

SUPPORTING INFORMATION**Formation of Carbocycles by Intramolecular Conjugate Displacement: Scope and Mechanistic Insights**

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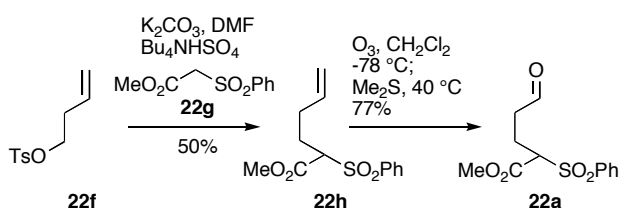
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Preparation of substrates for the all-carbon ICD reaction

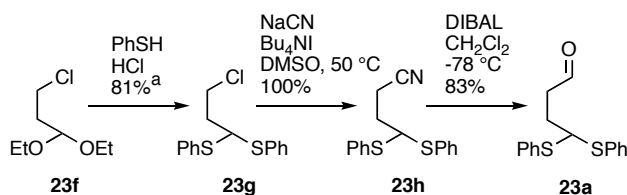
Aldehyde **20a** was a known compound,²⁶ readily made (40%) by methoxide-catalyzed Michael addition of dimethyl malonate to acrolein. The aromatic aldehyde **21a** was prepared by diborane reduction of the known²⁷ corresponding acid [2-(2-carboxyphenyl)malonic acid dimethyl ester] followed by PCC oxidation of the resulting benzylic alcohol (80% overall). The sulfone-ester aldehyde **22a** was made in two steps from **22f**²⁸ and the commercially available sulfone-ester **22g** (Scheme A).

Scheme A. Preparation of **22a**



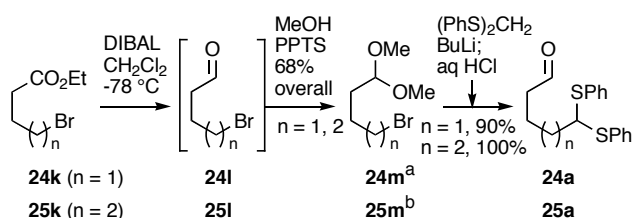
The bis(phenylthio) aldehyde **23a** was assembled in three straightforward steps (Scheme B), and the aldehydes **24a** and **25a** were made (Scheme C) by halide displacement from **24m** and **25m**, respectively, themselves obtained by the literature methods included in the Scheme.

Scheme B.^a Preparation of **23a**



^aLiterature reference: ^aReference 29.

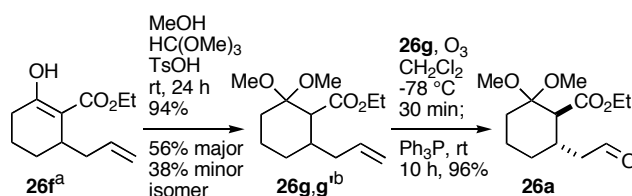
Scheme C.^a Preparation of **24a** and **25a**



^aLiterature references: ^aReference 30, ^bReference 31.

Our route to aldehyde **26a** (Scheme D) is the same as that reported³² for the corresponding methyl esters. The intermediate **26g,g'** was a mixture of cis and trans isomers, but only the major (trans) component was ozonized; consequently, **26a** was a single isomer.

Scheme D.^a Preparation of **26a**

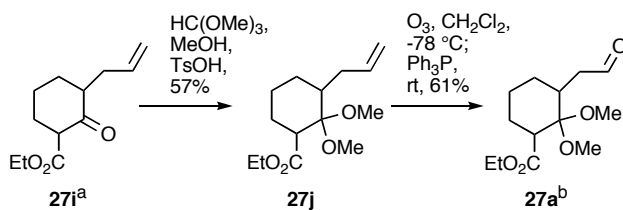


^aLiterature references and stereochemistry: ^aMethyl ester corresponding to **26f**: Reference 32.

^bWe assign the trans stereochemistry to the major isomer (**26g**) by analogy with the corresponding methyl ester series (Reference 32).

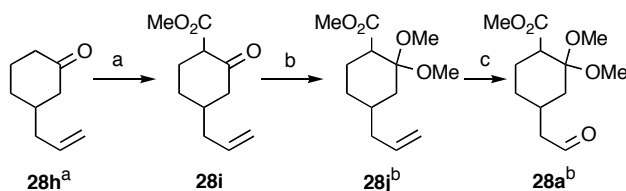
Aldehyde **27a** was available in two steps from **27i**³³ (Scheme E) by ketalization and ozonolysis, and a similar approach (Scheme F) was used for the isomeric aldehyde **28a**.

Scheme E.^a Preparation of **27a**



^aLiterature references and stereochemistry: ^aCompound **27i**: Reference 33. ^bSingle isomer.

Scheme F.^a Preparation of **28a**

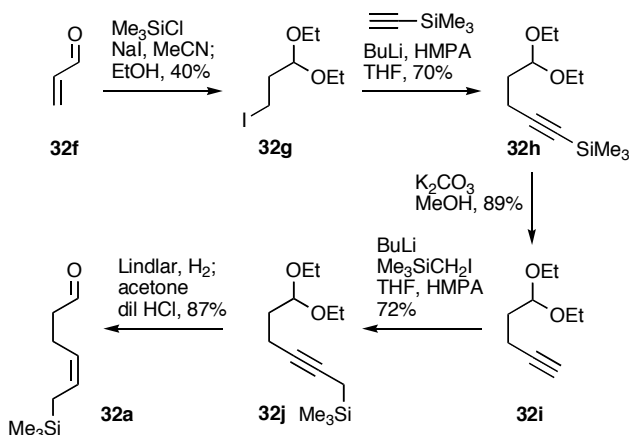


^aLiterature references, stereochemistry, reagents and conditions: ^aReaction details: ^aCompound **28h**: Reference 34. ^bSingle isomer. (a) NaH, (MeO)₂CO, THF, 89%. (b) HC(OMe)₃, MeOH, TsOH, 71%. (c) O₃, CH₂Cl₂, -78 °C, then Ph₃P, room temp, 6 h, 96%.

Both aldehydes **29a** and **30a** were known; the former³⁵ was made from 3-chloropropionaldehyde diethyl acetal, by displacement of chloride with cyanide, followed by DIBAL reduction, and the latter was conveniently available in a single step from cyclopentene by ozonolysis.³⁶

4-Nitrobutanal (**31a**) was prepared by Michael addition of MeNO₂ to acrolein, as reported in the literature.³⁷ Acrolein also served as the starting point for the preparation of the allylic silane **32a** (Scheme G). Treatment of acrolein with Me₃SiCl and NaI in MeCN, followed by

Scheme G. Preparation of **32a**

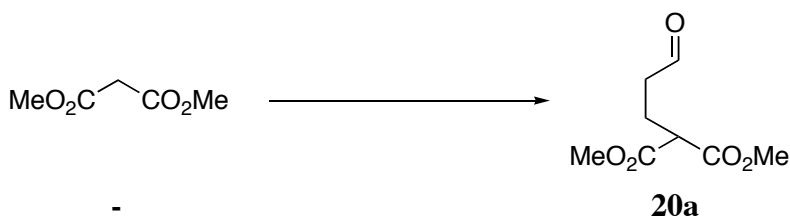


addition of EtOH gave iodide **32g**.³⁸ From that point, displacement with lithium (trimethylsilyl)acetylide (**32g**→**32h**), desilylation, reaction with Me₃SiCH₂I (**32i**→**32j**), Lindlar reduction and acid hydrolysis gave **32a**. We could have converted **32g** into **32j**, by using 3-(trimethylsilyl)-1-propynyllithium, but the present route is cheaper.

Experimental Section

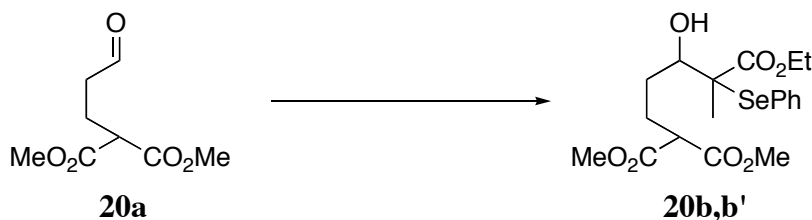
General Procedures. Solvents used for chromatography were distilled before use. Commercial thin layer chromatography plates (silica gel, Merck 60F-254) were used. Silica gel for flash chromatography was Merck type 60 (230–400 mesh). Dry solvents were prepared under an inert atmosphere and transferred by syringe or cannula. Dry THF and Et₂O were distilled from sodium and benzophenone ketyl. Dry MeCN, Et₃N and pyridine were distilled from CaH₂. The symbols s, d, t and q used for ¹³C NMR spectra indicate zero, one, two, or three attached hydrogens, respectively, the assignments being made by from APT spectra.

2-(3-Oxopropyl)malonic Acid Dimethyl Ester (**20a**).²⁶



Acrolein (3.9 mL, 58.865 mmol) was added dropwise over 30 min to a stirred and cooled (0 °C) solution of dimethyl malonate (6.0 g, 45.416 mmol) and sodium (10 mg, 0.454 mmol) in anhydrous MeOH (60 mL). The ice bath was left in place but not recharged and stirring was continued for 16 h. The solvent was evaporated and the residue was dissolved in Et₂O (150 mL). The solution was washed with water (25 mL) and brine (25 mL), dried (Na₂SO₄) and evaporated. Distillation of the residue under reduced pressure (100 °C, 0.5 mm Hg) gave **20a** as a colorless viscous liquid (4.6 g, 54%): ¹H NMR (CDCl₃, 500 MHz) δ 2.22 (q, *J* = 7.5 Hz, 2 H), 2.57 (td, *J* = 7.5, 1.0 Hz, 2 H), 3.45 (t, *J* = 7.5 Hz, 1 H), 3.74 (s, 6 H), 9.75 (t, *J* = 1.0 Hz, 1 H).

3-Hydroxy-6-methoxycarbonyl-2-methyl-2-(phenylseleno)heptanedioic Acid 1-Ethyl Ester 7-Methyl Ester (**20b,b'**).

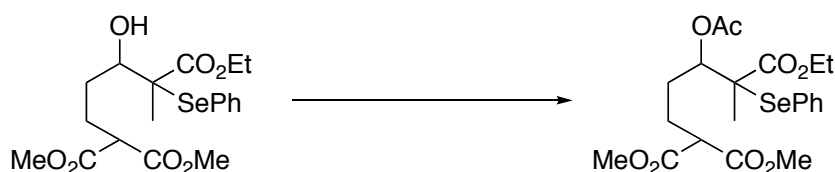


n-BuLi (2.5 M in hexane, 2.76 mL, 6.91 mmol) was added dropwise to a stirred and cooled (-78 °C) solution of *i*-Pr₂NH (1.01 mL, 7.17 mmol) in THF (10 mL). Stirring at -78 °C was continued for 40 min and a solution of **15**¹⁰ (1.912 g, 7.44 mmol) in THF (10 mL) was added over 3 min. Stirring was continued for 1 h and a solution of **20a**²⁶ (1.00g, 5.31 mmol) in THF (10 mL) was added dropwise over ca 3 min. The cold bath was left in place but not recharged and stirring was continued for 1.5 h. The mixture was quenched with saturated aqueous NH₄Cl (10 mL), the cooling bath was removed, stirring was continued for 15 min and the mixture was diluted with water (50 mL). The aqueous phase was extracted with EtOAc (3 x 10 mL) and the combined organic extracts were dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (4 x 18 cm), using 20% EtOAc-hexane, gave **20b** (less polar isomer, 480 mg, 20%) as a colorless viscous liquid and **20b'** (more polar isomer, 700 mg, 30%) as a colorless viscous liquid.

Compound **20b** had: FTIR (CH₂Cl₂ cast) 3512, 2954, 1734, 1438, 1248, 745 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.11 (t, *J* = 7.2 Hz, 3 H), 1.36 (s, 3 H), 1.35-1.43 (m, 1 H), 1.47-1.59 (m, 1 H), 1.91-2.0 (m, 1 H), 2.13-2.22 (m, 1 H), 3.11 (br s, 1 H), 3.40 (t, *J* = 7.6 Hz, 1 H), 3.69 (s, 6 H), 3.86 (dd, *J* = 10.0, 2.0 Hz, 1 H), 3.91-3.99 (m, 1 H), 4.0-4.08 (m, 1 H), 7.27-7.32 (m, 2 H), 7.36-7.41 (m, 1 H), 7.55-7.58 (m, 2 H); ¹³C NMR (CDCl₃, 100 MHz) δ 13.7 (q), 16.9 (q), 26.1 (t), 29.2 (t), 51.2 (d), 52.3 (2c, q), 57.1 (s), 61.0 (t), 72.5 (d), 126.2 (s), 128.8 (d), 129.4 (d), 137.9 (d), 169.5 (s), 169.6 (s), 172.9 (s); exact mass (electrospray) *m/z* calcd for C₁₉H₂₆NaO₇⁸⁰Se 469.0736, found 469.0735.

Compound **20b'** had: FTIR (CH₂Cl₂ cast) 3515, 2953, 1733, 1438, 1245 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.20 (t, *J* = 7.0 Hz, 3 H), 1.4 (s, 3 H), 1.39-1.47 (m, 1 H), 1.95-2.03 (m, 2 H), 2.18-2.45 (m, 1 H), 2.84 (d, *J* = 6.5 Hz, 1 H), 3.47 (t, 7.5 Hz, 1 H), 3.74 (s, 3 H), 3.76 (s, 3 H), 3.85 (dd, *J* = 9.5, 6.5 Hz, 1 H), 4.1 (q, *J* = 7.0 Hz, 2 H), 7.3-7.33 (m, 2 H), 7.38-7.42 (m, 1 H), 7.56-7.58 (m, 2 H); ¹³C NMR (CDCl₃, 125 MHz) δ 13.9 (q) 17.9 (q), 26.3 (t), 28.9 (t), 51.3 (d), 52.5 (2C, q), 54.3 (s), 61.3 (t), 74.8 (d), 126.4 (s), 128.8 (d), 129.5 (d), 138.1 (d), 169.72 (s), 169.78 (s), 173.8 (s); exact mass (electrospray) *m/z* calcd for C₁₉H₂₆NaO₇⁸⁰Se 469.0736, found 469.0739.

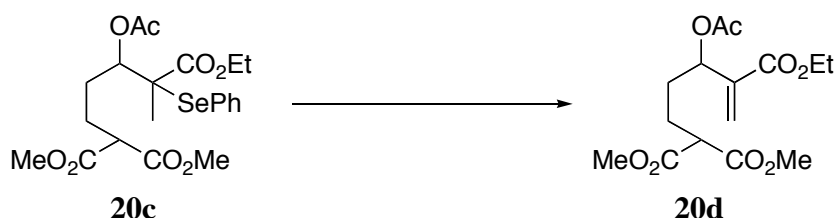
3-Acetoxy-6-methoxycarbonyl-2-methyl-2-(phenylseleno)heptanedioic Acid 1-Ethyl Ester 7-Methyl Ester (20c).



20b'**20c**

Pyridine (0.65 mL, 8.08 mmol) and AcCl (0.29 mL, 4.04 mmol) were added sequentially to a stirred and cooled (-10 °C, ice-acetone bath) solution of **20b'** (600 mg, 1.35 mmol) and DMAP (18 mg, 0.15 mmol) in CH₂Cl₂ (10 mL). The cooling bath was left in place but not recharged and stirring was continued for 12 h by which time the temperature had risen to 15 °C. The mixture was diluted with water (10 mL), acidified with hydrochloric acid (10%, 2 mL) and extracted with CH₂Cl₂ (3 x 10 mL). The combined organic extracts were dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (2 x 18 cm), using 20% EtOAc-hexane, gave **20c** (540 mg, 82%) as a viscous oil: FTIR (CH₂Cl₂ cast) 2983, 2954, 1737, 1438, 1231, 1020 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.06 (t, *J* = 7.0 Hz, 3 H), 1.47 (s, 3 H), 1.59-1.68 (m, 1 H), 1.94 (s, 3 H), 1.91-1.99 (m, 2 H), 2.17-2.24 (m, 1 H), 3.48 (t, *J* = 7.5 Hz, 1 H), 3.752 (s, 3 H), 3.754 (s, 3 H), 3.85 (dq, *J* = 10.75, 7.0 Hz, 1 H), 3.99 (dq, *J* = 10.75, 7.0 Hz, 1 H), 5.43 (dd, *J* = 10.5, 1.5 Hz, 1 H), 7.29-7.33 (m, 2 H), 7.38-7.41 (m, 1 H), 7.58-7.60 (m, 2 H); ¹³C NMR (CDCl₃, 125 MHz) δ 13.8 (q), 17.7 (q), 20.8 (q), 25.6 (t), 28.1 (t), 51.1 (d), 52.53 (q), 52.55 (q), 52.8 (s), 61.2 (t), 74.9 (d), 126.2 (s), 128.9 (d), 129.7 (d), 138.0 (d), 169.46 (s), 169.54 (s), 169.67 (s), 171.8 (s); exact mass (electrospray) *m/z* calcd for C₂₁H₂₈NaO₈⁸⁰Se 511.0842, found 511.0842.

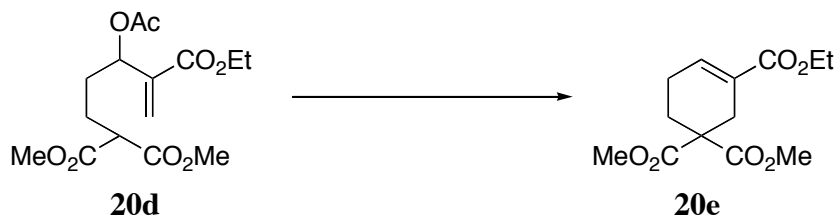
3-Acetoxy-6-methoxycarbonyl-2-methyleneheptanedioic Acid 1-Ethyl Ester 7-Methyl Ester (20d).



H₂O₂ (30%, 0.5 mL, 4.9 mmol) was added dropwise to a stirred and cooled (0 °C) solution of **20c** (200 mg, 0.41 mmol) in CH₂Cl₂ (3 mL). Stirring was continued at 0 °C for 1 h and the mixture was then quenched with saturated aqueous Na₂S₂O₃ (1 mL). The mixture was stirred at 0 °C for 5 min, the ice bath was removed and stirring was continued for 5 min. The mixture was diluted with water (5 mL) and extracted with CH₂Cl₂ (3 x 5 mL) and the combined organic extracts were washed with saturated aqueous NaHCO₃ (3 mL), dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (0.5 x 6 cm), using 20% EtOAc-hexane, gave **20d** (125 mg, 93%) as a colorless viscous liquid: FTIR (CH₂Cl₂ cast) 2957, 1739, 1634, 1437, 1235, 1024 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.29 (t, *J* = 7.5 Hz, 3 H), 1.67-1.75

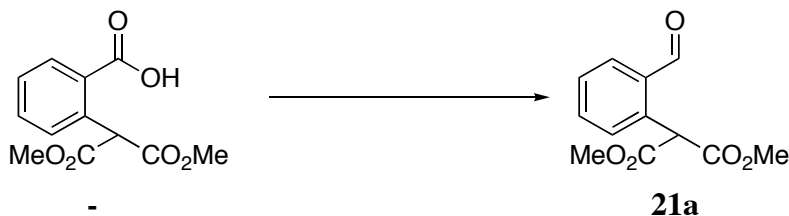
(m, 1 H), 1.78-1.85 (m, 1 H), 1.87-2.0 (m, 2 H), 2.08 (s, 3 H), 3.37 (dd, $J = 8.0, 7.0$ Hz, 1 H), 3.72 (s, 6 H), 4.17-4.26 (m, 2 H), 5.61 (dd, $J = 7.5, 4.5$ Hz, 1 H), 5.75 (m, 1 H), 6.29 (s, 1 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 14.1 (q), 21.0 (q), 24.5 (t), 31.5 (t), 51.1 (d), 52.50 (q), 52.52 (q), 61.0 (t), 71.1 (d), 125.3 (s), 139.6 (t), 165.0 (s), 169.4 (s), 169.5 (s), 169.8 (s); exact mass (electrospray) m/z calcd for $\text{C}_{15}\text{H}_{22}\text{NaO}_8$ 353.1207, found 353.1206.

Cyclohex-3-ene-1,1,3-tricarboxylic Acid 3-Ethyl Ester 1,1-Dimethyl Ester (20e).



DBU (0.07 mL, 0.48 mmol) was added dropwise to a stirred solution of **20d** (80 mg, 0.24 mmol) in MeCN (2.5 mL). Stirring was continued for 15 min and the mixture was filtered through a pad of silica gel (2 x 2 cm), using 50% EtOAc-hexanes (60 mL). Evaporation of the filtrate and flash chromatography of the residue over silica gel (0.5 x 8 cm), using 15% EtOAc-hexanes, gave **20e** (56 mg, 86%) as a colorless liquid: FTIR (CH_2Cl_2 cast) 2956, 2842, 1737, 1711, 1655, 1435, 1249, 1041 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.28 (t, $J = 7.0$ Hz, 3 H), 2.11 (d, $J = 7.0$ Hz, 1 H), 2.12 (d, $J = 6.0$ Hz, 1 H), 2.26-2.30 (m, 2 H), 2.82-2.83 (m, 2 H), 3.72 (s, 6 H), 4.19 (q, $J = 7.0$ Hz, 2 H), 6.93 (dddd, $J = 4.0, 4.0, 2.0, 2.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 14.2 (q), 23.1 (t), 26.7 (t), 29.6 (t), 52.7 (q), 52.9 (s), 60.5 (t), 127.9 (s), 137.7 (d), 166.4 (s), 171.5 (s); exact mass (electrospray) m/z calcd for $\text{C}_{13}\text{H}_{18}\text{NaO}_6$ 293.0996, found 293.0997.

2-(2-Formylphenyl)malonic Acid Dimethyl Ester (21a).



$\text{BH}_3\cdot\text{SMe}_2$ (10.1 M, 0.22 mL, 2.18 mmol) was added dropwise to a stirred and cooled (0 $^\circ\text{C}$) solution of 2-(2-carboxyphenyl)malonic acid dimethyl ester²⁷ (500 mg, 1.98 mmol) in THF (10 mL). Stirring was continued at 0 $^\circ\text{C}$ for 20 min and then at 50 $^\circ\text{C}$ for 3.5 h. The solvent was

evaporated and the residue was dissolved in CH_2Cl_2 (5 mL). The resulting solution was added to a stirred mixture of PCC (855 mg, 3.97 mmol) and 4 Å molecular sieves (855 mg) in CH_2Cl_2 (30 mL), and stirring was continued for 40 min. The solvent was evaporated, and the residue was filtered through a pad of Celite, using Et_2O as a rinse. Evaporation of the solvent and flash chromatography of the residue over silica gel (2.5 x 15 cm), using 1:2 EtOAc-hexane, gave **21a** (374 mg, 80%) as an oil: FTIR (CDCl_3 , cast) 3003, 2955, 2924, 2851, 2753, 1734, 1695, 1600, 1578, 1491, 1451, 1435 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 3.77 (s, 6 H), 5.90 (s, 1 H), 7.47 (dd, $J = 7.7, 0.4$ Hz, 1 H), 7.56 (td, $J = 7.5, 1.3$ Hz, 1 H), 7.61 (td, $J = 7.6, 1.6$ Hz, 1 H), 7.82 (dd, $J = 7.5, 1.6$ Hz, 1 H), 10.05 (s, 1 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 52.8 (q), 53.4 (d), 128.7 (d), 130.4 (d), 133.5 (s), 133.7 (s), 133.9 (d), 135.3 (d), 168.5 (s), 193.2 (d); exact mass (electrospray) m/z calcd for $\text{C}_{12}\text{H}_{12}\text{NaO}_5$ 259.0577, found 259.0575.

2-[2-[2-Ethoxycarbonyl-1-hydroxy-2-(phenylseleno)propyl]phenyl]malonic Acid Dimethyl Ester (21b,b').

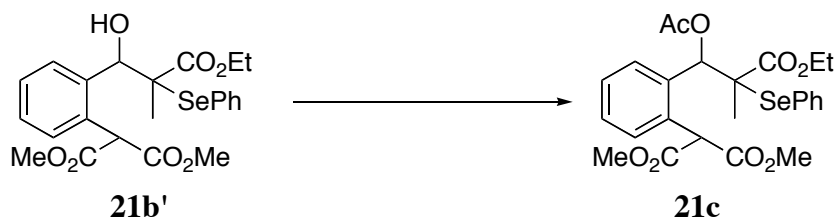


n-BuLi (1.6 M in hexane, 1.47 mL, 2.34 mmol) was added dropwise to a stirred and cooled (0 °C) solution of *i*-Pr₂NH (237.0 mg, 2.34 mmol) in THF (25 mL). Stirring at 0 °C was continued for 25 min. The mixture was then cooled to -78 °C and a solution of **15** (599.0 mg, 2.34 mmol) in THF (5 mL) was added dropwise. Stirring at -78 °C was continued for 70 min, and a solution of **21a** (220.0 mg, 0.94 mmol) in THF (6 mL) was added dropwise. Stirring at -78 °C was continued for 40 min, and the mixture was quenched with saturated aqueous NH_4Cl (10 mL). The cold bath was removed, stirring was continued for 15 min and the mixture was diluted with water (80 mL). The aqueous phase was extracted with EtOAc (3 x 40 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm), using 9:20 EtOAc-hexane, gave **21b** (less polar isomer, 135 mg, 40%) as a viscous oil containing an impurity which could not be removed, and pure **21b'** (more polar isomer, 135 mg, 40%) as a viscous oil.

Compound **21b'** had: FTIR (CDCl_3 cast) 3486, 2985, 2954, 1735, 1579, 1476, 1437 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.20 (dd, $J = 7.2, 7.1$, 3 H), 1.37 (s, 3 H), 3.73 (s, 3 H), 3.75 (s, 3 H), 3.84 (d, $J = 7.0$ Hz, 1 H), 4.09 (dq, $J = 10.8, 7.2$ Hz, 1 H), 4.17 (dq, $J = 10.8, 7.1$ Hz, 1 H),

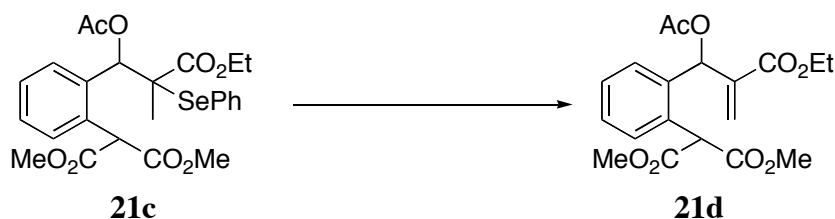
5.39 (s, 1 H), 5.45 (d, $J = 6.9$ Hz, 1 H), 7.26-7.32 (m, 3 H), 7.34-7.40 (m, 3 H), 7.48-7.50 (m, 2 H), 7.53-7.55 (m, 1 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 13.8 (q), 19.9 (q), 52.8 (q), 52.9 (q), 53.4 (d), 54.8 (s), 61.7 (t), 74.9 (d), 126.5 (s), 127.8 (d), 127.9 (d), 128.3 (d), 128.8 (d), 129.5 (d), 130.1 (d), 132.0 (s), 137.6 (s), 138.2 (d), 168.88 (s), 168.91 (s), 173.9 (s); exact mass (electrospray) m/z calcd for $\text{C}_{23}\text{H}_{26}\text{NaO}_7^{80}\text{Se}$ 517.0736, found 517.0740.

2-[2-[1-Acetoxy-2-ethoxycarbonyl-2-(phenylseleno)propyl]phenyl]malonic Acid Dimethyl Ester (21c).



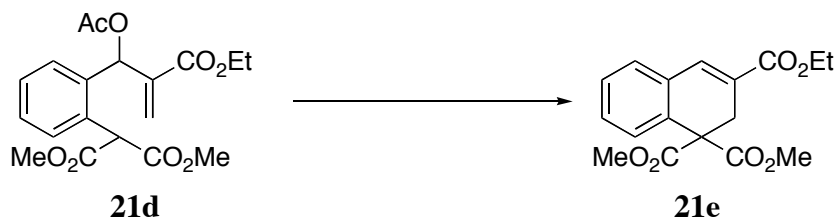
Pyridine (99.2 mg, 1.25 mmol) and AcCl (49.2 mg, 0.63 mmol) were added sequentially to a stirred and cooled (-10 °C, ice-acetone bath) solution of **21b'** (103 mg, 0.21 mmol) and DMAP (2.6 mg, 0.021 mmol) in CH_2Cl_2 (1 mL). The cold bath was left in place but not recharged and stirring was continued for 16 h, by which time the temperature had risen to room temperature. The mixture was diluted with water (5 mL), acidified with hydrochloric acid (1 M, 2 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1.5 x 15 cm), using 1:2 EtOAc-hexane, gave **21c** (89.4 mg, 80%) as an oil: FTIR (CDCl_3 cast) 2985, 2954, 1738, 1477, 1437 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.23 (dd, $J = 7.1$, 7.1 Hz, 3 H), 1.46 (s, 3 H), 1.96 (s, 3 H), 3.74 (s, 3 H), 3.80 (s, 3 H), 4.04 (dq, $J = 10.7$, 7.1 Hz, 1 H), 4.14 (dq, $J = 10.8$, 7.1 Hz, 1 H), 5.74 (s, 1 H), 6.73 (s, 1 H), 7.14-7.19 (m, 4 H), 7.28-7.32 (m, 2 H), 7.37 (dd, $J = 8.0$, 1.2 Hz, 1 H), 7.40-7.43 (m, 1 H), 7.57 (dd, $J = 7.9$, 1.3 Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.9 (q), 18.6 (q), 20.6 (q), 52.7 and 52.9 (these two signals incorporate two q and one d), 53.0 (s), 54.1 (d), 61.5 (t), 125.8 (s), 127.6 (d), 128.6 (d), 128.7 (d), 129.4 (d), 130.4 (d), 132.7 (s), 134.7 (s), 138.1 (d), 168.56 (s), 168.57 (s), 167.0 (s), 171.7 (s); exact mass (electrospray) m/z calcd for $\text{C}_{25}\text{H}_{28}\text{NaO}_8^{80}\text{Se}$ 559.0842, found 559.0845.

2-[2-(1-Acetoxy-2-ethoxycarbonylallyl)phenyl]malonic Acid Dimethyl Ester (21d).



H_2O_2 (30%, 0.18 mL, 1.8 mmol) was added dropwise to a stirred and cooled (0 °C) solution of **21c** (79 mg, 0.15 mmol) in CH_2Cl_2 (2 mL). Stirring was continued at 0 °C for 90 min and the mixture was quenched with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (1.0 mL). The mixture was stirred at 0 °C for 5 min, the ice bath was removed, stirring was continued for 30 min and the mixture was diluted with water (5 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (0.7 x 15 cm), using 1:2 EtOAc-hexane, gave **21d** (45 mg, 80%) as a viscous oil: FTIR (CDCl_3 cast) 2956, 1741, 1636, 1436 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.21 (t, J = 7.1 Hz, 3 H), 2.07 (s, 3 H), 3.73 (s, 3 H), 3.74 (s, 3 H), 4.16 (q, J = 7.1 Hz, 2 H), 5.24 (s, 1 H), 5.69 (d, J = 1.3 Hz, 1 H), 6.41 (s, 1 H), 6.86 (s, 1 H), 7.30-7.38 (m, 3 H), 7.47-7.49 (m, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.0 (q), 20.8 (q), 52.7 (q), 52.9 (d), 53.0 (q), 61.0 (t), 70.6 (d), 126.8 (s), 128.3 (d), 128.8 (d), 128.9 (d), 130.0 (d), 131.6 (s), 135.8 (s), 139.2 (t), 164.8 (s), 168.60 (s), 168.63 (s), 169.1 (s); exact mass (electrospray) m/z calcd for $\text{C}_{19}\text{H}_{22}\text{NaO}_8$ 401.1207, found 401.1207.

2H-Naphthalene-1,1,3-tricarboxylic Acid 3-Ethyl Ester 1,1-Dimethyl Ester (21e).



Cs_2CO_3 (45.3 mg, 0.139 mmol) was added to a stirred solution of **21d** (26.3 mg, 0.070 mmol) in THF (1 mL), and stirring at room temperature was continued for 40 min. Filtration of the mixture through a pad (ca 5 cm) of silica gel in a Pasteur pipette, using 1:1 EtOAc-hexane, gave **21e** (20.5 mg, 93%) as a colorless, viscous oil: FTIR (CDCl_3 cast) 3000, 2955, 1735, 1707, 1636, 1570, 1435 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.35 (t, J = 7.1 Hz, 3 H), 3.35 (d, J = 1.5 Hz, 2 H), 3.77 (s, 6 H), 4.29 (q, J = 7.1 Hz, 2 H), 7.25-7.29 (m, 2 H), 7.33-7.38 (m, 2 H), 7.50 (s, 1 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 14.3 (q), 30.0 (t), 53.1 (q), 59.2 (s), 60.9 (t), 127.0 (s),

127.9 (d), 128.7 (d), 128.88 (d), 129.89 (d), 131.9 (s), 132.6 (s), 135.5 (d), 166.2 (s), 170.8 (s); exact mass m/z calcd for $C_{17}H_{18}O_6$ 318.1104, found 318.1104.

2-[4-Benzenesulfonyl-3-hydroxy-4-(phenylseleno)pentyl]malonic Acid Dimethyl Ester (20f,f').



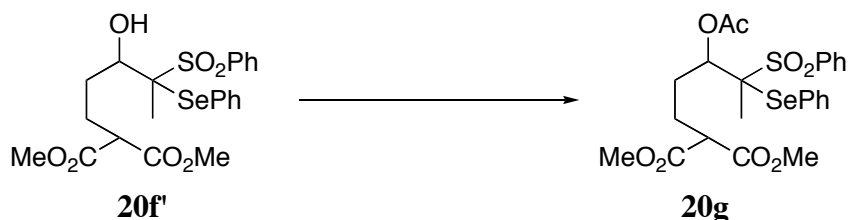
n-BuLi (1.6 M in hexane, 0.33 mL, 0.53 mmol) was added dropwise to a stirred and cooled (-78 °C) solution of **37**¹¹ (182.0 mg, 0.53 mmol) in THF (2 mL). Stirring at -78 °C was continued for 50 min. A solution of **20a** (70 mg, 0.37 mmol) in THF (1 mL) was added dropwise, and stirring at -78 °C was continued for 1 h. The mixture was quenched with saturated aqueous NH_4Cl (3 mL), the cold bath was removed, stirring was continued for 15 min and water (5 mL) was added. The aqueous phase was extracted with EtOAc (3 x 10 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm), using 2:5 EtOAc-hexane, gave **20f** (less polar isomer, 40 mg, 21%) as a viscous oil and **20f'** (more polar isomer, 50 mg, 26%) as a viscous oil.

Compound **20f** had: FTIR ($CDCl_3$ cast) 3498, 3061, 2953, 2866, 1750, 1734, 1583, 1477, 1438 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) δ 1.08 (s, 3 H), 1.58 (ddd, $J = 10.0, 10.0, 2.4$ Hz, 1 H), 1.94-2.05 (m, 2 H), 2.22-2.31 (m, 1 H), 3.46 (dd, $J = 7.2$ Hz, 1 H), 3.72 (s, 3 H), 3.75 (s, 3 H), 4.04 (d, $J = 7.2$ Hz, 1 H), 4.20 (s, 1 H), 7.25 (t, $J = 8.0$ Hz, 2 H), 7.37 (td, $J = 7.6, 0.8$ Hz, 1 H), 7.53 (dd, $J = 8.0, 1.2$ Hz, 2 H), 7.59 (t, $J = 7.6$ Hz, 2 H), 7.72 (td, $J = 7.6, 0.8$ Hz, 1 H), 7.92 (dd, $J = 8.0, 1.2$ Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.2, 25.0, 29.2, 51.1, 52.40, 52.42, 72.6, 77.5, 124.6, 128.64, 128.9, 129.5, 130.8, 134.1, 134.6, 138.9, 169.6, 169.7; exact mass (electrospray) m/z calcd for $C_{22}H_{26}NaO_7S^{80}Se$ 537.0457, found 537.0455.

Compound **20f'** had: FTIR ($CDCl_3$ cast) 3499, 3061, 2953, 1750, 1734, 1583, 1477, 1446, 1438 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) δ 1.08 (s, 3 H), 1.61-1.72 (m, 1 H), 1.93-2.03 (m, 1 H), 2.19-2.28 (m, 1 H), 2.32-2.39 (m, 1 H), 3.47 (s, 1 H), 3.48 (dd, $J = 7.2, 7.2$ Hz, 1 H), 3.75 (s, 3 H), 3.77 (s, 3 H), 4.08 (ddd, $J = 10.4, 5.6, 1.6$ Hz, 1 H), 7.21 (tt, $J = 7.6, 1.6$ Hz, 2 H), 7.29 (dt, $J = 6.8, 1.2$ Hz, 2 H), 7.35 (tt, $J = 7.2, 1.2$ Hz, 1 H), 7.60 (tt, $J = 7.6, 2.0$ Hz, 2 H), 7.72 (tt, $J = 7.6, 1.2$ Hz, 1 H), 8.04 (dt, $J = 7.2, 1.2$ Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.6, 26.2,

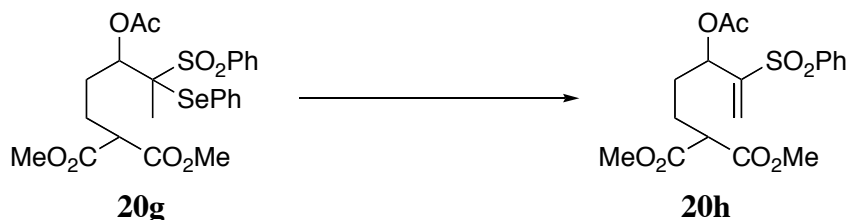
31.1, 51.1, 52.5, 74.6, 75.8, 125.1, 128.6, 128.9, 129.8, 131.5, 134.1, 136.0, 138.1, 169.7, 169.8; exact mass (electrospray) m/z calcd for $C_{22}H_{26}NaO_7S^{80}Se$ 537.0457, found 537.0452.

2-[3-Acetoxy-4-benzenesulfonyl-4-(phenylseleno)pentyl]malonic Acid Dimethyl Ester (20g).



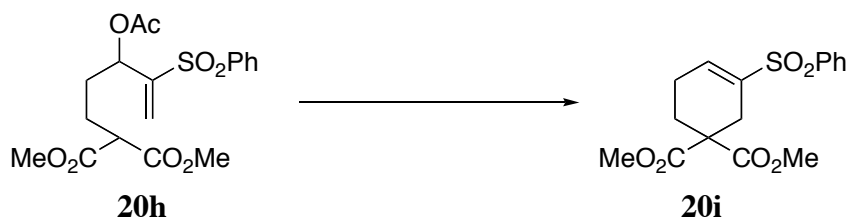
Pyridine (166.3 mg, 2.12 mmol) and AcCl (110 mg, 1.41 mmol) were added sequentially to a stirred and cooled ($-10\text{ }^{\circ}\text{C}$, ice-acetone bath) solution of **20f'** (181.2 mg, 0.35 mmol) and DMAP (6.1 mg, 0.05 mmol) in CH_2Cl_2 (2 mL). The cold bath was left in place but not recharged and stirring was continued for 12 h, by which time the temperature had risen to room temperature. The mixture was diluted with water (10 mL), acidified with hydrochloric acid (1 M, 5 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm), using 2:5 EtOAc-hexane, gave **20g** (130 mg, 67%) as an oil: FTIR (CDCl_3 cast) 3062, 2954, 1738, 1583, 1477, 1446, 1438 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.14 (s, 3 H), 1.73-1.83 (m, 1 H), 1.84-1.97 (m, 2 H), 1.99 (s, 3 H), 2.01-2.11 (m, 1 H), 3.42 (dd, $J = 7.2, 7.2$ Hz, 1 H), 3.69 (s, 3 H), 3.72 (s, 3 H), 5.42 (dd, $J = 10.0, 2.8$ Hz, 1 H), 7.31 (tt, $J = 7.6, 1.2$ Hz, 2 H), 7.41 (tt, $J = 7.6, 1.2$ Hz, 1 H), 7.55 (tt, $J = 8.0, 1.6$ Hz, 2 H), 7.66 (tt, $J = 7.2, 1.2$ Hz, 1 H), 7.74 (dt, $J = 8.0, 1.2$ Hz, 2 H), 7.96 (dt, $J = 8.0, 1.6$ Hz, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 20.65, 20.67, 24.6, 29.2, 50.7, 52.4, 52.5, 73.2, 74.4, 124.9, 128.7, 128.8, 129.8, 131.1, 133.7, 135.8, 139.1, 169.2, 169.3, 170.2; exact mass (electrospray) m/z calcd for $C_{24}H_{28}NaO_8S^{80}Se$ 579.0562, found 579.0561.

2-[3-Acetoxy-4-(benzenesulfonyl)pent-4-enyl]malonic Acid Dimethyl Ester (20h).



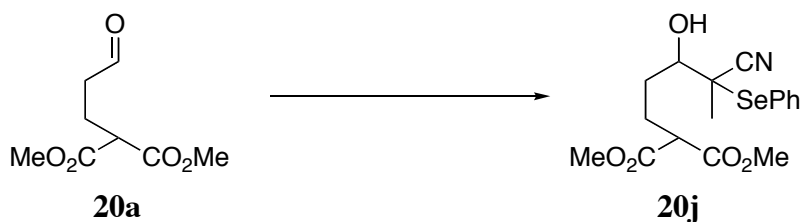
H_2O_2 (30%, 0.24 mL, 2.4 mmol) was added dropwise to a stirred and cooled (0 °C) solution of **20g** (110 mg, 0.20 mmol) in CH_2Cl_2 (2 mL). Stirring was continued at 0 °C for 1 h and the mixture was quenched with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (0.5 mL). The mixture was stirred at 0 °C for 5 min, the ice bath was removed, stirring was continued for 35 min and the mixture was diluted with water (5 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL) and the combined organic extracts were washed with saturated aqueous NaHCO_3 (3 mL), dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1 x 11 cm), using 1:3 EtOAc-hexane, gave **20h** (63 mg, 80%) as a viscous oil: FTIR (CDCl_3 cast) 2956, 1746, 1584, 1447, 1437 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.80 (s, 3 H), 1.79-1.97 (m, 4 H), 3.33 (dd, $J = 7.2, 7.2$ Hz, 1 H), 3.72 (s, 3 H), 3.73 (s, 3 H), 5.35-5.38 (m, 1 H), 6.07 (dd, $J = 1.2, 0.8$ Hz, 1 H), 6.54 (d, $J = 0.8$ Hz, 1 H), 7.54 (tt, $J = 7.2, 1.2$ Hz, 2 H), 7.64 (tt, $J = 7.6, 1.2$ Hz, 1 H), 7.87 (dt, $J = 7.2, 1.2$ Hz, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 20.5, 24.4, 31.7, 50.9, 52.6, 69.7, 126.5, 128.3, 129.2, 133.7, 139.1, 149.3, 169.2, 169.27, 169.30; exact mass (electrospray) m/z calcd for $\text{C}_{18}\text{H}_{22}\text{NaO}_8\text{S}$ 421.0928, found 421.0932.

3-(Benzenesulfonyl)cyclohex-3-ene-1,1-dicarboxylic Acid Dimethyl Ester (**20i**).



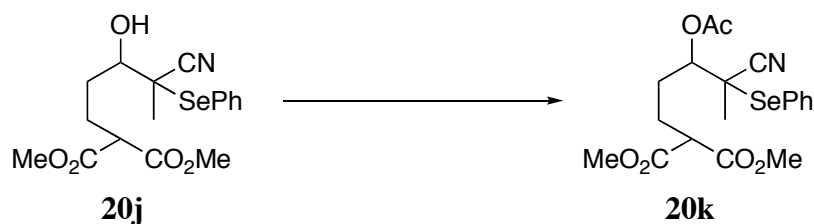
Cs_2CO_3 (13.4 mg, 0.041 mmol) was added to a stirred solution of **20h** (8.2 mg, 0.021 mmol) in THF (0.5 mL), and stirring at room temperature was continued for 4.5 h. Evaporation of the solvent and filtration of the residue through a pad (ca 5 cm) of silica gel in a Pasteur pipette, using 7:10 EtOAc-hexane, gave **20i** (7.0 mg, 91%) as a colorless viscous oil: FTIR (CDCl_3 cast) 2955, 2924, 2852, 1735, 1651, 1447, 1435 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 2.11 (t, $J = 6.4$ Hz, 2 H), 2.39-2.44 (m, 2 H), 2.74 (d, $J = 1.6$ Hz, 2 H), 3.56 (s, 6 H), 7.05-7.06 (m, 1 H), 7.55 (t, $J = 7.6$ Hz, 2 H), 7.62-7.65 (m, 1 H), 7.87 (d, $J = 7.6$ Hz, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 23.2 (t), 26.3 (t), 28.3 (t), 52.71 (s), 52.72 (q), 152.7 (s), 128.1 (d), 129.0 (d), 133.2 (d), 137.2 (s), 137.3 (d), 138.7 (s), 170.3 (s); exact mass (electrospray) m/z calcd for $\text{C}_{16}\text{H}_{18}\text{NaO}_6\text{S}$ 361.0716, found 361.0713.

2-[4-Cyano-3-hydroxy-4-(phenylseleno)pentyl]malonic Acid Dimethyl Ester (**20j**).



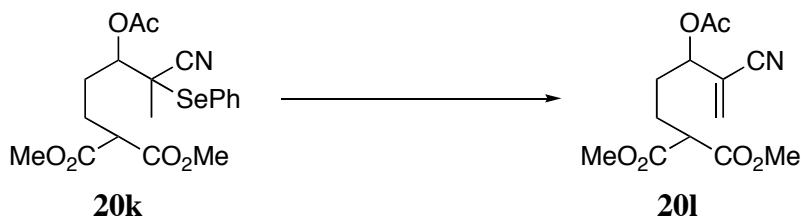
n-BuLi (1.6 M in hexane, 2.8 mL, 4.52 mmol) was added dropwise to a stirred and cooled (0 °C) solution of *i*-Pr₂NH (484.7 mg, 4.79 mmol) in THF (10 mL). Stirring at 0 °C was continued for 20 min, the mixture was cooled to -78 °C and a solution of **38**¹² (1.0 g, 4.79 mmol) in THF (8 mL) was added dropwise. Stirring at -78 °C was continued for 40 min, and a solution of **20a** (600 mg, 3.2 mmol) in THF (8 mL) was added dropwise. Stirring at -78 °C was continued for 80 min, and the mixture was quenched with saturated aqueous NH₄Cl (10 mL). The cold bath was removed, stirring was continued for 15 min and the mixture was diluted with water (50 mL). The aqueous phase was extracted with Et₂O (3 x 30 mL) and the combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (1.5 x 15 cm), using 7:20 EtOAc-hexane, gave **20j** (0.9 g, 71%) as a 1:1 mixture of diastereomers: FTIR (CH₂Cl₂ cast) 3474, 3056, 2954, 2226, 1736, 1578, 1477, 1438 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.56 (s, 1.5 H), 1.59 (s, 1.5 H), 1.53-1.68 (m, 1 H), 1.74-1.83 (m, 0.5 H), 1.93-2.05 (m, 1.5 H), 2.15-2.25 (m, 1 H), 2.59 (d, *J* = 6.0 Hz, 0.5 H), 2.70 (dd, *J* = 4.0, 1.6 Hz, 0.5 H), 3.42 (dd, *J* = 7.6, 7.6 Hz, 0.5 H), 3.45 (dd, *J* = 7.6, 7.6 Hz, 0.5 H), 3.55 (ddd, *J* = 10.4, 4.0, 2.0 Hz, 0.5 H), 3.62 (ddd, *J* = 10.4, 6.0, 2.0 Hz, 0.5 H), 3.72 (s, 1.5 H), 3.73 (s, 1.5 H), 3.75 (s, 1.5 H), 3.76 (s, 1.5 H), 7.38-7.43 (m, 2 H), 7.45-7.51 (m, 1 H), 7.74-7.77 (m, 2 H); ¹³C NMR (CDCl₃, 100 MHz) δ 19.4 (q), 21.6 (q), 25.5 (q), 25.7 (t), 29.3 (t), 29.4 (t), 43.0 (s), 43.3 (s), 50.93 (d), 50.95 (d), 52.51 (q), 52.54 (q), 52.6 (q), 72.7 (d), 74.8 (d), 120.7 (s), 121.1 (s), 124.8 (s), 125.0 (s), 129.4 (d), 129.5 (d), 130.2 (d), 130.4 (d), 137.65 (d), 137.70 (d), 137.9 (d), 169.45 (s), 169.49 (s), 169.54 (s); exact mass (electrospray) *m/z* calcd for C₁₇H₂₁NNaO₅⁸⁰Se 422.0477, found 422.0476.

2-[3-Acetoxy-4-cyano-4-(phenylseleno)pentyl]malonic Acid Dimethyl Ester (20k).



Pyridine (596.0 mg, 7.54 mmol) and AcCl (295.9 mg, 3.77 mmol) were added sequentially to a stirred and cooled (-10 °C, ice-acetone bath) solution of **20j** (500.0 mg, 1.26 mmol) and DMAP (17.0 mg, 0.14 mmol) in CH₂Cl₂ (12 mL). The cold bath was left in place but not recharged and stirring was continued for 9 h, by which time the temperature had risen to room temperature. The mixture was diluted with water (10 mL), acidified with hydrochloric acid (1 M, 8 mL) and extracted with CH₂Cl₂ (3 x 25 mL). The combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm), using 2:5 EtOAc-hexane, gave **20k** (497 mg, 90%) as an oil which was a 1:1 mixture of diastereomers: FTIR (CH₂Cl₂ cast) 2955, 2228, 1750, 1438 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.56 (s, 1.5 H), 1.58 (s, 1.5 H), 1.73-2.08 (m, 4 H), 2.127 (s, 1.5 H), 2.131 (s, 1.5 H), 3.41 (dd, *J* = 7.2, 7.2 Hz, 1 H), 3.74 (s, 1.5 H), 3.75 (s, 1.5 H), 3.755 (s, 1.5 H), 3.756 (s, 1.5 H), 5.11 (dd, *J* = 10.0, 2.0 Hz, 0.5 H), 5.16 (dd, *J* = 10.0, 2.0 Hz, 0.5 H), 7.41 (td, *J* = 8.0, 1.6 Hz, 2 H), 7.46-7.50 (m, 1 H), 7.77 (*J* = 8.1, 1.2 Hz, 2 H); ¹³C NMR (CDCl₃, 100 MHz) δ 20.55 (q), 20.57 (q), 22.2 (q), 22.3 (q), 24.88 (t), 24.92 (t), 28.0 (t), 29.2 (t), 39.6 (s), 50.65 (d), 50.71 (d), 52.5 (q), 52.56 (q), 52.57 (q), 74.1 (d), 74.3 (d), 120.0 (s), 120.3 (s), 124.9 (s), 125.1 (s), 129.37 (d), 129.44 (d), 130.3 (d), 130.4 (d), 137.8 (d), 138.1 (d), 169.1 (s), 169.16 (s), 169.17 (s), 169.9 (s), 170.0 (s); exact mass (electrospray) *m/z* calcd for C₁₉H₂₃NNaO₆⁸⁰Se 464.0583, found 464.0583.

2-(3-Acetoxy-4-cyanopent-4-enyl)malonic Acid Dimethyl Ester (20l).



H₂O₂ (30%, 0.83 mL, 8.2 mmol) was added dropwise to a stirred and cooled (0 °C) solution of **20k** (300 mg, 0.68 mmol) in CH₂Cl₂ (4 mL). Stirring was continued at 0 °C for 1 h and the mixture was quenched with saturated aqueous Na₂S₂O₃ (1.0 mL). The mixture was stirred at 0 °C for 5 min, the ice bath was removed, stirring was continued for 5 min and the mixture was diluted with water (10 mL). The aqueous phase was extracted with CH₂Cl₂ (3 x 10 mL) and the combined organic extracts were washed with saturated aqueous NaHCO₃ (3 mL), dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (2 x 13 cm), using 1:2 EtOAc-hexane, gave **20l** (180 mg, 94%) as a viscous oil: FTIR (neat) 3117, 3004,

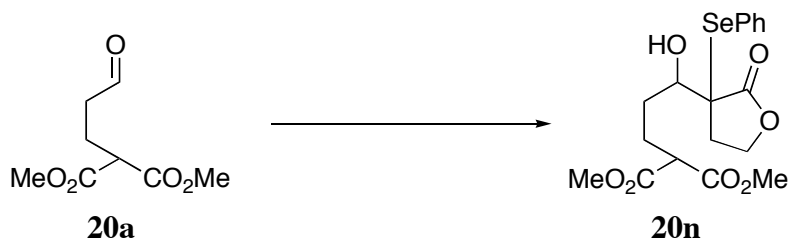
2957, 2849, 2228, 1744, 1626, 1437 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.74-2.01 (m, 4 H), 2.11 (s, 3 H), 3.39 (dd, $J = 7.2, 7.2$ Hz, 1 H), 3.75 (s, 6 H), 5.28 (dd, $J = 6.4, 6.4$ Hz, 1 H), 6.01 (d, $J = 0.8$ Hz, 1 H), 6.06 (s, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 20.8 (q), 24.1 (t), 30.4 (t), 50.9 (d), 52.7 (q), 72.4 (d), 115.9 (s), 122.2 (s), 133.1 (t), 169.1 (s), 169.12 (s), 169.7 (s); exact mass (electrospray) m/z calcd for $\text{C}_{13}\text{H}_{17}\text{NNaO}_6$ 306.0948, found 306.0946.

3-Cyanocyclohex-3-ene-1,1-dicarboxylic Acid Dimethyl Ester (**20m**).



Cs_2CO_3 (43.3 mg, 0.13 mmol) was added to a stirred solution of **20l** (18.8 mg, 0.066 mmol) in THF (2.5 mL), and stirring at room temperature was continued for 12 h. Evaporation of the solvent and filtration of the residue through a pad (ca 5 cm) of silica gel in a Pasteur pipette, using 7:10 EtOAc-hexane, gave **20m** (11.0 mg, 74%) as a colorless viscous oil: FTIR (CDCl_3 cast) 2957, 2845, 2219, 1737, 1642, 1452, 1435 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 2.15 (t, $J = 6.4$ Hz, 2 H), 2.31 (tdt, $J = 6.4, 4.4, 2.4$ Hz, 2 H), 2.78 (td, $J = 2.4, 2.0$ Hz, 2 H), 3.76 (s, 6 H), 6.59 (tt, $J = 4.4, 2.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 23.3 (t), 26.0 (t), 31.2 (t), 52.1 (s), 53.0 (q), 109.9 (s), 118.4 (s), 143.6 (d), 170.3 (s); exact mass m/z calcd for $\text{C}_{11}\text{H}_{13}\text{NO}_4$ 223.0845, found 223.0846.

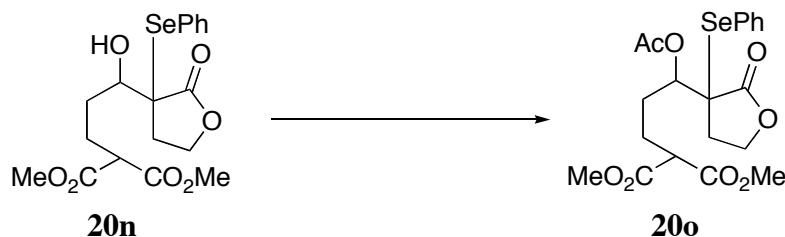
2-[3-Hydroxy-3-[2-oxo-3-(phenylseleno)tetrahydrofuran-3-yl]propyl]malonic Acid Dimethyl Ester (**20n**).



$n\text{-BuLi}$ (1.6 M in hexane, 1.5 mL, 2.37 mmol) was added dropwise to a stirred and cooled (-10°C , ice-acetone bath) solution of $i\text{-Pr}_2\text{NH}$ (240.0 mg, 2.37 mmol) in THF (10 mL). Stirring at -10°C was continued for 30 min, the mixture was cooled to -78°C and a solution of

39¹³ (572.0 mg, 2.37 mmol) in THF (10 mL) was then added dropwise. Stirring at -78 °C was continued for 1 h, and a solution of **20a** (297.0 mg, 1.58 mmol) in THF (4 mL) was added dropwise. Stirring at -78 °C was continued for 1 h, and the mixture was quenched with saturated aqueous NH₄Cl (3 mL). The cold bath was removed, stirring was continued for 15 min and the mixture was diluted with water (100 mL). The aqueous phase was extracted with EtOAc (3 x 30 mL) and the combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (3 x 15 cm), using 1:1 EtOAc-hexane, gave **20n** (601 mg, 86%) as an oil which was an inseparable 1:1 mixture of diastereomers: FTIR (CHCl₃ cast) 3502, 2954, 1750, 1576, 1477, 1438 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.32-1.40 (m, 0.5 H), 1.41-1.49 (m, 0.5 H), 1.82 (dddd, *J* = 13.6, 9.8, 9.8, 5.2 Hz, 0.5 H), 1.94-2.06 (m, 1.5 H), 2.11 (ddd, *J* = 14.3, 6.4, 0.8 Hz, 0.5 H), 2.16-2.32 (m, 2 H), 2.42 (ddd, *J* = 14.2, 10.5, 9.1 Hz, 0.5 H), 2.75 (ddd, *J* = 13.8, 10.8, 9.2 Hz, 0.5 H), 3.46 (dd, *J* = 7.5, 7.5 Hz, 0.5 H), 3.47 (dd, *J* = 7.2, 7.2 Hz, 0.5 H), 3.59 (dd, *J* = 1.9, 1.9 Hz, 0.5 H), 3.73 (s, 1.5 H), 3.74 (s, 1.5 H), 3.77 (s, 1.5 H), 3.78 (s, 1.5 H), 3.85 (ddd, *J* = 10.9, 4.6, 1.5 Hz, 0.5 H), 4.01 (ddd, *J* = 10.5, 9.0, 6.4 Hz, 0.5 H), 4.22 (ddd, *J* = 9.0, 9.0, 1.0 Hz, 0.5 H), 4.26-4.35 (m, 1 H), 7.31-7.38 (m, 2 H), 7.41-7.46 (m, 1 H), 7.62-7.65 (m, 1 H), 7.68-7.71 (m, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 25.4 (t), 25.8 (t), 28.4 (t), 28.8 (t), 29.6 (t), 31.8 (t), 51.5 (d), 52.43 (q), 52.5 (s), 54.6 (s), 65.5 (t), 65.6 (t), 71.1 (d), 73.2 (d), 124.3 (s), 124.9 (s), 129.2 (d), 130.01 (d), 130.04 (d), 137.9 (d), 138.2 (d), 169.57 (s), 169.58 (s), 169.64 (s), 176.1 (s), 176.7 (s); exact mass (electrospray) *m/z* calcd for C₁₈H₂₂NaO₇⁸⁰Se 453.0423, found 453.0422.

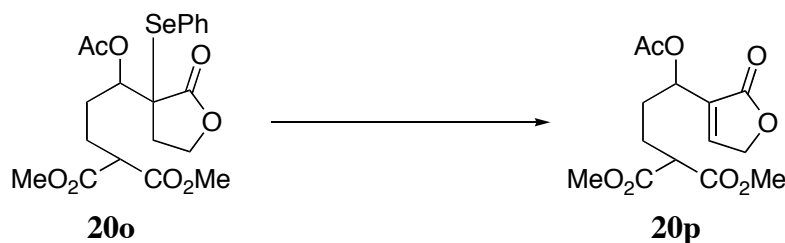
2-[3-Acetoxy-3-[2-oxo-3-(phenylseleno)tetrahydrofuran-3-yl]propyl]malonic Acid Dimethyl Ester (20o).



Pyridine (221.0 mg, 2.80 mmol) and AcCl (109.8 mg, 1.40 mmol) were added sequentially to a stirred and cooled (-10 °C, ice-acetone bath) solution of **20n** (200.0 mg, 0.47 mmol) and DMAP (6.0 mg, 0.05 mmol) in CH₂Cl₂ (5 mL). The cold bath was left in place but not recharged and stirring was continued for 5 h, by which time the temperature had risen to room temperature. The mixture was diluted with water (5 mL), acidified with hydrochloric acid (1 M, 1 mL) and extracted with CH₂Cl₂ (3 x 5 mL). The combined organic extracts were washed

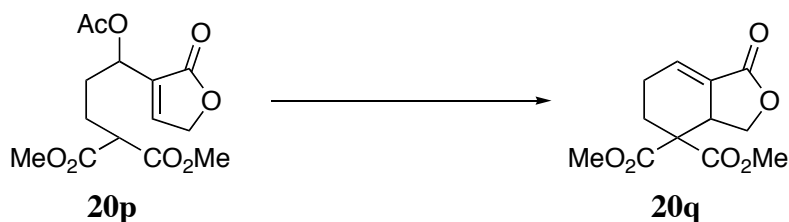
with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 x 15 cm), using 19:20 EtOAc-hexane, gave **20o** (190 mg, 87%) as an oil which was a 1.4:1.6 inseparable mixture of diastereomers: FTIR (CDCl_3 cast) 2955, 1752, 1478, 1438 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.59-1.70 (m, 1.0 H), 1.79-1.98 (m, 3.5 H), 2.04-2.14 (m, 2.5 H), 2.34-2.42 (m, 0.5 H), 2.53 (ddd, $J = 14.3, 10.2, 9.0$ Hz, 0.6 H), 2.68 (ddd, $J = 13.8, 10.7, 9.0$ Hz, 0.6 H), 3.38 (dd, $J = 8.5, 6.0, 0.6$ H), 3.47 (dd, $J = 7.4, 7.3$ Hz, 0.5 H), 3.69 (s, 1.6 H), 3.71 (s, 1.6 H), 3.76 (s, 1.4 H), 3.77 (s, 1.4 H), 4.23-4.34 (m, 2.2 H), 5.23 (dd, $J = 10.1, 2.2, 0.5$ H), 5.35 (dd, $J = 9.9, 2.5$ Hz, 0.6 H), 7.32- 7.38 (m, 2 H), 7.41-7.46 (m, 1 H), 7.64-7.68 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 20.7 (q), 20.9 (q), 25.1 (t), 25.2 (t), 28.2 (t), 28.5 (t), 30.8 (t), 31.5 (t), 50.8 (d), 51.0 (d), 51.6 (s), 52.5 (q), 52.6 (q), 65.0 (t), 65.2 (t), 72.3 (d), 72.4 (d), 124.4 (s), 125.4 (s), 129.2 (d), 129.4 (d), 130.1 (d), 130.3 (d), 137.8 (d), 138.1 (d), 169.3 (s), 169.4 (s), 169.5 (s), 170.4 (s), 173.3 (s), 173.9 (s); exact mass m/z calcd for $\text{C}_{20}\text{H}_{24}\text{O}_8^{80}\text{Se}$ 472.0636, found 472.0636.

2-[3-Acetoxy-3-(2-oxo-2,5-dihydrofuran-3-yl)propyl]malonic Acid Dimethyl Ester (20p).



H_2O_2 (30%, 0.41 mL, 4.0 mmol) was added dropwise to a stirred and cooled (0 °C) solution of **20o** (157 mg, 0.33 mmol) in CH_2Cl_2 (2 mL). Stirring was continued at 0 °C for 1 h and the mixture was quenched with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (1.0 mL). The mixture was stirred at 0 °C for 5 min, the ice bath was removed, stirring was continued for 10 min and the mixture was diluted with water (10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 10 mL) and the combined organic extracts were washed with saturated aqueous NaHCO_3 (3 mL), dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1 x 15 cm), using 17:10 EtOAc-hexane, gave **20p** (90 mg, 87%) as a viscous oil: FTIR (CDCl_3 cast) 2956, 1753, 1438 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.81-1.92 (m, 4 H), 2.08 (s, 3 H), 3.34-3.38 (m, 1 H), 3.70 (s, 6 H), 4.79-4.80 (m, 2 H), 5.56-5.58 (m, 1 H), 7.33 (dd, $J = 3.1, 1.6$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 20.7 (q), 24.0 (t), 29.7 (t), 50.8 (d), 52.5 (q), 68.1 (d), 70.2 (t), 132.5 (s), 146.9 (d), 169.2 (s), 169.3 (s), 169.7 (s), 171.3 (s); exact mass (electrospray) m/z calcd for $\text{C}_{14}\text{H}_{18}\text{NaO}_8$ 337.0894, found 337.0895.

1-Oxo-3,3a,5,6-tetrahydro-1H-isobenzofuran-4,4-dicarboxylic Acid Dimethyl Ester (20q).



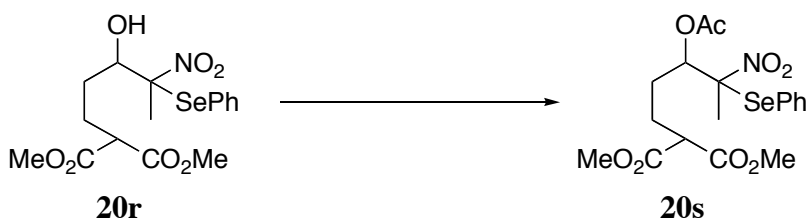
Cs_2CO_3 (29.1 mg, 0.089 mmol) was added to a stirred solution of **20p** (14.0 mg, 0.045 mmol) in THF (1 mL), and stirring at room temperature was continued for 3 h. Evaporation of the solvent and filtration of the residue through a pad (ca 5 cm) of silica gel in a Pasteur pipette, using 3:2 EtOAc-hexane, gave **20q** (11.0 mg, 97%) as a colorless viscous oil: FTIR (CDCl_3 cast) 2957, 2923, 1760, 1736, 1687 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.94 (ddd, $J = 13.9$, 10.3, 7.4 Hz, 1 H), 2.41-2.57 (m, 3 H), 3.35-3.41 (m, 1 H), 3.71 (s, 3 H), 3.79 (s, 3 H), 4.59-4.61 (m, 2 H), 6.84 (dd, $J = 7.0$, 3.5 Hz, 1 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 24.1 (t), 28.8 (t), 40.9 (d), 52.7 (q), 53.1 (q), 54.1 (s), 68.9 (t), 126.4 (s), 135.1 (d), 168.4 (s), 169.0 (s), 170.7 (s); exact mass m/z calcd for $\text{C}_{12}\text{H}_{14}\text{O}_6$ 254.0790, found 254.0784.

2-[3-Hydroxy-4-nitro-4-(phenylseleno)pentyl]malonic Acid Dimethyl Ester (20r).



DBU (23 mg, 0.15 mmol) was added to a stirred solution of **40**^{8c} (345 mg, 1.5 mmol) and aldehyde **20a** (94 mg, 0.5 mmol) in THF (3 mL). Stirring at room temperature was continued for 110 min. The reaction was quenched with hydrochloric acid (1 M, 3 mL) and the aqueous phase was extracted with CH_2Cl_2 (3 x 1 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1.5 x 15 cm), using 1:2 EtOAc, gave **20r** (124 mg, 59%) as an oil which consisted of two inseparable diastereoisomers contaminated by the starting aldehyde **20a**.

2-[3-Acetoxy-4-nitro-4-(phenylseleno)pentyl]malonic Acid Dimethyl Ester (20s).



Pyridine (147.6 mg, 1.87 mmol) and AcCl (73 mg, 0.93 mmol) were added sequentially to a stirred and cooled ($-10\text{ }^{\circ}\text{C}$, ice-acetone bath) solution of **20r** (130 mg, 0.31 mmol) and DMAP (3.7 mg, 0.03 mmol) in CH_2Cl_2 (1 mL). The cold bath was left in place but not recharged and stirring was continued for 6 h, by which time the temperature had risen to room temperature. The mixture was diluted with water (10 mL), acidified with hydrochloric acid (1 M, 3 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1 x 15 cm), using 9:20 EtOAc-hexane, gave **20s** (67 mg, 47%) as an oil which was an 8:5 mixture of diastereoisomers: FTIR (CHCl_3 cast) 2954, 1752, 1545, 1439 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.58-1.69 (m, 1.8 H), 1.77 (s, 2.5 H), 1.78-1.97 (m, 4.6 H), 2.15-2.25 (m, 1 H), 3.39 (dd, $J = 8.2, 6.5$ Hz, 0.23 H), 3.45 (dd, $J = 7.2, 7.2$ Hz, 0.74 H), 3.72 (s, 1.3 H), 3.76 (s, 4.6 H), 5.59 (dd, $J = 10.2, 1.7$ Hz, 0.74 H), 5.64 (dd, $J = 9.9, 2.2$ Hz, 0.23 H), 7.34-7.41 (m, 2 H), 7.44-7.50 (m, 1 H), 7.55-7.58 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 19.0 (q), 20.5 (q), 20.7 (q), 20.8 (q), 25.1 (t), 25.3 (t), 28.2 (t), 28.9 (t), 50.6 (d), 50.8 (d), 52.55 (q), 52.59 (q), 73.6 (d), 74.0 (d), 92.0 (s), 92.9 (s), 124.8 (s), 125.4 (s), 129.4 (d), 129.6 (d), 130.5 (d), 137.6 (d), 137.7 (d), 169.1 (s), 169.2 (s), 169.3 (s), 169.9 (s); exact mass m/z calcd for $\text{C}_{18}\text{H}_{23}\text{NO}_8^{80}\text{Se}$ 461.0589, found 461.0590.

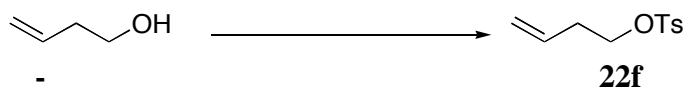
2-(3-Acetoxy-4-nitropent-4-enyl)malonic Acid Dimethyl Ester (20t).



H_2O_2 (30%, 0.14 mL, 1.37 mmol) was added dropwise to a stirred and cooled ($0\text{ }^{\circ}\text{C}$) solution of **20s** (51 mg, 0.11 mmol) in CH_2Cl_2 (1 mL). Stirring was continued at $0\text{ }^{\circ}\text{C}$ for 1.5 h and the mixture was quenched with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (1.0 mL). The mixture was stirred at $0\text{ }^{\circ}\text{C}$ for 5 min, the ice bath was removed, stirring was continued for 1 h and the mixture was diluted with water (10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 10

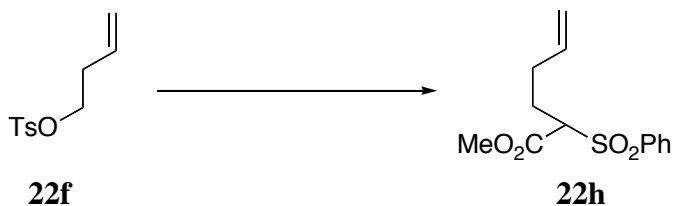
mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (0.7 x 15 cm), using 7:20 EtOAc-hexane, gave **20t** (13.7 mg, 41%) as a viscous oil. The material contained minor impurities (^1H NMR); the compound is unstable and partial decomposition occurred on chromatography: ^1H NMR (CDCl_3 , 300 MHz) δ 1.78-2.03 (m, 4 H), 2.11 (s, 3 H), 3.40 (dd, $J = 7.0, 7.0$ Hz, 1 H), 3.74 (s, 6 H), 5.85-5.89 (m, 2 H), 6.62 (d, $J = 2.4$ Hz, 1 H).

Toluene-4-sulfonic Acid But-3-enyl Ester (22f).²⁸



TsCl (2.91 g, 15.25 mmol) and Et_3N (1.54 g, 15.25 mmol) were added sequentially to a stirred solution of 3-buten-1-ol (1.0 g, 13.98 mmol) and DMAP (17.0 mg, 0.139 mmol) in CH_2Cl_2 (50 mL), and the mixture was stirred at room temperature for 24 h and then poured into water (40 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (4 x 15 cm), using 3:25 EtOAc-hexane, gave **22f** (2.25 g, 100%) as an oil.

2-(Phenylsulfonyl)hex-5-enoic Acid Methyl Ester (22h).



K_2CO_3 (1.29 g, 9.35 mmol) and $n\text{-Bu}_4\text{NHSO}_4$ (158 mg, 0.47 mmol) were added to a solution of **22g** (1.0 g, 4.67 mmol) and **22f** (0.757 g, 4.67 mmol) in DMF (24 mL). The mixture was stirred at 80 °C for 24 h, cooled to room temperature and diluted with water (250 mL). The aqueous phase was extracted with EtOAc (3 x 40 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (3.5 x 15 cm), using 1:2 EtOAc-hexane, gave **22h** (626 mg, 50%) as an oil: FTIR (CHCl_3 cast) 3070, 2954, 1742, 1641, 1448 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.99-2.20 (m, 4 H), 3.66 (s, 3 H), 3.97 (dd, $J = 10.2, 3.7$ Hz, 1 H), 4.98-5.01 (m, 1 H), 5.02-5.03 (m, 1 H), 5.63-

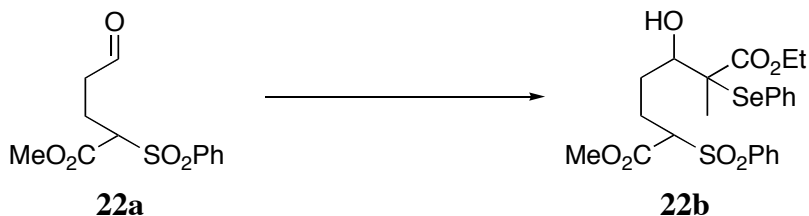
5.73 (m, 1 H), 7.55-7.59 (m, 2 H), 7.66-7.71 (m, 1 H), 7.85-7.88 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 25.9 (t), 30.8 (t), 52.9 (q), 70.0 (d), 116.8 (t), 129.0 (d), 129.3 (d), 134.3 (d), 135.6 (d), 137.1 (s), 116.3 (s); exact mass m/z calcd for $\text{C}_9\text{H}_{10}\text{O}_4\text{S}$ ($\text{M} - \text{C}_4\text{H}_6$) 214.0300, found 214.0305.

2-(Benzenesulfonyl)-5-oxopentanoic Acid Methyl Ester (22a).



O_3 was bubbled into a stirred and cooled ($-78\text{ }^\circ\text{C}$) solution **22h** (577.0 mg, 2.15 mmol) in CH_2Cl_2 (50 mL) until the solution became blue and then the excess of O_3 was removed by bubbling oxygen through the mixture. Me_2S (400 mg, 6.26 mmol) was added to the mixture, the cold bath was removed and replaced by a prewarmed water bath at $40\text{ }^\circ\text{C}$. Stirring at $40\text{ }^\circ\text{C}$ was continued for 2 h, and then the solvent was evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm), using 7:10 EtOAc-hexane, gave **22a** (400 mg, 77%) as a colorless oil: FTIR (CHCl_3 cast) 3067, 3008, 2955, 1741, 1585, 1479, 1448 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 2.18-2.31 (m, 1 H), 2.39 (dddd, $J = 14.3, 7.7, 6.7, 5.0$ Hz, 1 H), 2.54-2.74 (m, 2 H), 3.65 (s, 3 H), 4.07 (dd, $J = 9.7, 5.0$ Hz, 1 H), 7.55-7.61 (m, 2 H), 7.67-7.73 (m, 1 H), 7.85-7.91 (m, 2 H), 9.71 (t, $J = 1.2$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 19.5 (t), 40.3 (t), 53.1 (q), 69.2 (d), 129.1 (d), 129.2 (d), 134.4 (d), 137.0 (s), 165.9 (s), 199.5 (d); exact mass (electrospray) m/z calcd for $\text{C}_{12}\text{H}_{14}\text{NaO}_5\text{S}$ 293.0454, found 293.0455.

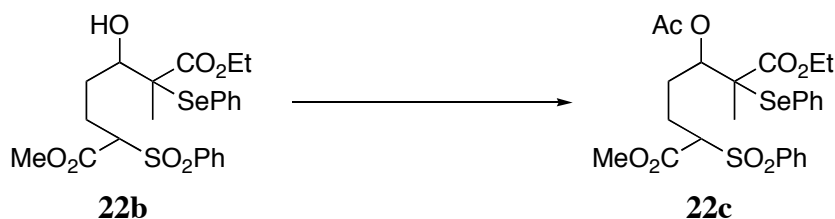
6-Benzenesulfonyl-3-hydroxy-2-methyl-2-(phenylseleno)heptanedioic Acid 1-Ethyl Ester 7-Methyl Ester (22b).



$n\text{-BuLi}$ (1.6 M in hexane, 0.83 mL, 1.33 mmol) was added dropwise to a stirred and cooled ($-10\text{ }^\circ\text{C}$, ice-acetone bath) solution of $i\text{-Pr}_2\text{NH}$ (134.0 mg, 1.33 mmol) in THF (4 mL).

Stirring at -10 °C was continued for 25 min, the mixture was cooled to -78 °C and a solution of **15** (342.0 mg, 1.33 mmol) in THF (1 mL) was then added dropwise. Stirring at -78 °C was continued for 50 min, and a solution of **22a** (240.0 mg, 0.89 mmol) in THF (3 mL) was added dropwise. Stirring at -78 °C was continued for 40 min, and the mixture was quenched with saturated aqueous NH₄Cl (3 mL). The cold bath was removed, stirring was continued for 15 min and the mixture was diluted with water (50 mL). The aqueous phase was extracted with EtOAc (3 x 20 mL) and the combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm), using 4:5 EtOAc-hexane, gave **22b** (290 mg, 62%) as an inseparable 10:8:6:5 mixture of four diastereoisomers: FTIR (CDCl₃ cast) 3515, 3060, 2954, 2927, 2854, 1740, 1584, 1448 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.11-1.22 (m, 3 H), 1.32-1.58 (m, 4 H), 1.96-2.01 (m, 1.5 H), 2.13-2.37 (m, 1.5 H), 2.82 (t, *J* = 6.8 Hz, 0.6 H), 3.06 (s, 0.2 H), 3.12 (s, 0.2 H), 3.63 (s, 0.6 H), 3.64 (s, 0.6 H), 3.67 (s, 0.8 H), 3.70 (s, 1 H), 3.75-3.86 (m, 1 H), 3.91-4.15 (m, 3 H), 7.27-7.34 (m, 2 H), 7.37-7.44 (m, 1 H), 7.50-7.60 (m, 4 H), 7.66-7.72 (m, 1 H), 7.85-7.90 (m, 2 H); ¹³C NMR (CDCl₃, 100 MHz) δ 13.70 (q), 13.72 (q), 13.82 (q), 13.84 (q), 16.99 (q), 17.02 (q), 17.5 (q), 17.8 (q), 24.1 (t), 24.3 (t), 24.5 (t), 24.7 (t), 28.1 (t), 28.56 (t), 28.62 (t), 52.8 (q), 52.85 (q), 52.88 (q), 53.9 (s), 54.1 (s), 56.8 (s), 61.1 (t), 61.2 (t), 61.4 (t), 70.3 (d), 70.38 (d), 70.42 (d), 71.8 (d), 72.8 (d), 74.2 (d), 74.8 (d), 126.00 (s), 126.03 (s), 126.2 (s), 128.80 (d), 128.84 (d), 128.9 (d), 128.95 (d), 128.96 (d), 129.1 (d), 129.2 (d), 129.3 (d), 129.48 (d), 129.53 (d), 134.11 (s), 134.13 (s), 134.14 (s), 134.2 (s), 137.0 (d), 137.1 (d), 137.9 (d), 138.0 (d), 166.17 (s), 166.22 (s), 166.26 (s), 166.34 (s), 172.9 (s), 173.6 (s), 173.8 (s); exact mass (electrospray) *m/z* calcd for C₂₃H₂₈NaO₇S⁸⁰Se 551.0613, found 551.0614.

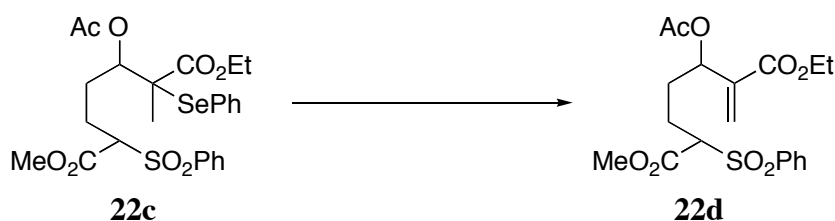
3-Acetoxy-6-benzenesulfonyl-2-methyl-2-(phenylseleno)heptanedioic Acid 1-Ethyl Ester 7-Methyl Ester (22c).



Pyridine (86.9 mg, 1.10 mmol) and AcCl (43.1 mg, 0.55 mmol) were added sequentially to a stirred and cooled (-10 °C, ice-acetone bath) solution of **22b** (mixture of four diastereoisomers) (96.5 mg, 0.18 mmol) and DMAP (2.2 mg, 0.018 mmol) in CH₂Cl₂ (1 mL). The cold bath was left in place but not recharged and stirring was continued for 5 h, by which

time the temperature had risen to room temperature. The mixture was diluted with water (5 mL), acidified with hydrochloric acid (1 M, 1 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1.5 x 15 cm), using 13:20 EtOAc-hexane, gave **22c** (84 mg, 81%) as an oil which was a 29:29:21:21 mixture of diastereomers (^1H NMR): FTIR (CHCl_3 cast) 3062, 2982, 2954, 1743, 1584, 1477, 1448, 1439 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 0.98-1.18 (m, 3 H), 1.42-1.79 (m, 4 H), 1.86 (s, 1 H), 1.92 (s, 1 H), 1.95-2.28 (m, 4 H), 3.61 (s, 0.6 H), 3.63 (s, 0.5 H), 3.72 (s, 1.6 H), 3.74-4.05 (m, 2.5 H), 4.11 (dd, J = 10.8, 4.4 Hz, 0.3 H), 4.26 (dd, J = 10.9, 4.3 Hz, 0.3 H), 5.28-5.45 (m, 1 H), 7.25-7.31 (m, 2 H), 7.36-7.41 (m, 1 H), 7.52-7.60 (m, 4 H), 7.66-7.72 (m, 1 H), 7.82-7.91 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.66 (q), 13.70 (q), 13.8 (q), 17.6 (q), 17.8 (q), 17.86 (q), 17.90 (q), 20.6 (q), 20.8 (q), 20.9 (q), 21.1 (q), 23.1 (t), 23.3 (t), 24.1 (t), 24.5 (t), 27.3 (t), 28.0 (t), 28.1 (t), 29.2 (t), 52.5 (s), 52.6 (s), 52.92 (q), 52.93 (q), 53.0 (q), 53.1 (q), 54.1 (s), 54.3 (s), 61.2 (t), 61.3 (t), 61.4 (t), 69.2 (d), 69.4 (d), 70.2 (d), 70.4 (d), 73.0 (d), 73.9 (d), 74.1 (d), 75.0 (d), 125.9 (s), 126.1 (s), 126.57 (s), 126.59 (s), 128.8 (d), 128.95 (d), 128.98 (d), 129.02 (d), 129.1 (d), 129.21 (d), 129.24 (d), 129.28 (d), 129.33 (d), 129.4 (d), 129.6 (d), 129.7 (d), 134.2 (d), 134.3 (d), 136.85 (s), 136.93 (s), 137.25 (s), 137.30 (s), 137.96 (d), 138.01 (d), 165.8 (s), 166.0 (s), 166.05 (s), 166.14 (s), 169.6 (s), 170.46 (s), 170.49 (s), 170.98 (s), 171.01 (s), 171.6 (s), 171.8 (s); exact mass (electrospray) m/z calcd for $\text{C}_{25}\text{H}_{30}\text{NaO}_8\text{S}^{80}\text{Se}$ 593.0719, found 593.0717.

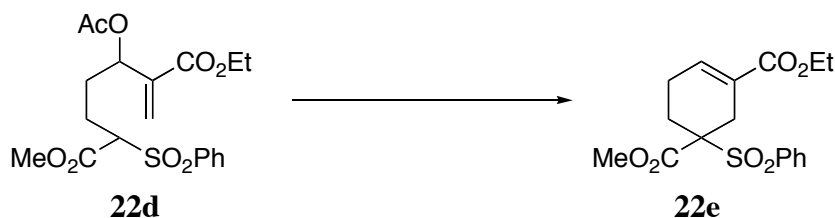
3-Acetoxy-6-benzenesulfonyl-2-methyleneheptanedioic Acid 1-Ethyl Ester 7-Methyl Ester (22d).



H_2O_2 (30%, 0.17 mL, 1.7 mmol) was added dropwise to a stirred and cooled (0 °C) solution of **22c** (four diastereoisomers) (81 mg, 0.14 mmol) in CH_2Cl_2 (2 mL). Stirring was continued at 0 °C for 90 min and the mixture was quenched with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (1.0 mL). The mixture was stirred at 0 °C for 5 min, the ice bath was removed, stirring was continued for 10 min and the mixture was diluted with water (5 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL) and the combined organic extracts were washed with saturated aqueous NaHCO_3 (5 mL), dried (Na_2SO_4) and evaporated. Flash chromatography of the residue

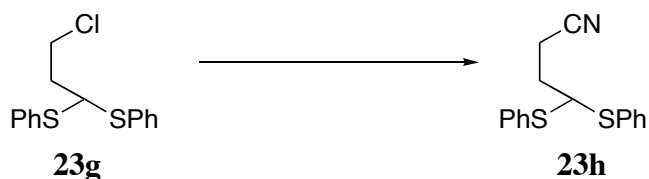
over silica gel (0.7 x 15 cm), using 1:1 EtOAc-hexane, gave **22d** (44 mg, 76%) as a viscous oil which was a 1:1 mixture of diastereomers: FTIR (CDCl₃ cast) 2955, 2971, 2854, 1743, 1634, 1585, 1448 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.28 (t, *J* = 7.1 Hz, 1.5 H), 1.29 (t, *J* = 7.1 Hz, 1.5 H), 1.69-1.87 (m, 2 H), 1.98- 2.15 (m, 5 H), 3.63 (s, 1.5 H), 3.65 (s, 1.5 H), 3.94 (dd, *J* = 10.5, 3.9 Hz, 0.5 H), 4.00-4.03 (m, 0.5 H), 4.16-4.25 (m, 2 H), 5.54 (dd, *J* = 7.2, 4.7 Hz, 0.5 H), 5.59 (dd, *J* = 7.8, 3.8 Hz, 0.5 H), 5.72 (t, *J* = 1.0 Hz, 0.5 H), 5.74 (t, *J* = 0.9 Hz, 0.5 H), 6.27 (s, 0.5 H), 6.29 (s, 0.5 H), 7.56-7.59 (m, 2 H), 7.67-7.71 (m, 1 H), 7.84-7.87 (m, 2 H); ¹³C NMR (CDCl₃, 125 MHz) δ 14.0 (q), 20.88 (q), 20.93 (q), 22.3 (t), 22.5 (t), 30.8 (t), 31.1 (t), 52.90 (q), 52.94 (q), 60.98 (t), 61.01 (t), 69.8 (d), 70.27 (d), 70.28 (d), 70.7 (d), 125.3 (s), 125.6 (s), 129.055 (d), 129.063 (d), 129.15 (d), 129.17 (d), 134.28 (d), 134.32 (d), 137.0 (s), 137.1 (s), 139.06 (t), 139.13 (t), 164.78 (s), 164.83 (s), 165.9 (s), 166.1 (s), 169.61 (s), 169.64 (s); exact mass (electrospray) *m/z* calcd for C₁₉H₂₄NaO₈S 435.1084, found 435.1081.

1-(Benzenesulfonyl)cyclohex-3-ene-1,3-dicarboxylic Acid 3-Ethyl Ester 1-Methyl Ester (22e).



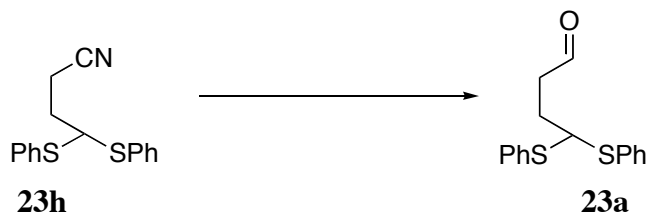
Cs₂CO₃ (40.0 mg, 0.123 mmol) was added to a stirred solution of **22d** (25.3 mg, 0.061 mmol) in THF (2.4 mL), and stirring at room temperature was continued for 45 min. Filtration of the mixture through a pad (ca 5 cm) of silica gel in a Pasteur pipette, using 2:1 EtOAc-hexane, gave **22e** (20.0 mg, 93%) as a colorless viscous oil: FTIR (CDCl₃ cast) 3066, 2981, 2953, 1736, 1709, 1655, 1584, 1448, 1435 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.28 (t, *J* = 7.1 Hz, 3 H), 2.03 (ddd, *J* = 12.9, 11.3, 6.4 Hz, 1 H), 2.22-2.31 (m, 1 H), 2.41-2.48 (m, 1 H), 2.53 (dddd, *J* = 12.9, 6.3, 2.5, 2.5 Hz, 1 H), 2.80 (dddd, *J* = 17.2, 4.3, 2.6, 2.6 Hz, 1 H), 3.21 (dddd, *J* = 17.2, 2.4, 1.4, 1.4 Hz, 1 H), 3.62 (s, 3 H), 4.18 (q, *J* = 7.2 Hz, 2 H), 6.91 (ddd, *J* = 5.0, 2.5, 2.5 Hz, 1 H), 7.56-7.59 (m, 2 H), 7.68-7.71 (m, 1 H), 7.82-7.85 (m, 2 H); ¹³C NMR (CDCl₃, 125 MHz) δ 14.2 (q), 23.5 (t), 23.8 (t), 26.9 (t), 53.2 (q), 60.8 (t), 72.0 (s), 127.3 (s), 128.9 (d), 130.2 (d), 134.4 (d), 135.4 (s), 137.6 (d), 165.9 (s), 167.4 (s); exact mass *m/z* calcd for C₁₇H₂₀O₆S 352.0981, found 352.0981.

4,4-Bis(phenylthio)butyronitrile (23h).



A solution of **23g**²⁹ (200 mg, 0.68 mmol) in DMSO (2.5 mL) was added to a stirred mixture of NaCN (166.6 mg, 3.4 mmol) and Bu₄NI (26 mg, 0.07 mmol) in DMSO (2.5 mL), and the resulting mixture was stirred at 50 °C for 15 h, cooled to room temperature and diluted with water (20 mL). The aqueous phase was extracted with EtOAc (3 x 15) and the combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (1.5 x 15 cm), using 7:20 EtOAc-hexane, gave **23h** (193 mg, 100%) as a liquid: FTIR (CDCl₃ cast) 3058, 2929, 2248, 1582, 1479, 1439, 1419 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 2.15 (tq, *J* = 7.2, 6.9 Hz, 2 H), 2.68 (t, *J* = 7.2 Hz, 2 H), 4.45 (t, *J* = 6.9 Hz, 1 H), 7.33-7.37 (m, 6 H), 7.48-7.51 (m, 4 H); ¹³C NMR (CDCl₃, 125 MHz) δ 15.1 (t), 31.2 (t), 56.9 (d), 118.7 (s), 128.5 (d), 129.2 (d), 132.7 (s), 133.3 (d); exact mass *m/z* calcd for C₁₆H₁₅NS₂ 285.0646, found 285.0647.

4,4-Bis(phenylthio)butyraldehyde (**23a**).³⁹



DIBAL-H (1.0 M in PhMe, 2.63 mL, 2.63 mmol) was added dropwise to a stirred and cooled (-78 °C) solution of **23h** (500 mg, 1.75 mmol) in CH₂Cl₂ (10 mL). Stirring at -78 °C was continued for 2 h, and the mixture was quenched with hydrochloric acid (1 M, 10 mL). The cold bath was removed, stirring was continued for 30 min and the mixture was diluted with water (10 mL). The aqueous phase was extracted with CH₂Cl₂ (3 x 10 mL) and the combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (2 x 15 cm), using 1:5 EtOAc-hexane, gave **23a** (419 mg, 83%) as a liquid: FTIR (CH₂Cl₂ cast) 3057, 2926, 2827, 2724, 1723, 1479, 1438 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 2.19 (td, *J* = 7.2, 6.7 Hz, 2 H), 2.81 (td, *J* = 7.2, 1.0 Hz, 2 H), 4.49 (t, *J* = 6.7 Hz, 1 H), 7.28-7.35 (m, 6 H), 7.46-7.49 (m, 4 H), 9.77 (t, *J* = 1.0 Hz, 1 H); ¹³C NMR (CDCl₃, 100

MHz) δ 28.2 (t), 41.1 (t), 57.4 (d), 127.9 (d), 129.0 (d), 132.8 (d), 133.6 (s), 200.8 (d); exact mass m/z calcd for $C_{16}H_{16}OS_2$ 288.0643, found 288.0640.

3-Hydroxy-2-methyl-2-(phenylseleno)-6,6-bis(phenylthio)hexanoic Acid Ethyl Ester (23b,b').



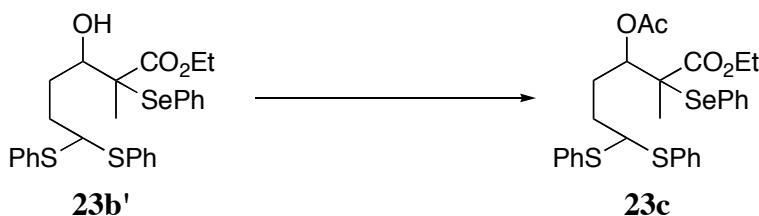
n-BuLi (1.5 M in hexane, 0.34 mL, 0.51 mmol) was added dropwise to a stirred and cooled (0 °C) solution of *i*-Pr₂NH (51.6 mg, 0.51 mmol) in THF (2 mL). Stirring at 0 °C was continued for 15 min, the mixture was cooled to -78 °C, and a solution of **15** (131 mg, 0.51 mmol) in THF (1 mL) was added dropwise. Stirring at -78 °C was continued for 50 min, and a solution of **23a** (105 mg, 0.36 mmol) in THF (1 mL) was added dropwise. Stirring at -78 °C was continued for 90 min, and the mixture was quenched with saturated aqueous NH₄Cl (10 mL). The cold bath was removed, stirring was continued for 15 min and the mixture was diluted with water (10 mL). The aqueous phase was extracted with EtOAc (3 x 5 mL) and the combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (2 x 15 cm), using 9:50 EtOAc-hexane and then 13:50 EtOAc-hexane, gave **23b** (less polar isomer) (55 mg, 28%) as a viscous oil and **23b'** (more polar isomer) (120 mg, 61%) as a viscous oil.

Compound **23b** had: FTIR (CDCl₃ cast) 3504, 3072, 3057, 2980, 2933, 2868, 1718, 1582, 1475, 1438 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.14 (t, *J* = 7.1 Hz, 3 H), 1.42 (s, 3 H), 1.73-1.79 (m, 1 H), 1.80-1.87 (m, 1 H), 1.94 (dddd, *J* = 14.3, 9.2, 6.3, 6.2 Hz, 1 H), 2.17-2.25 (m, 1 H), 3.00 (s, 1 H), 3.87 (dd, *J* = 9.7, 2.0 Hz, 1 H), 4.02 (dq, *J* = 10.8, 7.1 Hz, 1 H), 4.09 (dq, *J* = 10.8, 7.1 Hz, 1 H), 4.47 (dd, *J* = 6.7, 6.7 Hz, 1 H), 7.27-7.34 (m, 8 H), 7.41-7.48 (m, 5 H), 7.59-7.61 (m, 2 H); ¹³C NMR (CDCl₃, 125 MHz) δ 13.9 (q), 17.2 (q), 29.1 (t), 33.2 (t), 57.3 (s), 58.0 (d), 61.2 (t), 72.6 (d), 126.3 (s), 127.6 (d), 128.8 (d), 129.5 (d), 132.6 (d), 132.7 (d), 134.05 (s), 134.12 (s), 138.1 (d), 173.1 (s); exact mass m/z calcd for C₂₇H₃₀O₃S₂⁸⁰Se 546.0801, found 546.0813.

Compound **23b'** had: FTIR (CH₂Cl₂ cast) 3498, 3072, 3057, 2980, 2957, 2933, 1721, 1706, 1582, 1476, 1438 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.21 (t, *J* = 7.1 Hz, 3 H), 1.42 (s, 3 H), 1.63-1.71 (m, 1 H), 1.87-1.94 (m, 1 H), 2.17-2.30 (m, 2 H), 2.76 (d, *J* = 6.9 Hz, 1 H), 3.79

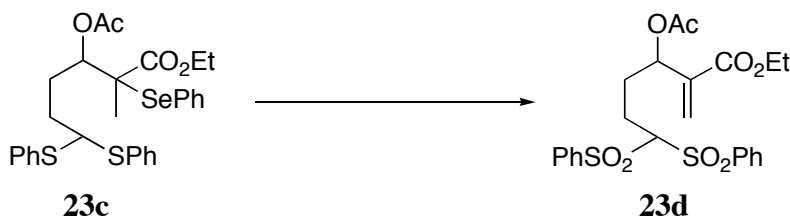
(ddd, $J = 10.7, 6.9, 1.4$ Hz, 1 H), 4.11 (q, $J = 7.1$ Hz, 2 H), 4.51 (dd, $J = 6.4, 6.4$ Hz, 1 H), 7.25-7.34 (m, 8 H), 7.36-7.40 (m, 1 H), 7.48-7.51 (m, 4 H), 7.53-7.55 (m, 2 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 14.0 (q), 18.1 (q), 28.8 (t), 33.2 (t), 54.4 (s), 58.1 (d), 61.4 (t), 75.0 (d), 126.5 (s), 127.70 (d), 127.72 (d), 128.8 (d), 128.9 (d), 129.4 (d), 132.7 (d), 132.8 (d), 134.09 (s), 134.14 (s), 138.1 (d), 174.0 (s); exact mass m/z calcd for $\text{C}_{27}\text{H}_{30}\text{O}_3\text{S}_2^{80}\text{Se}$ 546.0801, found 546.0793.

3-Acetoxy-2-methyl-2-(phenylseleno)-6,6-bis(phenylthio)hexanoic Acid Ethyl Ester (23c).



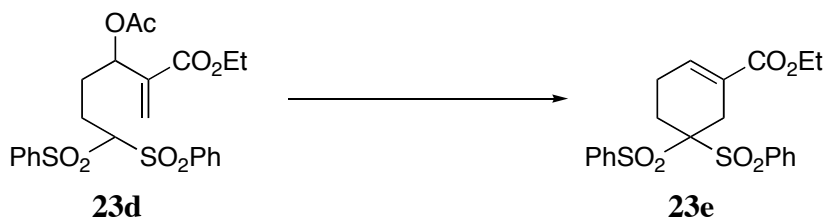
Pyridine (98.0 mg, 1.23 mmol) and AcCl (48.4 mg, 0.62 mmol) were added sequentially to a stirred and cooled (-10°C , ice-acetone bath) solution of **23b'** (112 mg, 0.21 mmol) and DMAP (2 mg, 0.02 mmol) in CH_2Cl_2 (2 mL). The cold bath was left in place but not recharged and stirring was continued for 13 h, by which time the temperature had risen to room temperature. The mixture was diluted with water (10 mL), acidified with hydrochloric acid (1 M, 2 mL) and extracted with CH_2Cl_2 (3 x 8 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1 x 15 cm), using 1:4 EtOAc-hexane, gave **23c** (90 mg, 74%) as an oil: FTIR (CDCl_3 cast) 3057, 2981, 2932, 1745, 1725, 1582, 1476, 1439 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.06 (t, $J = 7.1$ Hz, 3 H), 1.51 (s, 3 H), 1.82 (s, 3 H), 1.85-1.99 (m, 3 H), 2.51-2.60 (m, 1 H), 3.86 (dq, $J = 10.8, 7.1$ Hz, 1 H), 4.00 (dq, $J = 10.8, 7.1$ Hz, 1 H), 4.50 (dd, $J = 6.2, 6.2$ Hz, 1 H), 5.36 (dd, $J = 10.1, 1.7$ Hz, 1 H), 7.24-7.40 (m, 9 H), 7.49-7.52 (m, 4 H), 7.56-7.58 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.8 (q), 17.7 (q), 20.7 (q), 27.8 (t), 32.2 (t), 52.8 (s), 57.9 (d), 61.1 (t), 75.0 (d), 126.2 (s), 127.8 (d), 127.9 (d), 128.91 (d), 128.94 (d), 129.6 (d), 132.9 (d), 133.1 (d), 133.87 (s), 133.90 (s), 138.1 (d), 169.5 (s), 171.9 (s); exact mass m/z calcd for $\text{C}_{29}\text{H}_{32}\text{O}_4\text{S}_2^{80}\text{Se}$ 588.0907, found 588.0916.

2-[1-Acetoxy-4,4-bis(benzenesulfonyl)butyl]acrylic Acid Ethyl Ester (23d).

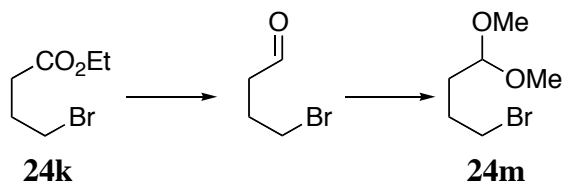


m-CPBA (70-75%, 164 mg, 0.66 mmol) was added to a solution of **23c** (39 mg, 0.066 mmol) in CH₂Cl₂ (2 mL), and the mixture was stirred at 40 °C for 23 h, cooled to room temperature and evaporated. Flash chromatography of the residue over silica gel (0.7 x 15 cm), using 15:20 EtOAc-hexane, gave **23d** (23 mg, 81%) as a viscous oil: FTIR (CH₂Cl₂ cast) 3066, 2983, 2933, 1743, 1635, 1584, 1448 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.31 (t, *J* = 7.1 Hz, 3 H), 1.99-2.05 (m, 1 H), 2.06 (s, 3 H), 2.16-2.30 (m, 3 H), 4.19-4.28 (m, 2 H), 4.51-4.53 (m, 1 H), 5.57 (dd, *J* = 8.0, 2.9 Hz, 1 H), 5.73 (dd, *J* = 1.1, 1.1 Hz, 1 H), 6.29 (dd, *J* = 0.7, 0.7 Hz, 1 H), 7.55-7.59 (m, 4 H), 7.67-7.71 (m, 2 H), 7.93-7.95 (m, 4 H); ¹³C NMR (CDCl₃, 125 MHz) δ 14.1 (q), 21.0 (q), 21.4 (t), 31.8 (t), 61.1 (t), 70.4 (d), 82.6 (d), 125.4 (t), 129.08 (d), 129.11 (d), 129.57 (d), 129.61 (d), 134.56 (d), 134.57 (d), 137.7 (s), 137.8 (s), 139.1 (s), 164.9 (s), 169.7 (s); exact mass (electrospray) *m/z* calcd for C₂₃H₂₆NaO₈S₂ 517.0961, found 517.0961.

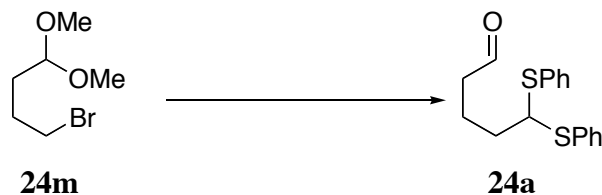
5,5-Bis(benzenesulfonyl)cyclohex-1-enecarboxylic Acid Ethyl Ester (23e).



Cs₂CO₃ (20.0 mg, 0.062 mmol) was added to a stirred solution of **23d** (15.2 mg, 0.031 mmol) in THF (1 mL), and stirring at room temperature was continued for 2 h. Evaporation of the solvent and filtration of the residue through a pad (ca 5 cm) of silica gel in a Pasteur pipette, using 1:1 EtOAc-hexane, gave **23e** (13.2 mg, 99%) as a colorless viscous oil: FTIR (CH₂Cl₂ cast) 3066, 2982, 1707, 1663, 1583, 1448 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.27 (t, *J* = 7.1 Hz, 3 H), 2.42 (t, *J* = 6.5 Hz, 2 H), 2.56-2.62 (m, 2 H), 3.12 (ddd, *J* = 2.1, 2.1, 2.1 Hz, 2 H), 4.18 (q, *J* = 7.2 Hz, 2 H), 7.01 (dddd, *J* = 4.0, 4.0, 2.0, 2.0 Hz, 1 H), 7.56-7.60 (m, 4 H), 7.69-7.73 (m, 2 H), 8.01-8.03 (m, 4 H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.2 (q), 23.0 (t), 23.3 (t), 25.4 (t), 60.8 (t), 86.7 (s), 125.5 (s), 128.8 (d), 131.2 (d), 134.7 (d), 136.3 (s), 138.0 (d), 165.5 (s); exact mass *m/z* calcd for C₂₁H₂₂O₆S₂ 434.0858, found 434.0859.

4-Bromo-1,1-dimethoxybutane (24m).³⁰

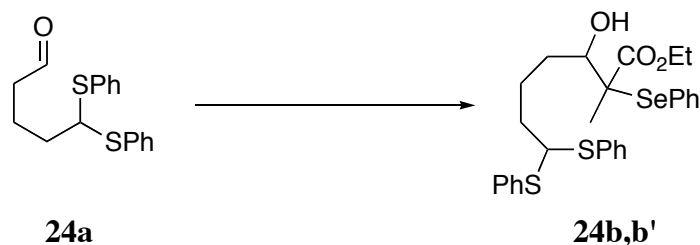
DIBAL-H (1.0 M in PhMe, 6.2 mL) was added slowly to a stirred and cooled (-78 °C) solution of **24k** (1.0 g, 5.12 mmol) in CH₂Cl₂ (50 mL), the internal temperature being kept below -75 °C. Stirring at -78 °C was continued for 40 min, and MeOH (2.2 mL) and saturated aqueous Rochelle salt (97 mL) were added. The cold bath was removed and vigorous stirring was continued for 2 h. The aqueous phase was extracted with CH₂Cl₂ (2 x 50 mL) and the combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. The residue was dissolved in MeOH (20 mL), pyridinium *p*-toluene sulfonate (64 mg, 0.26 mmol) was added, and stirring at room temperature was continued for 7 h. The mixture was diluted with water (100 mL) and the aqueous phase was extracted with EtOAc (3 x 80 mL). The combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm), using 17:25 EtOAc-hexane, gave **24m** (691 mg, 68%) as an oil.

5,5-Bis(phenylthio)pentanal (24a).

n-BuLi (1.5 M in hexane, 2.8 mL, 4.19 mmol) was added dropwise to a stirred and cooled (0 °C) solution of (PhS)₂CH₂ (885.3 mg, 3.81 mmol) in THF (20 mL).²⁹ Stirring at 0 °C was continued for 15 min, and a solution of **24m** (250 mg, 1.27 mmol) in THF (2 mL) was added rapidly in one portion. Stirring at 0 °C was continued for 1.5 h, and hydrochloric acid (4 M, 2.5 mL) was added. The cold bath was removed, stirring was continued for 1 h and the mixture was diluted with water (100 mL). The aqueous phase was extracted with EtOAc (3 x 50 mL) and the combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (1.5 x 15 cm), using 1:3 EtOAc-hexane, gave **24a** (345 mg, 90%) as a liquid: FTIR (CDCl₃ cast) 3057, 2934, 2826, 2723, 1722, 1582, 1480, 1439

cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.85-2.00 (m, 4 H), 2.42 (td, $J = 7.2, 1.5$ Hz, 2 H), 4.40 (t, $J = 6.4$ Hz, 1 H), 7.26-7.35 (m, 6 H), 7.46-7.49 (m, 4 H), 9.72 (t, $J = 1.5$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 19.7 (t), 35.16 (t), 43.2 (t), 58.2 (d), 127.9 (d), 129.0 (d), 132.8 (d), 134.0 (s), 201.6 (d); exact mass m/z calcd for $\text{C}_{17}\text{H}_{18}\text{OS}_2$ 302.0799, found 302.0801.

3-Hydroxy-2-methyl-2-(phenylseleno)-7,7-bis(phenylthio)heptanoic Acid Ethyl Ester (24b,b').

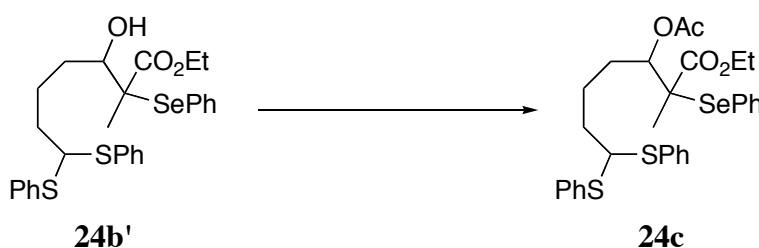


$n\text{-BuLi}$ (1.5 M in hexane, 0.41 mL, 0.62 mmol) was added dropwise to a stirred and cooled ($0\text{ }^{\circ}\text{C}$) solution of $i\text{-Pr}_2\text{NH}$ (62.7 mg, 0.62 mmol) in THF (3 mL). Stirring at $0\text{ }^{\circ}\text{C}$ was continued for 15 min, the mixture was cooled to $-78\text{ }^{\circ}\text{C}$, and a solution of **15** (159.3 mg, 0.62 mmol) in THF (2 mL) was then added dropwise. Stirring at $-78\text{ }^{\circ}\text{C}$ was continued for 1 h, and a solution of **24a** (124 mg, 0.41 mmol) in THF (1 mL) was added dropwise. Stirring at $-78\text{ }^{\circ}\text{C}$ was continued for 40 min, and the mixture was quenched with saturated aqueous NH_4Cl (5 mL). The cold bath was removed, stirring was continued for 15 min and the mixture was diluted with water (40 mL). The aqueous phase was extracted with EtOAc (3 x 20 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 x 15 cm), using 3:20 EtOAc-hexane and then 1:5 EtOAc-hexane, gave **24b** (less polar isomer) (84 mg, 37%) as a viscous oil and **24b'** (more polar) (110 mg, 48%) as a viscous oil.

Compound **24b** had: FTIR (CH_2Cl_2 cast) 3498, 3057, 2979, 2937, 2867, 1720, 1582, 1476, 1438 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.12 (t, $J = 7.1$ Hz, 3 H), 1.28-1.37 (m, 1 H), 1.38 (s, 3 H), 1.49-1.57 (m, 1 H), 1.66-1.74 (m, 1 H), 1.83-1.99 (m, 3 H), 2.95 (dd, $J = 2.9, 1.7$ Hz, 1 H), 3.86 (ddd, $J = 9.8, 2.3, 2.3$ Hz, 1 H), 3.98 (dq, $J = 10.8, 7.1$ Hz, 1 H), 4.06 (dq, $J = 10.8, 7.1$ Hz, 1 H), 4.39 (dd, $J = 6.5, 6.5$ Hz, 1 H), 7.25-7.33 (m, 8 H), 7.39-7.50 (m, 5 H), 7.58-7.60 (m, 2 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 13.8 (q), 17.0 (q), 24.5 (t), 31.3 (t), 35.6 (t), 57.4 (s), 58.4 (d), 61.1 (t), 72.6 (d), 126.4 (s), 127.6 (d), 128.82 (d), 128.84 (d), 128.86 (d), 128.93 (d), 129.5 (d), 132.7 (d), 132.8 (d), 134.2 (s), 134.3 (s), 138.0 (d), 173.1 (s); exact mass (electrospray) m/z calcd for $\text{C}_{28}\text{H}_{32}\text{NaO}_3\text{S}_2^{80}\text{Se}$ 583.0850, found 583.0842.

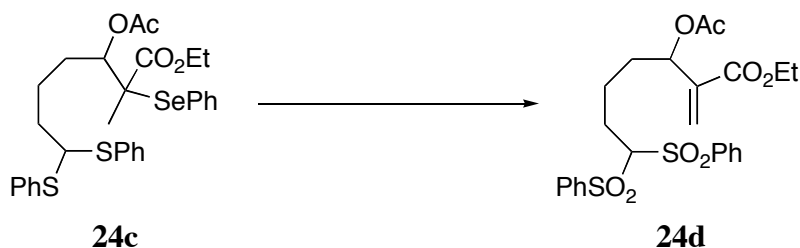
Compound **24b'** had: FTIR (CH₂Cl₂ cast) 3502, 3072, 3057, 2979, 2937, 2866, 1722, 1582, 1476, 1438 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.20 (t, *J* = 7.1 Hz, 3 H), 1.31-1.37 (m, 1 H), 1.39 (s, 3 H), 1.64-1.75 (m, 1 H), 1.83-1.95 (m, 4 H), 2.77 (s, 1 H), 3.84 (d, *J* = 10.3 Hz, 1 H), 4.10 (q, *J* = 7.1 Hz, 2 H), 4.42 (t, *J* = 6.4 Hz, 1 H), 7.27-7.34 (m, 8 H), 7.38-7.42 (m, 1 H), 7.46-7.50 (m, 4 H), 7.55-7.57 (m, 2 H); ¹³C NMR (CDCl₃, 100 MHz) δ 13.9 (q), 18.0 (q), 24.5 (t), 30.8 (t), 35.7 (t), 54.6 (s), 58.5 (d), 61.3 (t), 75.0 (d), 126.5 (s), 127.7 (d), 128.8 (d), 128.85 (d), 128.86 (d), 129.4 (d), 132.78 (d), 132.80 (d), 134.18 (s), 134.19 (s), 138.0 (d), 173.9 (s); exact mass (electrospray) *m/z* calcd for C₇₈H₇₂NaO₄S₇⁸⁰Se 583.0850, found 583.0849.

3-Acetoxy-2-methyl-2-(phenylseleno)-7,7-bis(phenylthio)heptanoic Acid Ethyl Ester (24c).



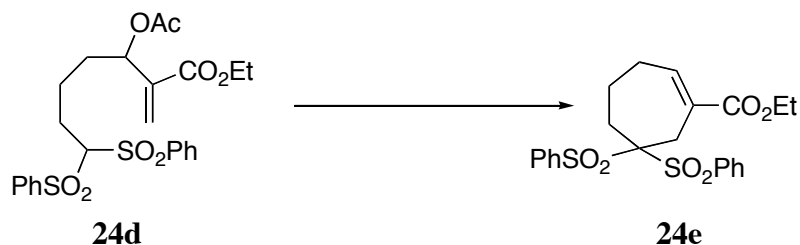
Pyridine (93.4 mg, 1.18 mmol) and AcCl (46.3 mg, 0.59 mmol) were added sequentially to a stirred and cooled (-10 °C, ice-acetone bath) solution of **24b'** (110 mg, 0.197 mmol) and DMAP (2.5 mg, 0.02 mmol) in CH₂Cl₂ (2 mL). The cold bath was left in place but not recharged and stirring was continued for 16 h, by which time the temperature had risen to room temperature. The mixture was diluted with water (10 mL), acidified with hydrochloric acid (1 M, 2 mL) and extracted with CH₂Cl₂ (3 x 10 mL). The combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (1 x 15 cm), using 17:100 EtOAc-hexane, gave **24c** (84 mg, 71%) as an oil: FTIR (CHCl₃ cast) 3057, 2981, 2936, 1745, 1725, 1582, 1476, 1438 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.09 (t, *J* = 7.1 Hz, 3 H), 1.48 (s, 3 H), 1.51-1.60 (m, 1 H), 1.62-1.72 (m, 2 H), 1.86 (dddd, *J* = 14.3, 14.3, 6.8, 6.8 Hz, 1 H), 1.91-2.00 (m, 1 H), 1.94 (s, 3 H), 2.03-2.12 (m, 1 H), 3.89 (dq, *J* = 10.7, 7.1 Hz, 1 H), 4.02 (dq, *J* = 10.7, 7.1 Hz, 1 H), 4.40 (dd, *J* = 6.8, 6.8 Hz, 1 H), 5.44 (dd, *J* = 10.1, 1.8 Hz, 1 H), 7.28-7.35 (m, 8 H), 7.37-7.42 (m, 1 H), 7.46-7.49 (m, 4 H), 7.56-7.59 (m, 2 H); ¹³C NMR (CDCl₃, 100 MHz) δ 13.8 (q), 17.9 (q), 20.9 (q), 24.02 (t), 30.0 (t), 35.7 (t), 53.0 (s), 58.2 (d), 61.1 (t), 75.4 (d), 126.3 (s), 127.6 (d), 127.7 (d), 128.87 (d), 128.90 (d), 129.6 (d), 132.7 (d), 132.9 (d), 134.16 (s), 134.22 (s), 138.0 (d), 169.5 (s), 172.0 (s); exact mass (electrospray) *m/z* calcd for C₃₀H₃₄NaO₄S₂⁸⁰Se 625.0956, found 625.09501.

2-[1-Acetoxy-5,5-bis(benzenesulfonyl)pentyl]acrylic Acid Ethyl Ester (24d).



m-CPBA (70-75%, 151.8 mg, ca 0.62 mmol) was added to a solution of **24c** (37 mg, 0.062 mmol) in CH₂Cl₂ (2 mL), and the mixture was stirred at 40 °C for 23 h, cooled to room temperature and evaporated. Flash chromatography of the residue over silica gel (0.7 x 15 cm), using 3:5 EtOAc-hexane, gave **24d** (19.8 mg, 65%) as a viscous oil: FTIR (CDCl₃ cast) 3064, 2981, 2928, 1739, 1584, 1478, 1448 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.31 (t, *J* = 7.1 Hz, 3 H), 1.59-1.79 (m, 4 H), 2.08 (s, 3 H), 2.18 (dd, *J* = 13.4, 7.0 Hz, 2 H), 4.18-4.29 (m, 2 H), 4.41 (dd, *J* = 5.7, 5.7 Hz, 1 H), 5.55 (dd, *J* = 6.3, 4.0 Hz, 1 H), 5.73 (s, 1 H), 6.28 (s, 1 H), 7.56-7.60 (m, 4 H), 7.69-7.72 (m, 2 H), 7.94-7.96 (m, 4 H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.1 (q), 21.0 (q), 23.8 (t), 25.2 (t), 33.3 (t), 61.0 (t), 71.0 (d), 83.3 (d), 125.2 (t), 129.1 (d), 129.55 (d), 129.58 (d), 134.6 (d), 137.7 (s), 137.8 (s), 139.6 (s), 165.0 (s), 169.8 (s); exact mass (electrospray) *m/z* calcd for C₂₄H₂₈NaO₈S₂ 531.1118, found 531.1112.

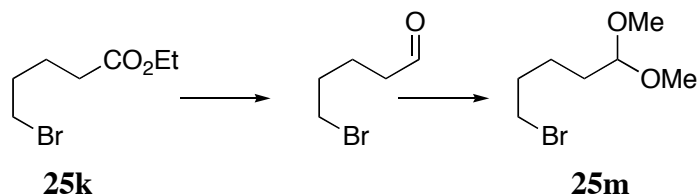
6,6-Bis(benzenesulfonyl)cyclohept-1-enecarboxylic Acid Ethyl Ester (24e).



Cs₂CO₃ (25.7 mg, 0.079 mmol) was added to a stirred solution of **24d** (20.0 mg, 0.039 mmol) in THF (1 mL), and stirring at room temperature was continued for 2 h. Evaporation of the solvent and filtration of the residue through a pad (ca 5 cm) of silica gel in a Pasteur pipette, using 2:5 EtOAc-hexane, gave **24e** (16.6 mg, 95%) as a colorless viscous oil: FTIR (CDCl₃ cast) 3067, 2927, 1704, 1650, 1583, 1466, 1448 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.28 (t, *J* = 7.1 Hz, 3 H), 1.68-1.74 (m, 2 H), 2.43 (dd, *J* = 11.7, 6.5 Hz, 2 H), 2.52-2.54 (m, 2 H), 3.51 (s, 2 H), 4.21 (q, *J* = 7.1 Hz, 2 H), 6.95 (dd, *J* = 5.0, 5.0 Hz, 1 H), 7.56-7.60 (m, 4 H), 7.68-7.72 (m, 2 H),

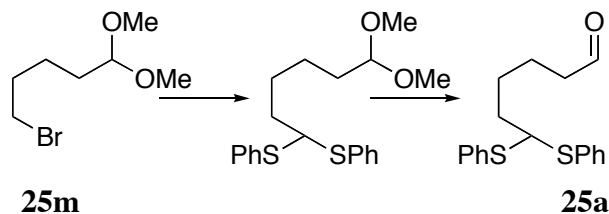
8.05-8.08 (m, 4 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.2 (q), 19.1 (t), 25.7 (t), 28.3 (t), 30.3 (t), 61.2 (t), 91.0 (s), 127.0 (s), 128.7 (s), 131.4 (d), 134.5 (d), 136.7 (s), 140.4 (d), 166.9 (s); exact mass (electrospray) m/z calcd for $\text{C}_{22}\text{H}_{24}\text{NaO}_6\text{S}_2$ 471.0907, found 471.0906.

5-Bromo-1,1-dimethoxypentane (25m).³¹



DIBAL-H (1.0 M in PhMe, 5.7 mL) was added slowly to a stirred and cooled ($-78\text{ }^{\circ}\text{C}$) solution of **25k** (1.0 g, 4.8 mmol) in CH_2Cl_2 (50 mL), the internal temperature being kept below $-75\text{ }^{\circ}\text{C}$. Stirring at $-78\text{ }^{\circ}\text{C}$ was continued for 40 min, and MeOH (2.5 mL) and saturated aqueous Rochelle salt (100 mL) were added. The cold bath was removed, and vigorous stirring was continued for 2 h. The aqueous phase was extracted with CH_2Cl_2 (2 x 50 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. The residue was dissolved in MeOH (20 mL), pyridinium *p*-toluenesulfonate (60 mg, 0.24 mmol) was added, and stirring at room temperature was continued for 7 h. The mixture was diluted with water (150 mL) and the aqueous phase was extracted with EtOAc (3 x 80 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm), using 17:25 EtOAc-hexane, gave **25m** (681 mg, 68%) as an oil.

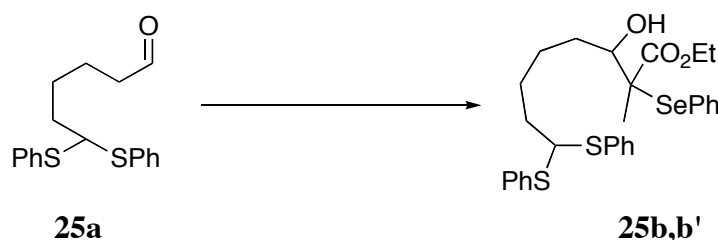
6,6-Bis(phenylthio)hexanal (25a).



n-BuLi (1.5 M in hexane, 2.1 mL, 3.13 mmol) was added dropwise to a stirred and cooled ($0\text{ }^{\circ}\text{C}$) solution of $(\text{PhS})_2\text{CH}_2$ (660 mg, 2.84 mmol) in THF (14 mL).²⁹ Stirring at $0\text{ }^{\circ}\text{C}$ was continued for 15 min, and a solution of **25m** (200 mg, 0.95 mmol) in THF (2 mL) was added rapidly in one portion. Stirring at $0\text{ }^{\circ}\text{C}$ was continued for 3.5 h, and hydrochloric acid (4 M, 2.2

mL) was added. The cold bath was removed, stirring was continued for 1 h and the mixture was diluted with water (100 mL). The aqueous phase was extracted with EtOAc (3 x 50 mL) and the combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (2 x 15 cm), using 1:5 EtOAc-hexane, gave **25a** (300 mg, 100%) as a liquid: FTIR (CH₂Cl₂ cast) 3057, 2938, 2860, 2722, 1723, 1582, 1480, 1439, 1408 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.54-1.71 (m, 4 H), 1.86 (dd, *J* = 14.8, 6.6 Hz, 2 H), 2.41 (td, *J* = 7.0, 1.5 Hz, 2 H), 4.39 (t, *J* = 6.6 Hz, 1 H), 7.27-7.37 (m, 6 H), 7.45-7.49 (m, 4 H), 9.74 (t, *J* = 1.6 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 21.4 (t), 26.5 (t), 35.5 (t), 43.6 (t), 58.2 (d), 127.8 (d), 128.9 (d), 132.8 (d), 134.1 (s), 202.2 (d); exact mass *m/z* calcd for C₁₈H₂₀OS₂ 316.0956, found 316.0954.

3-Hydroxy-2-methyl-2-(phenylseleno)-8,8-bis(phenylthio)octanoic Acid Ethyl Ester (25b,b').



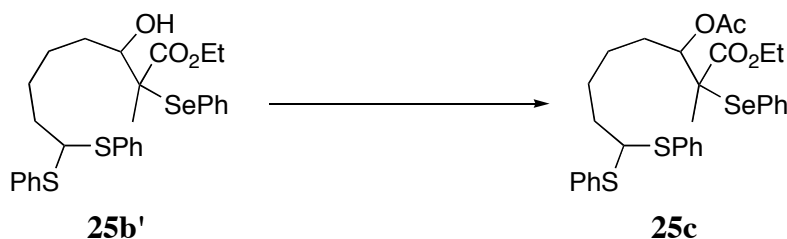
n-BuLi (1.5 M in hexane, 0.51 mL, 0.76 mmol) was added dropwise to a stirred and cooled (0 °C) solution of *i*-Pr₂NH (76.9 mg, 0.76 mmol) in THF (3 mL). Stirring at 0 °C was continued for 15 min, the mixture was cooled to -78 °C, and a solution of **15** (195.3 mg, 0.76 mmol) in THF (2 mL) was then added dropwise. Stirring at -78 °C was continued for 1 h, and a solution of **25a** (150 mg, 0.48 mmol) in THF (1 mL) was added dropwise. Stirring at -78 °C was continued for 40 min, and the mixture was quenched with saturated aqueous NH₄Cl (5 mL). The cold bath was removed, stirring was continued for 15 min and the mixture was diluted with water (40 mL). The aqueous phase was extracted with EtOAc (3 x 20 mL) and the combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (2 x 15 cm), using 4:25 EtOAc-hexane and then 1:5 EtOAc-hexane, gave **25b** (less polar isomer) (85 mg, 31%) as a viscous oil and **25b'** (more polar isomer) (130 mg, 48%) as a viscous oil.

Compound **25b** had: FTIR (CH₂Cl₂ cast) 3498, 3057, 2979, 2937, 2858, 1720, 1582, 1476, 1438 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.14 (t, *J* = 7.1 Hz, 3 H), 1.27-1.36 (m, 2 H), 1.39 (s, 3 H), 1.47-1.68 (m, 4 H), 1.80-1.89 (m, 2 H), 2.97 (s, 1 H), 3.86 (dd, *J* = 9.8, 1.6 Hz, 1 H), 4.00 (dq, *J* = 10.8, 7.1 Hz, 1 H), 4.08 (dq, *J* = 10.8, 7.2 Hz, 1 H), 4.39 (t, *J* = 4.4 Hz, 1 H),

7.25-7.33 (m, 8 H), 7.39-7.49 (m, 5 H), 7.59-7.61 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.9 (q), 17.0 (q), 26.3 (t), 26.9 (t), 31.6 (t), 35.6 (t), 57.5 (s), 58.3 (d), 61.1 (t), 72.7 (d), 126.4 (s), 127.6 (d), 128.8 (d), 129.5 (d), 132.7 (d), 134.3 (s), 138.0 (d), 173.1 (s); exact mass (electrospray) m/z calcd for $\text{C}_{29}\text{H}_{34}\text{NaO}_3\text{S}_2^{80}\text{Se}$ 597.1007, found 597.1011.

Compound **25b'** had: FTIR (CH_2Cl_2 cast) 3504, 3057, 2979, 2939, 2858, 1721, 1582, 1476, 1457, 1438 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.21 (t, $J = 7.1$ Hz, 3 H), 1.27-1.38 (m, 2 H), 1.40 (s, 3 H), 1.57-1.76 (m, 3 H), 1.82-1.91 (m, 3 H), 2.80 (s, 1 H), 3.84 (d, $J = 9.0$ Hz, 1 H), 4.11 (qd, $J = 7.1, 1.6$ Hz, 2 H), 4.43 (t, $J = 6.7$ Hz, 1 H), 7.28-7.34 (m, 8 H), 7.37-7.42 (m, 1 H), 7.45-7.49 (m, 4 H), 7.56-7.58 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.9 (q), 18.3 (q), 26.2 (t), 26.9 (t), 31.3 (t), 35.7 (t), 54.7 (s), 58.3 (d), 61.3 (t), 75.2 (d), 126.6 (s), 127.6 (d), 128.8 (d), 128.9 (d), 129.37 (d), 132.65 (d), 132.68 (d), 134.3 (s), 138.1 (d), 174.0 (s); exact mass (electrospray) m/z calcd for $\text{C}_{29}\text{H}_{34}\text{NaO}_3\text{S}_2^{80}\text{Se}$ 597.1007, found 597.1012.

3-Acetoxy-2-methyl-2-(phenylseleno)-8,8-bis(phenylthio)octanoic Acid Ethyl Ester (25c).



Pyridine (107.6 mg, 1.36 mmol) and AcCl (53.4 mg, 0.68 mmol) were added sequentially to a stirred and cooled (-10°C , ice-acetone bath) solution of **25b'** (130 mg, 0.227 mmol) and DMAP (2.8 mg, 0.02 mmol) in CH_2Cl_2 (2 mL). The cold bath was left in place but not recharged and stirring was continued for 16 h, by which time the temperature had risen to room temperature. The mixture was diluted with water (10 mL), acidified with hydrochloric acid (1 M, 2 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1.5 x 15 cm), using 9:50 EtOAc-hexane, gave **25c** (104 mg, 75%) as an oil: FTIR (CDCl_3 cast) 3057, 2981, 2937, 2859, 1744, 1725, 1582, 1477, 1438 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.09 (t, $J = 7.1$ Hz, 3 H), 1.29-1.36 (m, 2 H), 1.49 (s, 3 H), 1.52-1.77 (m, 3 H), 1.87 (dd, $J = 14.8, 7.4$ Hz, 2 H), 1.94 (s, 3 H), 2.03-2.12 (m, 1 H), 3.88 (dq, $J = 10.8, 7.1$ Hz, 1 H), 4.02 (dq, $J = 10.8, 7.1$ Hz, 1 H), 4.42 (dd, $J = 6.6, 6.6$ Hz, 1 H), 5.43 (dd, $J = 10.5, 1.7$ Hz, 1 H), 7.27-7.34 (m, 8 H), 7.37-7.42 (m, 1 H), 7.46-7.49 (m, 4 H), 7.57-7.60 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.8 (q), 17.9 (q), 20.9 (q), 25.9 (t), 27.0 (t), 30.3 (t), 35.6 (t), 53.0 (s), 58.3 (d), 61.1 (t), 75.6 (d),

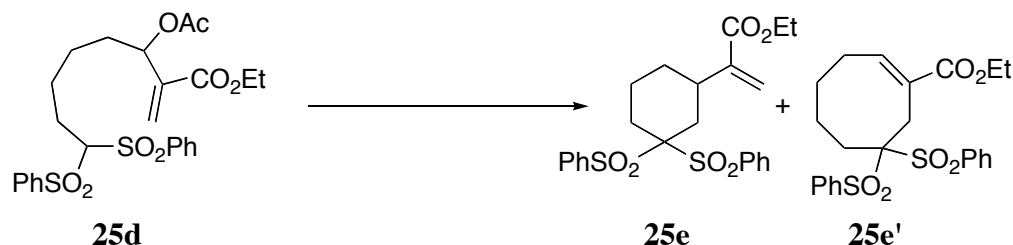
126.3 (s), 127.6 (d), 127.7 (d), 28.9 (d), 129.6 (d), 132.70 (d), 132.73 (d), 134.2 (s), 138.0 (d), 169.6 (s), 172.1 (s); exact mass (electrospray) m/z calcd for $C_{31}H_{36}NaO_4S_2^{80}Se$ 639.1113, found 639.1108.

2-[1-Acetoxy-6,6-bis(benzenesulfonyl)hexyl]acrylic Acid Ethyl Ester (25d).



m-CPBA (70-75%, 204 mg, 0.83 mmol) was added to a stirred solution of **25c** (51 mg, 0.083 mmol) in CH_2Cl_2 (2 mL), and the mixture was stirred at 40 °C for 23 h, cooled to room temperature and evaporated. Flash chromatography of the residue over silica gel (0.7 x 15 cm), using 3:5 EtOAc-hexane, gave **25d** (35.4 mg, 82%) as a viscous oil: FTIR ($CDCl_3$ cast) 3067, 2933, 2869, 1738, 1632, 1584, 1478, 1448 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) δ 1.31 (t, $J = 7.1$ Hz, 3 H), 1.24-1.33 (m, 2 H), 1.56-1.65 (m, 3 H), 1.66-1.76 (m, 1 H), 2.08 (s, 3 H), 2.13-2.18 (m, 2 H), 4.23 (qd, $J = 7.1, 1.8$ Hz, 2 H), 4.37 (t, $J = 5.6$ Hz, 1 H), 5.57 (dd, $J = 7.7, 4.4$ Hz, 1 H), 5.73 (s, 1 H), 6.28 (s, 1 H), 7.56-7.60 (m, 4 H), 7.68-7.72 (m, 2 H), 7.94-7.96 (m, 4 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1 (q), 21.1 (q), 24.8 (t), 25.4 (t), 27.8 (t), 33.6 (t), 60.9 (t), 71.4 (d), 83.6 (d), 124.9 (t), 129.1 (d), 129.6 (d), 134.5 (d), 137.82 (d), 137.85 (s), 140.1 (s), 165.2 (s), 169.9 (s); exact mass (electrospray) m/z calcd for $C_{25}H_{30}NaO_8S_2$ 545.1274, found 545.1277.

7,7-Bis(benzenesulfonyl)cyclooct-1-enecarboxylic Acid Ethyl Ester (25e') and 2-[3,3-Bis(benzenesulfonyl)cyclohexyl]acrylic Acid Ethyl Ester (25e).



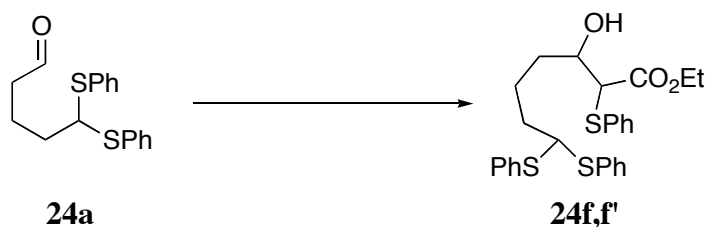
Cs_2CO_3 (43.7 mg, 0.134 mmol) was added to a stirred solution of **25d** (35.0 mg, 0.067 mmol) in THF (2 mL). Stirring at room temperature was continued for 1.5 h, and the solvent

was evaporated. Flash chromatography of the residue over silica gel (0.7 x 15 cm), using 60:1 CH₂Cl₂-EtOAc, gave **25e** (10.9 mg, 49%) as a white solid and **25e'** (6.5 mg, 29.4%) as a viscous oil.

Compound **25e'** had: FTIR (CDCl₃ cast) 3067, 2925, 2854, 1711, 1648, 1583, 1467, 1447 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.23 (t, *J* = 7.1 Hz, 3 H), 1.71-1.76 (m, 2 H), 2.01-2.05 (m, 2 H), 2.22-2.26 (m, 2 H), 2.37-2.39 (m, 2 H), 3.56 (s, 2 H), 4.19 (q, *J* = 7.1 Hz, 2 H), 7.05 (t, *J* = 8.3 Hz, 1 H), 7.57-7.60 (m, 4 H), 7.68-7.72 (m, 2 H), 8.05-8.07 (m, 4 H); ¹³C NMR (CDCl₃, 125 MHz) δ 14.1 (q), 26.7 (t), 27.0 (t), 27.7 (t), 27.9 (t), 29.7 (t), 61.0 (t), 92.3 (s), 128.5 (s), 129.4 (d), 131.4 (d), 134.4 (d), 137.1 (s), 142.0 (d), 167.1 (s); exact mass (electrospray) *m/z* calcd for C₂₃H₂₆NaO₆S₂ 485.1063, found 485.1062.

Compound **25e** had: mp 213-215 °C; FTIR (CDCl₃ cast) 3094, 3056, 2966, 2930, 2871, 2856, 1710, 1620, 1581, 1479, 1449, 1419 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.10 (dddd, *J* = 13.3, 13.0, 3.8, 3.6 Hz, 1 H), 1.39 (t, *J* = 7.1 Hz, 3 H), 1.52-1.60 (m, 2 H), 1.74-1.84 (m, 2 H), 2.05-2.19 (m, 2 H), 2.57 (dddd, *J* = 13.4, 13.4, 13.1, 3.8 Hz, 1 H), 3.71 (dd, *J* = 12.6, 4.4 Hz, 1 H), 4.29-4.40 (m, 2 H), 6.61 (s, 1 H), 6.64 (s, 1 H), 7.51-7.57 (m, 4 H), 7.63-7.69 (m, 2 H), 8.03-8.06 (m, 2 H), 8.16-8.19 (m, 2 H); ¹³C NMR (CDCl₃, 125 MHz) δ 14.3 (q), 21.0 (t), 25.2 (t), 32.0 (t), 32.1 (t), 40.2 (d), 61.3 (t), 91.6 (s), 128.2 (d), 128.9 (d), 129.9 (t), 131.41 (d), 131.44 (d), 134.0 (d), 134.3 (d), 137.0 (s), 139.8 (s), 140.1 (s), 168.7 (s); exact mass (electrospray) *m/z* calcd for C₂₃H₂₆NaO₆S₂ 485.1063, found 485.1066.

3-Hydroxy-2,7,7-tris(phenylthio)heptanoic Acid Ethyl Ester (**24f,f'**).



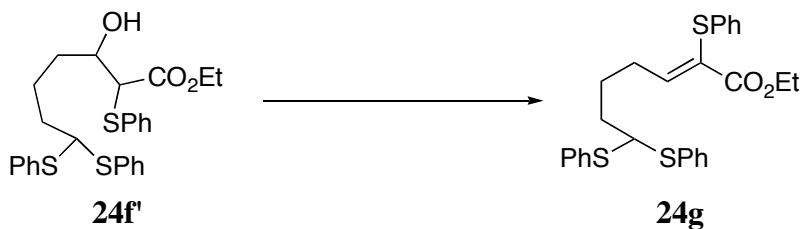
n-BuLi (1.3 M in hexane, 0.68 mL, 0.88 mmol) was added dropwise to a stirred and cooled (0 °C) solution of *i*-Pr₂NH (89.0 mg, 0.88 mmol) in THF (4 mL). Stirring at 0 °C was continued for 15 min, the mixture was cooled to -78 °C, and a solution of (phenylthio)acetic acid ethyl ester¹⁴ (172.5 mg, 0.88 mmol) in THF (2.5 mL) was then added dropwise. Stirring at -78 °C was continued for 40 min, and a solution of **24a** (190 mg, 0.63 mmol) in THF (2 mL) was added dropwise. Stirring at -78 °C was continued for 70 min and the mixture was quenched with saturated aqueous NH₄Cl (5 mL). The cold bath was removed, stirring was continued for 15 min and the mixture was diluted with water (50 mL). The aqueous phase was extracted with EtOAc

(3 x 20 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm), using 1:3 Et_2O -hexane, 9:20 Et_2O -hexane and then 7:10 Et_2O -hexane, gave **24f** (less polar isomer) (91 mg, 29%) as a viscous oil, which appeared to contain an impurity (NMR), and **24f'** (more polar isomer) (130 mg, 41%) as a viscous oil.

Compound **24f** had: FTIR (CDCl_3 cast) 3514, 3058, 2933, 1727, 1583, 1480, 1439 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 0.90 (t, $J = 7.4$ Hz, 0.7 H), 1.20 (t, $J = 7.1$ Hz, 2.3 H), 1.27-1.38 (m, 0.5 H), 1.51-1.77 (m, 2.5 H), 1.81-1.91 (m, 3 H), 2.71 (d, $J = 6.6$ Hz, 0.2 H), 3.12 (dd, $J = 2.9, 0.8$ Hz, 0.8 H), 3.59 (d, $J = 5.7$ Hz, 0.8 H), 3.63 (d, $J = 7.1$ Hz, 0.2 H), 3.86-3.91 (m, 0.2 H), 3.91-3.98 (m, 0.8 H), 4.09-4.22 (m, 2 H), 4.40 (dd, $J = 6.5, 6.5$ Hz, 1 H), 7.25-7.34 (m, 9 H), 7.44-7.52 (m, 6 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.6 (q), 134.0 (q), 19.0 (t), 23.19 (t), 23.23 (t), 30.4 (t), 33.2 (t), 33.6 (t), 35.50 (t), 35.53 (t), 59.0 (d), 57.7 (d), 58.2 (d), 58.3 (d), 61.4 (t), 65.3 (t), 70.2 (t), 71.4 (t), 127.66 (d), 127.68 (d), 128.1 (d), 128.2 (d), 128.8 (d), 128.85 (d), 128.86 (d), 129.06 (d), 129.07 (d), 132.72 (d), 132.74 (d), 132.76 (d), 132.9 (d), 133.0 (d), 133.3 (s), 134.11 (s), 134.14 (s), 171.66 (s), 171.72 (s); exact mass (electrospray) m/z calcd for $\text{C}_{27}\text{H}_{30}\text{NaO}_3\text{S}_3$ 521.1249, found 521.1252.

Compound **24f'** had: FTIR (CDCl_3 cast) 3497, 3058, 2980, 2917, 2849, 1729, 1583, 1480, 1474, 1439 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.21 (t, $J = 7.1$ Hz, 3 H), 1.44-1.59 (m, 1 H), 1.66-1.75 (m, 1 H), 1.78-1.89 (m, 4 H), 2.70 (d, $J = 6.6$ Hz, 1 H), 3.61 (d, $J = 7.1$ Hz, 1 H), 3.89 (dddd, $J = 8.5, 6.8, 6.8, 2.6$ Hz, 1 H), 4.10-4.21 (m, 2 H), 4.39 (dd, $J = 6.4, 6.4$ Hz, 1 H), 7.27-7.33 (m, 9 H), 7.45-7.48 (m, 6 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.0 (q), 23.2 (t), 33.6 (t), 35.5 (t), 56.0 (d), 58.3 (d), 61.4 (t), 71.4 (d), 127.7 (d), 128.2 (d), 128.9 (d), 129.1 (d), 132.8 (d), 133.1 (d), 134.1 (d), 171.6 (s); exact mass (electrospray) m/z calcd for $\text{C}_{27}\text{H}_{30}\text{NaO}_3\text{S}_3$ 521.1249, found 521.1248.

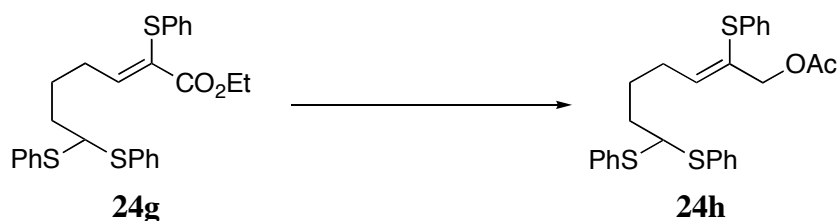
(Z)-2,7,7-Tris(phenylthio)hept-2-enoic Acid Ethyl Ester (24g).



MsCl (24.8 mg, 0.216 mmol) and Et_3N (43.7 mg, 0.432 mmol) were added sequentially to a stirred and cooled (0°C) solution of **24f'** (36 mg, 0.072 mmol) in CH_2Cl_2 (1 mL). Stirring at 0°C was continued for 3 h and DBU (65.8 mg, 0.432 mmol) was added. The cold bath was

removed, stirring was continued for 3 h and the mixture was diluted with water (3 mL) and acidified with hydrochloric acid (1 M, 3 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1 x 15 cm), using 2:25 EtOAc-hexane, gave **24g** (24 mg, 69%) as an oil: FTIR (CDCl_3 cast) 3073, 3058, 2980, 2935, 2859, 1712, 1608, 1583, 1479, 1439 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.09 (t, $J = 7.1$ Hz, 3 H), 1.79-1.92 (m, 4 H), 2.51 (t, $J = 7.1$ Hz, 2 H), 4.11 (q, 7.1 Hz, 2 H), 4.39 (t, $J = 1.0$ Hz, 1 H), 7.13-7.35 (m, 12 H), 7.44-7.47 (m, 4 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.9 (q), 25.8 (t), 30.1 (t), 35.3 (t), 58.2 (d), 61.5 (t), 126.1 (d), 127.5 (s), 127.8 (d), 128.2 (d), 128.9 (d), 132.9 (d), 133.9 (s), 135.8 (s), 151.7 (d), 165.2 (s); exact mass (electrospray) m/z calcd for $\text{C}_{27}\text{H}_{28}\text{NaO}_2\text{S}_3$ 503.1144, found 503.1143. We assign the *Z* geometry by analogy with the assignment to **25h**.

Acetic Acid (Z)-2,7,7-tris(phenylthio)hept-2-enyl Ester (24h).

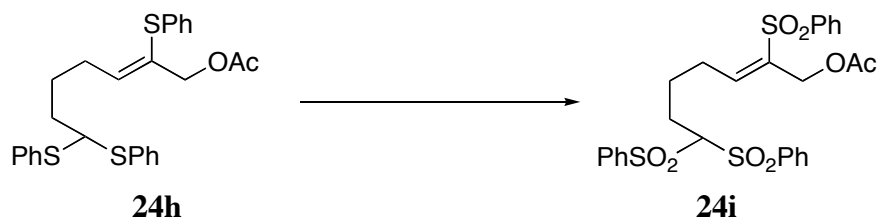


DIBAL-H (1.0 M in PhMe, 0.1 mL, 0.1 mmol) was added dropwise to a stirred and cooled ($-78\text{ }^{\circ}\text{C}$) solution of **24g** (14.1 mg, 0.029 mmol) in CH_2Cl_2 (1 mL), and stirring at $-78\text{ }^{\circ}\text{C}$ was continued for 15 min. The cold bath was removed and stirring was continued for 15 min. MeOH (0.4 mL) and saturated aqueous Rochelle salt (1 mL) were added sequentially, and stirring was continued for 30 min. The aqueous phase was extracted with CH_2Cl_2 (2 x 1 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. The residual crude alcohol (9.4 mg, 86%) was used directly for the next step.

Pyridine (12 mg, 0.15 mmol) and AcCl (5.9 mg, 0.075 mmol) were added sequentially to a stirred and cooled ($-10\text{ }^{\circ}\text{C}$, ice-acetone bath) solution of the above crude alcohol (9.4 mg, 0.025 mmol) and DMAP (0.4 mg, 0.003 mmol) in CH_2Cl_2 (0.5 mL). The cold bath was left in place but not recharged and stirring was continued for 16 h, by which time the temperature had risen to room temperature. The mixture was diluted with water (2 mL), acidified with hydrochloric acid (1 M, 0.1 mL) and extracted with CH_2Cl_2 (3 x 2 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (0.7 x 7.5 cm), using 1:10 EtOAc-hexane, gave **24h** (7 mg, 58% from **24g**) as an oil: FTIR (CDCl_3 cast) 3058, 3019, 2934, 2856, 1741, 1583, 1478, 1438 cm^{-1} ; ^1H NMR (CDCl_3 , 500

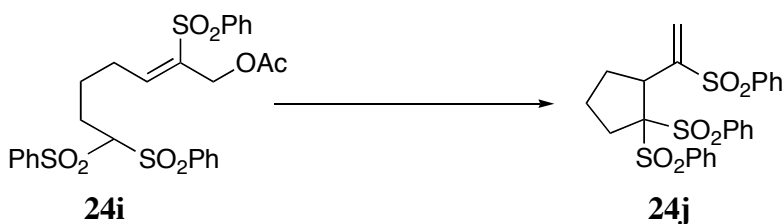
MHz) δ 1.74-1.80 (m, 2 H), 1.85-1.90 (m, 2 H), 2.00 (s, 3 H), 2.39 (q, $J = 7.3$ Hz, 2 H), 4.41 (t, $J = 6.6$ Hz, 1 H), 4.54 (d, $J = 0.6$ Hz, 2 H), 6.17 (t, $J = 7.2$ Hz, 1 H), 7.18-7.22 (m, 1 H), 7.27-7.32 (m, 10 H), 7.45-7.47 (m, 4 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 20.8 (q), 26.3 (t), 29.0 (t), 35.2 (t), 58.3 (d), 66.9 (t), 126.5 (d), 127.8 (d), 128.6 (s), 128.9 (d), 129.0 (d), 129.5 (d), 132.9 (d), 134.1 (s), 134.2 (s), 139.6 (d), 170.4 (s); exact mass (electrospray) m/z calcd for $\text{C}_{27}\text{H}_{28}\text{NaO}_2\text{S}_3$ 503.1144, found 503.1145. We assign the *Z* geometry by analogy with the assignment to **25h**.

Acetic Acid (Z)-2,7,7-Tris(benzenesulfonyl)hept-2-enyl Ester (24i).



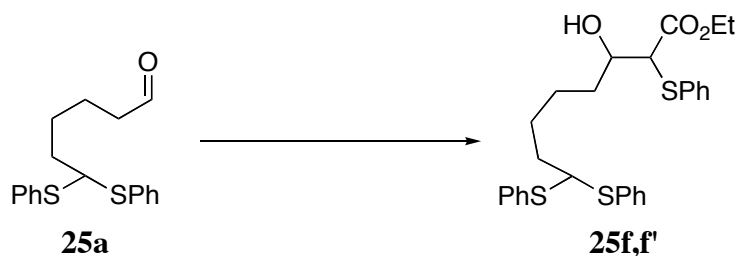
m-CPBA (70-75%, 39 mg, 0.158 mmol) was added to a solution of **24h** (6.3 mg, 0.013 mmol) in CH_2Cl_2 (1 mL), and the mixture was stirred at 40 °C for 24 h, cooled to room temperature and evaporated. Flash chromatography of the residue over silica gel (0.7 x 7 cm), using 4:5 EtOAc-hexane, gave **24i** (5.5 mg, 73%) as a viscous oil: FTIR (CDCl_3 cast) 3060, 2934, 1742, 1640, 1580, 1447 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.83-1.89 (tt, $J = 15.0, 15.0$ Hz, 2 H), 1.92 (s, 3 H), 2.21-2.25 (m, 2 H), 2.70 (q, $J = 7.7$ Hz, 2 H), 4.59 (t, $J = 5.7$ Hz, 1 H), 4.79 (s, 2 H), 6.39 (t, $J = 8.0$ Hz, 1 H), 7.55-7.59 (m, 6 H), 7.63-7.66 (m, 1 H), 7.69-7.72 (m, 2 H), 7.92-7.96 (m, 6 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 20.7 (q), 24.9 (t), 26.8 (t), 27.6 (t), 63.8 (t), 82.5 (d), 127.6 (d), 129.1 (d), 129.3 (d), 129.6 (d), 133.7 (d), 134.6 (d), 137.6 (s), 137.8 (s), 141.1 (s), 147.4 (d), 170.0 (s); exact mass (electrospray) m/z calcd for $\text{C}_{27}\text{H}_{28}\text{NaO}_8\text{S}_3$ 599.0839, found 599.0842.

[[1-[2,2-Bis(phenylsulfonyl)cyclopent-1-yl]ethenyl]sulfonyl]benzene (24j).



Cs_2CO_3 (6.0 mg, 0.018 mmol) was added to a stirred solution of **24i** (5.10 mg, 0.0089 mmol) in THF (0.5 mL). Stirring at room temperature was continued for 1 h, and the solvent was evaporated. Flash chromatography of the residue over silica gel (0.7 x 7 cm), using 3:5 EtOAc-hexane, gave **24j** (3.9 mg, 85%) as a viscous oil: FTIR (CDCl_3 cast) 3066, 2962, 2925, 1583, 1478, 1447 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.44-1.52 (m, 1 H), 1.83-1.92 (m, 2 H), 2.20-2.08 (m, 1 H), 2.19-2.25 (m, 1 H), 2.60 (ddd, $J = 15.2, 9.5, 6.9$ Hz, 1 H), 4.13 (ddd, $J = 10.5, 1.2$ Hz, 1 H), 6.38 (d, $J = 2.5$ Hz, 1 H), 6.77 (dd, $J = 2.5, 1.2$ Hz, 1 H), 7.53-7.59 (m, 6 H), 7.61-7.64 (m, 1 H), 7.68-7.71 (m, 2 H), 7.91-7.93 (m, 2 H), 8.09-8.11 (m, 4 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 22.1 (t), 33.8 (t), 34.5 (t), 47.5 (d), 96.0 (s), 128.1 (d), 128.6 (d), 128.9 (d), 129.1 (d), 130.8 (t), 131.0 (d), 131.9 (d), 133.4 (d), 134.6 (d), 134.8 (d), 136.5 (s), 138.4 (s), 140.1 (s), 147.0 (s); exact mass (electrospray) m/z calcd for $\text{C}_{25}\text{H}_{24}\text{NaO}_6\text{S}_3$ 539.0627, found 539.0622.

3-Hydroxy-2,8,8-tris(phenylthio)octanoic Acid Ethyl Ester (**25f,f'**).



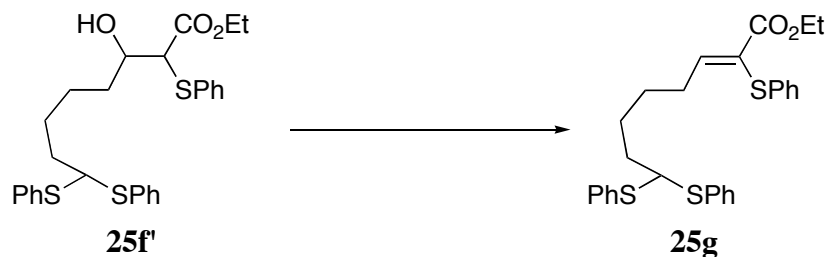
$n\text{-BuLi}$ (1.3 M in hexane, 0.95 mL, 1.23 mmol) was added dropwise to a stirred and cooled (0 °C) solution of $i\text{-Pr}_2\text{NH}$ (124.4 mg, 1.23 mmol) in THF (6 mL). Stirring at 0 °C was continued for 15 min, the mixture was cooled to -78 °C, and a solution of (phenylthio)acetic acid ethyl ester¹⁴ (241.1 mg, 1.23 mmol) in THF (1 mL) was then added dropwise. Stirring at -78 °C was continued for 40 min, and a solution of **25a** (277.5 mg, 0.88 mmol) in THF (1.5 mL) was added dropwise. Stirring at -78 °C was continued for 1 h, and the mixture was quenched with saturated aqueous NH_4Cl (5 mL). The cold bath was removed, stirring was continued for 15 min and the mixture was diluted with water (50 mL). The aqueous phase was extracted with EtOAc (3 x 20 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm), using 1:3 Et_2O -hexane and then 2:5 Et_2O -hexane, gave **25f** (less polar isomer) (166 mg, 37%) as a viscous oil and **25f'** (more polar isomer) (200 mg, 44%) as a viscous oil.

Compound **25f** had: FTIR (CDCl_3 cast) 3512, 3073, 3058, 3018, 2979, 2938, 2859, 1728, 1583, 1480, 1439 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.22 (t, $J = 7.1$ Hz, 3 H), 1.32-1.39

(m, 1 H), 1.48-1.71 (m, 5 H), 1.86 (dd, $J = 14.9, 7.3$ Hz, 2 H), 3.11 (dd, $J = 2.9, 0.7$ Hz, 1 H), 3.59 (d, $J = 5.8$ Hz, 1 H), 3.96 (ddd, $J = 8.8, 6.4, 3.4$ Hz, 1 H), 4.11-4.22 (m, 2 H), 4.41 (dd, $J = 6.7, 6.7$ Hz, 1 H), 7.26-7.34 (m, 9 H), 7.45-7.48 (m, 4 H), 7.50-7.52 (m, 2 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 14.0 (q), 25.1 (t), 26.8 (t), 33.7 (t), 35.6 (t), 57.8 (d), 58.3 (d), 61.4 (t), 70.3 (d), 127.6 (d), 128.0 (d), 128.8 (d), 129.0 (d), 132.7 (d), 132.9 (d), 133.4 (s), 134.2 (s), 171.7 (s); exact mass (electrospray) m/z calcd for $\text{C}_{28}\text{H}_{32}\text{NaO}_3\text{S}_3$ 535.1406, found 535.1403.

Compound **25f'** had: FTIR (CDCl_3 cast) 3497, 3058, 2981, 2938, 2859, 1729, 1583, 1480, 1439 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.15 (t, $J = 7.1$ Hz, 3 H), 1.27-1.36 (m, 1 H), 1.41-1.50 (m, 2 H), 1.54-1.66 (m, 2 H), 1.72-1.77 (m, 1 H), 1.82 (dd, $J = 14.8, 7.3$ Hz, 2 H), 2.71 (d, $J = 6.7$ Hz, 1 H), 3.56 (d, $J = 7.0$ Hz, 1 H), 3.85 (dddd, $J = 8.7, 6.9, 6.9, 3.4$ Hz, 1 H), 4.06-4.15 (m, 2 H), 4.36 (dd, $J = 6.7, 6.7$ Hz, 1 H), 7.21-7.28 (m, 9 H), 7.40-7.44 (m, 6 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 14.0 (q), 25.9 (t), 26.7 (t), 34.0 (t), 35.6 (t), 56.1 (d), 58.3 (d), 61.4 (t), 71.4 (d), 127.6 (d), 128.1 (d), 128.8 (d), 129.0 (d), 132.6 (d), 132.7 (d), 132.9 (s), 133.0 (d), 134.2 (s), 171.6 (s); exact mass (electrospray) m/z calcd for $\text{C}_{28}\text{H}_{32}\text{NaO}_3\text{S}_3$ 535.1406, found 535.1407.

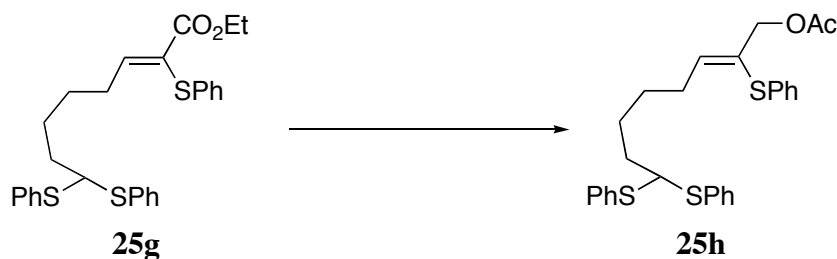
(Z)-2,8,8-Tris(phenylthio)octanoic Acid Ethyl Ester (25g).



MsCl (143.3 mg, 1.25 mmol) and Et_3N (254 mg, 2.51 mmol) were added sequentially to a stirred and cooled (0°C) solution of **25f'** (214 mg, 0.42 mmol) in CH_2Cl_2 (3 mL). Stirring at 0°C was continued for 2.5 h, DBU (382 mg, 2.51 mmol) was added and stirring at 0°C was continued for 3 h. The mixture was diluted with water (5 mL) and acidified with hydrochloric acid (1 M, 3 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 10 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1.5 x 15 cm), using 1:10 EtOAc-hexane, gave **25g** (110 mg, 53%) as an oil: FTIR (CHCl_3 cast) 3057, 2980, 2935, 2857, 1710, 1608, 1583, 1478, 1438 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.09 (t, $J = 7.1$ Hz, 3 H), 1.48 (dddd, $J = 7.7$ Hz, 2 H), 1.65-1.71 (m, 2 H), 1.85-1.90 (m, 2 H), 2.51 (dd, $J = 15.0, 7.5$ Hz, 2 H), 4.12 (q, $J = 7.1$ Hz, 2 H), 4.39 (t, $J = 13.4$ Hz, 1 H), 7.14-7.18 (m, 1 H), 7.22-7.33 (m, 10 H), 7.34-7.37 (t, $J = 7.5$ Hz, 1 H), 7.45-7.47 (m, 4 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 13.9 (q), 26.7 (t), 27.8 (t), 30.5 (t), 35.5 (t), 58.3 (d),

61.5 (t), 126.0 (d), 127.1 (s), 127.7 (d), 128.2 (d), 128.9 (d), 132.8 (d), 134.2 (s), 135.9 (s), 152.3 (d), 165.3 (s); exact mass (electrospray) m/z calcd for $C_{28}H_{30}NaO_2S_3$ 517.1300, found 517.1301. We assign a *Z* geometry based on the assignment made to the derived acetate **25h**.

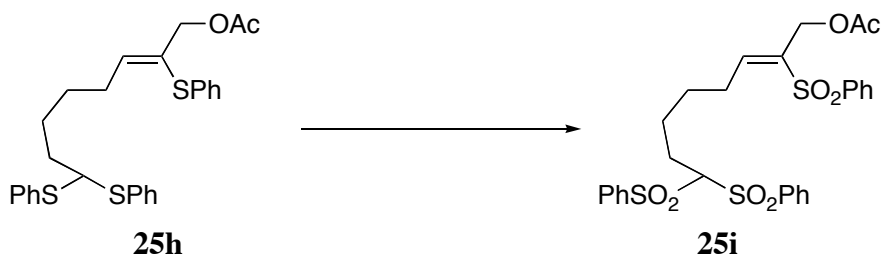
Acetic Acid (Z)-2,8,8-Tris(phenylthio)oct-2-enyl Ester (25h).



DIBAL-H (1.0 M in PhMe, 0.44 mL, 0.44 mmol) was added dropwise to a stirred and cooled (-78 °C) solution of **25g** (73.0 mg, 0.148 mmol) in CH_2Cl_2 (5 mL), and stirring at -78 °C was continued for 15 min. The cold bath was removed and stirring was continued for 15 min. MeOH (2 mL) and saturated aqueous Rochelle salt (4 mL) were added sequentially, and stirring was continued for 30 min. The aqueous phase was extracted with CH_2Cl_2 (2 x 1 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. The residual crude alcohol was used directly for the next step.

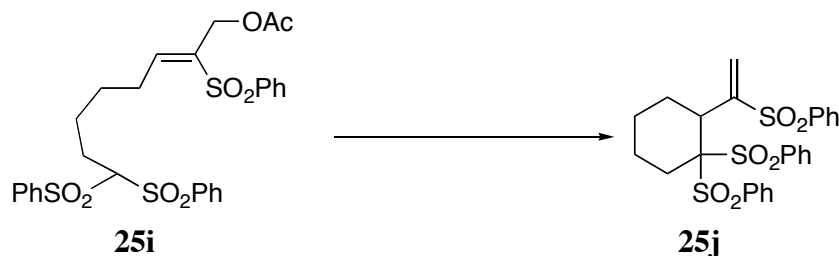
Pyridine (70.4 mg, 0.89 mmol) and AcCl (34.5 mg, 0.44 mmol) were added sequentially to a stirred and cooled (-10 °C, ice-acetone bath) solution of the above crude alcohol and DMAP (1.8 mg, 0.015 mmol) in CH_2Cl_2 (2 mL). The cold bath was left in place but not recharged and stirring was continued for 16 h, by which time the temperature had risen to room temperature. The mixture was diluted with water (10 mL), acidified with hydrochloric acid (1 M, 5 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1.0 x 7.5 cm), using 3:25 EtOAc-hexane, gave **25h** (53.4 mg, 73% from **25g**) as an oil: FTIR ($CDCl_3$ cast) 3057, 2932, 2855, 1740, 1582, 1478, 1438 cm^{-1} ; 1H NMR ($CDCl_3$, 500 MHz) δ 1.42 (tt, J = 15.2, 15.2 Hz, 2 H), 1.63-1.69 (m, 2 H), 1.85-1.89 (m, 2 H), 2.00 (s, 3 H), 2.38 (dd, J = 14.9, 7.4 Hz, 2 H), 4.40 (t, J = 6.7 Hz, 1 H), 4.57 (d, J = 0.9 Hz, 2 H), 6.21 (tt, J = 7.2, 1.2 Hz, 1 H), 7.18-7.21 (m, 1 H), 7.26-7.33 (m, 10 H), 7.45-7.47 (m, 4 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.8 (q), 26.7 (t), 28.3 (t), 29.4 (t), 35.6 (t), 58.4 (d), 67.0 (t), 126.4 (d), 127.7 (d), 128.2 (s), 128.9 (d), 129.0 (d), 129.5 (d), 132.7 (d), 134.2 (s), 134.3 (s), 140.3 (d), 170.4 (s); exact mass (electrospray) m/z calcd for $C_{28}H_{30}NaO_2S_3$ 517.1300, found 517.1305. TROESY measurements [nOe between vinyl hydrogen and CH_2O] suggested that the double bond has *Z* geometry.

Acetic Acid (Z)-2,8,8-Tris(benzenesulfonyl)oct-2-enyl Ester (25i**).**



m-CPBA (70-75%, 146 mg, 0.59 mmol) was added to a solution of **25h** (24.4 mg, 0.049 mmol) in CH₂Cl₂ (1 mL), and the mixture was stirred at 40 °C for 24 h, cooled to room temperature and evaporated. Flash chromatography of the residue over silica gel (0.7 x 15 cm), using 9:10 EtOAc-hexane, gave **25i** (22 mg, 76%) as a viscous oil: FTIR (CDCl₃ cast) 3066, 2928, 1743, 1639, 1584, 1448 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.39 (quintet, *J* = 15.3 Hz, 2 H), 1.60-1.67 (m, 2 H), 1.92 (s, 3 H), 2.15-2.19 (m, 2 H), 2.62 (dd, *J* = 15.3, 7.7 Hz, 2 H), 4.41 (t, *J* = 5.7 Hz, 1 H), 4.82 (s, 2 H), 6.40 (t, *J* = 7.9 Hz, 1 H), 7.54-7.64 (m, 7 H), 7.68-7.71 (m, 2 H), 7.91-7.96 (m, 6 H); ¹³C NMR (CDCl₃, 125 MHz) δ 20.7 (q), 25.2 (t), 27.5 (t), 28.0 (t), 28.1 (t), 64.0 (t), 83.3 (d), 127.5 (d), 129.1 (d), 129.3 (d), 133.5 (d), 134.6 (d), 136.9 (s), 137.8 (s), 141.4 (s), 148.7 (d), 170.1 (s); exact mass (electrospray) *m/z* calcd for C₂₈H₃₀NaO₈S₃ 613.0995, found 613.0996.

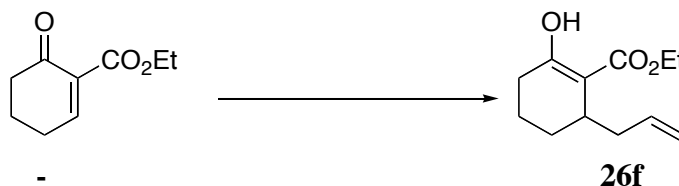
[[1-[2,2-Bis(phenylsulfonyl)cyclohex-1-yl]ethenyl]sulfonyl]benzene (25j**).**



Cs₂CO₃ (13.9 mg, 0.043 mmol) was added to a stirred solution of **25i** (12.6 mg, 0.021 mmol) in THF (0.5 mL). Stirring at room temperature was continued for 2 h and the solvent was evaporated. Flash chromatography of the residue over silica gel (0.7 x 7 cm), using 3:2 Et₂O-hexane, gave **25j** (5.3 mg, 47%) as a viscous oil: FTIR (CH₂Cl₂ cast) 3066, 2932, 2858, 1583, 1478, 1447 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.22-1.26 (m, 1 H), 1.54-1.60 (m, 1 H), 1.72-1.76 (m, 1 H), 1.86-1.98 (m, 3 H), 2.03-2.06 (m, 1 H), 2.40 (ddd, *J* = 15.7, 12.8, 3.9 Hz, 1 H), 3.87 (dd, *J* = 11.6, 4.1 Hz, 1 H), 6.28 (d, *J* = 3.0 Hz, 1 H), 7.01 (d, *J* = 3.0 Hz, 1 H), 7.52-7.59

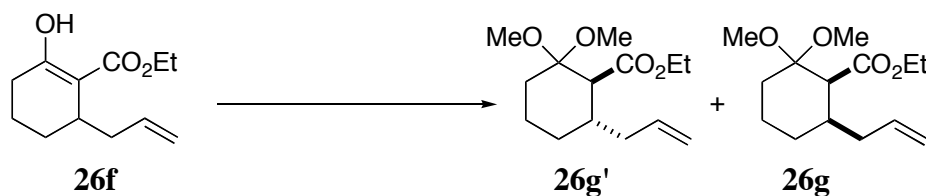
(m, 6 H), 7.61-7.64 (m, 1 H), 7.66-7.71 (m, 2 H), 8.02 (dd, $J = 8.4, 1.3$ Hz, 2 H), 8.09 (dd, $J = 8.5, 1.1$ Hz, 2 H), 8.21 (dd, $J = 8.4, 1.0$ Hz, 2 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 20.8 (t), 24.6 (t), 32.0 (t), 32.4 (t), 41.5 (d), 92.0 (s), 128.5 (d), 128.6 (d), 128.9 (d), 129.1 (d), 129.8 (t), 131.0 (d), 132.0 (d), 133.4 (d), 134.3 (d), 134.5 (d), 137.2 (s), 139.5 (s), 140.3 (s), 150.4 (s); exact mass (electrospray) m/z calcd for $\text{C}_{26}\text{H}_{26}\text{NaO}_6\text{S}_3$ 553.0784, found 553.0782.

2-Allyl-6-oxocyclohexanecarboxylic Acid Ethyl Ester (26f).



TiCl_4 (21 mL, 20.62 mmol) and allyltrimethylsilane (4.4 mL, 27.5 mmol) were added dropwise (over ca 10 min) to a stirred and cooled (-78°C) solution of ethyl 6-oxocyclohex-1-enecarboxylate⁴⁰ (2.6 g, 19.6 mmol) in CH_2Cl_2 (50 mL). Stirring was continued for 20 min and aqueous Na_2CO_3 (20%, 50 mL) was added. The cold bath was removed and the aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (3 x 16 cm), using 20% EtOAc-hexane, gave **26f** (3.81 g, 92%) as a colorless oil which was an inseparable equilibrium mixture of keto-enol tautomers (^{13}C NMR): FTIR (CH_2Cl_2 cast) 3076, 2979, 2940, 2870, 1743, 1714, 1642, 1614, 1216, 915 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 1.31-1.39 (m, 3 H), 1.42-1.83 (m, 3 H), 1.96-2.45 (5 H), 2.50-2.57 (m, 0.7 H), 2.63-2.68 (m, 0.4 H), 3.20 (dd, $J = 11.1, 1.2$ Hz, 0.5 H), 4.19-4.37 (m, 2 H), 5.02-5.15 (m, 2 H), 5.74-5.91 (m, 1 H), 12.47 (s, 0.4 H); exact mass (electrospray) m/z calcd for $\text{C}_{12}\text{H}_{18}\text{NaO}_3$ 233.1148, found 233.1147.

Trans-6-Allyl-2,2-dimethoxycyclohexanecarboxylic Acid Ethyl Ester (26g') and Cis-6-Allyl-2,2-dimethoxycyclohexanecarboxylic Acid Ethyl Ester (26g).



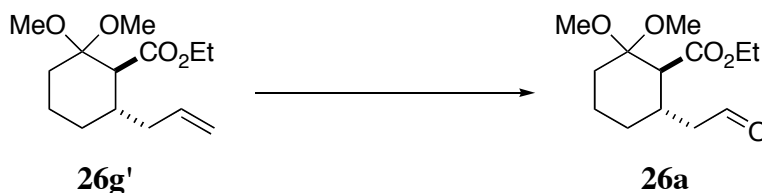
$p\text{-TsOH}\cdot\text{H}_2\text{O}$ (171 mg, 0.9 mmol) was added to a stirred solution of **26f** (3.75 g, 17.83 mmol) and $\text{HC}(\text{OMe})_3$ (2.54 mL, 23.18 mmol) in dry MeOH (35 mL). Stirring was continued

for 24 h and the mixture was quenched with saturated aqueous NaHCO_3 (20 mL), diluted with water (30 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (4 x 20 cm), using 15% EtOAc-hexanes gave **26g** (less polar isomer) (1.75 g, 38%, cis-isomer) as a viscous oil and **26g'** (more polar isomer) (2.55g, 56%, major, trans-isomer) as a viscous oil.

Compound **26g** had: FTIR (CH_2Cl_2 cast) 2942, 2832, 1734, 1641, 1447, 1182, 916 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.26 (t, $J = 7.2$ Hz, 3 H), 1.29-1.48 (m, 2 H), 1.56-1.70 (m, 2 H), 1.74-1.83 (m, 2 H), 1.87-2.03 (m, 3 H), 3.01 (dd, $J = 4.4, 1.6$ Hz, 1 H), 3.14 (s, 3 H), 3.2 (s, 3 H), 4.14 (q, $J = 7.2$ Hz, 2 H), 4.98-5.02 (m, 2 H), 5.73-5.83 (m, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.2 (q), 21.6 (t), 26.0 (t), 27.6 (t), 37.1 (d), 38.5 (t), 47.3 (q), 47.8 (q), 50.3 (d), 59.9 (t), 100.8 (s), 116.3 (t), 136.6 (d), 171.4 (s); exact mass (electrospray) m/z calcd for $\text{C}_{14}\text{H}_{24}\text{NaO}_4$ 279.1567, found 179.1565.

Compound **26g'** had: FTIR (CH_2Cl_2 cast) 2943, 2833, 1736, 1640, 1448, 1177, 1050, 913 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.10-1.18 (m, 1 H), 1.26 (t, $J = 7.2$ Hz, 3 H), 1.38-1.60 (m, 3 H), 1.80-1.88 (m, 1 H), 1.95-2.06 (m, 3 H), 2.14-2.20 (m, 1 H), 2.59 (d, $J = 6.4$ Hz, 1 H), 3.20 (s, 3 H), 3.21 (s, 3 H), 4.14 (q, $J = 7.2$ Hz, 2 H), 4.98-5.02 (m, 2 H), 5.67-5.78 (m, 1 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 14.1 (q), 19.7 (t), 27.5 (t), 30.2 (t), 36.7 (d), 38.0 (t), 48.2 (q), 48.6 (q), 53.2 (d), 60.1 (t), 100.8 (s), 116.4 (t), 136.9 (d), 172.4 (s); exact mass (electrospray) calcd for $\text{C}_{14}\text{H}_{24}\text{NaO}_4$ 279.15668, found 279.15672.

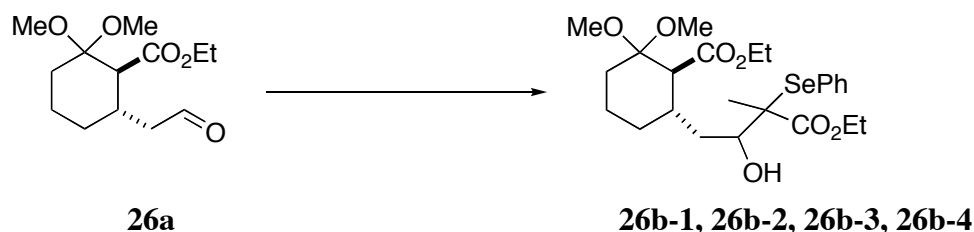
Trans-2,2-Dimethoxy-6-(2-oxoethyl)cyclohexanecarboxylic Acid Ethyl Ester (26a).



O_3 was bubbled into a stirred and cooled (-78°C) solution of **26g'** (2.1 g, 8.2 mmol) in CH_2Cl_2 (100 mL) for 30 min, by which time a blue color persisted. O_2 was passed through the solution for 30 min and Ph_3P (3 g, 11.4 mmol) was then added. The cold bath was removed after 30 min and stirring was continued for 10 h. Evaporation of the solvent and flash chromatography of the residue over silica gel (4 x 18 cm), using 20% EtOAc-hexane, gave **26a** (2.02 g, 96%) as a colorless viscous oil: FTIR (CH_2Cl_2 cast) 2946, 1734, 1181, 1049 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.16-1.22 (m, 1 H), 1.25 (t, $J = 7.0$ Hz, 3 H), 1.49-1.54 (m, 2 H), 1.62-1.67 (m, 1 H), 1.92-2.02 (m, 2 H), 2.45 (ddd, $J = 18.0, 9.5, 2.0$ Hz, 1 H), 2.54-2.60 (m, 2 H), 2.65-2.66 (m, 1 H), 3.18 (s, 3 H), 3.19 (s, 3 H), 4.10-4.17 (m, 2 H), 9.69-9.70 (m, 1 H); ^{13}C

NMR (CDCl₃, 125 MHz) δ 14.1 (q), 19.1 (t), 27.6 (t), 29.3 (t), 31.1 (d), 48.0 (t), 48.2 (q), 48.3 (q), 52.1 (d), 60.4 (t), 100.5 (s), 171.9 (s), 201.9 (d). The aldehyde is sensitive and attempts to obtain its mass spectrum invariably led to the mass spectrum of the derived carboxylic acid.

6-[3-Ethoxycarbonyl-2-hydroxy-3-(phenylseleno)butyl]-2,2-dimethoxycyclohexane-carboxylic Acid Ethyl Ester (26b-1, 26b-2, 26b-3, 26b-4).



n-BuLi (2.5 M in hexane, 3.29 mL, 8.23 mmol) was added over ca 5 min to a stirred and cooled (-78 °C) solution of *i*-Pr₂NH (1.25 mL, 8.88 mmol) in THF (15 mL). Stirring was continued for 40 min and a solution of **15** (2.368 g, 9.21 mmol) in THF (10 mL plus 2 mL as a rinse) was added over ca 5 min. Stirring was continued for 1 h and a solution of **26a** (1.7 g, 6.58 mmol) in THF (10 mL plus 2 mL as a rinse) was added over ca 5 min. Stirring at -78 °C was continued for 3 h and the mixture was quenched with saturated aqueous NH₄Cl (10 mL). The cold bath was removed, stirring was continued for 10 min and the mixture was diluted with water (50 mL) and extracted with EtOAc (3 x 20 mL). The combined organic extracts were dried (Na₂SO₄) and evaporated. ¹H NMR analysis of the crude residue indicated a 30:25:24:21 mixture of 4 diastereomers. Flash chromatography of the residue over silica gel (4 x 22 cm), using 15% EtOAc-hexane, gave **26b** as four fractions: **26b-1** (least polar) (520 mg, 15%, single isomer) as a viscous oil, **26b-2** and **26b-3** (1.2 g, 35%, mixture of two diastereoisomers) as a viscous oil and **26b-4** (most polar) (610 mg, 18%, single isomer) as a viscous oil.

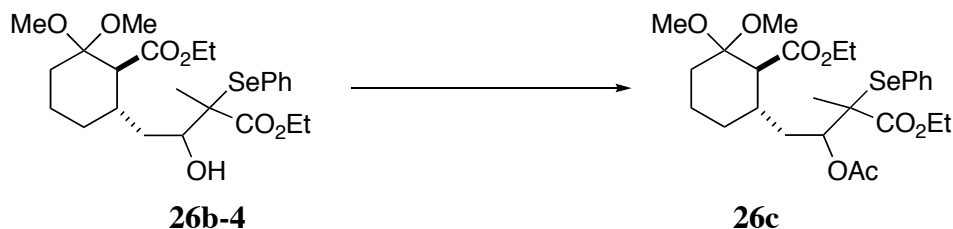
Compound **26b-1** had: FTIR (CH₂Cl₂ cast) 3507, 2938, 1722, 1246, 1050, 744 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.16 (t, *J* = 7.2 Hz, 3 H), 1.26 (t, *J* = 7.2 Hz, 3 H), 1.37 (s, 3 H), 1.50-1.55 (m, 4 H), 1.64-1.72 (m, 2 H), 1.96-2.05 (m, 2 H), 2.15-2.20 (m, 1 H), 2.71 (d, *J* = 5.2 Hz, 1 H), 3.15 (s, 3 H), 3.20 (s, 3 H), 3.99-4.20 (m, 5 H), 7.29-7.34 (m, 2 H), 7.38-7.42 (m, 1 H), 7.58-7.63 (m, 2 H); ¹³C NMR (CDCl₃, 100 MHz) δ 13.8 (q), 14.1 (q), 17.5 (q), 19.2 (t), 28.5 (t), 29.3 (t), 34.6 (d), 36.0 (t), 48.07 (q), 48.12 (q), 51.5 (d), 57.6 (s), 60.1 (t), 61.1 (t), 72.3 (d), 100.7 (s), 126.6 (s), 128.8 (d), 129.3 (d), 138.0 (d), 172.4 (s), 173.4 (s); exact mass (electrospray) *m/z* calcd for C₂₄H₃₆NaO₇⁸⁰Se 539.1519, found 539.1512.

The middle fraction containing compounds **26b-2** and **26b-3** had: (data on a fraction containing a 76:24 mixture of diastereomers) FTIR (CH₂Cl₂ cast) 3507, 2939, 1727, 1439, 1247,

1051, 744 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.09 (t, $J = 7.2$ Hz, 0.7 H), 1.18 (t, $J = 7.2$ Hz, 2.3 H), 1.24-1.29 (m, 4 H), 1.39 (s, 2.3 H), 1.42 (s, 0.7 H), 1.44-1.57 (m, 2 H), 1.62-1.72 (m, 1 H), 1.89-2.26 (m, 4 H), 2.77 (br d, $J = 4.8$ Hz, 0.3 H), 2.83 (br d, $J = 3.6$ Hz, 0.7 H), 2.92 (br d, $J = 7.6$ Hz, 0.7 H), 3.08 (br d, $J = 2.8$ Hz, 0.3 H), 3.16 (s, 0.7 H), 3.18 (s, 2.3 H), 3.20 (s, 0.7 H), 3.24 (s, 2.3 H), 3.94-4.22 (m, 5 H), 7.28-7.32 (m, 2 H), 7.36-7.41 (m, 1 H), 7.58-7.63 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.8 (q), 13.9 (q), 14.2 (q), 16.9 (q), 18.7 (t), 18.8 (q), 19.2 (t), 25.7 (t), 28.7 (t), 29.2 (t), 29.3 (t), 34.0 (d), 34.3 (d), 35.5 (t), 35.9 (t), 48.0 (q), 48.05 (q), 48.1 (q), 50.8 (d), 52.3 (d), 55.2 (s), 57.4 (s), 60.3 (t), 61.0 (t), 61.2 (t), 70.9 (d), 74.5 (d), 100.7 (s), 100.8 (s), 126.6 (s), 126.9 (s), 128.7 (d), 128.8 (d), 129.3 (d), 129.4 (d), 138.0 (d), 138.2 (d), 172.4 (s), 172.5 (s), 172.8 (s), 174.0 (s); exact mass (electrospray) m/z calcd for $\text{C}_{24}\text{H}_{36}\text{NaO}_7^{80}\text{Se}$ 539.1519, found 539.1520.

Compound **26b-4** had: FTIR (CH_2Cl_2 cast) 3502, 2941, 2833, 1728, 1439, 1246, 1051, 744 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.19 (t, $J = 7.2$ Hz, 3 H), 1.24-1.30 (m, 1 H), 1.25 (t, $J = 7.2$ Hz, 3 H), 1.37-1.46 (m, 1 H), 1.38 (s, 3 H), 1.50-1.58 (m, 2 H), 1.65-1.71 (m, 1 H), 1.94-2.07 (m, 3 H), 2.24 (dddd, $J = 9.6, 9.6, 5.2, 5.2$ Hz, 1 H), 2.77 (dd, $J = 5.2, 0.8$ Hz, 1 H), 3.01-3.02 (m, 1 H), 3.201 (s, 3 H), 3.204 (s, 3 H), 3.99-4.03 (m, 1 H), 4.04-4.20 (m, 4 H), 7.27-7.31 (m, 2 H), 7.35-7.40 (m, 1 H), 7.55-7.58 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.9 (q), 14.1 (q), 18.3 (q), 19.0 (t), 26.1 (t), 29.5 (t), 33.8 (d), 35.4 (t), 48.13 (q), 48.20 (q), 52.8 (d), 54.9 (s), 60.3 (t), 61.2 (t), 73.4 (d), 100.8 (s), 126.7 (s), 128.7 (d), 129.3 (d), 138.0 (d), 172.4 (s), 173.8 (s); exact mass (electrospray) m/z calcd for $\text{C}_{24}\text{H}_{36}\text{NaO}_7^{80}\text{Se}$ 539.1519, found 539.1513.

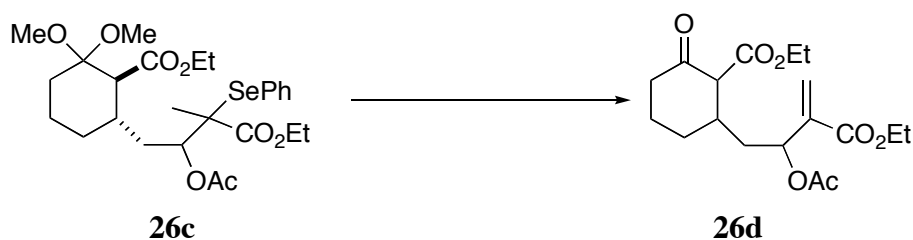
Trans-6-[2-Acetoxy-3-ethoxycarbonyl-3-(phenylseleno)butyl]-2,2-dimethoxycyclohexanecarboxylic Acid Ethyl Ester (26c).



Pyridine (0.55 mL, 6.75 mmol) and AcCl (0.25 mL, 3.38 mmol) were added dropwise to a stirred and cooled ($0\text{ }^{\circ}\text{C}$) solution of **26b-4** (580 mg, 1.125 mmol) and DMAP (15 mg, 0.12 mmol) in CH_2Cl_2 (8 mL). The ice bath was left in place but not recharged and stirring was continued for 12 h. The mixture was quenched with water (15 mL), acidified with hydrochloric acid (10%, 1 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 x 20 cm),

using 15% EtOAc-hexane, gave **26c** (435 mg, 69%) as a viscous oil: FTIR (CH_2Cl_2 cast) 2942, 2833, 1744, 1723, 1370, 1237, 744 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.07 (t, $J = 7.2$ Hz, 3 H), 1.25 (t, $J = 7.2$ Hz, 3 H), 1.29-1.38 (m, 1 H), 1.45 (s, 3 H), 1.46-1.69 (m, 4 H), 1.78-1.91 (m, 1 H), 1.94 (s, 3 H), 1.95-2.13 (m, 2 H), 2.18-2.28 (m, 1 H), 2.58 (d, $J = 5.6$ Hz, 1 H), 3.19 (s, 3 H), 3.22 (s, 3 H), 3.82-3.90 (m, 1 H), 3.94-4.02 (m, 1 H), 4.08-4.16 (m, 2 H), 5.65 (d, $J = 10.4$ Hz, 1 H), 7.26-7.32 (m, 2 H), 7.36-7.40 (m, 1 H), 7.57-7.60 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.8 (q), 14.2 (q), 18.0 (q), 19.2 (t), 20.9 (q), 26.2 (t), 29.9 (t), 33.2 (d), 34.6 (t), 48.1 (q), 48.4 (q), 53.3 (s), 54.1 (d), 60.2 (t), 61.2 (t), 73.6 (d), 100.6 (s), 126.4 (s), 128.9 (d), 129.5 (d), 137.9 (d), 169.7 (s), 172.0 (s), 172.11 (s); exact mass (electrospray) m/z calcd for $\text{C}_{26}\text{H}_{38}\text{NaO}_8^{80}\text{Se}$ 581.1624, found 581.1625.

2-(2-Acetoxy-3-ethoxycarbonylbut-3-enyl)-6-oxocyclohexanecarboxylic Acid Ethyl Ester (26d).

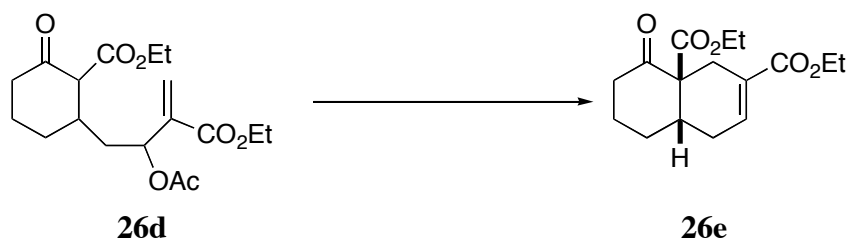


H_2O_2 (30%, 1 mL, 9.79 mmol) was added dropwise to a stirred and cooled (-5 $^\circ\text{C}$, ice-acetone bath) solution of **26c** (400 mg, 0.717 mmol) in THF (10 mL) and water (1 mL). The cold bath was left in place but not recharged and stirring was continued for 3 h, by which time the temperature had risen to 0 $^\circ\text{C}$. The mixture was quenched with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (3 mL) and stirred at 0 $^\circ\text{C}$ for 5 min. The cold bath was removed, stirring was continued for 5 min, and the mixture was diluted with water (15 mL) and extracted with EtOAc (3 x 10 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 x 18 cm), using 25% EtOAc-hexane, gave **26d** (150 mg, 59%) as a viscous oil which was an equilibrium mixture of tautomers (^{13}C NMR): FTIR (CH_2Cl_2 cast) 2982, 2941, 1744, 1715, 1644, 1369, 1233 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.26-1.38 (m, 6 H), 1.42-1.53 (m, 1 H), 1.60-1.81 (m, 4 H), 1.86-1.92 (m, 1 H), 2.10-2.11 (two s, 3 H), 2.19-2.36 (m, 2 H), 2.46-2.51 (m, 0.2 H), 2.64-2.69 (m, 0.7 H), 3.07 (dd, $J = 10.8, 0.8$ Hz, 0.2 H), 4.14-4.29 (m, 4 H), 5.69-5.77 (m, 2 H), 6.24-6.27 (m, 1 H), 12.40 (s, 0.7 H); ^{13}C NMR (CDCl_3 , 100 MHz) (enol form) δ 14.1 (q), 14.2 (q), 16.9 (t), 21.0 (q), 24.7 (t), 28.3 (d), 29.0 (t), 38.9 (t), 60.2 (t), 60.9 (t), 69.9 (d), 101.6 (s), 123.9 (s), 140.2 (t), 165.1 (s), 170.0 (s), 172.3 (s), 173.1 (s); (keto

form) δ 24.5 (t), 28.4 (t), 37.8 (d), 40.0 (t), 41.1 (t), 61.0 (t), 63.4 (d), 68.7 (d), 124.5 (s), 140.2 (t), 205.7 (s); exact mass (electrospray) m/z calcd for $C_{18}H_{26}NaO_7$ 377.1571, found 377.1573.

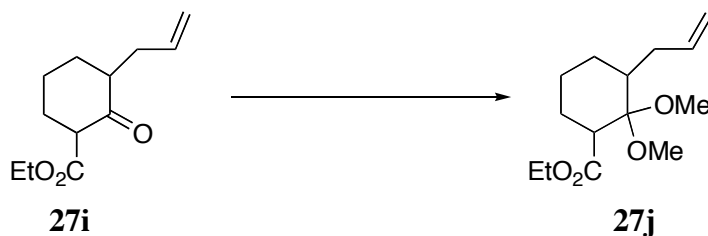
In this oxidation the acetal was hydrolyzed, presumably by $PhSe(O)OH$.

Cis-8-Oxo-4,4a,5,6,7,8-hexahydro-1H-naphthalene-2,8a-dicarboxylic Acid Diethyl Ester (26e).



DBU (0.04 mL, 0.3 mmol) was added dropwise to a stirred solution of **26d** (52 mg, 0.146 mmol) in MeCN (1.5 mL). Stirring was continued for 30 min and the mixture was filtered through a pad of silica gel (2 x 2 cm), using 50% EtOAc-hexane (60 mL). Evaporation of the filtrate and flash chromatography of the residue over silica gel (0.5 x 8 cm), using 10% EtOAc-hexane, gave **26e** (36 mg, 84%) as a colorless oil. The stereochemical assignment is tentative and is based on analogy:¹⁵ FTIR (CH_2Cl_2 cast) 2939, 1713, 1660, 1427, 1245, 1096, 723 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) δ 1.25 (t, $J = 7.2$ Hz, 3 H), 1.29 (t, $J = 7.2$ Hz, 3 H), 1.60-1.70 (m, 1 H), 1.80-1.91 (m, 2 H), 1.99-2.15 (m, 2 H), 2.27-2.36 (m, 1 H), 2.40-2.47 (m, 1 H), 2.51-2.58 (m, 1 H), 2.70-2.76 (m, 3 H), 4.15-4.27 (m, 4 H), 6.90 (dddd, $J = 4.0, 4.0, 2.0, 2.0$ Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1 (q), 14.2 (q), 23.9 (t), 26.5 (t), 26.6 (t), 28.2 (t), 36.2 (d), 38.0 (t), 6.56 (t), 60.61 (s), 61.4 (t), 126.8 (s), 136.4 (d), 166.2 (s), 171.6 (s), 207.3 (s); exact mass (electrospray) m/z calcd for $C_{16}H_{22}NaO_5$ 317.1359, found 317.1357.

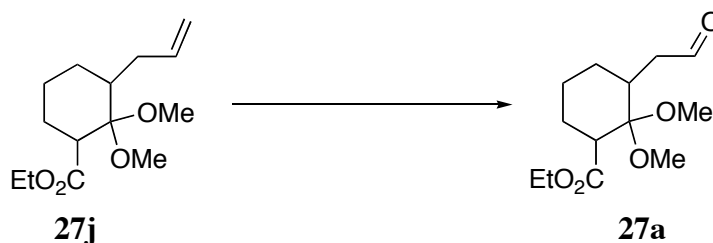
3-Allyl-2,2-dimethoxycyclohexanecarboxylic Acid Ethyl Ester (27j).



p -TsOH.H₂O (285 mg, 1.49 mmol) was added to a stirred solution of **27i**³³ (6.0 g, 28.53 mmol) and $HC(OMe)_3$ (4.4 mL, 40.5 mmol) in MeOH (80 mL). Stirring was continued for 24 h

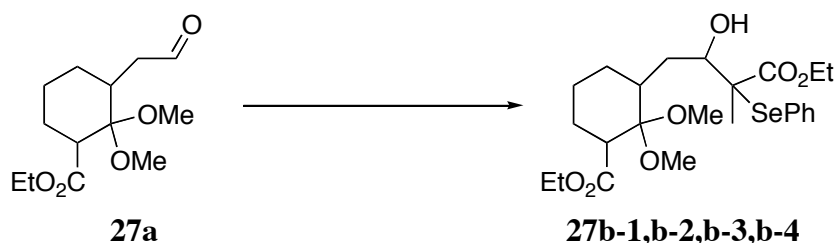
and the mixture was quenched with saturated aqueous NaHCO_3 (15 mL), diluted with water (100 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (4 x 20 cm), using 10% EtOAc-hexane, gave **27j** (4.13 g, 57%) as a colorless liquid which was very largely a single isomer, but contained impurities (^{13}C NMR): FTIR (CH_2Cl_2 cast) 2941, 2866, 1734, 1640, 1445, 1201, 1053, 910 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.26 (t, $J = 7.2$ Hz, 3 H), 1.39-1.96 (m, 7 H), 2.09-2.15 (m, 1 H), 2.49-2.54 (m, 1 H), 2.73 (dd, $J = 8.4, 4.4$ Hz, 1 H), 3.23 (s, 3 H), 3.25 (s, 3 H), 4.09-4.21 (m, 2 H), 4.95-5.07 (m, 2 H), 5.66-5.80 (m, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.1 (q), 20.0 (t), 25.3 (t), 26.7 (t), 32.5 (t), 40.7 (d), 46.9 (d), 49.0 (q), 49.1 (q), 60.3 (t), 101.8 (s), 115.6 (t), 137.9 (d), 173.4 (s); exact mass (electrospray) m/z calcd for $\text{C}_{14}\text{H}_{24}\text{NaO}_4$ 279.1567, found 279.1565.

2,2-Dimethoxy-3-(2-oxoethyl)cyclohexanecarboxylic Acid Ethyl Ester (27a).



O_3 was bubbled into a stirred and cooled (-78°C) solution of **27j** (2.45 g, 9.55 mmol) in CH_2Cl_2 (120 mL) for 30 min, by which time a blue color persisted. O_2 was passed through the solution for 30 min and Ph_3P (3.26 g, 12.42 mmol) was then added. The cold bath was removed and stirring was continued for 8 h. Evaporation of the solvent and flash chromatography of the residue over silica gel (4 x 20 cm), using 15% EtOAc-hexane, gave **27a** (1.51 g, 61%) as colorless oil which was a single isomer: FTIR (CH_2Cl_2 cast) 2945, 2868, 1735, 1132, 901 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 1.23 (t, $J = 7.2$ Hz, 3 H), 1.33-1.48 (m, 2 H), 1.58-1.86 (m, 4 H), 2.23 (ddd, $J = 16.5, 8.7, 2.4$ Hz, 1 H), 2.74-2.82 (m, 2 H), 2.86-2.98 (m, 1 H), 3.20 (s, 3 H), 3.22 (s, 3 H), 4.06-4.16 (m, 2 H), 9.64 (t, $J = 2.4$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 14.1 (q), 20.4 (t), 26.6 (t), 28.1 (t), 35.9 (d), 44.4 (t), 46.8 (d), 48.9 (q), 49.7 (q), 60.3 (t), 100.8 (s), 172.7 (s), 201.9 (d); exact mass (electrospray) m/z calcd for $\text{C}_{13}\text{H}_{22}\text{NaO}_6$ 297.1309, found 297.1308 (the aldehyde is sensitive, and attempts to obtain its mass spectrum invariably led to the mass spectrum of the derived carboxylic acid).

3-[3-Ethoxycarbonyl-2-hydroxy-3-(phenylseleno)butyl]-2,2-dimethoxycyclohexane-carboxylic Acid Ethyl Ester (27b-1, 27b-2, 27b-3, 27b-4).



n-BuLi (2.5 M in hexane, 3.4 mL, 8.43 mmol) was added dropwise over ca 5 min to a stirred and cooled (-78 °C) solution of *i*-Pr₂NH (1.26 mL, 8.95 mmol) in THF (10 mL). Stirring was continued for 40 min and a solution of **15** (2.3 g, 8.95 mmol) in THF (10 mL plus 1 mL as a rinse) was added over 5 min. Stirring was continued for 1 h and a solution of **27a** (1.36 g, 5.26 mmol) in THF (10 mL plus 1 mL as a rinse) was added over 5 min. Stirring at -78 °C was continued for 4 h and the mixture was quenched with saturated aqueous NH₄Cl (10 mL). The cold bath was removed, stirring was continued for 10 min and the mixture was diluted with water (50 mL) and extracted with EtOAc (3 x 15 mL). The combined organic extracts were dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (4 x 28 cm), using 15% EtOAc-hexane, gave a less polar isomer **27b-1** (510 mg, 19%), a 72:28 mixture of diastereoisomers **27b-2** and **27b-3** (1.25 g, 46%) and a more polar isomer **27b-4** (780 mg, 29%) as viscous oils. The stereochemical configuration at the carbinol carbon is the same in **27b-1** and **27b-2**, while the opposite configuration applies to **27b-3** and **27b-4** at the carbinol center.

Compound **27b-1** had: FTIR (CH₂Cl₂ cast) 3510, 2940, 2867, 1723, 1247, 744 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.13 (t, *J* = 7.2 Hz, 3 H), 1.24 (t, *J* = 7.2 Hz, 3 H), 1.36-1.51 (m, 2 H), 1.44 (s, 3 H), 1.57-1.87 (m, 6 H), 2.26-2.32 (m, 1 H), 2.70 (dd, *J* = 8.4 4.4 Hz, 1 H), 3.16 (s, 3 H), 3.22 (s, 3 H), 3.95-4.15 (m, 5 H), 7.29-7.33 (m, 2 H), 7.37-7.42 (m, 1 H), 7.59-7.63 (m, 2 H); ¹³C NMR (CDCl₃, 100 MHz) δ 13.7 (q), 14.1 (q), 16.9 (q), 20.3 (t), 26.8 (t), 27.8 (t), 31.4 (t), 39.9 (d), 46.9 (q), 48.7 (q), 49.2 (d), 57.9 (s), 60.2 (t), 61.0 (t), 73.6 (d), 102.1 (s), 126.7 (s), 128.7 (d), 129.3 (d), 138.0 (d), 173.1 (s), 173.2 (s); exact mass (electrospray) *m/z* calcd for C₂₄H₃₆NaO₇⁸⁰Se 539.1519, found 539.1519.

The mixture of compounds **27b-2** and **27b-3** had: FTIR (CH₂Cl₂ cast) 3514, 2939, 2866, 1724, 1247, 1053 744 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.10 (t, *J* = 7.2 Hz, 1 H), 1.19 (t, *J* = 7.2 Hz, 2 H), 1.24-1.34 (m, 4 H), 1.38-1.48 (m, 1 H), 1.43 (s, 2 H), 1.46 (s, 1 H), 1.51-1.88 (m, 5 H), 2.29-2.40 (m, 2 H), 2.60 (dd, *J* = 10.0, 4.0 Hz, 0.28 H), 2.75 (dd, *J* = 8.4, 4.4 Hz, 0.72 H), 2.80-2.98 (br s, 1 H), 3.24 (s, 1 H), 3.25-3.26 (two s, 3 H), 3.28 (s, 3 H), 3.94-4.18 (m, 5 H),

7.27-7.33 (m, 2 H), 7.36-7.42 (m, 1 H), 7.59-7.63 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.7 (q), 13.9 (q), 14.0 (q), 16.7 (q), 18.2 (q), 19.7 (t), 20.2 (t), 25.8 (t), 26.6 (t), 67.9 (t), 28.1 (t), 30.4 (t), 30.8 (t), 38.1 (d), 40.1 (d), 46.90 (q), 46.96 (q), 48.6 (q), 48.86 (d), 48.89 (q), 49.3 (d), 55.1 (s), 57.5 (s), 60.2 (t), 60.3 (t), 60.9 (t), 61.1 (t), 71.1 (d), 76.9 (d), 101.9 (s), 102.1 (s), 126.6 (s), 126.7 (s), 128.6 (d), 128.7 (d), 129.2 (d), 129.3 (d), 137.9 (d), 138.1 (d), 172.6 (s), 173.2 (s), 173.2 (s), 173.9 (s); exact mass (electrospray) m/z calcd for $\text{C}_{24}\text{H}_{36}\text{NaO}_7^{80}\text{Se}$ 539.1519, found 539.1518.

Compound **27b-4** had: FTIR (CH_2Cl_2 cast) 3507, 2941, 2866, 1725, 1439, 1246, 1158, 743 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.19 (t, $J = 7.2$ Hz, 3 H), 1.27 (t, $J = 7.2$ Hz, 3 H), 1.44-1.52 (m, 2 H), 1.45 (s, 3 H), 1.60-1.89 (m, 6 H), 2.39-2.42 (m, 1 H), 2.68 (dd, $J = 10.0, 4.0$ Hz, 1 H), 3.06 (br s, 1 H), 3.24 (s, 3 H), 3.26 (s, 3 H), 3.99 (dd, $J = 9.6, 2.4$ Hz, 1 H), 4.08 (q, $J = 7.2$ Hz, 2 H), 4.16 (q, $J = 7.2$ Hz, 2 H), 7.26-7.32 (m, 2 H), 7.36-7.41 (m, 1 H), 7.56-7.58 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.8 (q), 14.0 (q), 17.9 (q), 19.9 (t), 25.7 (t), 26.6 (t), 29.6 (t), 37.6 (d), 47.0 (d), 48.8 (q), 48.9 (q), 54.8 (s), 60.3 (t), 61.1 (t), 73.4 (d), 102.0 (s), 126.6 (s), 128.7 (d), 129.2 (d), 137.8 (d), 173.3 (s), 173.7 (s); exact mass (electrospray) m/z calcd for $\text{C}_{24}\text{H}_{36}\text{NaO}_7^{80}\text{Se}$ 539.1519, found 539.1518.

3-(3-Ethoxycarbonyl-2-hydroxybut-3-enyl)-2,2-dimethoxycyclohexanecarboxylic Acid Ethyl Ester (27c-1).



H_2O_2 (30%, 0.2 mL, 1.96 mmol) was added dropwise to a stirred and cooled ($-10\text{ }^\circ\text{C}$, ice-acetone bath) solution of **27b-1** (100 mg, 0.193 mmol) in CH_2Cl_2 (4 mL). The mixture was stirred vigorously for 1 h and quenched with saturated aqueous NaHCO_3 (1 mL) and saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (1 mL). The cold bath was removed after 5 min, stirring was continued for 10 min and the mixture was diluted with water (10 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (0.5 x 8 cm), using 20% EtOAc-hexane, gave **27c-1** (63 mg, 91%) as a colorless liquid: FTIR (CH_2Cl_2 cast) 3510, 2942, 2868, 2837, 1718, 1628, 1177, 1051 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.25 (t, $J = 7.0$ Hz, 3 H), 1.31 (t, $J = 7.0$ Hz, 3 H), 1.38-1.48 (m, 2

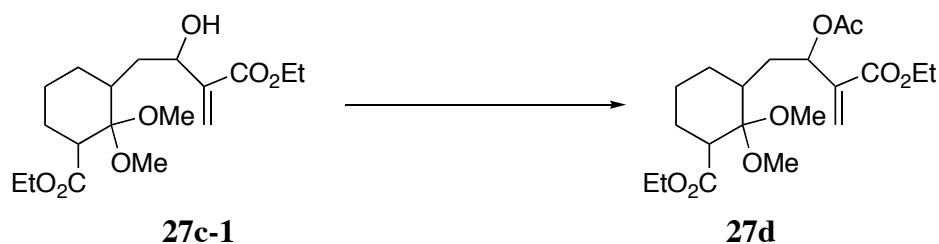
H), 1.55-1.63 (m, 3 H), 1.70-1.76 (m, 1 H), 1.79-1.86 (m, 1 H), 2.19-2.25 (m, 2 H), 2.78 (dd, $J = 7.5, 4.5$ Hz, 1 H), 3.251 (s, 3 H), 3.252 (s, 3 H), 3.38 (br s, 1 H), 4.13 (q, $J = 7.0$ Hz, 2 H), 4.18-4.26 (m, 2 H), 4.56 (m, 1 H), 5.91 (t, $J = 1.5$ Hz, 1 H), 6.28 (m, 1 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 14.1 (q), 14.2 (q), 20.5 (t), 26.9 (t), 28.8 (t), 35.1 (t), 36.9 (d), 47.1 (q), 48.6 (q), 49.7 (d), 60.3 (t), 60.6 (t), 70.6 (d), 101.8 (s), 125.3 (s), 142.2 (t), 166.5 (s), 173.0 (s); exact mass (electrospray) m/z calcd for $\text{C}_{18}\text{H}_{30}\text{NaO}_7$ 381.1884, found 381.1893.

3-(3-Ethoxycarbonyl-2-hydroxybut-3-enyl)-2,2-dimethoxycyclohexanecarboxylic Acid Ethyl Ester (27c-4).



H_2O_2 (30%, 1.5 mL, 14.69 mmol) was added dropwise to a stirred and cooled (-10°C , ice-acetone bath) solution of **27b-4** (730 mg, 1.416 mmol) in CH_2Cl_2 (15 mL). Stirring was continued for 1 h and the mixture was quenched with saturated aqueous NaHCO_3 (5 mL) and saturated aqueous in $\text{Na}_2\text{S}_2\text{O}_3$ (5 mL). The cold bath was removed after 10 min, stirring was continued for 10 min and the mixture was diluted with water (10 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 x 20 cm), using 25% EtOAc-hexane, gave **27c-4** (494 mg, 97%) as a viscous oil: FTIR (CH_2Cl_2 cast) 3501, 2941, 2867, 1714, 1629, 1374, 1061 cm^{-1} ; ^1H NMR (CDCl_3 , 400 mg) δ 1.24 (t, $J = 7.2$ Hz, 3 H), 1.30 (t, $J = 7.2$ Hz, 3 H), 1.36-1.65 (m, 4 H), 1.66-1.76 (m, 2 H), 1.79-1.89 (m, 2 H), 2.41-2.47 (m, 1 H), 2.69 (dd, $J = 8.8, 4.4$ Hz, 1 H), 3.03 (br d, $J = 4.4$ Hz, 1 H), 3.23 (s, 3 H), 3.26 (s, 3 H), 4.13 (q, $J = 7.2$ Hz, 2 H), 4.17-4.25 (m, 2 H), 4.42 (br d, $J = 10.0$ Hz, 1 H), 5.90 (t, $J = 1.6$ Hz, 1 H), 6.23 (dd, $J = 1.6, 0.8$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.08 (q), 14.14 (q), 20.1 (t), 26.86 (t), 26.9 (t), 36.1 (t), 38.0 (d), 47.1 (q), 48.8 (q), 49.3 (d), 60.4 (t), 60.6 (t), 69.8 (d), 101.9 (s), 124.2 (s), 143.6 (t), 166.4 (s), 173.2 (s); exact mass (electrospray) m/z calcd for $\text{C}_{18}\text{H}_{30}\text{NaO}_7$ 381.1884, found 381.1882.

3-(2-Acetoxy-3-ethoxycarbonylbut-3-enyl)-2,2-dimethoxycyclohexanecarboxylic Acid Ethyl Ester (27d).



Pyridine (0.05 mL, 0.56 mmol) and AcCl (0.02 mL, 0.28 mmol) were added dropwise to a stirred and cooled (0 °C) solution of **27c-1** (50 mg, 0.139 mmol) and DMAP (3 mg, 0.02 mmol) in CH₂Cl₂ (2 mL). Stirring was continued for 2 h and the mixture was quenched with water (5 mL), acidified with hydrochloric acid (10%, 0.5 mL) and extracted with CH₂Cl₂ (3 x 5 mL). The combined organic extracts were dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (0.5 x 8 cm), using 20% EtOAc-hexane, gave **27d** (52 mg, 94%) as a viscous oil: FTIR (CH₂Cl₂ cast) 2944, 2868, 1739, 1635, 1371, 1236, 1049 cm⁻¹; ¹H NMR (CDCl₃, 400 mg) δ 1.22 (t, *J* = 7.2 Hz, 3 H), 1.29 (t, *J* = 7.2 Hz, 3 H), 1.41-1.51 (m, 2 H), 1.55-1.86 (m, 5 H), 2.03 (s, 3 H), 2.11-2.24 (m, 2 H), 2.67 (dd, *J* = 8.4, 4.4 Hz, 1 H), 3.20 (s, 3 H) 3.21 (s, 3 H), 4.04-4.16 (m, 2 H), 4.18-4.27 (m, 2 H), 5.65 (t, *J* = 6.4 Hz, 1 H), 5.82 (m, 1 H), 6.29 (m, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.0 (q), 20.1 (t), 21.0 (q), 26.4 (t), 27.1 (t), 32.7 (t), 38.0 (d), 46.9 (q), 48.7 (q), 49.1 (d), 60.1 (t), 60.7 (t), 71.8 (d), 101.6 (s), 125.6 (s), 140.2 (t), 165.2 (s), 169.7 (s), 173.0 (s); exact mass (electrospray) *m/z* calcd for C₂₀H₃₂NaO₈ 423.1989, found 423.1986.

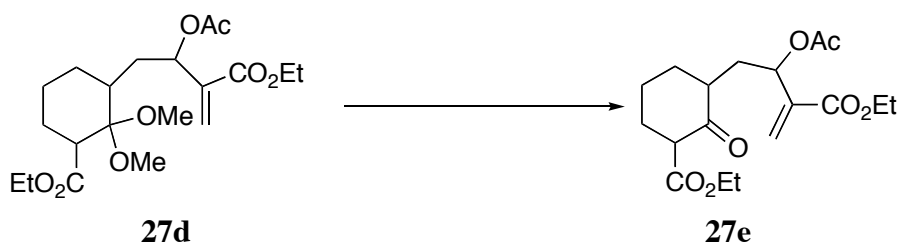
3-(2-Acetoxy-3-ethoxycarbonylbut-3-enyl)-2,2-dimethoxycyclohexanecarboxylic Acid Ethyl Ester (27d').



Pyridine (0.09 mL, 1.172 mmol) and AcCl (0.04 mL, 0.586 mmol) were added dropwise to a stirred and cooled (0 °C) solution of **27c-4** (105 mg, 0.293 mmol) and DMAP (6 mg, 0.045 mmol) in CH₂Cl₂ (3 mL). Stirring was continued for 2 h and the mixture was quenched with water (5 mL), acidified with hydrochloric acid (10%, 0.5 mL) and extracted with CH₂Cl₂ (3 x 5 mL). The combined organic extracts were dried (Na₂SO₄) and evaporated. Flash

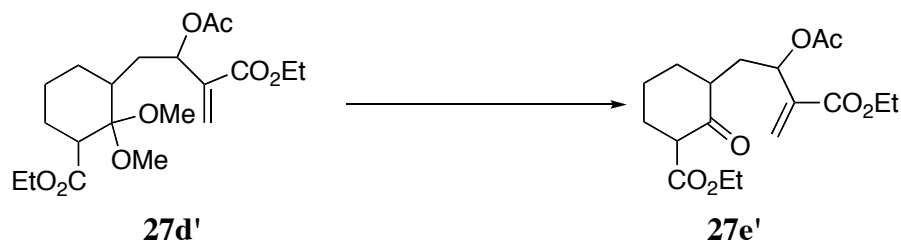
chromatography of the residue over silica gel (2 x 10 cm), using 20% EtOAc-hexane, gave **27d'** (105 mg, 90%) as a viscous oil which was used without full characterization: FTIR (CH_2Cl_2 cast) 2981, 2942, 2869, 1745, 1634, 1371, 1232 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.24 (t, $J = 7.2$ Hz, 3 H), 1.29 (t, $J = 7.2$ Hz, 3 H), 1.42-1.87 (m, 9 H), 2.08 (s, 3 H), 2.62 (dd, $J = 9.6, 4.0$ Hz, 1 H), 3.21 (s, 3 H), 3.24 (s, 3 H), 4.06-4.28 (m, 4 H), 5.61-5.64 (m, 1 H), 5.74 (t, $J = 1.2$ Hz, 1 H), 6.25 (br s, 1 H); exact mass (electrospray) m/z calcd for $\text{C}_{20}\text{H}_{32}\text{NaO}_8$ 423.1989, found 423.1991.

3-(2-Acetoxy-3-ethoxycarbonylbut-3-enyl)-2-oxocyclohexanecarboxylic Acid Ethyl Ester (27e).



A mixture of **27d** (84 mg, 0.209 mmol) and Amberlyst-15 (150 mg) in acetone (4 mL) was stirred for 1 h and filtered through a pad of silica gel (2 x 2 cm), using 70% EtOAc-hexane (50 mL). The filtrate was evaporated to give **27e** (67 mg, 91% as a viscous oil which was an inseparable mixture of keto-enol tautomers: FTIR (CH_2Cl_2 cast) 2982, 2938, 2865, 1744, 1716, 1648, 1371, 1235, 1026, 818 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.28-1.38 (m, 6 H), 1.45-2.07 (m, 5 H), 2.09 (s, 3 H), 2.11-2.34 (m, 1.7 H), 2.41-2.49 (m, 1.8 H), 2.69-2.75 (m, 0.3 H), 3.39-3.53 (m, 0.8 H), 4.20-4.32 (m, 4 H), 5.67-5.72 (m, 0.8 H), 5.82-5.88 (m, 1.2 H), 6.33-6.36 (m, 1 H), 12.42 (s, 0.2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.06 (q), 14.10 (q), 14.13 (q), 14.24 (q), 20.0 (t), 20.98 (q), 21.02 (q), 21.1 (q), 21.7 (t), 22.6 (t), 24.2 (t), 27.9 (t), 30.4 (t), 30.8 (t), 33.5 (t), 33.9 (t), 34.4 (t), 35.0 (t), 35.7 (d), 37.0 (t), 45.8 (d), 47.6 (d), 56.0 (d), 57.7 (d), 60.2 (t), 60.81 (t), 60.86 (t), 60.90 (t), 60.92 (t), 60.96 (t), 61.2 (t), 70.5 (d), 70.6 (d), 70.8 (d), 97.9 (s), 125.6 (s), 125.7 (s), 140.0 (t), 140.27 (t), 140.29 (t), 165.1 (s), 165.3 (s), 169.65 (s), 169.77 (s), 169.79 (s), 169.87 (s), 172.8 (s), 173.5 (s), 205.9 (s), 206.8 (s); exact mass (electrospray) m/z calcd for $\text{C}_{18}\text{H}_{26}\text{NaO}_7$ 377.1571, found 377.1571.

3-(2-Acetoxy-3-ethoxycarbonylbut-3-enyl)-2-oxocyclohexanecarboxylic Acid Ethyl Ester (27e').



A mixture of **27d'** (95 mg, 0.237 mmol) and Amberlyst-15 (200 mg) in acetone (4 mL) was stirred for 1 h and filtered through a pad of silica gel (2 x 2 cm), using 70% EtOAc-hexane (50 mL). The filtrate was evaporated to give **27e'** (80 mg, 95%) as a viscous oil which was an inseparable mixture of keto-enol tautomers: FTIR (CH₂Cl₂ cast) 2982, 2939, 2864, 1744, 1715, 1649, 1371, 1230, 1025 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.29-1.36 (m, 6 H), 1.41-2.09 (m, 5 H), 2.11-2.15 (three s, 3 H), 2.21-2.48 (m, 3.7 H), 2.67-2.73 (m, 0.3 H), 3.4-3.52 (m, 0.7 H), 4.19-4.31 (m, 4 H), 5.70 (br d, *J* = 10.0 Hz, 0.65 H), 5.77-5.83 (m, 1.35 H), 6.30-6.32 (m, 1 H), 12.43 (s, 0.3 H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.0 (q), 14.1 (q), 14.2 (q), 19.5 (t), 20.8 (q), 20.9 (q), 21.0 (q), 21.3 (t), 22.6 (t), 23.9 (t), 26.4 (t), 30.3 (t), 30.6 (t), 33.0 (t), 33.8 (t), 34.2 (t), 35.1 (d), 36.9 (t), 46.1 (d), 47.4 (d), 55.8 (d), 57.7 (d), 60.2 (t), 60.82 (t), 60.86 (t), 61.1 (t), 69.1 (d), 69.2 (d), 69.5 (d), 98.1 (s), 124.5 (s), 124.66 (s), 124.69 (s), 140.1 (t), 140.3 (t), 140.4 (t), 164.9 (s), 165.0 (s), 169.67 (s), 169.74 (s), 169.81 (s), 169.86 (s), 169.92 (s), 172.8 (s), 173.2 (s), 206.4 (s), 207.1 (s); exact mass (electrospray) *m/z* calcd for C₁₈H₂₆NaO₇ 377.1571, found 377.1572.

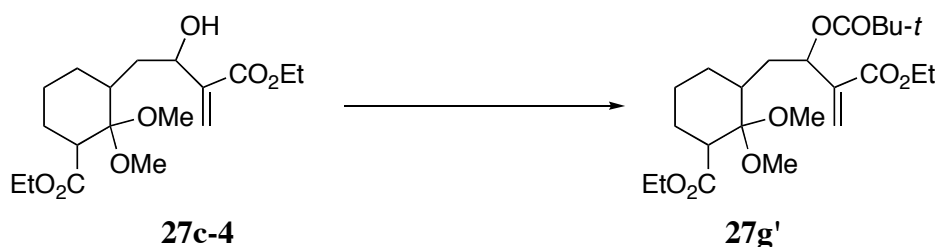
3-[2-(2,2-Dimethylpropionyloxy)-3-ethoxycarbonylbut-3-enyl]-2,2-dimethoxycyclohexanecarboxylic Acid Ethyl Ester (27g).



i-Pr₂NEt (0.2 mL, 1.024 mmol) and *t*-BuCOCl (0.06 mL, 0.512 mmol) were added dropwise to a stirred and cooled (0 °C) solution of **27c-1** (92 mg, 0.256 mmol) and DMAP (5 mg, 0.04 mmol) in CH₂Cl₂ (3 mL). The cold bath was removed after 15 min and stirring was continued for 16 h. The mixture was quenched with water (5 mL) and the aqueous phase was extracted with CH₂Cl₂ (3 x 5 mL). The combined organic extracts were dried (Na₂SO₄) and

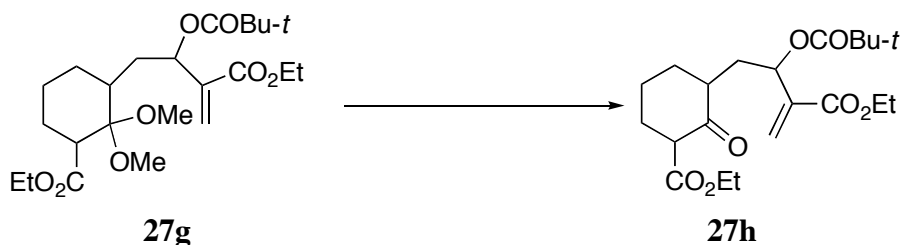
evaporated. Flash chromatography of the residue over silica gel (2 x 16 cm), using 20% EtOAc-hexane, gave **27g** (79 mg, 70%) and unreacted **27c-1** (5 mg, 5%) as viscous oils. Compound **27g** had: FTIR (CH₂Cl₂ cast); ¹H NMR (CDCl₃, 500 mg) δ 1.2 (s, 9 H), 1.25 (t, *J* = 7.0 Hz, 3 H), 1.31 (t, *J* = 7.0 Hz, 3 H), 1.39-1.55 (m, 2 H), 1.58-1.84 (m, 5 H), 2.14-2.24 (m, 2 H), 2.70 (dd, *J* = 9.0, 4.0 Hz, 1 H), 3.21 (s, 3 H), 3.23 (s, 3 H), 4.08-4.17 (m, 2 H), 4.18-4.28 (m, 2 H), 5.63 (ddd, *J* = 7.0, 6.0, 1.0 Hz, 1 H), 5.80 (t, *J* = 1.0 Hz, 1 H), 6.28 (d, *J* = 1.0 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.10 (q), 14.13 (q), 20.2 (t), 26.6 (t), 27.1 (q), 27.3 (t), 32.9 (t), 38.1 (d), 38.7 (s), 47.0 (d), 48.8 (q), 49.2 (q), 60.3 (t), 60.9 (t), 71.8 (d), 101.7 (s), 125.1 (s), 140.9 (t), 165.4 (s), 173.2 (s), 177.2 (s); exact mass (electrospray) *m/z* calcd for C₂₃H₃₈NaO₈ 465.2459, found 465.2455.

3-[2-(2,2-Dimethylpropionyloxy)-3-ethoxycarbonylbut-3-enyl]-2,2-dimethoxycyclohexanecarboxylic Acid Ethyl Ester (27g'**).**



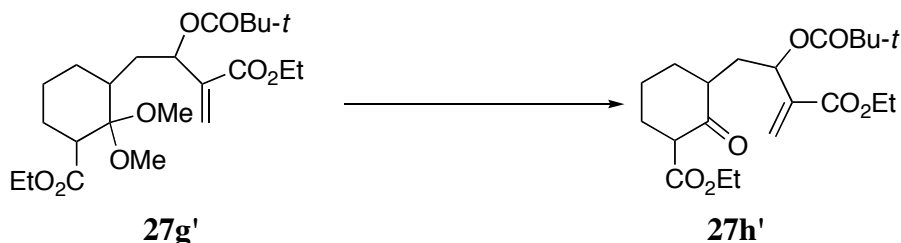
i-Pr₂NEt (0.38 mL, 2.2 mmol) and *t*-BuCOCl (0.14 mL, 1.1 mmol) were added dropwise to a stirred and cooled (0 °C) solution of **27c-4** (198 mg, 0.55 mmol) and DMAP (7 mg, 0.06 mmol) in CH₂Cl₂ (8 mL). The ice bath was removed after 1 h, stirring was continued for 24 h and the mixture was diluted with water (8 mL) and extracted with CH₂Cl₂ (3 x 5 mL). The combined organic extracts were dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (2 x 18 cm), using 15% EtOAc-hexane, gave **27g'** (236 mg, 97%) as a viscous oil: FTIR (CH₂Cl₂ cast) 2958, 2871, 1733, 1632, 1148, 946 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.21 (s, 9 H), 1.23 (t, *J* = 7.0 Hz, 3 H), 1.29 (t, *J* = 7.0 Hz, 3 H), 1.41-1.64 (m, 3 H), 1.67-1.74 (m, 3 H), 1.78-1.85 (m, 1 H), 1.91-1.98 (m, 1 H), 2.14-2.17 (m, 1 H), 2.62 (dd, *J* = 10.0, 4.0 Hz, 1 H), 3.21 (s, 3 H), 3.22 (s, 3 H), 4.06-4.26 (m, 4 H), 5.58 (br d, *J* = 9.5 Hz, 1 H), 5.70 (t, *J* = 1.0 Hz, 1 H), 6.22 (m, 1 H); ¹³C NMR (CDCl₃, 125 MHz) δ 14.1 (q), 19.8 (t), 25.0 (t), 26.6 (t), 27.1 (q), 32.9 (t), 37.2 (d), 38.8 (s), 46.9 (q), 48.7 (d), 49.0 (q), 60.3 (t), 60.9 (t), 69.5 (d), 101.8 (s), 123.7 (s), 141.3 (t), 165.1 (s), 173.3 (s), 177.3 (s); exact mass (electrospray) *m/z* calcd for C₂₃H₃₈NaO₈ 465.2459, found 465.2457.

3-[2-(2,2-Dimethylpropionyloxy)-3-ethoxycarbonylbut-3-enyl]-2-oxocyclohexane-carboxylic Acid Ethyl Ester (27h).



A mixture of **27g** (35 mg, 0.08 mmol) and Amberlyst-15 (70 mg) in acetone (3 mL, reagent grade) was stirred for 1 h and filtered through a pad of silica gel (2 x 2 cm), using 70% EtOAc-hexane (30 mL). The filtrate was evaporated and the residual viscous oil [30 mg, 95%, a keto-enol mixture of tautomers (^1H NMR)], was used without further purification in the next step. The material (**27h**) had: FTIR (CH_2Cl_2 cast) 2979, 2872, 1732, 1650, 1283, 1148, 1029 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 1.246-1.252 (m, 9 H), 1.28-1.40 (m, 6 H), 1.44-1.92 (m, 5 H), 1.94-2.51 (m, 3.7 H), 2.66-2.76 (m, 0.5 H), 3.38-3.50 (m, 0.7 H), 4.16-4.35 (m, 4 H), 5.62-5.66 (m, 0.7 H), 5.79-5.85 (m, 1.2 H), 6.32-6.35 (m, 1 H), 12.42 (s, 0.26 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.10 (q), 14.12 (q), 14.15 (q), 14.3 (q), 19.9 (t), 21.7 (t), 22.7 (t), 24.2 (t), 27.0 (q), 27.1 (q), 28.0 (t), 30.3 (t), 30.8 (t), 33.7 (t), 34.0 (t), 34.3 (t), 35.0 (t), 35.7 (d), 37.1 (t), 38.7 (s), 46.0 (d), 47.9 (d), 56.1 (d), 57.7 (d), 60.2 (t), 60.9 (t), 60.95 (t), 60.99 (t), 61.3 (t), 70.3 (d), 70.4 (d), 70.7 (d), 97.8 (s), 125.1 (s), 125.3 (s), 140.6 (t), 140.8 (t), 165.27 (s), 165.31 (s), 169.8 (s), 172.9 (s), 173.5 (s), 177.0 (s), 177.1 (s), 205.8 (s), 206.6 (s); exact mass (electrospray) m/z calcd for $\text{C}_{21}\text{H}_{32}\text{NaO}_7$ 419.2040, found 419.2043.

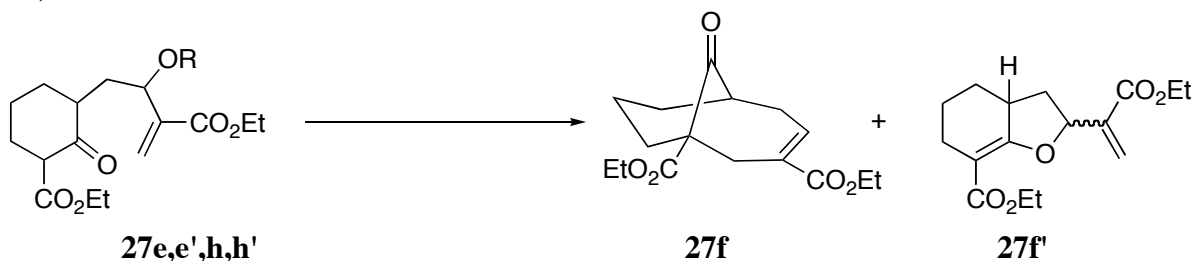
3-[2-(2,2-Dimethylpropionyloxy)-3-ethoxycarbonylbut-3-enyl]-2-oxocyclohexane-carboxylic Acid Ethyl Ester (27h').



A mixture of **27g'** (235 mg, 0.53 mmol) and Amberlyst-15 (500 mg) in acetone (6 mL) was stirred for 1 h and filtered through a pad of silica gel (2 x 2 cm), using 70% EtOAc-hexane

(50 mL). The filtrate was evaporated and the residual viscous oil [208 mg, 99%, a keto-enol mixture of tautomers (^1H NMR)], was used without further purification in the next step. The material (**27h'**) had: FTIR (CH_2Cl_2 cast) 2978, 2873, 1733, 1716, 1652, 1293, 1147 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.19-1.22 (m, 9 H), 1.23-1.30 (m, 6 H), 1.32-1.86 (m, 5 H), 1.92-2.05 (m, 0.6 H), 2.15-2.43 (m, 4 H), 2.61-2.69 (m, 0.4 H), 3.32-3.40 (m, 0.6 H), 4.08-4.26 (m, 4 H), 5.59-5.65 (m, 0.6 H), 5.68-5.75 (m, 1.4 H), 6.23-6.24 (m, 1 H), 12.34 (s, 0.4 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.1 (q), 14.13 (q), 14.2 (q), 19.6 (t), 21.6 (t), 22.7 (t), 24.1 (t), 26.4 (t), 27.0 (q), 27.1 (q), 29.2 (q), 30.3 (t), 30.7 (t), 32.7 (t), 33.7 (t), 33.8 (t), 34.0 (t), 35.3 (d), 37.1 (t), 38.76 (s), 38.82 (s), 45.6 (d), 47.5 (d), 56.1 (d), 57.8 (d), 60.2 (t), 60.86 (t), 60.91 (t), 61.2 (t), 68.7 (d), 68.84 (d), 68.88 (d), 98.1 (s), 124.2 (s), 124.34 (s), 124.37 (s), 140.5 (t), 140.8 (t), 164.98 (s), 165.04 (s), 169.7 (s), 169.8 (s), 172.9 (s), 173.4 (s), 177.1 (s), 177.2 (s), 177.3 (s), 206.3 (s), 207.0 (s); exact mass (electrospray) m/z calcd for $\text{C}_{21}\text{H}_{32}\text{NaO}_7$ 419.2040, found 419.2044.

10-Oxobicyclo[4.3.1]dec-3-ene-1,3-dicarboxylic Acid Diethyl Ester (27f) and 2-(1-Ethoxycarbonylvinyl)-2,3,3a,4,5,6-hexahydrobenzofuran-7-carboxylic Acid Ethyl Ester (27f').



(a)

DBU (0.02 mL, 0.14 mmol) was added dropwise to a stirred solution of **27e** (R = Ac, less polar isomer) (26 mg, 0.073 mmol) in MeCN (2 mL). Stirring was continued for 30 min and the mixture was filtered through a pad of silica gel (2 x 2 cm), using 60% EtOAc-hexane (30 mL). Evaporation of the filtrate and flash chromatography of the residue over silica gel (0.5 x 8 cm), using 10% EtOAc-hexane, gave **27f'** (17 mg, 79%) and **27f** (1 mg, ca 5%) as viscous oils. Compound **27f'** is a mixture of diastereoisomers (ca 7:3) with the ethoxycarbonylvinyl substituent cis and trans to the ring fusion hydrogen.

Compound **27f'** had: FTIR (CH_2Cl_2 cast) 2982, 2938, 1714, 1660, 1448, 1269, 1146, 1036 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) (inseparable 72:28 mixture of diastereoisomers) δ 1.17-1.36 (m, 8 H), 1.43-1.53 (m, 1 H), 1.90-1.96 (m, 1.35 H), 2.0-2.1 (m, 1 H), 2.15 (dd, J = 12.5, 7.5 Hz, 0.3 H), 2.22-2.32 (m, 1 H), 2.38-2.44 (m, 1 H), 2.54-2.57 (m, 0.3 H), 2.69-2.81 (m, 1.4

H), 4.12-4.31 (m, 4 H), 5.14-5.18 (m, 0.7 H), 5.41 (br d, $J = 8.5$ Hz, 0.3 H), 5.80-5.81 (m, 0.28 H), 6.16-6.17 (m, 0.72 H), 6.30-6.31 (m, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.06 (q), 14.38 (q), 22.1 (t), 22.2 (t), 23.9 (t), 27.1 (t), 27.4 (t), 34.8 (t), 37.4 (d), 38.2 (t), 41.7 (d), 59.41 (t), 59.47 (t), 60.72 (t), 60.76 (t), 79.6 (d), 80.5 (d), 97.5 (s), 97.6 (s), 124.3 (s), 124.5 (s), 139.1 (t), 139.5 (t), 165.12 (s), 165.14 (s), 166.6 (s), 166.7 (s), 167.0 (s), 167.4 (s); exact mass (electrospray) m/z calcd for $\text{C}_{16}\text{H}_{22}\text{NaO}_5$ 317.1359, found 317.1357.

Compound **27f** had: FTIR (CH_2Cl_2 cast) 2981, 2934, 1737, 1710, 1633, 1447, 1281, 1072, 1037 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.24 (t, $J = 7.0$ Hz, 3 H), 1.29 (t, $J = 7.0$ Hz, 3 H), 1.59-1.65 (m, 1 H), 1.91-2.10 (m, 3 H), 2.18 (dt, $J = 14.5, 12.5, 4.5$ Hz, 1 H), 2.41-2.51 (m, 2 H), 2.64 (dt, $J = 15.5, 6.5$ Hz, 1 H), 2.82-2.87 (m, 1 H), 2.94 (dd, $J = 15.5, 2.0$ Hz, 1 H), 3.07 (dd, $J = 15.5, 0.5$ Hz, 1 H), 4.14-4.24 (m, 4 H), 7.13 (t, $J = 6.5$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 13.9 (q), 14.2 (q), 17.7 (t), 29.9 (t), 30.7 (t), 32.6 (t), 35.1 (t), 47.3 (d), 60.5 (s), 60.9 (t), 61.2 (t), 134.3 (s), 140.2 (t), 166.7 (s), 172.6 (s), 211.1 (s); exact mass (electrospray) m/z calcd for $\text{C}_{16}\text{H}_{22}\text{NaO}_5$ 317.1359, found 317.1354.

(b)

DBU (0.027 mL, 0.18 mmol) was added dropwise to a stirred solution of **27e'** (R = Ac, more polar isomer) (32 mg, 0.09 mmol) in MeCN (2 mL). Stirring was continued for 50 min and the mixture was filtered through a pad of silica gel (2 x 2 cm), using 60% EtOAc-hexane (30 mL). Evaporation of the filtrate and flash chromatography of the residue over silica gel (0.5 x 8 cm), using 10% EtOAc-hexane, gave **27f'** (10 mg, 38%) and **27f** (14 mg, 53%) as viscous oils. Compound **27f'** is a mixture of diastereoisomers (ca 7:3) with the ethoxycarbonylvinyl substituent cis and trans to the ring fusion hydrogen.

(c)

DBU (0.027 mL, 0.18 mmol) was added dropwise to a stirred solution of **27h** (R = Piv, less polar isomer) (25 mg, 0.06 mmol) in MeCN (2 mL). Stirring was continued for 30 min and the mixture was filtered through a pad of silica gel (2 x 2 cm), using 60% EtOAc-hexane (30 mL). Evaporation of the filtrate and flash chromatography of the residue over silica gel (0.5 x 8 cm), using 10% EtOAc-hexane, gave **27f'** (14 mg, 80%) and **27f** (1 mg, 5%) as viscous oils. Compound **27f'** is a mixture of diastereoisomers (ca 7:3) with the ethoxycarbonylvinyl substituent cis and trans to the ring fusion hydrogen.

(d)

DBU (18 mg, 0.12 mmol) was added dropwise to a stirred solution of **27h'** (R = Piv, more polar isomer) (25 mg, 0.06 mmol) in MeCN (1.5 mL). Stirring was continued for 20 min

and the mixture was filtered through a pad of silica gel (2 x 2 cm), using 60% EtOAc-hexane (30 mL). Evaporation of the filtrate and flash chromatography of the residue over silica gel (0.5 x 8 cm), using 10% EtOAc-hexane, gave **27f'** (9 mg, 51%) and **27f** (4 mg, 23%) as viscous oils. Compound **27f'** is a mixture of diastereoisomers (ca 7:3) with the ethoxycarbonylvinyl substituent cis and trans to the ring fusion hydrogen.

(e)

DBU (0.024 mL, 0.16 mmol) was added dropwise to a stirred solution of **27h'** (R = Piv, more polar isomer) (30 mg, 0.075 mmol) in MeCN (2 mL). Stirring was continued for 2.5 h and the mixture was filtered through a pad of silica gel (2 x 2 cm), using 60% EtOAc-hexane (30 mL). Evaporation of the filtrate and flash chromatography of the residue over silica gel (0.5 x 8 cm), using 10% EtOAc-hexane, gave **27f** (16 mg, 73%) (and no **27f'**) as a viscous oil.

Conversion of **27f'** into **27f**.



(a)

DBU (0.02 mL, 0.14 mmol) was added dropwise to a stirred solution of **27f'** (20 mg, 0.068 mmol) in MeCN (2 mL). Stirring was continued for 12 h and the mixture was filtered through a pad of silica gel (2 x 2 cm), using 60% EtOAc-hexane (30 mL). Evaporation of the filtrate and flash chromatography of the residue over silica gel (0.5 x 8 cm), using 10% EtOAc-hexane, gave **27f** (15 mg, 75%) as a viscous oil.

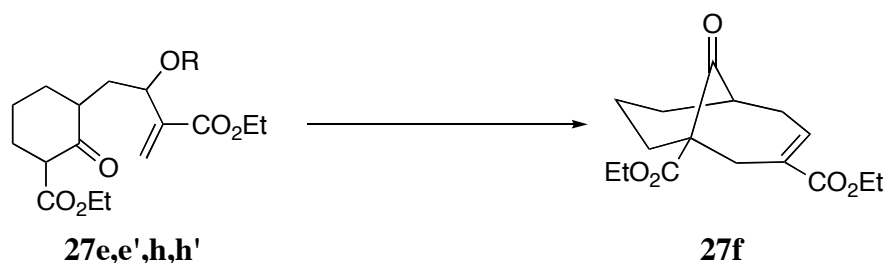
(b)

Cs₂CO₃ (2.2 mg, 0.00068 mmol) was added to a stirred solution of **27f'** (1.0 mg, 0.0034 mmol) in dry MeCN (0.5 mL) and stirring at room temperature was continued for 12 h. The mixture was filtered through a pad (0.5 x 4 cm) of Celite in a Pasteur pipette, using EtOAc. Evaporation of the filtrate gave a residue which was examined by ¹H NMR. The characteristic signals for **27f** were not observed; the main signals were attributable to the starting material **27f'**.

Compounds **27f'** have characteristic signals at δ 6.30 ppm and 6.18 ppm, and compound **27f** has a characteristic signal at δ 7.14 ppm.

The NMR solution was evaporated and the residue was dissolved in MeCN (0.5 mL). Cs_2CO_3 (2.2 mg, 0.0068 mmol) was added and the mixture was refluxed for 2 h, cooled, and filtered through a pad (0.5 x 4 cm) of Celite in a Pasteur pipette, using EtOAc. Evaporation of the filtrate gave a residue which was examined by ^1H NMR. The spectrum indicated that extensive decomposition had occurred and the characteristic signals for **27f** and **27f'** were absent.

10-Oxobicyclo[4.3.1]dec-3-ene-1,3-dicarboxylic Acid Diethyl Ester (27f).



Specific examples of the Cs_2CO_3 reactions

(a)

A mixture of **27e** (R = OAc, less polar isomer) (31 mg, 0.087 mmol) and Cs_2CO_3 (57 mg, 0.174 mmol) in MeCN (1.5 mL) was refluxed for 1 h, cooled to room temperature and filtered through a pad of silica gel (2 x 2 cm), using EtOAc (20 mL). Evaporation of the filtrate gave **27f** (26 mg, 100%) as a colorless liquid, which was pure by ^1H NMR.

(b)

A mixture of **27e'** (R = OAc, more polar isomer) (61 mg, 0.172 mmol) and Cs_2CO_3 (112 mg, 0.344 mmol) in MeCN (2 mL) was refluxed for 45 min, cooled to room temperature and filtered through a pad of silica gel (2 x 2 cm), using EtOAc (20 mL). Evaporation of the filtrate gave **27f** (50 mg, 99%) as a colorless liquid, which was pure by ^1H NMR.

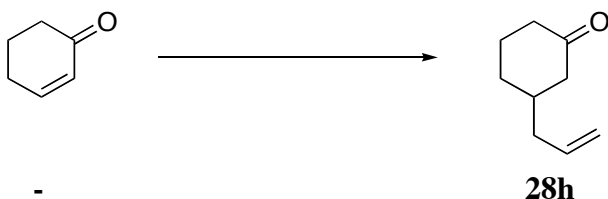
(c)

A mixture of **27h** (R = OPiv, less polar isomer) (6 mg, 0.015 mmol) and Cs_2CO_3 (10 mg, 0.03 mmol) in MeCN (1 mL) was refluxed for 1 h, cooled to room temperature and filtered through a pad of silica gel (2 x 2 cm), using EtOAc (20 mL). Evaporation of the filtrate and flash chromatography of the residue over silica gel (0.5 x 8 cm), using 20% EtOAc-hexane, gave **27f** (5 mg, 100%) as a colorless liquid.

(d)

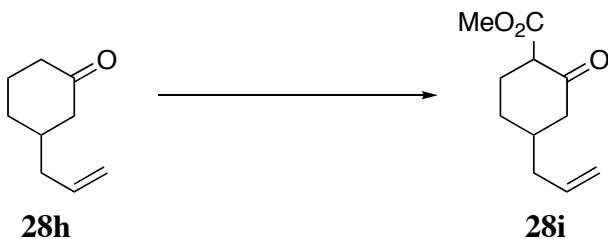
A mixture of **27h'** (130 mg, 0.327 mmol) and Cs_2CO_3 (214 mg, 0.656 mmol) in MeCN (5 mL) was refluxed for 1 h, cooled to room temperature and filtered through a pad of silica gel (2 x 2 cm), using EtOAc (20 mL). Evaporation of the filtrate and flash chromatography of the residue over silica gel (0.5 x 8 cm), using 20% EtOAc-hexane, gave **27f** (95 mg, 99%) as a colorless liquid.

3-Allylcyclohexanone (**28h**).³⁴



TiCl_4 (7.9 mL, 71.78 mmol) was added dropwise over ca 20 min by syringe pump to a stirred and cooled ($-78\text{ }^\circ\text{C}$) solution of 2-cyclohexenone (6.0 g, 62.415 mmol) in CH_2Cl_2 (100 mL). After 5 min, a solution of allyltrimethylsilane (11.0 mL, 68.656 mmol) in CH_2Cl_2 (50 mL) was added dropwise over ca 15 min (syringe pump). Stirring was continued at $-78\text{ }^\circ\text{C}$ for 1.5 h and then the cold bath was replaced by one at $-30\text{ }^\circ\text{C}$, and stirring was continued for 15 min. Water (100 mL) was added and the cold bath was removed. The mixture was extracted with Et_2O (3 x 25 mL) and the combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (4 x 18 cm), using 10% EtOAc-hexane, gave **28h** (6.82 g, 79%) as a viscous oil.

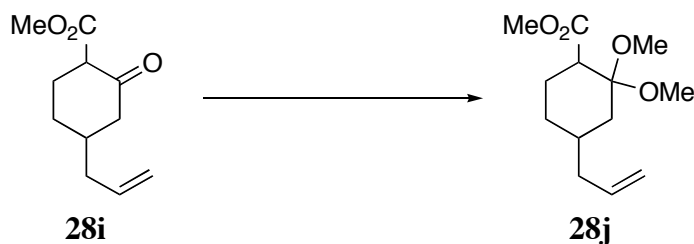
4-Allyl-2-oxocyclohexanecarboxylic Acid Ethyl Ester (**28i**).



A solution of **28h** (1.0 g, 7.235 mmol) in THF (20 mL) was added dropwise over 1 h by syringe pump to a refluxing suspension of NaH (732 mg, 28.94 mmol) and $(\text{MeO})_2\text{CO}$ (1.83 mL, 21.705 mmol) in THF (30 mL). The mixture was refluxed for 2 h, cooled to room temperature

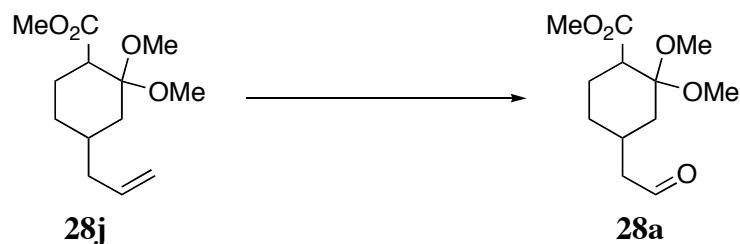
and then to 0 °C (ice bath), and quenched by slow addition of water (5 mL) and saturated aqueous NH_4Cl (20 mL). The cold bath was removed, stirring was continued for 10 min and the mixture was diluted with water (50 mL) and extracted with Et_2O (3 x 25 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (3 x 18 cm), using 15% EtOAc -hexane, gave **28i** (1.26 g, 89%) as a viscous oil which was an inseparable mixture of keto-enol tautomers: FTIR (CH_2Cl_2 cast) 3358, 2923, 2852, 1734, 1463, 1031 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.25 (dtd, J = 13.0, 10.5, 5.5 Hz, 0.8 H, enol form), 1.61-1.86 (m, 2 H), 1.99-2.05 (m, 1.2 H), 2.10-2.22 (m, 3.2 H), 2.36-2.42 (m, 2 H), 3.79 (s, 3 H), 5.06-5.11 (m, 2 H), 5.78-5.86 (m, 1 H), 12.14 (s, 0.8 H, enol form); ^{13}C NMR (CDCl_3 , 125 MHz) (enolic form) δ 21.9 (t), 28.1 (t), 33.1 (d), 35.0 (t), 40.1 (t), 51.3 (q), 97.3 (s), 116.4 (t), 136.2 (d), 171.5 (s), 172.9 (s); exact mass (electrospray) m/z calcd for $\text{C}_{11}\text{H}_{16}\text{NaO}_3$ 219.0992, found 219.0992.

4-Allyl-2,2-dimethoxycyclohexanecarboxylic Acid Ethyl Ester (**28j**).



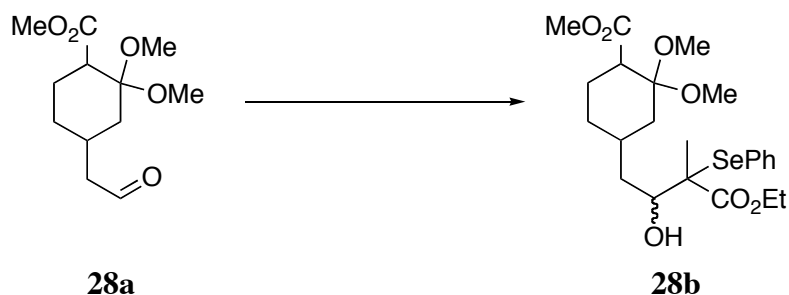
$\text{HC}(\text{OMe})_2$ (1.38 mL, 12.636 mmol) and $p\text{-TsOH}\cdot\text{H}_2\text{O}$ (61 mg, 0.32 mmol) were added to a stirred solution of **28i** (1.24 g, 6.318 mmol) in dry MeOH (25 mL). The mixture was stirred for 4 days and then refluxed for 12 h. The solvent was evaporated and the residue was diluted with CH_2Cl_2 (50 mL). The mixture was quenched with saturated aqueous NaHCO_3 (5 mL), diluted with water (50 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 x 25 cm), using 15% EtOAc -hexane, gave **28j** (1.08 g, 71%) as a viscous oil which was a single isomer: FTIR (CH_2Cl_2 cast) 2950, 2832, 1741, 1641, 1436, 1171, 1051 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.34-1.43 (m, 1 H), 1.47-1.55 (m, 2 H), 1.66-1.80 (m, 3 H), 1.85-1.89 (m, 1 H), 1.96-2.05 (m, 2 H), 2.96-2.98 (m, 1 H), 3.12 (s, 3 H), 3.18 (s, 3 H), 3.65 (s, 3 H), 4.96-5.01 (m, 2 H), 5.76 (ddt, J = 17.5, 10.0, 7.0 Hz, 1 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 25.6 (t), 26.9 (t), 33.6 (d), 34.3 (t), 41.0 (t), 44.8 (d), 47.2 (q), 47.8 (q), 51.4 (q), 100.6 (s), 115.9 (t), 136.8 (d), 172.9 (s); exact mass (electrospray) m/z calcd for $\text{C}_{13}\text{H}_{22}\text{NaO}_4$ 265.1410, found 265.1411.

2,2-Dimethoxy-4-(2-oxoethyl)cyclohexanecarboxylic Acid Ethyl Ester (**28a**).



O₃ was bubbled into a stirred and cooled (-78 °C) solution of **28j** (1.4 g, 5.778 mmol) in CH₂Cl₂ (100 mL) until a blue color persisted (ca 30 min). O₂ was passed through the solution for 30 min and Ph₃P (1.97 g, 7.511 mmol) was then added. The cold bath was removed and stirring was continued for 6 h. Evaporation of the solvent and flash chromatography of the residue over silica gel (3 x 25 cm), using 15% EtOAc-hexane, gave **28a** (1.36 g, 96%) as a viscous oil which was a single isomer: FTIR (CH₂Cl₂ cast) 2952, 2834, 1737, 1436, 1196, 1049 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.46-1.55 (m, 2 H), 1.74-1.82 (m, 3 H), 1.88-1.92 (m, 1 H), 2.07-2.16 (m, 1 H), 2.39 (dd, *J* = 7.0, 1.5 Hz, 2 H), 3.0-3.02 (m, 1 H), 3.188 (s, 3 H), 3.194 (s, 3 H), 3.67 (s, 3 H), 9.78 (t, *J* = 2.0 Hz, 1 H); ¹³C NMR (CDCl₃, 125 MHz) δ 25.4 (t), 26.9 (t), 28.5 (d), 34.4 (t), 44.5 (d), 47.3 (q), 47.8 (q), 50.5 (t), 51.5 (q), 100.0 (s), 172.8 (s), 201.8 (d); exact mass (electrospray) *m/z* calcd for C₁₂H₂₀NaO₅ 267.1203, found 267.1207.

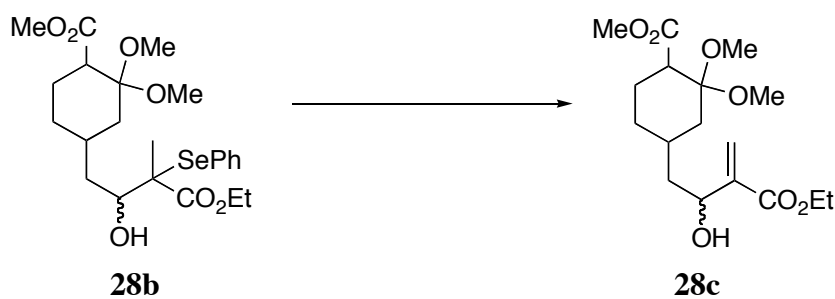
4-[3-Ethoxycarbonyl-2-hydroxy-3-(phenylseleno)butyl]-2,2-dimethoxycyclohexane-carboxylic Acid Ethyl Ester (28b).



n-BuLi (2.5 M in hexane, 3.27 mL, 8.166 mmol) was added dropwise over 3 min to a stirred and cooled (-78 °C) solution of *i*-Pr₂NH (1.27 mL, 8.983 mmol) in THF (20 mL). Stirring at -78 °C was continued for 40 min and a solution of **15** (2.38 g, 9.26 mmol) in THF (8 mL plus 2 mL as a rinse) was added dropwise over 5 min. Stirring was continued for 1.5 h at -78 °C and a solution of **28a** (1.33 g, 5.44 mmol) in THF (8 mL plus 2 mL as a rinse) was added over 5 min. Stirring was continued for 2 h and the mixture was quenched with saturated aqueous NH₄Cl (10 mL). The cold bath was removed, stirring was continued for 15 min and the mixture was diluted

with water (25 mL) and extracted with EtOAc (3 x 15 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 x 22 cm), using 20% EtOAc-hexane, gave **28b** (2.57 g, 94%) as a viscous oil which was an inseparable mixture of diastereoisomers: FTIR (CH_2Cl_2 cast) 3508, 2945, 2831, 1725, 1438, 1051, 744 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.11-1.22 (m, 3 H), 1.37-1.38 (m, 3 H), 1.42-2.03 (m, 8 H), 2.89-3.08 (m, 2 H), 3.15-3.21 (m, 6 H), 3.65-3.68 (m, 3 H), 3.96-4.15 (m, 3 H), 7.28-7.33 (m, 2 H), 7.37-7.42 (m, 1 H), 7.56-7.61 (m, 2 H); exact mass (electrospray) m/z calcd for $\text{C}_{23}\text{H}_{34}\text{NaO}_7^{80}\text{Se}$ 525.1362, found 525.1363.

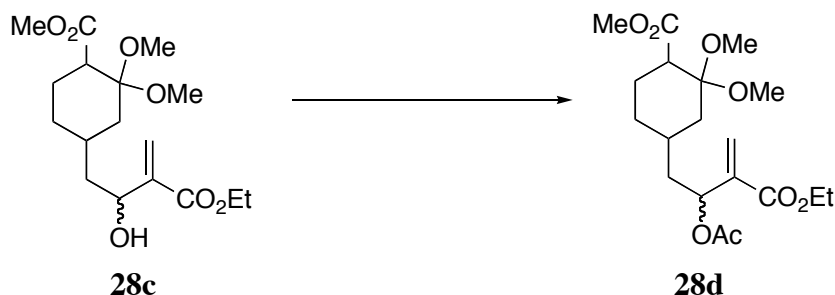
4-(3-Ethoxycarbonyl-2-hydroxybut-3-enyl)-2,2-dimethoxycyclohexanecarboxylic Acid Ethyl Ester (28c).



H_2O_2 (30%, 0.55 mL, 5.38 mmol) was added dropwise over 2 min to a stirred and cooled (-10°C) solution of **28b** (250 mg, 0.498 mmol) in CH_2Cl_2 (5 mL). Stirring was continued at -10°C for 1 h and the mixture was quenched with saturated aqueous NaHCO_3 (1 mL) followed by saturated $\text{Na}_2\text{S}_2\text{O}_3$ (3 mL). The cold bath was removed after 10 min, stirring was continued for 5 min and the mixture was diluted with water (10 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 x 16 cm), using 15% EtOAc-hexane, gave **28c** (168 mg, 98%) as a viscous oil which was a 1:1 inseparable mixture of diastereoisomers which must differ in stereochemistry only at the hydroxyl-bearing carbon: FTIR (CH_2Cl_2 cast) 3476, 2949, 2833, 1738, 1715, 1628, 1436, 1171, 1053 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.32 (t, $J = 7.2$ Hz, 3 H), 1.34-2.04 (m, 9 H), 2.59 (dd, $J = 18.4, 7.2$ Hz, 1 H), 2.99-3.01 (m, 1 H), 3.15 (s, 1.4 H), 3.17 (s, 1.6 H), 3.20 (s, 1.4 H), 3.21 (s, 1.6 H), 3.67 (s, 3 H), 4.21-4.27 (m, 2 H), 4.48-4.55 (m, 1 H), 5.77-5.78 (m, 1 H), 6.207-6.21 (m, 1 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 14.1 (q), 25.6 (t), 25.7 (t), 26.4 (t), 27.9 (t), 30.3 (d), 30.4 (d), 33.9 (t), 35.4 (t), 43.0 (t), 43.4 (t), 44.85 (d), 44.94 (d), 47.27 (q), 47.29 (q), 47.8 (q), 47.82 (q), 51.4 (q), 60.8 (t), 69.2 (d), 69.5 (d), 100.365 (s), 100.373

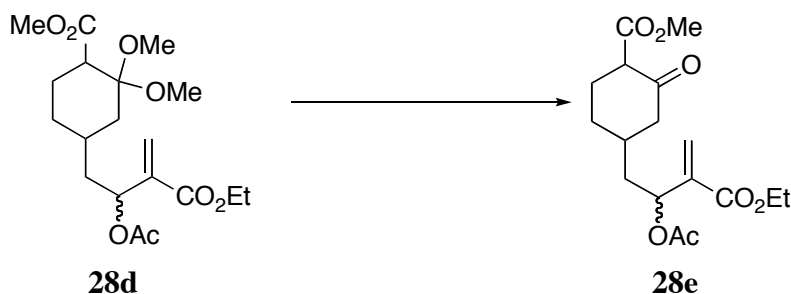
(s), 124.4 (s), 124.5 (s), 143.1 (t), 143.2 (t), 166.55 (s), 166.58 (s), 172.9 (s); exact mass (electrospray) m/z calcd for $C_{17}H_{28}NaO_7$ 367.1727, found 367.1730.

4-(2-Acetoxy-3-ethoxycarbonylbut-3-enyl)-2,2-dimethoxycyclohexanecarboxylic Acid Ethyl Ester (28d).



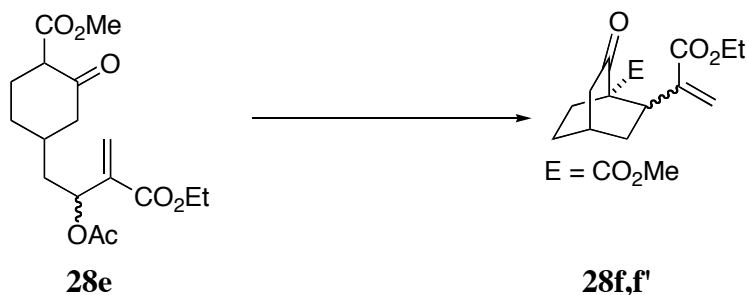
Pyridine (0.7 mL, 8.592 mmol) and AcCl (0.31 mL, 4.296 mmol) were added dropwise to a stirred and cooled (0 °C) solution of **28c** (740 mg, 2.148 mmol) and DMAP (39 mg, 0.322 mmol) in CH_2Cl_2 (10 mL). Stirring at 0 °C was continued for 2 h and the mixture was quenched with water (35 mL), followed by hydrochloric acid (10%, 2 mL). The mixture was extracted with CH_2Cl_2 (3 x 15 mL) and the combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 x 20 cm), using 20% EtOAc-hexane, gave **28d** (736 mg, 89%) as a viscous oil which was an inseparable (1:1) mixture of diastereoisomers which must differ in stereochemistry only at the acetoxy-bearing carbon: FTIR (CH_2Cl_2) 2951, 1742, 1633, 1369, 1235, 957 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) δ 1.27-1.31 (m, 3 H), 1.34-1.48 (m, 1.5 H), 1.52-1.83 (m, 7 H), 1.95-1.99 (m, 0.5 H), 2.06 (s, 1.5 H), 2.07 (s, 1.5 H), 2.94-2.98 (m, 1 H), 3.09 (s, 1.5 H), 3.12 (s, 1.5 H), 3.17 (s, 1.5 H), 3.18 (s, 1.5 H), 3.648 (s, 1.5 H), 3.65 (s, 1.5 H), 4.15-4.27 (m, 2 H), 5.68-5.72 (m, 2 H), 6.23-6.25 (m, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1 (q), 14.13 (q), 21.1 (q), 25.5 (t), 25.6 (t), 26.3 (t), 27.5 (t), 30.5 (d), 30.7 (d), 33.9 (t), 35.2 (t), 41.5 (t), 41.7 (t), 44.6 (d), 44.9 (d), 47.1 (q), 47.2 (q), 47.77 (q), 47.80 (q), 51.4 (q), 60.9 (t), 69.9 (d), 69.95 (d), 100.2 (s), 100.3 (s), 124.3 (s), 124.5 (s), 140.95 (t), 140.99 (t), 165.1 (s), 169.83 (s), 169.89 (s), 172.8 (s); exact mass (electrospray) m/z calcd for $C_{19}H_{30}NaO_8$ 409.1833, found 409.1835.

4-(2-Acetoxy-3-ethoxycarbonylbut-3-enyl)-2-oxocyclohexanecarboxylic Acid Ethyl Ester (28e).



A mixture of **28d** (700 mg, 1.811 mmol) and Amberlyst-15 (1.5 g) in acetone (reagent grade, 10 mL) was stirred at room temperature for 1.5 h and then filtered through a pad of silica gel (2 x 4 cm), using EtOAc (30 mL). Evaporation of the filtrate and flash chromatography of the residue over silica gel (2 x 20 cm), using 20% EtOAc-hexane, gave **28e** (605 mg, 98%) as an equilibrium mixture of keto-enol tautomers: FTIR (CH_2Cl_2) 2983, 2938, 1745, 1716, 1659, 1621, 1443, 1222, 1027 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.26-1.34 (m, 3 H), 1.64-2.66 (m, 11 H), 3.33-3.38 (m, 0.4 H), 3.70-3.77 (m, 3 H), 4.11-4.30 (m, 2 H), 5.61-5.81 (m, 2 H), 6.26-6.33 (m, 1 H), 12.08 (s, 0.25 H), 12.09 (s, 0.25 H); exact mass (electrospray) m/z calcd for $\text{C}_{17}\text{H}_{24}\text{NaO}_7$ 363.1414, found 363.1412.

2-(1-Ethoxycarbonylvinyl)-6-oxobicyclo[2.2.2]octane-1-carboxylic Acid Methyl Ester (28f,f').



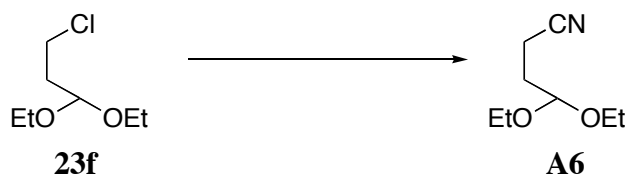
(a) DBU (0.1 mL, 0.68 mmol) was added dropwise to a stirred solution of **28e** (116 mg, 0.34 mmol) in MeCN (5 mL). Stirring was continued for 1 h and the mixture was then filtered through a pad of silica gel (2 x 2 cm), using 60% EtOAc-hexane (60 mL). Evaporation of the filtrate and flash chromatography of the residue over silica gel (2 x 20 cm), using 10% EtOAc-hexane, gave **28f** (12 mg, 13%) and **28f'** (66 mg, 69%) as viscous oils. Compound **28f'** had: FTIR (CH_2Cl_2) 2951, 2876, 1721, 1626, 1262 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.29 (t, $J = 7.5$ Hz, 3 H), 1.66 (ddt, $J = 13.5, 8.0, 2.0$ Hz, 1 H), 1.74-1.80 (m, 2 H), 2.11-2.25 (m, 4 H), 2.38 (dt, $J = 19.0, 3.0$ Hz, 1 H), 2.48 (dt, $J = 18.5, 3.0$ Hz, 1 H), 3.31 (dd, $J = 11.0, 7.5$ Hz, 1 H), 3.63 (s, 3

H), 4.14-4.25 (m, 2 H), 5.38 (s, 1 H), 6.10 (s, 1 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 14.2 (q), 23.8 (t), 27.6 (d), 29.1 (t), 34.6 (t), 41.8 (d), 44.6 (t), 51.7 (q), 57.9 (s), 60.7 (t), 123.9 (s), 143.7 (t), 166.6 (s), 170.9 (s), 208.2 (s); exact mass (electrospray) m/z calcd for $\text{C}_{15}\text{H}_{20}\text{NaO}_5$ 303.1203, found 303.1203.

The minor isomer (**28f**) was not obtained pure, a small signal at δ 6.95 ppm indicated the presence of **28g** (ca 3% yield).

(b) Cs_2CO_3 (48.9 mg, 0.15 mmol) was added to a stirred solution of **28e** (25.5 mg, 0.075 mmol) in dry MeCN (1.5 mL) and the mixture was heated at 80 °C for 30 min, cooled, and filtered through a pad (0.5 cm x 4 cm) of Celite in a Pasteur pipette, using EtOAc. Evaporation of the solvent and flash chromatography of the residue over silica gel (0.5 x 4.5 cm) in a Pasteur pipette, using 1:5 EtOAc-hexane, and then 2:5 EtOAc-hexane, gave **28g** (2.4 mg, 11%): FTIR (CH_2Cl_2) 2953, 1744, 1712, 1645, 1433 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.28 (t, $J = 7.5$ Hz, 3 H), 1.83 (dddd, $J = 16.0, 8.5, 8.0, 2.0, 1.5$ Hz, 1 H), 1.98 (ddd, $J = 14.0, 7.5, 3.5$ Hz, 1 H), 2.17 (dq, $J = 14.0, 8.8, 3.3$ Hz, 1 H), 2.27 (ddd, $J = 16.0, 2.0, 1.5$ Hz, 1 H), 2.41-2.54 (m, 2 H), 2.57-2.64 (m, 1 H), 2.64-2.70 (m, 2 H), 2.72-2.73 (m, 1 H), 3.58 (d, $J = 17.5$ Hz, 1 H), 3.72 (s, 3 H), 4.18 (q, $J = 7.5$ Hz, 2 H), 6.94 (td, $J = 5.8, 1.5$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 14.2 (q), 23.8 (t), 27.2 (d), 30.1 (t), 33.1 (t), 37.0 (t), 42.7 (t), 52.7 (q), 58.3 (s), 61.1 (t), 129.6 (s), 138.6 (d), 167.9 (s), 173.2 (s), 210.3 (s); exact mass (electrospray) m/z calcd for $\text{C}_{15}\text{H}_{20}\text{NaO}_5$ 303.1203, found 303.1203.

4,4-Diethoxybutyronitrile (**A6**).⁴¹



A solution of **23f** (2.00 g, 12.0 mmol) in dry DMSO (3 mL) was added to a stirred mixture of NaCN (2.94 mg, 60.0 mmol) and Bu_4NI (443.0 mg, 1.20 mmol) in DMSO (30 mL), and the resulting mixture was stirred at 50 °C for 15 h, cooled to room temperature, diluted with water (120 mL) and extracted with EtOAc (3 x 50 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (4 x 15 cm), using 8:25 EtOAc-hexane, gave 4,4-diethoxybutyronitrile (**A6**) (1.76 g, 94%) as a liquid: ^1H NMR (CDCl_3 , 400 MHz) δ 1.22 (t, $J = 7.2$ Hz, 6 H), 1.95 (td, $J = 7.2, 4.2$ Hz, 2 H), 2.44 (t, $J = 7.2$ Hz, 2 H), 3.53 (dq, $J = 9.6, 7.2$ Hz, 2 H), 3.69 (dq, $J = 9.6, 7.2$ Hz, 2

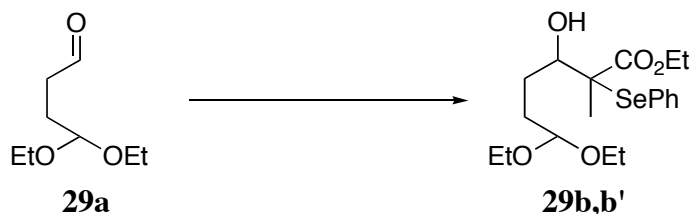
H), 4.59 (t, $J = 5.6$ Hz, 1 H; ^{13}C NMR (CDCl_3 , 100 MHz) δ 12.5 (t), 15.2 (q), 29.6 (t), 62.4 (t), 100.8 (d), 119.5 (s).

4,4-Diethoxybutyraldehyde (29a).³⁵



DIBAL-H (1.0 M in CH_2Cl_2 , 1.93 mL, 1.93 mmol) was added dropwise to stirred and cooled (-78°C , dry ice, acetone) solution of 4,4-diethoxybutyronitrile (202.0 mg, 1.29 mmol) in CH_2Cl_2 . The dry-ice (but not the acetone) was removed from the cold bath, and stirring was continued for 1 h, by which time the mixture had reached room temperature. Acetone (0.3 mL), EtOAc (0.3 mL) and pH 7.0 buffer (0.3 mL) were added sequentially, and the mixture was stirred vigorously for 20 min. Na_2SO_4 was added and stirring was continued for 3 h. The solid was filtered off, and the solvent was evaporated. Flash chromatography of the residue over silica gel (1.5 x 15 cm), using 1:4 EtOAc-hexane, gave **29a** (140 mg, 68%) as a liquid: ^1H NMR (CDCl_3 , 400 MHz) δ 1.16 (t, $J = 7.2$ Hz, 6 H), 1.93 (td, $J = 7.2, 5.6$ Hz, 2 H), 2.49 (td, $J = 7.2, 1.6$ Hz, 2 H), 3.45 (dq, $J = 9.6, 7.2$ Hz, 2 H), 3.62 (dq, $J = 9.6, 7.2$ Hz, 2 H), 4.47 (t, $J = 5.6$ Hz, 1 H), 9.74 (t, $J = 1.6$ Hz, 1 H).

6,6-Diethoxy-3-hydroxy-2-methyl-2-(phenylseleno)hexanoic Acid Ethyl Ester (29b,b').



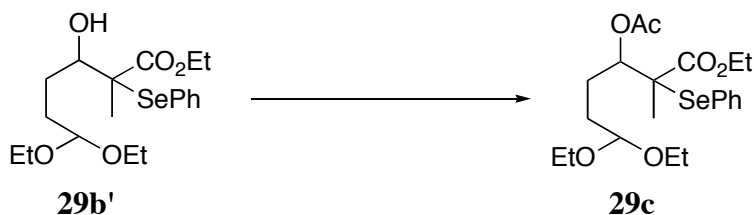
$n\text{-BuLi}$ (1.5 M in hexane, 0.65 mL, 0.98 mmol) was added dropwise to a stirred and cooled (0°C) solution of $i\text{-Pr}_2\text{NH}$ (98.7 mg, 0.98 mmol) in THF (5 mL). Stirring at 0°C was continued for 15 min, the mixture was cooled to -78°C , and a solution of **15** (252 mg, 0.98 mmol) in THF (3 mL) was added dropwise. Stirring at -78°C was continued for 1 h, and a solution of **29a** (120 mg, 0.75 mmol) in THF (2 mL) was added dropwise. Stirring at -78°C was

continued for 40 min, and the mixture was quenched with saturated aqueous NH_4Cl (5 mL). The cold bath was removed, stirring was continued for 15 min and the mixture was diluted with water (40 mL). The aqueous phase was extracted with EtOAc (3 x 20 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 x 15 cm), using 13:50 EtOAc-hexane, gave **29b** (less polar isomer) (64 mg, 21%) as a viscous oil and **29b'** (more polar isomer) (132 mg, 42%) as a viscous oil.

Compound **29b** had: FTIR (CH_2Cl_2 cast) 3505, 3058, 2976, 2931, 2877, 1720, 1476, 1439 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.13 (t, $J = 7.1$ Hz, 3 H), 1.18 (t, $J = 7.1$ Hz, 3 H), 1.18 (t, $J = 7.0$ Hz, 3 H), 1.42 (s, 3 H), 1.42-1.50 (m, 1 H), 1.53-1.63 (m, 1 H), 1.65-1.73 (m, 1 H), 1.91 (dddd, $J = 14.3, 9.0, 5.4, 5.4$ Hz, 1 H), 3.21 (s, 1 H), 3.47 (dq, $J = 9.4, 7.1$ Hz, 2 H), 3.62 (dq, $J = 10.1, 7.1, 3.1$ Hz, 2 H), 3.91 (dd, $J = 9.9, 2.2$ Hz, 1 H), 3.94-4.10 (m, 2 H), 4.49 (dd, $J = 5.5, 5.5$ Hz, 1 H), 7.28-7.32 (m, 2 H), 7.37-7.41 (m, 1 H), 7.59-7.62 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.8 (q), 15.3 (q), 17.1 (q), 27.0 (t), 31.0 (t), 57.3 (s), 61.0 (t), 61.1 (t), 61.2 (t), 73.1 (d), 102.6 (d), 126.6 (s), 128.8 (d), 129.4 (d), 138.1 (d), 173.1 (s); exact mass m/z calcd for $\text{C}_{19}\text{H}_{30}\text{O}_5^{80}\text{Se}$ 418.1259, found 418.1246.

Compound **29b'** had: FTIR (CH_2Cl_2 cast) 3492, 3058, 2976, 2932, 2878, 1724, 1579, 1477, 1439 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.18-1.23 (m, 9 H), 1.42 (s, 3 H), 1.44-1.50 (m, 1 H), 1.66-1.74 (m, 1 H), 1.93 (dddd, $J = 9.7, 9.7, 5.2, 5.2$ Hz, 1 H), 1.96-2.05 (m, 1 H), 2.99 (s, 1 H), 3.51 (dq, $J = 9.4, 7.1$ Hz, 2 H), 3.66 (dq, $J = 9.4, 7.1$ Hz, 2 H), 3.89 (dd, $J = 10.7, 1.1$ Hz, 1 H), 4.10 (q, $J = 7.1$ Hz, 2 H), 4.54 (dd, $J = 5.4, 5.4$ Hz, 1 H), 7.28-7.32 (m, 2 H), 7.37-7.41 (m, 1 H), 7.57-7.59 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.9 (q), 15.3 (q), 18.2 (q), 26.6 (t), 30.9 (t), 54.7 (s), 61.0 (t), 61.2 (t), 61.3 (t), 73.3 (d), 102.7 (d), 126.7 (s), 128.8 (d), 129.4 (d), 138.1 (d), 174.0 (s); exact mass m/z calcd for $\text{C}_{19}\text{H}_{30}\text{O}_5^{80}\text{Se}$ 418.1259, found 418.1255.

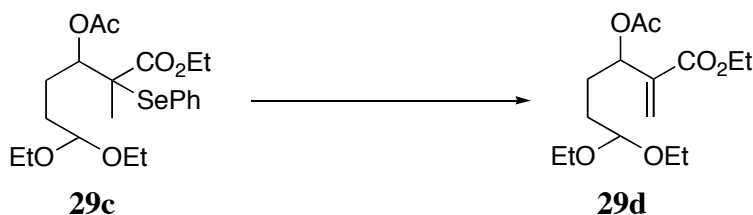
3-Acetoxy-6,6-diethoxy-2-methyl-2-(phenylseleno)hexanoic Acid Ethyl Ester (**29c**).



Pyridine (500 mg, 6.33 mmol) and AcCl (249 mg, 3.17 mmol) were added sequentially to a stirred and cooled ($-10\text{ }^{\circ}\text{C}$, ice-acetone bath) solution of **29b'** (440 mg, 1.06 mmol) and DMAP (13 mg, 0.11 mmol) in CH_2Cl_2 (3 mL). The cold bath was left in place but not recharged and stirring was continued for 6 h, by which time the temperature had risen to room temperature.

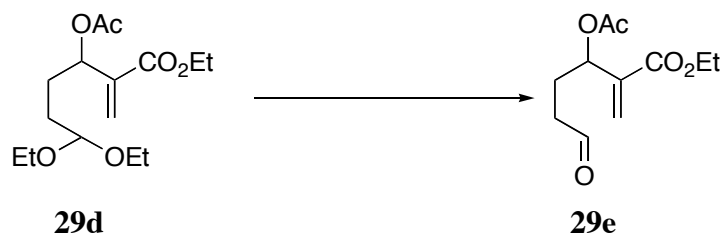
The mixture was diluted with water (10 mL), acidified with saturated aqueous NH_4Cl (5 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm), using 11:50 EtOAc-hexane, gave **29c** (400 mg, 82%) as an oil: FTIR (CH_2Cl_2 cast) 3058, 2977, 2933, 2877, 1747, 1727, 1578, 1477, 1439 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.08 (t, $J = 7.1$ Hz, 3 H), 1.221 (t, $J = 7.1$ Hz, 3 H), 1.222 (t, $J = 7.1$ Hz, 3 H), 1.50 (s, 3 H), 1.59-1.71 (m, 3 H), 1.93 (s, 3 H), 2.18-2.28 (m, 1 H), 3.51 (dq, $J = 9.4, 7.0, 4.8$ Hz, 2 H), 3.66 (dq, $J = 9.4, 7.1$ Hz, 2 H), 3.88 (dq, $J = 10.7, 7.1$ Hz, 1 H), 4.01 (dq, $J = 10.7, 7.1$ Hz, 1 H), 4.53 (dd, $J = 5.3, 5.3$ Hz, 1 H), 5.43-5.45 (m, 1 H), 7.29-7.32 (m, 2 H), 7.37-7.41 (m, 1 H), 7.59-7.61 (m, 2 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 13.8 (q), 15.3 (q), 17.8 (q), 20.9 (q), 25.5 (t), 30.5 (t), 53.0 (s), 61.1 (t), 61.2 (t), 61.3 (t), 75.6 (d), 102.4 (d), 126.3 (s), 128.9 (d), 129.5 (d), 138.0 (d), 169.6 (s), 172.1 (s); exact mass m/z calcd for $\text{C}_{21}\text{H}_{32}\text{O}_6$ ^{80}Se 460.1364, found 460.1361.

2-(1-Acetoxy-4,4-diethoxybutyl)acrylic Acid Ethyl Ester (29d).



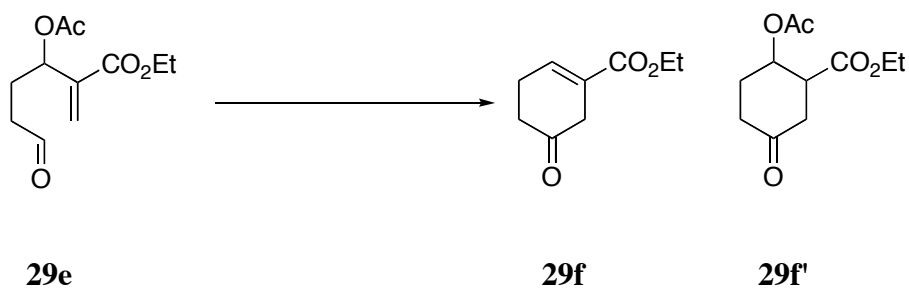
H_2O_2 (30%, 0.95 mL, 9.3 mmol) was added dropwise to a stirred and cooled (0 °C) solution of **29c** (421 mg, 0.92 mmol) in CH_2Cl_2 (5 mL). Stirring was continued at 0 °C for 40 min and the mixture was quenched with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (4 mL). The mixture was stirred at 0 °C for 5 min, the ice bath was removed, stirring was continued for 5 min and the mixture was diluted with water (10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 10 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1.5 x 15 cm), using 23:100 EtOAc-hexane, gave **29d** (260 mg, 94%) as a oil: FTIR (CDCl_3 cast) 2977, 2933, 2878, 1747, 1719, 1633, 1446 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.18 (t, $J = 7.1$ Hz, 6 H), 1.29 (t, $J = 7.1$ Hz, 3 H), 1.58-1.77 (m, 3 H), 1.82-1.90 (m, 1 H), 2.06 (s, 3 H), 3.47 (dq, $J = 9.4, 7.1$ Hz, 2 H), 3.61 (dq, $J = 9.3, 7.0, 0.6$ Hz, 2 H), 4.16-4.27 (m, 2 H), 4.47 (dd, $J = 5.6, 5.6$ Hz, 1 H), 5.63 (ddd, $J = 7.7, 4.5, 0.8$ Hz, 1 H), 5.74 (dd, $J = 1.1, 1.1$ Hz, 1 H), 6.27 (s, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.1 (q), 15.3 (q), 21.0 (q), 29.2 (t), 29.3 (t), 60.9 (t), 61.11 (t), 61.14 (t), 71.4 (d), 102.4 (d), 125.0 (t), 140.1 (s), 165.2 (s), 169.8 (s); exact mass (electrospray) m/z calcd for $\text{C}_{15}\text{H}_{26}\text{NaO}_6$ 325.1622, found 325.1620.

2-(1-Acetoxy-4-oxobutyl)acrylic Acid Ethyl Ester (29e).



Hydrochloric acid (4 M, 0.11 mL, 0.42 mmol) was added to a stirred solution of **29d** (128 mg, 0.42 mmol) in acetone (4 mL), and stirring was continued at room temperature for 1.5 h. The mixture was diluted with water (20 mL) and the aqueous phase was extracted with Et₂O (3 x 10 mL). The combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (1 x 15 cm), using 2:5 EtOAc-hexane, gave **29e** (90 mg, 94%) as a liquid: FTIR (CH₂Cl₂ cast) 2983, 2939, 2830, 2728, 1745, 1723, 1634, 1446 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.31 (t, *J* = 7.1 Hz, 3 H), 2.04 (dddd, *J* = 14.7, 14.7, 7.5, 7.5 Hz, 1 H), 2.07 (s, 3 H), 2.17 (dddd, *J* = 11.7, 7.4, 7.3, 4.4 Hz, 1 H), 2.50 (td, *J* = 7.5, 1.4 Hz, 2 H), 4.18-4.29 (m, 2 H), 5.65 (ddd, *J* = 7.6, 4.4, 1.2 Hz, 1 H), 5.76 (t, *J* = 1.0, 1.0 Hz, 1 H), 6.32 (s, 1 H), 7.53 (t, *J* = 1.2 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.1 (q), 21.0 (q), 26.5 (t), 39.6 (t), 61.1 (t), 70.8 (d), 125.4 (t), 139.5 (s), 164.9 (s), 169.6 (s), 201.0 (d); exact mass (electrospray) *m/z* calcd for C₁₁H₁₆NaO₅ 251.0890, found 251.0888.

5-Oxocyclohex-1-enecarboxylic Acid Ethyl Ester (29f) and 2-Acetoxy-5-oxocyclohexanecarboxylic Acid Ethyl Ester (29f').



Et₃N (26.6 mg, 0.263 mmol) was added to a solution of **29e** (40 mg, 0.175 mmol) and 3-benzyl-5-(2-hydroxyethyl)-4-methylthiazolium chloride (**45**) (4.7 mg, 0.018 mmol) in 1,4-dioxane (0.4 mL) contained in a thick-walled vial. The vial was closed with a Teflon-lined screw-on cap and the mixture was stirred at 70 °C for 10 h, cooled to room temperature, diluted with water (5 mL) and extracted with EtOAc (3 x 5 mL). The combined organic extracts were

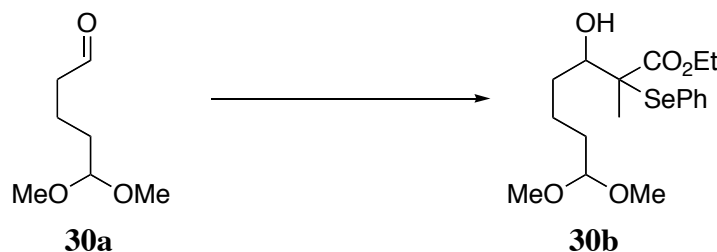
washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (0.7 x 15 cm), using 1:4 EtOAc-hexane, gave a 2:3 mixture of **29f** and **29f'** (25 mg, 86%) as an oil.

DBU (61.1 mg, 0.4 mmol) was added to a solution of the above 2:3 mixture in MeCN (0.5 ml). The mixture was stirred at 50 °C overnight, cooled to room temperature, diluted with water (5 mL) and acidified with hydrochloric acid (1 M, 1 mL). The aqueous phase was extracted with EtOAc (3 x 5 mL) and the combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (0.7 x 7 cm), using 1:4 EtOAc-hexane, gave the acetate **29f'** (ca 1 mg, 3.5%) as an oil (and no **29f**): FTIR (CHCl_3 cast) 2985, 2942, 1739, 1720, 1655, 1448 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 1.24-1.28 (m, 5 H), 1.93-2.06 (m, 1 H), 2.08 (s, 3 H), 2.36-2.51 (m, 4 H), 4.11-4.27 (m, 2 H), 5.65-5.69 (m, 1 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 13.49 (q), 13.99 (q), 20.71 (d), 26.06 (t), 35.30 (t), 60.05 (t), 61.87 (t), 76.54 (d), 170.01 (s), 170.14 (s), 211.60 (s); exact mass (electrospray) m/z calcd for $\text{C}_{11}\text{H}_{16}\text{NaO}_5$ 251.0890, found 251.0891.

The above experiment was done in an attempt to establish if **29f** is derived from **29f'**; it appears, however, that **29f** is not stable for a prolonged time under these conditions, and all we accomplished by this experiment was the isolation of pure **29f'**.

By subtracting the signals of **29f'** from the NMR spectrum of the mixture of **29f** and **29f'**, it was possible to identify the NMR signals of **29f**: ^1H NMR (CDCl_3 , 400 MHz) δ 1.29 (td, $J = 7.1, 0.5$ Hz, 3 H), 2.37-2.50 (m, 2 H), 2.61-2.66 (m, 2 H), 3.14 (dd, $J = 2.1, 2.1$ Hz, 2 H), 4.08-4.24 (m, 2 H), 7.16 (dddd, $J = 4.0, 4.0, 1.9, 1.9$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.2 (q), 25.1 (t), 37.3 (t), 39.0 (t), 60.8 (t), 128.7 (s), 137.9 (d), 165.7 (s), 208.2 (s).

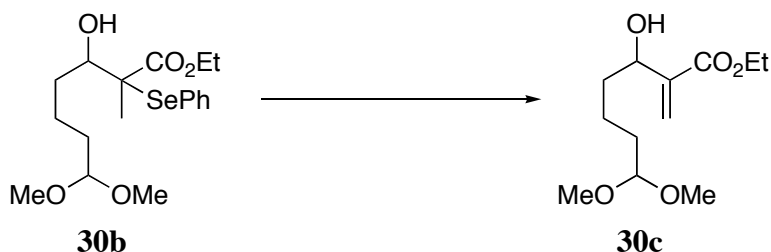
3-Hydroxy-7,7-dimethoxy-2-methyl-2-(phenylseleno)heptanoic Acid Ethyl Ester (**30b**).



n-BuLi (2.5 M in hexane, 9.03 mL, 22.57 mmol) was added dropwise over 5 min to a stirred and cooled (-78 °C) solution of *i*-Pr₂NH (3.47 mL, 24.624 mmol) in THF (50 mL). Stirring was continued for 45 min and a solution of **15** (6.07 g, 23.6 mmol) in THF (15 mL plus

2 mL as a rinse) was added over 10 min. Stirring at $-78\text{ }^{\circ}\text{C}$ was continued for 3 h and a solution of **30a**³⁶ (3.0 g, 20.52 mmol) in THF (15 mL plus 2 mL as a rinse) was added dropwise over 10 min. The mixture was stirred for 1.5 h, and quenched with water (10 mL) and saturated aqueous NH_4Cl (15 mL). The cold bath was removed, stirring was continued for 10 min and the mixture was diluted with water (100 mL) and extracted with EtOAc (3 x 25 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (3 x 20 cm), using 20% EtOAc-hexane, gave **30b** (8.02 g, 97%) as a viscous oil which was a 60:40 mixture of diastereoisomers: FTIR (CH_2Cl_2 cast) 3477, 2980, 2947, 2830, 1721, 1250, 1129, 744 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 1.14 (t, $J = 7.0$ Hz, 1.2 H), 1.21 (t, $J = 7.0$ Hz, 1.8 H), 1.32-1.44 (m, 5.4 H), 1.52-1.71 (m, 4 H), 1.87-1.92 (m, 0.6 H), 2.82 (d, $J = 7.0$ Hz, 0.6 H), 2.97 (dd, $J = 3.0, 1.5$ Hz, 0.4 H), 3.30-3.33 (m, 6 H), 3.85-3.90 (m, 1 H), 3.96-4.14 (m, 2 H), 4.33-4.40 (m, 1 H), 7.29-7.33 (m, 2 H), 7.38-7.42 (m, 1 H), 7.56-7.60 (m, 2 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 13.8 (q), 14.0 (q), 17.0 (q), 18.2 (q), 21.99 (t), 22.01 (t), 31.2 (t), 31.6 (t), 32.27 (t), 32.34 (t), 52.64 (q), 52.69 (q), 52.74 (q), 52.81 (q), 54.8 (s), 57.5 (s), 61.0 (t), 61.2 (t), 72.8 (d), 75.2 (d), 104.48 (d), 104.53 (d), 126.5 (s), 126.6 (s), 128.77 (d), 128.83 (d), 129.36 (d), 129.44 (d), 138.04 (d), 138.07 (d), 173.1 (s), 174.0 (s); exact mass (electrospray) m/z calcd for $\text{C}_{18}\text{H}_{28}\text{NaO}_5^{80}\text{Se}$ 427.0994, found 427.0997.

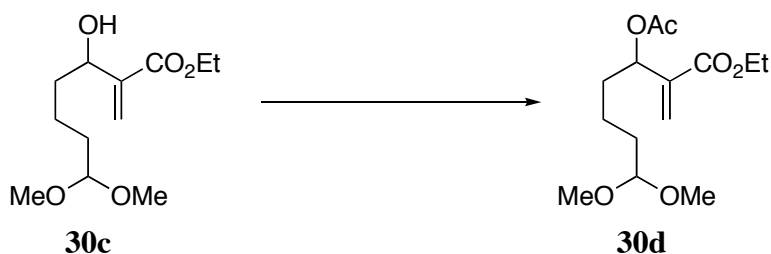
2-(1-Hydroxy-5,5-dimethoxypentyl)acrylic Acid Ethyl Ester (30c).



H_2O_2 (30%, 5 mL, 49 mmol) was added dropwise over 2 min to a stirred and cooled ($-10\text{ }^{\circ}\text{C}$) solution of **30b** (2.0 g, 4.958 mmol) in CH_2Cl_2 (20 mL). Stirring at $-10\text{ }^{\circ}\text{C}$ was continued for 1 h and the mixture was quenched with saturated aqueous NaHCO_3 (8 mL), followed by dropwise addition of saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (8 mL). The cold bath was removed after 10 min, stirring was continued for 5 min and the mixture was diluted with water (30 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 x 18 cm), using 15% EtOAc-hexane, gave **30c** (1.2 g, 98%) as a viscous oil: FTIR (CH_2Cl_2 cast) 3454, 2983, 2948, 2832, 1714, 1629, 1128, 954 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.31 (t, $J = 7.2$ Hz, 3 H), 1.36-1.73

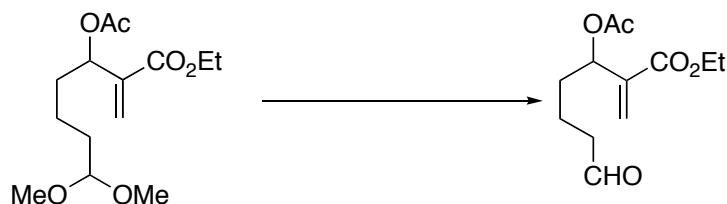
(m, 6 H), 2.68 (d, $J = 6.8$ Hz, 1 H), 3.304 (s, 3 H), 3.307 (s, 3 H), 4.23 (q, $J = 7.2$ Hz, 2 H), 4.36 (t, $J = 5.6$ Hz, 1 H), 4.36-4.41 (m, 1 H), 4.778-4.783 (m, 1 H), 6.22 (d, $J = 0.8$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.0 (q), 20.9 (t), 32.1 (t), 35.8 (t), 52.6 (q), 52.7 (q), 60.7 (t), 71.5 (d), 104.4 (d), 124.6 (s), 142.5 (t), 166.4 (s); exact mass (electrospray) m/z calcd for $\text{C}_{12}\text{H}_{22}\text{NaO}_5$ 269.1359, found 269.1356.

2-(1-Acetoxy-5,5-dimethoxypentyl)acrylic Acid Ethyl Ester (30d).



Pyridine (1.56 mL, 19.324 mmol) and AcCl (0.51 mL, 7.23 mmol) were added dropwise over ca 5 min to a stirred and cooled ($0\text{ }^{\circ}\text{C}$) solution of **30c** (1.19 g, 4.831 mmol) and DMAP (90 mg, 0.73 mmol) in CH_2Cl_2 (20 mL). Stirring at $0\text{ }^{\circ}\text{C}$ was continued for 1 h and the mixture was quenched with water (5 mL). The cold bath was removed, stirring was continued for 10 min and the mixture was diluted with water (15 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (3 x 16 cm), using 20% EtOAc -hexane, gave **30d** (1.292 g, 93%) as a viscous oil: FTIR (CH_2Cl_2 cast) 2983, 2947, 2831, 1746, 1719, 1633, 1240, 956 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.31 (t, $J = 7.2$ Hz, 3 H), 1.34-1.47 (m, 2 H), 1.54-1.84 (m, 4 H), 2.08 (s, 3 H), 3.309 (s, 3 H), 3.311 (s, 3 H), 4.18-4.29 (m, 2 H), 4.34 (t, $J = 5.6$ Hz, 1 H), 5.62 (dd, $J = 8.0$, 4.4 Hz, 1 H), 5.74-5.75 (m, 1 H), 6.281-6.283 (m, 1 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 14.1 (q), 20.4 (t), 21.1 (q), 32.1 (t), 34.0 (t), 52.7 (q), 52.8 (q), 60.9 (t), 71.7 (d), 104.3 (s), 124.8 (s), 140.2 (t), 165.2 (s), 169.9 (s); exact mass (electrospray) m/z calcd for $\text{C}_{14}\text{H}_{24}\text{NaO}_6$ 311.1465, found 311.1460.

2-(1-Acetoxy-5-oxopentyl)acrylic Acid Ethyl Ester (30e).



30d**30e**

Hydrochloric acid (10%, 4 mL) was added to a stirred and cooled (0 °C) solution of **30d** (650 mg, 2.254 mmol) in THF (12 mL). The ice bath was removed after 2 h, stirring was continued for 3 h and the mixture was diluted with water (30 mL) and extracted with EtOAc (3 x 10 mL). The combined organic extracts were dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (2 x 2 cm), using 50% EtOAc-hexane (80 mL), gave **30e** (525 mg, 96%) as a colorless liquid: FTIR (CH₂Cl₂ cast) 2941, 1743, 1372, 1235, 1029 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.29 (t, *J* = 7.2 Hz, 3 H), 1.56-1.83 (m, 4 H), 2.07 (s, 3 H), 2.40-2.53 (m, 2 H), 4.15-4.27 (m, 2 H), 5.59-5.62 (m, 1 H), 5.75 (t, *J* = 1.2 Hz, 1 H), 6.27 (t, *J* = 0.4 Hz, 1 H), 9.74 (t, *J* = 1.6 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.1 (q), 17.8 (t), 21.0 (q), 33.5 (t), 43.2 (t), 60.9 (t), 71.2 (d), 125.0 (s), 139.9 (t), 165.1 (s), 169.8 (s), 201.7 (d); exact mass (electrospray) *m/z* calcd for C₁₂H₁₈NaO₅ 265.1047, found 265.1045.

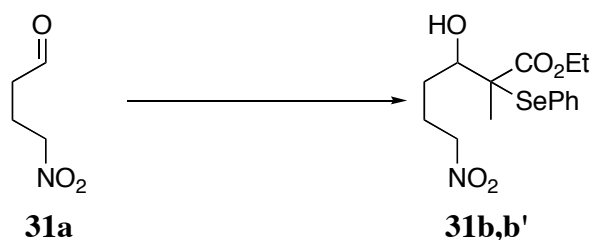
5-Formylcyclohex-1-enecarboxylic Acid Ethyl Ester (30f).**(a) Use of pyrrolidine**

A solution of pyrrolidine (4 mg, 0.06 mmol) in PhH (2 mL) was added over 1 min to a stirred solution of **30e** (150 mg, 0.619 mmol) in PhH (1 mL). The reaction flask was lowered into a preheated oil bath and the mixture was refluxed for 18 h. Evaporation of the solvent and flash chromatography of the residue over silica gel (0.5 x 8 cm), using 20% EtOAc-hexane, gave **30f** (36 mg, 32%) as a viscous liquid: FTIR (CH₂Cl₂ cast) 2982, 2933, 2714, 1711, 1651, 1251, 1089, 720 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.29 (t, *J* = 7.5 Hz, 3 H), 1.63-1.7 (m, 1 H), 1.95-2.01 (m, 1 H), 2.22-2.37 (m, 2 H), 2.42-2.61 (m, 3 H), 4.20 (q, *J* = 7.5 Hz, 2 H), 6.98-7.0 (m, 1 H), 9.72 (br s, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.2 (q), 21.0 (t), 23.4 (t), 24.2 (t), 45.6 (d), 60.4 (t), 128.5 (s), 138.9 (d), 166.7 (s), 203.2 (d); exact mass (electrospray) *m/z* calcd for C₁₀H₁₄NaO₃ 205.0835, found 205.0836.

(b) Use of proline-derived catalyst 46

A solution of the proline-derived catalyst **46**¹⁸ (15 mg, 0.046 mmol) in dry MeCN (3 mL) was added to a stirred solution of **30e** (68 mg, 0.28 mmol) in MeCN (1 mL). The reaction flask was lowered into a preheated oil bath and the mixture was refluxed for 15 h, cooled to room temperature and filtered through a pad of silica gel (2 x 2 cm), using 60% EtOAc-hexane (60 mL). Evaporation of the solvent and flash chromatography of the residue over silica gel (0.5 x 8 cm), using 10% EtOAc-hexane, gave **30f** (27 mg, 53%, 69% after correction for recovered **30e**) as a viscous liquid and **30e** (16 mg, 24%) as pure (¹H NMR) viscous oils. Compound **30f** had: $[\alpha]_D -0.64$ (CH₂Cl₂, c 0.5 g/100).

3-Hydroxy-2-methyl-6-nitro-2-(phenylseleno)hexanoic Acid Ethyl Ester (**31b,b'**).



n-BuLi (1.6 M in hexane, 1.04 mL, 1.67 mmol) was added dropwise to a stirred and cooled (-78 °C) solution of *i*-Pr₂NH (168.7 mg, 1.67 mmol) in THF (8 mL). Stirring at -78 °C was continued for 1 h, and a solution of **15** (429.0 mg, 1.67 mmol) in THF (1 mL) was then added dropwise. Stirring at -78 °C was continued for 85 min, and a solution of **31a**³⁷ (150 mg, 1.28 mmol) in THF (1 mL) was added dropwise. Stirring at -78 °C was continued for 40 min, and the mixture was quenched with saturated aqueous NH₄Cl (10 mL). The cold bath was removed, stirring was continued for 15 min, the mixture was diluted with water (30 mL) and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm), using 1:2 EtOAc-hexane, gave **31b** (less polar isomer) (91 mg, 19%) as a viscous oil and **31b'** (more polar isomer) (160 mg, 33%) as a viscous oil.

Compound **31b** had: FTIR (CDCl₃ cast) 3508, 3059, 2980, 2935, 1717, 1552, 1476, 1438 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.15 (dd, *J* = 7.1, 7.1 Hz, 3 H), 1.37 (s, 3 H), 1.46-1.52 (m, 1 H), 1.64 (dddd, *J* = 14.2, 10.2, 8.5, 5.8 Hz, 1 H), 2.08-2.16 (m, 1 H), 2.24-2.32 (m, 1 H), 3.19 (dd, *J* = 2.3, 2.3 Hz, 1 H), 3.87 (td, *J* = 10.2, 2.3 Hz, 1 H), 4.02 (dq, *J* = 10.8, 7.1 Hz, 1 H), 4.09 (dq, *J* = 10.8, 7.1 Hz, 1 H), 4.37-4.48 (m, 2 H), 7.31-7.35 (m, 2 H), 7.40-7.44 (m, 1 H), 7.57-7.59 (m, 2 H); ¹³C NMR (CDCl₃, 125 MHz) δ 13.8 (q), 17.1 (q), 24.8 (t), 28.1 (t), 56.9 (s), 61.3 (t), 72.2 (d), 75.3 (t), 126.0 (s), 129.0 (d), 129.7 (d), 138.0 (d), 173.1 (s); exact mass *m/z* calcd for C₁₅H₂₁NO₅⁸⁰Se 375.0580, found 375.0584.

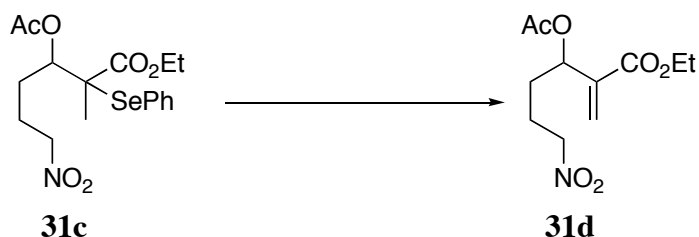
Compound **31b'** had: FTIR (CDCl₃ cast) 3509, 2980, 2938, 1717, 1551, 1476, 1438 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.22 (t, *J* = 7.2 Hz, 3 H), 1.41 (s, 3 H), 1.44-1.52 (m, 1 H), 2.01-2.15 (m, 2 H), 2.23-2.32 (m, 1 H), 2.93 (dd, *J* = 6.6, 1.0 Hz, 1 H), 3.86 (ddd, *J* = 10.7, 6.6, 1.7 Hz, 1 H), 4.12 (q, *J* = 7.2 Hz, 1 H), 4.13 (q, *J* = 7.2 Hz, 1 H), 4.40-4.51 (m, 2 H), 7.31-7.34 (m, 2 H), 7.39-7.43 (m, 1 H), 7.55-7.57 (m, 2 H); ¹³C NMR (CDCl₃, 125 MHz) δ 13.9 (q), 17.9 (q), 24.9 (t), 27.9 (t), 54.0 (s), 61.5 (t), 74.6 (d), 75.4 (t), 126.2 (s), 128.9 (d), 129.6 (d), 138.0 (d), 174.0 (s); exact mass *m/z* calcd for C₁₅H₂₁NO₅⁸⁰Se 375.0580, found 375.0580.

3-Acetoxy-2-methyl-6-nitro-2-(phenylseleno)hexanoic Acid Ethyl Ester (31c).



Pyridine (187.9 mg, 2.38 mmol) and AcCl (93.3 mg, 1.19 mmol) were added sequentially to a stirred and cooled (-10 °C, ice-acetone bath) solution of **31b'** (148 mg, 0.40 mmol) and DMAP (4.8 mg, 0.040 mmol) in CH₂Cl₂ (3 mL). The cold bath was left in place but not recharged and stirring was continued for 13 h, by which time the temperature had risen to room temperature. The mixture was diluted with water (5 mL), acidified with hydrochloric acid (1 M, 2 mL) and extracted with CH₂Cl₂ (3 x 5 mL). The combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (1.5 x 15 cm), using 19:50 EtOAc-hexane, gave **31c** (127 mg, 77%) as an oil: FTIR (CDCl₃ cast) 3058, 2982, 2936, 1743, 1725, 1669, 1552, 1477, 1439 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.09 (t, *J* = 7.2 Hz, 3 H), 1.49 (s, 3 H), 1.68 (dddd, *J* = 14.1, 10.5, 9.3, 4.8 Hz, 1 H), 1.96 (s, 3 H), 1.96-2.11 (m, 2 H), 2.23-2.30 (m, 1 H), 3.90 (dq, *J* = 10.8, 7.2 Hz, 1 H), 4.03 (dq, *J* = 10.8, 7.2 Hz, 1 H), 4.43 (dd, *J* = 6.7, 6.6 Hz, 2 H), 5.41 (dd, *J* = 10.6, 1.7 Hz, 1 H), 7.31-7.34 (m, 2 H), 7.39-7.43 (m, 1 H), 7.56-7.59 (m, 2 H); ¹³C NMR (CDCl₃, 125 MHz) δ 13.8 (q), 17.6 (q), 20.8 (q), 24.1 (t), 27.3 (t), 52.4 (s), 61.3 (s), 74.5 (d), 74.9 (t), 126.0 (s), 129.0 (d), 129.8 (d), 137.9 (d), 169.9 (s), 171.8 (s); exact mass *m/z* calcd for C₁₇H₂₃NO₆⁸⁰Se 417.0691, found 417.0692.

2-(1-Acetoxy-4-nitrobutyl)acrylic Acid Ethyl Ester (31d).



H₂O₂ (30%, 0.36 mL, 3.52 mmol) was added dropwise to a stirred and cooled (0 °C) solution of **31c** (123 mg, 0.30 mmol) in CH₂Cl₂ (3 mL). Stirring was continued at 0 °C for 70 min and the mixture was quenched with saturated aqueous Na₂S₂O₃ (2.0 mL). The mixture was stirred at 0 °C for 5 min, the ice bath was removed, stirring was continued for 30 min, and water (10 mL) was added. The aqueous phase was extracted with CH₂Cl₂ (3 x 10 mL) and the combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (1 x 15 cm), using 7:20 EtOAc-hexane, gave **31d** (60 mg, 78%) as a viscous oil: FTIR (CDCl₃ cast) 2983, 2940, 1743, 1633, 1553, 1436 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 1.30 (t, *J* = 7.1 Hz, 3 H), 1.75-1.82 (m, 1 H), 1.88 (dddd, *J* = 14.0, 10.0, 6.1, 4.2 Hz, 1 H), 1.99-2.09 (m, 2 H), 2.09 (s, 3 H), 4.18-4.27 (m, 2 H), 4.40 (dd, *J* = 7.0, 6.9 Hz, 2 H), 5.64 (dd, *J* = 7.7, 4.1 Hz, 1 H), 5.77 (s, 1 H), 6.31 (s, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.1 (q), 20.9 (q), 23.2 (t), 30.7 (t), 61.1 (t), 70.6 (d), 74.9 (t), 125.4 (t), 139.4 (s), 164.9 (s), 169.7 (s); exact mass (electrospray) *m/z* calcd for C₁₁H₁₇NNaO₆ 282.0948, found 282.0947.

5-Nitrocyclohex-1-enecarboxylic Acid Ethyl Ester (**31e**).



Cs₂CO₃ (66.2 mg, 0.203 mmol) was added to a stirred solution of **31d** (26.3 mg, 0.102 mmol) in THF (1 mL), and stirring at room temperature was continued for 4.5 h. Evaporation of the solvent and flash chromatography of the residue over silica gel (0.7 x 7 cm), using 1:2 EtOAc-hexane, gave **31e** (15 mg, 75%) as a colorless viscous oil: FTIR (CDCl₃ cast) 2982, 2938, 2907, 1712, 1655, 1548, 1462, 1445, 1430 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.30 (t, *J* = 7.2 Hz, 3 H), 2.14-2.49 (m, 4 H), 2.84-2.98 (m, 2 H), 4.21 (q, *J* = 7.2 Hz, 2 H), 4.67 (dddd, *J* = 9.6, 8.0, 6.0, 4.0 Hz, 1 H), 7.00 (dddd, *J* = 3.6, 3.6, 1.8, 1.8 Hz, 1 H); ¹³C NMR (CDCl₃, 100

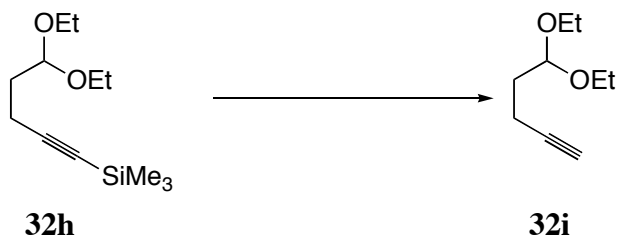
MHz) δ 14.2 (q), 23.6 (t), 25.8 (t), 28.2 (t), 60.1 (t), 80.4 (d), 126.9 (s), 137.8 (d), 165.9 (s); exact mass m/z calcd for $C_9H_{13}NO_4$ 199.0845, found 199.0846.

(5,5-Diethoxypent-1-ynyl)trimethylsilane (32h).⁴²

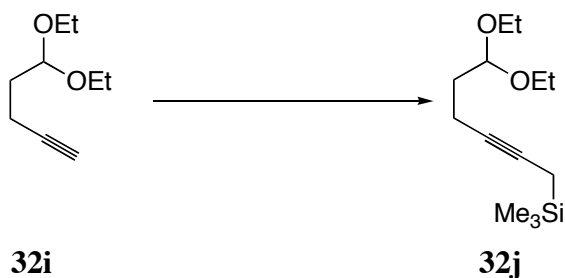


n-BuLi (1.3 M, 5.8 mL, 7.57 mmol) was added to a stirred and cooled ($-78\text{ }^{\circ}\text{C}$) solution of trimethylsilylacetylene (0.744 g, 7.57 mmol) in THF (35 mL). The mixture was stirred at $0\text{ }^{\circ}\text{C}$ for 10 min and then recooled to $-78\text{ }^{\circ}\text{C}$. A solution of HMPA (7.4 g, 41.3 mmol) in THF (7 mL) was added, stirring was continued for 10 min, and a solution of **32g** (1.78 g, 6.9 mmol) in THF (10 mL) was added dropwise. The cold bath was left in place but not recharged and stirring was continued overnight. The mixture was quenched with saturated aqueous NH_4Cl (30 mL) and diluted with water (200 mL). The aqueous phase was extracted with Et_2O (3 x 60 mL) and the combined organic extracts were washed with brine, dried (MgSO_4) and evaporated. Flash chromatography of the residue over silica gel (4 x 15 cm), using 0.9:25 EtOAc-hexane, gave **32h** (1.104 mg, 70%) as a colorless liquid.

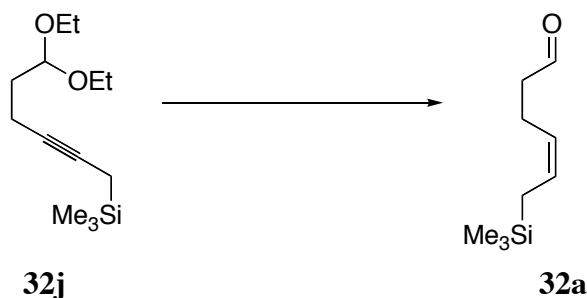
4-Pentynyl Diethyl Acetal (32i).⁴²



K_2CO_3 (2.67 g, 19.4 mmol) was added to a stirred solution of **32h** (1.104 g, 4.84 mmol) in anhydrous MeOH (100 mL) (N_2 atmosphere). Stirring at room temperature was continued for 2.5 h. The mixture was concentrated to 50 mL and diluted with water (250 mL). The aqueous phase was extracted with Et_2O (3 x 60 mL) and the combined organic extracts were washed with brine, dried (MgSO_4) and evaporated to give **32i** as a liquid (669 mg, 89%).

(6,6-Diethoxyhex-2-ynyl)trimethylsilane (32j).⁴³

n-BuLi (1.3 M, 4.5 mL, 5.85 mmol) was added to a stirred and cooled (-78 °C) solution of **32i** (760 mg, 4.87 mmol) in THF (20 mL). The mixture was stirred at 0 °C for 15 min and HMPA (5.1 mL) was added. The mixture was cooled to -78 °C and iodomethyltrimethylsilane (1.25 g, 5.85 mmol) was added dropwise. The cold bath was left in place but not recharged and stirring was continued overnight. The mixture was quenched with saturated aqueous NH₄Cl (20 mL) and diluted with water (150 mL). The aqueous phase was extracted with Et₂O (3 x 30 mL) and the combined organic extracts were washed with brine, dried (MgSO₄) and evaporated. Flash chromatography of the residue over silica gel (2 x 15 cm), using 1:20 EtOAc-hexane, gave **32j** (852 mg, 72%) as a colorless liquid: FTIR (CH₂Cl₂ cast) 2975, 2960, 2933, 2901, 2881, 2222, 2177 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ -0.09 (s, 9 H), 1.21 (t, *J* = 5.8 Hz, 6 H), 1.41 (t, *J* = 2.7 Hz, 2 H), 1.77 (td, *J* = 7.2, 5.8 Hz, 2 H), 2.22 (tt, *J* = 7.2, 2.7 Hz, 2 H), 3.51 (dq, *J* = 9.5, 7.1 Hz, 2 H), 3.66 (dq, *J* = 9.5, 7.1 Hz, 2 H), 4.61 (t, *J* = 5.8 Hz, 1 H); ¹³C NMR (CDCl₃, 125 MHz) δ -2.1 (q), 6.9 (t), 14.6 (t), 15.4 (q), 33.5 (t), 61.5 (t), 77.7 (s), 77.8 (s), 102.0 (d); exact mass (electrospray) *m/z* calcd for C₁₃H₂₆NaO₂Si 265.1594, found 265.1594.

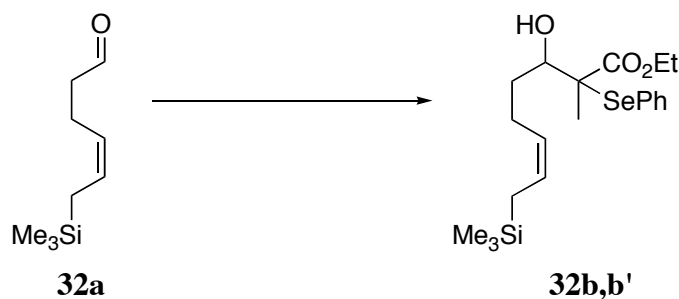
(Z)-6-(Trimethylsilyl)hex-4-enal (32a).⁴⁴

N₂ was bubbled through a solution of **32j** (256 mg, 1.06 mmol) in MeOH (1 mL) for 10 min, and then 10% Pd/BaSO₄ (5.8 mg) and quinoline (5.8 mg, 0.48 mmol) were added. Stirring at room temperature was continued for 5 min, and the mixture was purged with a stream of H₂.

for 10 sec. The flask was connected to a sloping manifold apparatus filled with H₂. The flask was removed when rapid absorption of H₂ stopped (a little more than the calculated amount), and the solid was filtered off through a pad of Celite, using Et₂O as a rinse. Evaporation of the filtrate gave the crude product (251 mg, 97%).

The above crude product was dissolved in acetone (2 mL), and hydrochloric acid (1 M, 1.1 mL) was added. The solution was stirred at room temperature for 2 h, diluted with water (20 mL), and extracted with Et₂O (3 x 15 mL). The combined organic extracts were washed with saturated aqueous NaHCO₃ and brine, dried (MgSO₄) and evaporated, to give crude **32a** (157 mg, 87% over two steps), which was used directly in the next step: ¹H NMR (CDCl₃, 300 MHz) δ -0.01 (s, 9 H), 1.47-1.51 (m, 2 H), 2.31-2.37 (m, 2 H), 2.45-2.51 (m, 2 H), 5.23 (dtt, *J* = 10.5, 6.9, 1.5 Hz, 1 H), 5.47 (dtt, *J* = 10.5, 8.7, 1.5 Hz, 1 H), 9.78 (t, *J* = 1.5 Hz, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ -1.9 (q), 18.5 (t), 19.8 (t), 43.8 (t), 124.7 (d), 127.3 (d), 202.3 (d).

(Z)-3-Hydroxy-2-methyl-2-(phenylseleno)-8-(trimethylsilyl)oct-6-enoic Acid Ethyl Ester (32b,b').

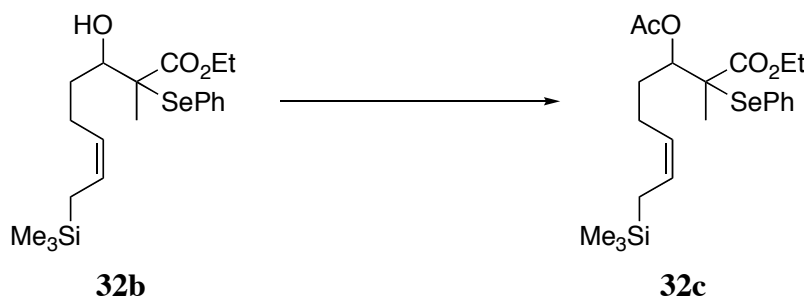


n-BuLi (1.3 M in hexane, 1.07 mL, 1.39 mmol) was added dropwise to a stirred and cooled (0 °C) solution of *i*-Pr₂NH (141 mg, 1.39 mmol) in THF (6 mL). Stirring at 0 °C was continued for 10 min, the mixture was cooled to -78 °C, and a solution of **15** (357.2 mg, 1.39 mmol) in THF (1 mL) was then added dropwise. Stirring at -78 °C was continued for 30 min, and a solution of **32a** (157 mg, 0.92 mmol) in THF (1.5 mL) was added dropwise. Stirring at -78 °C was continued for 50 min, and the mixture was quenched with saturated aqueous NH₄Cl (5 mL). The cold bath was removed, stirring was continued for 15 min, the mixture was diluted with water (25 mL) and the aqueous phase was extracted with Et₂O (3 x 20 mL). The combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm), using successively 1:20 EtOAc-hexane, 8% EtOAc-hexane, and 10% EtOAc-hexane, gave **32b** (less polar isomer) (80 mg, 20%) as a viscous oil and **32b'** (more polar isomer) (133 mg, 34%) as a viscous oil.

Compound **32b** had: FTIR (CDCl_3 cast) 3515, 3058, 2953, 1721, 1476, 1438 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ -0.01 (s, 9 H), 1.12 (t, $J = 7.5$ Hz, 3 H), 1.33-1.41 (m, 4 H), 1.47 (dddd, $J = 13.7, 13.7, 13.6, 8.5$ Hz, 2 H), 1.59 (dddd, $J = 23.4, 19.9, 17.1, 10.7$ Hz, 1 H), 2.06-2.14 (m, 1 H), 2.20-2.27 (m, 1 H), 2.96 (dd, $J = 2.7, 1.7$ Hz, 1 H), 3.93 (ddd, $J = 9.8, 2.8, 1.9$ Hz, 1 H), 3.95-4.09 (m, 2 H), 5.20-5.25 (m, 1 H), 5.40 (dddd, $J = 10.1, 8.7, 8.7, 1.4, 1.4$ Hz, 1 H), 7.29-7.32 (m, 2 H), 7.37-7.41 (m, 1 H), 7.59-7.61 (m, 2 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ -1.8 (q), 13.8 (q), 17.1 (q), 18.4 (t), 24.2 (t), 31.9 (t), 57.5 (s), 61.0 (t), 72.6 (d), 126.3 (d), 126.48 (d), 126.54 (s), 128.8 (d), 129.4 (d), 138.0 (d), 173.1 (s); exact mass (electrospray) m/z calcd for $\text{C}_{20}\text{H}_{32}\text{NaO}_3^{80}\text{SeSi}$ 451.1178, found 451.1176.

Compound **32b'** had: FTIR (CDCl_3 cast) 3507, 3059, 3002, 2953, 1704, 1476, 1438 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 0.01 (s, 9 H), 1.19 (t, $J = 7.5$ Hz, 3 H), 1.41 (s, 3 H), 1.44-1.55 (m, 3 H), 1.90 (dddd, $J = 13.6, 8.9, 7.3, 1.5$ Hz, 1 H), 2.11 (dddd, $J = 14.6, 8.7, 7.3, 7.2, 1.5$ Hz, 1 H), 2.24-2.31 (m, 1 H), 2.82 (d, $J = 6.0$ Hz, 1 H), 3.90 (ddd, $J = 10.4, 6.8, 1.3$ Hz, 1 H), 4.06-4.13 (m, 2 H), 5.26-5.31 (m, 1 H), 5.45 (dddd, $J = 10.2, 8.6, 8.6, 1.5, 1.5$ Hz, 1 H), 7.28-7.32 (m, 2 H), 7.37-7.40 (m, 1 H), 7.56-7.59 m, 2 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ -1.8 (q), 13.9 (q), 18.3 (q), 18.5 (t), 24.2 (t), 31.6 (t), 54.7 (s), 61.2 (t), 75.0 (d), 126.4 (d), 126.5 (d), 126.7 (s), 128.7 (d), 129.3 (d), 138.1 (d), 174.0 (s); exact mass (electrospray) m/z calcd for $\text{C}_{20}\text{H}_{32}\text{NaO}_3^{80}\text{SeSi}$ 451.1178, found 451.1181.

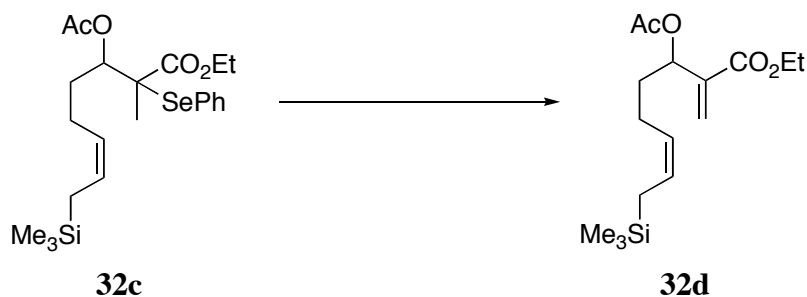
(Z)-3-Acetoxy-2-methyl-2-(phenylseleno)-8-(trimethylsilyl)oct-6-enoic Acid Ethyl Ester (32c).



Pyridine (88.6 mg, 1.12 mmol) and AcCl (44.1 mg, 0.56 mmol) were added sequentially to a stirred and cooled (-10 $^{\circ}\text{C}$, ice-acetone bath) solution of **32b** (80 mg, 0.19 mmol) and DMAP (2.3 mg, 0.018 mmol) in CH_2Cl_2 (1.5 mL). Stirring at -10 $^{\circ}\text{C}$ was continued for 30 min, the cold bath was removed and stirring was continued for 2.5 h. The mixture was quenched with hydrochloric acid (1 M, 3 mL) and diluted with water (10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 10 mL) and the combined organic extracts were washed with brine,

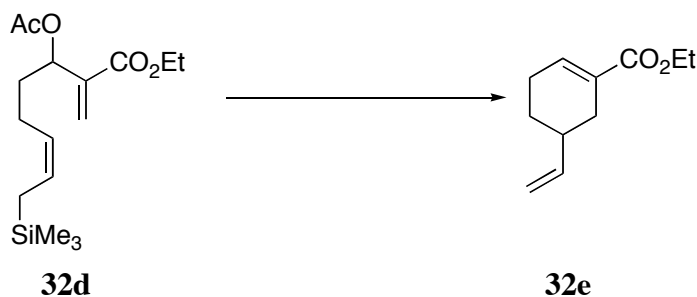
dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1 x 15 cm), using 1.3:20 EtOAc-hexane, gave **32c** (74 mg, 84%) as an oil: FTIR (CDCl_3 cast) 2954, 1745, 1727, 1439 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ -0.02 (s, 9 H), 1.07 (t, $J = 7.5$ Hz, 3 H), 1.37-1.50 (m, 3 H), 1.52 (s, 3 H), 1.65 (dddd, $J = 15.0, 9.9, 7.4, 7.4$ Hz, 1 H), 1.99 (ddd, $J = 7.4, 7.3, 7.3$ Hz, 2 H), 2.16 (s, 3 H), 3.83 (dq, $J = 10.8, 7.2$ Hz, 1 H), 3.97 (dq, $J = 10.8, 7.2$ Hz, 1 H), 5.18-5.23 (m, 1 H), 5.37-7.43 (m, 1 H), 5.58 (dd, $J = 10.0, 1.2$ Hz, 1 H), 7.29-7.32 (m, 2 H), 7.37-7.40 (m, 1 H), 7.61-7.63 (m, 2 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ -1.8 (q), 13.7 (q), 17.9 (q), 18.4 (t), 21.1 (q), 24.0 (t), 31.9 (t), 54.8 (s), 61.0 (t), 74.7 (d), 125.8 (d), 126.4 (d), 126.9 (s), 128.7 (d), 129.4 (d), 138.0 (d), 170.5 (s), 171.3 (s); exact mass (electrospray) m/z calcd for $\text{C}_{22}\text{H}_{34}\text{NaO}_4^{80}\text{SeSi}$ 493.1284, found 493.1289.

(Z)-3-Acetoxy-2-methylene-8-(trimethylsilyl)oct-6-enoic Acid Ethyl Ester (32d).



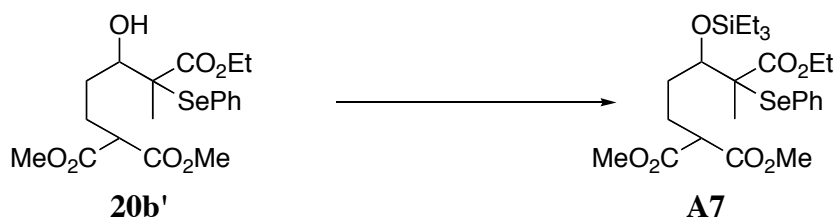
H_2O_2 (30%, 127.6 mg, 1.13 mmol) was added dropwise to a stirred and cooled (0 °C) solution of **32c** (44 mg, 0.094 mmol) in CH_2Cl_2 (1 mL). Stirring was continued at 0 °C for 1.3 h and the mixture was quenched with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (2 mL). The mixture was stirred at 0 °C for 20 min, the ice bath was removed, stirring was continued for 5 min and the mixture was diluted with water (10 mL) and the aqueous phase was extracted with CH_2Cl_2 (3 x 8 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (0.7 x 15 cm), using 7:100 EtOAc-hexane, gave **32d** (25.2 mg, 86%) as an oil: FTIR (CDCl_3 cast) 2955, 1749, 1721, 1632 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ -0.02 (s, 9 H), 1.30 (t, $J = 7.2$ Hz, 3 H), 1.43 (d, $J = 8.4$ Hz, 2 H), 1.72 (ddd, $J = 14.2, 14.0, 6.9$ Hz, 1 H), 1.77-1.85 (m, 1 H), 2.03 (ddd, $J = 7.7, 7.7, 7.3$ Hz, 2 H), 3.08 (s, 3 H), 4.17 (m, 2 H), 5.19-5.26 (m, 1 H), 5.41 (dddd, $J = 10.2, 8.7, 8.7, 1.5, 1.5$ Hz, 1 H), 5.62 (dd, $J = 8.0, 4.4$ Hz, 1 H), 5.74 (dd, $J = 0.8, 0.8$ Hz, 1 H), 6.27 (dd, $J = 0.8, 0.8$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ -1.8 (q), 14.1 (q), 18.4 (t), 21.1 (q), 23.0 (t), 34.3 (t), 60.8 (t), 71.6 (d), 124.7 (s), 125.8 (d), 126.5 (d), 140.4 (t), 165.2 (s), 169.9 (s); exact mass (electrospray) m/z calcd for $\text{C}_{16}\text{H}_{28}\text{NaO}_4\text{Si}$ 335.1649, found 335.1645.

5-Vinylcyclohex-1-enecarboxylic Acid Ethyl Ester (32e).



TiCl₄ (14.5 mg, 0.076 mmol) that had been frozen (-78 °C), placed under vacuum, allowed to melt under N₂, and subjected to this freeze-thaw cycle three times, was added to a stirred and cooled (-40 °C) solution of **32d** (19.8 mg, 0.063 mmol) in CH₂Cl₂ (0.6 mL). Stirring at -40 °C was continued for 5 min. The mixture was quenched with water (5 mL) and the aqueous phase was extracted with CH₂Cl₂ (3 x 5 mL). The combined organic extracts were washed with saturated aqueous NaHCO₃ and brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (0.7 x 7 cm), using 3:100 EtOAc-hexane, gave **32e** (10.3 mg, 90%) as a colorless liquid: FTIR (CDCl₃ cast) 3081, 2980, 2930, 1711, 1651, 1434 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.29 (t, *J* = 7.6 Hz, 3 H), 1.33-1.41 (m, 1 H), 1.77-1.84 (m, 1 H), 1.98-2.06 (m, 1 H), 2.18-2.35 (m, 3 H), (dddd, *J* = 17.5, 5.1, 2.7, 2.6, 1.3 Hz, 1 H), 1.19 (q, *J* = 7.6 Hz, 2 H), 5.03 (dddd, *J* = 23.4, 10.4, 1.5, 1.5 Hz, 2 H), 5.85 (ddd, *J* = 17.1, 0.4, 6.4 Hz, 1 H), 6.96-7.00 (m, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.3 (q), 25.4 (t), 27.3 (t), 29.7 (t), 37.1 (d), 60.2 (t), 113.1 (t), 129.7 (s), 139.0 (d), 142.7 (d), 167.4 (s); exact mass *m/z* calcd for C₁₁H₁₆O₂ 180.1150, found 180.1151.

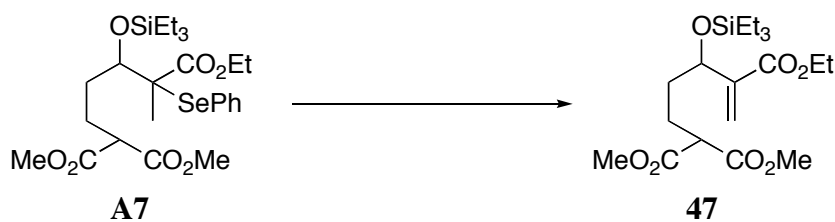
6-Methoxycarbonyl-2-methyl-2-(phenylseleno)-3-[(triethylsilyl)oxy]heptanedioic Acid 1-Ethyl Ester 7-Methyl Ester (A7).



Et₃SiOSO₂CF₃ (0.5 mL, 2.142 mmol) was added dropwise over ca 2 min to a stirred and cooled (-78 °C) solution of **20b'** (530 mg, 1.19 mmol) and 2,6-lutidine (0.42 mL, 3.57 mmol) in CH₂Cl₂ (10 mL). Stirring at -78 °C was continued for 2 h and the mixture was quenched with

water (5 mL) and saturated aqueous NaHCO_3 (3 mL). The cold bath was removed, stirring was continued for 10 min and the mixture was diluted with water (5 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 x 16 cm), using 15% EtOAc-hexane, gave 6-methoxycarbonyl-2-methyl-2-(phenylseleno)-3-[(triethylsilyl)oxy]heptanedioic acid 1-ethyl ester 7-methyl ester (**A7**) (658 mg, 99%) as a colorless oil: FTIR (CH_2Cl_2 cast) 2954, 2916, 2876, 1754, 1737, 1437, 1242, 741 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 0.54 (q, $J = 8.0$ Hz, 6 H), 0.88 (t, $J = 8.0$ Hz, 9 H), 1.12 (t, $J = 7.2$ Hz, 3 H), 1.42-1.51 (m, 1 H), 1.49 (s, 3 H), 1.84-1.92 (m, 1 H), 2.06-2.20 (m, 2 H), 3.40 (t, $J = 7.2$ Hz, 1 H), 3.77 (s, 3 H), 3.79 (s, 3 H), 3.87-4.03 (m, 2 H), 4.21 (br d, $J = 8.4$ Hz, 1 H), 7.27-7.32 (m, 2 H), 7.37-7.40 (m, 1 H), 7.56-7.59 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 5.3 (t), 6.8 (q), 13.6 (q), 16.3 (q), 26.6 (t), 30.8 (t), 51.7 (d), 52.4 (q), 52.43 (q), 55.7 (s), 60.8 (t), 75.0 (d), 126.6 (s), 128.6 (d), 129.2 (d), 137.8 (d), 169.5 (s), 169.6 (s), 172.6 (s); exact mass (electrospray) m/z calcd for $\text{C}_{25}\text{H}_{40}\text{NaO}_7^{80}\text{SeSi}$ 583.1601, found 583.1590.

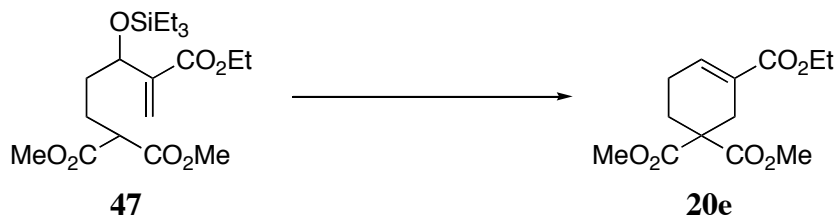
6-Methoxycarbonyl-2-methylene-3-[(triethylsilyl)oxy]heptanedioic Acid 1-Ethyl Ester 7-Methyl Ester (47).



H_2O_2 (30%, 1.25 mL, 12.24 mmol) was added dropwise over 2 min to a stirred and cooled (-10°C , ice-acetone cold bath) solution of 6-methoxycarbonyl-2-methyl-2-(phenylseleno)-3-[(triethylsilyl)oxy]heptanedioic acid 1-ethyl ester 7-methyl ester (**A7**) (655 mg, 1.17 mmol) in CH_2Cl_2 (10 mL). Stirring was continued for 1 h and the mixture was quenched with saturated aqueous NaHCO_3 (3 mL), followed by dropwise addition of saturated $\text{Na}_2\text{S}_2\text{O}_3$ (5 mL). The cold bath was removed after 10 min, stirring was continued for 10 min and the mixture was diluted with water (25 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 x 18 cm), using 5% EtOAc-hexane, gave **47** (453 mg, 96%) as a colorless oil: FTIR (CH_2Cl_2 cast) 2956, 2878, 1756, 1739, 1714, 1631, 1095, 743 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 0.59 (q, $J = 7.6$ Hz, 6 H), 0.94 (t, $J = 7.6$ Hz, 9 H), 1.30 (t, $J = 7.2$ Hz, 3 H), 1.50-1.59 (m, 1 H), 1.63-1.71 (m, 1 H), 1.89-1.99 (m, 2 H), 3.37 (t, $J = 7.6$ Hz, 1 H), 3.719 (s, 3 H), 3.722 (s, 3 H),

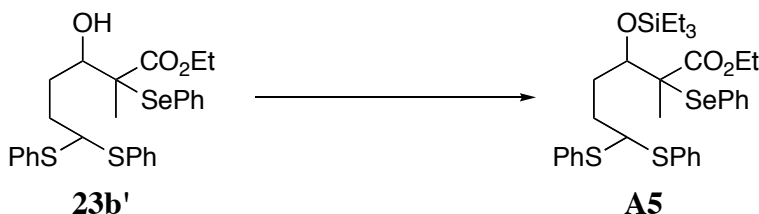
4.15–4.26 (m, 2 H), 4.66 (dd, $J = 5.6, 4.4$ Hz, 1 H), 5.93 (t, $J = 1.6$ Hz, 1 H), 6.27 (dd, $J = 1.6, 0.8$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 4.6 (t), 6.7 (q), 14.0 (q), 24.0 (t), 34.6 (t), 51.4 (d), 52.26 (q), 52.28 (q), 60.5 (t), 69.4 (d), 124.8 (s), 143.2 (t), 165.9 (s), 169.62 (s), 169.7 (s); exact mass (electrospray) m/z calcd for $\text{C}_{19}\text{H}_{34}\text{NaO}_7\text{Si}$ 425.1966, found 425.1969.

Cyclohex-3-ene-1,1,3-tricarboxylic Acid 3-Ethyl Ester 1,1-Dimethyl Ester (20e**) from **47**.**



DBU (0.04 mL, 0.248 mmol) was added dropwise to a stirred solution of **47** (50 mg, 0.124 mmol) in MeCN (2 mL). The mixture was stirred for 1.5 h and then filtered through a pad of silica gel (2 x 2 cm), using 50% EtOAc-hexane (25 mL). Evaporation of the filtrate and flash chromatography of the residue over silica gel (0.5 x 8 cm), using 20% EtOAc-hexane, gave **20e** (32 mg, 96%) as a viscous oil.

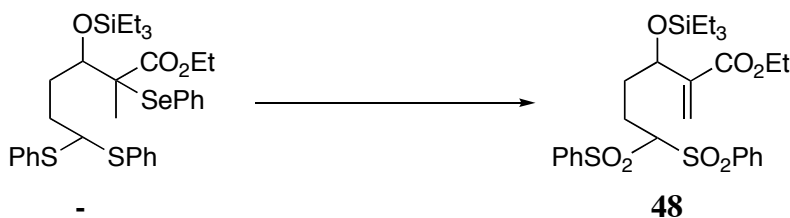
2-Methyl-2-(phenylseleno)-6,6-bis(phenylthio)-3-[(triethylsilyl)oxy]hexanoic Acid Ethyl Ester (A5**).**



$\text{Me}_3\text{SiOSO}_2\text{CF}_3$ (291 mg, 1.1 mmol) was added dropwise to a stirred and cooled (-78°C) solution of **23b'** (326 mg, 0.6 mmol) and 2,6-lutidine (192.9 mg, 1.8 mmol) in dry CH_2Cl_2 (3 mL). Stirring at -78°C was continued for 1.5 h and the mixture was quenched with water (5 mL) and saturated aqueous NaHCO_3 (3 mL). The cold bath was removed and stirring was continued for 15 min. The aqueous phase was extracted with CH_2Cl_2 (3 x 10 mL) and the combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2.4 x 15 cm), using 1:20 EtOAc-hexane, gave 2-methyl-2-(phenylseleno)-

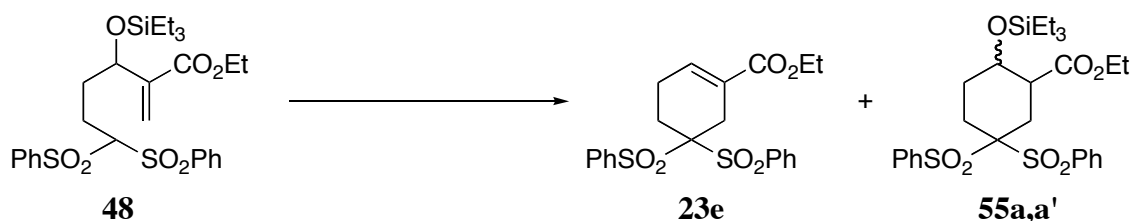
6,6-bis(phenylthio)-3-[(triethylsilyl)oxy]hexanoic acid ethyl ester (**A5**) (338 mg, 85%) as an oil: FTIR (CDCl₃ cast) 3073, 3058, 2955, 2911, 2875, 1720, 1583, 1475, 1439 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 0.61-0.75 (m, 6 H), 0.99 (t, *J* = 8.0 Hz, 9 H), 1.02 (t, *J* = 7.0 Hz, 3 H), 1.57 (s, 3 H), 1.73-1.81 (m, 3 H), 1.97-2.05 (m, 1 H), 3.72-3.84 (m, 2 H), 4.33- 4.37 (m, 2 H), 7.27-7.33 (m, 8 H), 7.35-7.38 (m, 1 H), 7.45-7.48 (m, 4 H), 7.58-7.60 (m, 2 H); ¹³C NMR (CDCl₃, 125 MHz) δ 5.6 (t), 7.1 (q), 13.8 (q), 18.2 (q), 32.9 (t), 33.5 (t), 58.4 (s), 58.5 (d), 60.7 (t), 76.1 (d), 127.6 (s), 127.76 (d), 127.78 (d), 128.6 (d), 128.89 (d), 128.90 (d), 129.0 (d), 132.8 (d), 132.9 (d), 133.9 (s), 134.1 (s), 138.0 (d), 171.9 (s); exact mass (electrospray) *m/z* calcd for C₃₃H₄₄NaO₃S₂⁸⁰SeSi 683.1559, found 683.1558.

2-[4,4-Bis(benzenesulfonyl)-1-[(triethylsilyl)oxy]butyl]acrylic Acid Ethyl Ester (48).



NaHCO₃ (706 mg, 8.4 mmol) was added to a stirred and cooled (0 °C) solution of 2-methyl-2-(phenylseleno)-6,6-bis(phenylthio)-3-[(triethylsilyl)oxy]hexanoic acid ethyl ester (231 mg, 0.35 mmol) in CH₂Cl₂ (3 mL), followed by *m*-CPBA (70%, 1.04 g, 4.2 mmol). Stirring at 0 °C was continued for 5 min and the cold bath was removed. Stirring was continued for 30 min and the mixture was quenched with saturated aqueous NaHCO₃ (5 mL) and saturated aqueous Na₂S₂O₃ (5 mL). The mixture was extracted with CH₂Cl₂ (3 x 10 mL), and the combined organic extracts were dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (1 x 15 cm), using 1:5 EtOAc-hexane and then 1:3 EtOAc-hexane, gave **48** (175 mg, 88%) as an oil: FTIR (CDCl₃ cast) 3066, 2957, 2912, 2877, 1712, 1631, 1585, 1448 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 0.55 (q, *J* = 8.0 Hz, 6 H), 0.91 (t, *J* = 8.0 Hz, 9 H), 1.31 (t, *J* = 7.0 Hz, 3 H), 1.87 (ddt, *J* = 13.5, 11.0, 5.0 Hz, 1 H), 1.99-2.06 (m, 1 H), 2.09-2.32 (m, 2 H), 4.17-4.26 (m, 2 H), 4.49 (dd, *J* = 6.5, 5.0 Hz, 1 H), 4.66 (t, *J* = 10.0 Hz, 1 H), 5.84 (t, *J* = 1.5 Hz, 1 H), 6.25 (dd, *J* = 1.5, 1.0 Hz, 1 H), 7.54-7.59 (m, 4 H), 7.67-7.71 (m, 2 H), 7.94-7.97 (m, 4 H); ¹³C NMR (CDCl₃, 125 MHz) δ 4.7 (t), 6.8 (q), 14.1 (q), 21.0 (t), 34.8 (t), 60.7 (t), 69.3 (d), 83.7 (d), 125.3 (s), 128.96 (d), 128.99 (d), 129.7 (d), 134.39 (d), 134.41 (d), 137.9 (s), 142.6 (t), 165.7 (s); exact mass (electrospray) *m/z* calcd for C₂₇H₃₈NaO₇S₂Si 589.1721, found 589.1723.

5,5-Bis(benzenesulfonyl)-2-[(triethylsilyl)oxy]cyclohexanecarboxylic Acid Ethyl Ester (55a,a'**).**



DBU (38.7 mg, 0.25 mmol) was added dropwise to a stirred solution of **48** (72 mg, 0.13 mmol) in dry MeCN (2.5 mL). Stirring at room temperature was continued for 40 min and the mixture was filtered through a pad (ca 5 cm) of silica gel in a Pasteur pipette, using 4:5 EtOAc-hexane. The filtrate was evaporated and preparative TLC of the residue, using CH₂Cl₂, gave **23e** (15 mg, 27%), **55a** (the less polar isomer, trans) (32 mg, 44%) as an oil and **55a'** (the more polar isomer, cis) (4 mg, 5.6%) as an oil.

Compound **55a** had: FTIR (CDCl₃ cast) 3067, 2955, 2876, 1734, 1584, 1448 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 0.58 (q, *J* = 8.0 Hz, 6 H), 0.94 (t, *J* = 8.0 Hz, 9 H), 1.28 (t, *J* = 7.0 Hz, 3 H), 1.94 (dddd, *J* = 12.5, 5.0, 5.0, 3.5 Hz, 1 H), 2.23 (dddd, *J* = 13.5, 13.5, 9.0, 4.5 Hz, 1 H), 2.32-2.38 (m, 2 H), 2.47 (ddd, *J* = 15.5, 13.5, 5.0 Hz, 1 H), 2.63 (dd, *J* = 15.5, 13.0 Hz, 1 H), 3.30 (ddd, *J* = 13.0, 9.5, 3.0 Hz, 1 H), 3.90 (ddd, *J* = 10.5, 10.5, 4.5 Hz, 1 H), 4.09-4.18 (m, 2 H), 7.59-7.64 (m, 4 H), 7.70-7.75 (m, 2 H), 8.01-8.03 (m, 2 H), 8.12-8.14 (m, 2 H); ¹³C NMR (CDCl₃, 125 MHz) δ 4.9 (t), 6.7 (q), 14.1 (q), 25.4 (t), 28.6 (t), 30.0 (t), 47.0 (d), 60.8 (t), 70.4 (d), 86.2 (s), 128.58 (d), 128.63 (d), 131.2 (d), 131.6 (d), 134.6 (d), 134.7 (d), 136.0 (s), 136.1 (s), 173.4 (s); exact mass (electrospray) *m/z* calcd for C₂₇H₃₈NaO₇S₂Si 589.1721, found 589.1721.

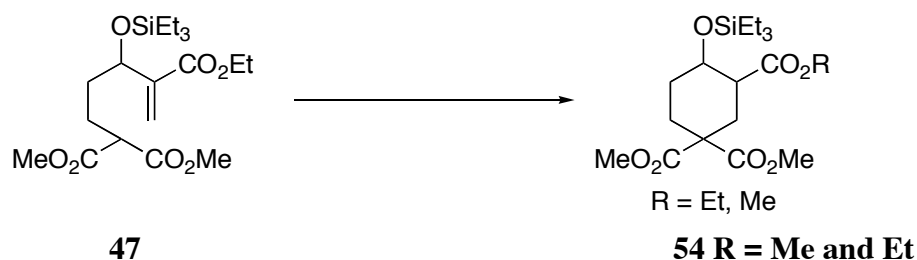
Compound **55a'** had: FTIR (CDCl₃ cast) 3066, 2956, 2911, 2877, 1735, 1584, 1448 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 0.40 (q, *J* = 8.0 Hz, 6 H), 0.81 (t, *J* = 8.0 Hz, 9 H), 1.28 (t, *J* = 7.0 Hz, 3 H), 1.77 (dddd, *J* = 13.5, 4.0, 4.0, 2.5 Hz, 1 H), 2.28 (dddd, *J* = 14.5, 4.0, 2.5, 2.0 Hz, 1 H), 2.36 (dddd, *J* = 13.5, 13.5, 4.0, 1.5 Hz, 1 H), 2.48 (ddd, *J* = 14.0, 14.0, 4.5 Hz, 1 H), 2.57 (ddd, *J* = 15.0, 4.5, 2.0 Hz, 1 H), 2.71 (dd, *J* = 15.0, 12.5 Hz, 1 H), 3.42 (ddd, *J* = 12.5, 4.5, 2.5 Hz, 1 H), 4.06 (dq, *J* = 11.0, 7.0 Hz, 1 H), 4.21 (dq, *J* = 11.0, 7.0 Hz, 1 H), 4.49 (ddd, *J* = 4.0, 2.0, 2.0 Hz, 1 H), 7.55-7.64 (m, 4 H), 7.67-7.70 (m, 1 H), 7.72-7.75 (m, 1 H), 7.96-7.98 (m, 2 H), 8.09-8.12 (m, 2 H); ¹³C NMR (CDCl₃, 125 MHz) δ 4.7 (t), 6.7 (q), 14.1 (q), 20.2 (t), 22.7 (t), 29.4 (t), 44.1 (d), 60.8 (t), 65.7 (d), 87.2 (s), 128.6 (d), 128.7 (d), 131.2 (d), 131.4 (d), 134.4 (d), 134.6 (d), 135.9 (s), 137.0 (s), 172.0 (s); exact mass (electrospray) *m/z* calcd for C₂₇H₃₈NaO₇S₂Si 589.1721, found 589.1723.

Stability of **55a** and **55a'** to DBU.

DBU (4.0 mg, 0.026 mmol) was added to a solution of **55a** (7.5 mg, 0.013 mmol) in CD₃CN (0.7 mL) in an NMR tube. No change was observed after 45 min (¹H NMR, 400 MHz).

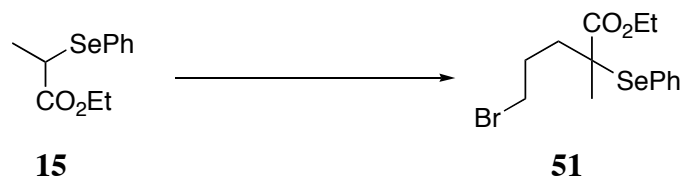
DBU (2.15 mg, 0.014 mmol) was added to a solution of **55a'** (4 mg, 0.007 mmol) in CD₃CN (0.7 mL) in an NMR tube. No change was observed after 45 min (¹H NMR, 500 MHz).

4-[(Triethylsilyl)oxy]cyclohexane-1,1,3-tricarboxylic Acid 3-Ethyl Ester 1,1-Dimethyl Ester (**54**, R = Et) and 4-[(Triethylsilyl)oxy]cyclohexane-1,1,3-tricarboxylic Acid Trimethyl Ester (**54**, R = Me).



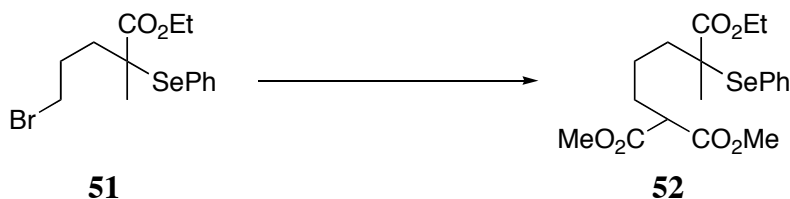
DBU (10.8 mg, 0.071 mmol) was added into a stirred solution of **47** (14.3 mg, 0.036 mmol) in MeOH (0.1 mL). Stirring at room temperature was continued for 34.5 h and the mixture was filtered through a pad (ca 5 cm) of silica gel in a Pasteur pipette, using EtOAc. Evaporation of the filtrate and flash chromatography of the residue over silica gel (0.7 x 7 cm), using 1:6 EtOAc-hexane and then 1:3 EtOAc-hexane, gave **54** as an inseparable 7.6:2.4 mixture of 3-ethyl 1,1-dimethyl and trimethyl esters, respectively (4 mg, 28%) as an oil: FTIR (CDCl₃, cast) 2955, 2914, 2878, 1736, 1435 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 0.85-0.93 (m, 6 H), 1.25-1.29 (m, 9 H), 1.61 (t, *J* = 7.0 Hz, 2.6 H), 1.88 (dddd, *J* = 14.0, 14.0, 4.5, 2.0 Hz, 1 H), 2.09 (dddd, *J* = 14.5, 3.5, 3.5, 3.5 Hz, 1 H), 2.43 (dddd, *J* = 13.5, 4.5, 3.0, 3.0 Hz, 1 H), 2.50 (ddd, *J* = 14.0, 13.5, 4.0 Hz, 1 H), 2.61 (ddd, *J* = 13.5, 13.5, 2.5 Hz, 1 H), 2.71 (dddd, *J* = 14.0, 3.5, 3.5, 3.5 Hz, 1 H), 2.94 (dddd, *J* = 13.0, 13.0, 4.0, 2.5 Hz, 1 H), 4.02 (s, 1 H), 4.06 (s, 3 H), 4.07 (s, 3 H), 4.40 (dq, *J* = 11.0, 7.0 Hz, 1 H), 4.52 (dq, *J* = 11.0, 7.0 Hz, 1 H), 4.73-4.77 (m, 1 H); ¹³C NMR (CDCl₃, 125 MHz) δ 4.85 (t), 4.89 (t), 6.75 (q), 6.78 (q), 14.1 (q), 24.27 (t), 24.29 (t), 26.2 (t), 30.40 (t), 30.43 (t), 45.1 (d), 45.2 (d), 51.5 (q), 52.5 (q), 52.7 (q), 54.3 (s), 60.5 (t), 66.6 (d), 66.7 (d), 171.5 (s), 172.17 (s), 172.23 (s), 172.6 (s), 173.0 (s); exact mass (electrospray) *m/z* calcd for C₁₉H₃₄NaO₇Si (**54**, R = Et) 425.1966, found 425.1966; *m/z* calcd for C₁₈H₃₂NaO₇Si (**54**, R = Me) 411.1810, found 411.1810.

5-Bromo-2-methyl-2-(phenylseleno)pentanoic Acid Ethyl Ester (**51**).



n-BuLi (2.5 M in hexane, 1.76 mL, 4.4 mmol) was added dropwise over ca 2 min to a stirred and cooled (-78 °C) solution of *i*-Pr₂NH (0.68 mL, 4.8 mmol) in THF (8 mL). Stirring at -78 °C was continued for 45 min and a solution of **15** (1.028 g, 4.0 mmol) in THF (3 mL plus 1 mL as a rinse) was added over 5 min. Stirring was continued for 1.5 h at -78 °C and a solution of 1,3-dibromopropane (1.615 g, 8.0 mmol) in a mixture of THF (3 mL) and HMPA (1 mL) was added over 5 min. The mixture was stirred at -78 °C for 2 h, the cold bath was removed and stirring was continued for 2 h. The mixture was re-cooled to 0 °C and quenched with water (1 mL) and saturated aqueous NH₄Cl (5 mL). The cold bath was removed, stirring was continued for 10 min and the mixture was diluted with water (50 mL) and extracted with EtOAc (3 x 20 mL). The combined organic extracts were dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (3 x 20 cm), using 4% EtOAc-hexane, gave **51** (1.27 g, 84%) as a viscous oil: FTIR (CH₂Cl₂ cast) 2978, 2932, 1720, 1244, 1155, 742 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.19 (t, *J* = 7.2 Hz, 3 H), 1.51 (s, 3 H), 1.79-1.93 (m, 2 H), 1.97-2.09 (m, 2 H), 3.34-3.39 (m, 2 H), 4.03-4.15 (m, 2 H), 7.29-7.34 (m, 2 H), 7.37-7.42 (m, 1 H), 7.57-7.60 (m, 2 H); ¹³C NMR (CDCl₃, 100 MHz) δ 13.9 (q), 22.8 (q), 29.0 (t), 33.0 (t), 37.2 (t), 49.1 (s), 61.0 (t), 127.0 (s), 128.7 (d), 129.2 (d), 137.9 (d), 173.5 (s); exact mass (electrospray) *m/z* calcd for C₁₄H₁₉⁷⁹BrNaO₂⁸⁰Se 400.9626, found 400.9624.

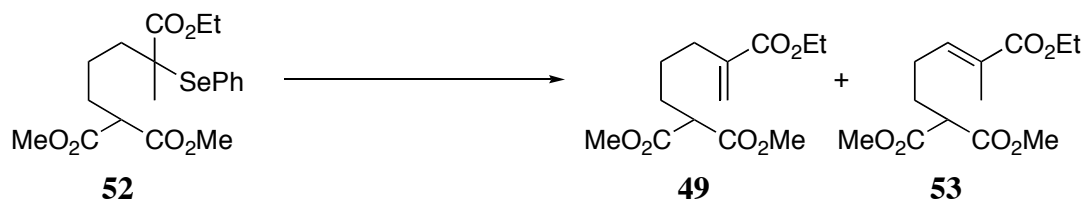
6-Methoxycarbonyl-2-methyl-2-(phenylseleno)heptanedioic Acid 1-Ethyl Ester 7-Methyl Ester (52).



A solution of dimethyl malonate (0.5 mL, 4.23 mmol) in THF (8 mL) was added dropwise over ca 10 min to a stirred suspension of NaH (95% w/w, 100 mg, 3.966 mmol) in THF (10 mL). Stirring at room temperature was continued for 1.5 h and a solution of **51** (1.0 g, 2.644 mmol) in THF (10 mL plus 2 mL as a rinse) was added dropwise over ca 5 min. The mixture was refluxed for 16 h, cooled to room temperature and then to 0 °C, and quenched with water (5 mL) and

saturated aqueous NH_4Cl (5 mL). The mixture was stirred at room temperature for 10 min and diluted with water (25 mL). The aqueous phase was extracted with EtOAc (3 x 15 mL) and the combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2 x 18 cm), using 15% EtOAc-hexane, gave **52** (955 mg, 84%) as a viscous oil: FTIR (CH_2Cl_2) 2954, 1753, 1736, 1721, 1438, 1157 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.17 (t, $J = 7.2$ Hz, 3 H) 1.2-1.31 (m, 1 H), 1.43-1.53 (m, 1 H), 1.47 (s, 3 H), 1.75 (ddd, $J = 13.6, 12.0, 4.4$ Hz, 1 H), 1.84-1.97 (m, 3 H), 3.34 (t, $J = 7.4$ Hz, 1 H), 3.71 (s, 3 H), 3.72 (s, 3 H), 4.0-4.13 (m, 2 H), 7.27-7.32 (m, 2 H), 7.36-7.40 (m, 1 H), 7.55-7.57 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.0 (q), 22.7 (q), 23.5 (t), 28.8 (t), 38.0 (t), 49.6 (s), 51.4 (d), 52.5 (q), 61.0 (t), 127.2 (s), 128.7 (d), 129.2 (d), 137.9 (d), 169.6 (s), 173.7 (s); exact mass (electrospray) m/z calcd for $\text{C}_{19}\text{H}_{26}\text{NaO}_6^{80}\text{Se}$ 453.0787, found 453.0794.

2-Methoxycarbonyl-6-methyleneheptanedioic Acid 7-Ethyl Ester 1-Methyl Ester (49) and 6-Methoxycarbonyl-2-methylhept-2-enedioic Acid 1-Ethyl Ester 7-Methyl Ester (53).

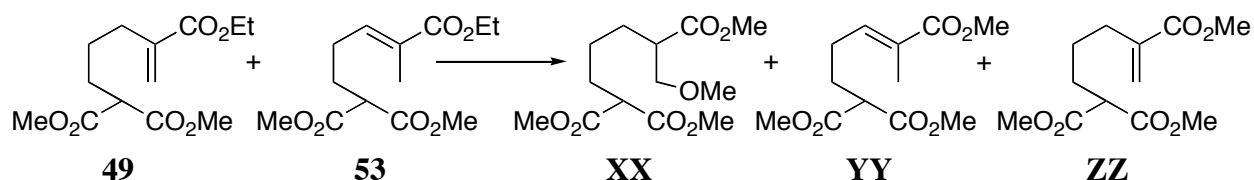


H_2O_2 (30%, 0.25 mL, 2.45 mmol) was added dropwise over 2 min to a stirred and cooled (-10°C , ice-acetone bath) solution of **52** (100 mg, 0.23 mmol) in CH_2Cl_2 (5 mL). Stirring at -10°C was continued for 1 h and the mixture was quenched with saturated aqueous NaHCO_3 (2 mL), followed by dropwise addition of $\text{Na}_2\text{S}_2\text{O}_3$ (3 mL). The cold bath was removed after 10 min, stirring was continued for 10 min and the mixture was diluted with water (10 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (0.5 x 8 cm), using 15% EtOAc-hexane, gave an inseparable 1:3 mixture of **53** (minor isomer) and **49** (59 mg, 94% in total): FTIR (CH_2Cl_2 cast) 2956, 1754, 1737, 1715, 1632, 1437, 1156 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.26-1.30 (m, 3 H), 1.46-1.53 (m, 1.5 H), 1.795-1.80 (m, 0.75 H), 1.88-1.94 (m, 1.5 H), 2.02-2.07 (m, 0.5 H), 2.19-2.25 (m, 0.5 H), 2.30-2.33 (m, 1.5 H), 3.36 (t, $J = 7.4$ Hz, 1 H), 3.72 (s, 4.5 H), 3.73 (s, 1.5 H), 4.14-4.21 (m, 2 H), 5.51-5.52 (m, 0.75 H), 6.135-6.138 (m, 0.75 H), 6.65-6.69 (m, 0.25 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 12.3 (q), 14.15 (q), 14.23 (q), 26.0 (t), 26.2 (t), 27.6 (t), 28.3 (t), 31.4 (t), 50.9 (d), 51.4 (q), 52.4 (q), 52.5 (d), 60.5 (t), 60.6 (t), 124.9 (s), 129.3 (s), 139.5 (d),

140.0 (t), 167.0 (s), 167.8 (s), 169.4 (s), 169.7 (s); exact mass (electrospray) m/z calcd for (**49** and **54**) $C_{13}H_{20}NaO_6$ 295.1152, found 295.1153.

Compound **53** probably has *E* geometry, based on the chemical shift of the vinyl H (δ 6.7).

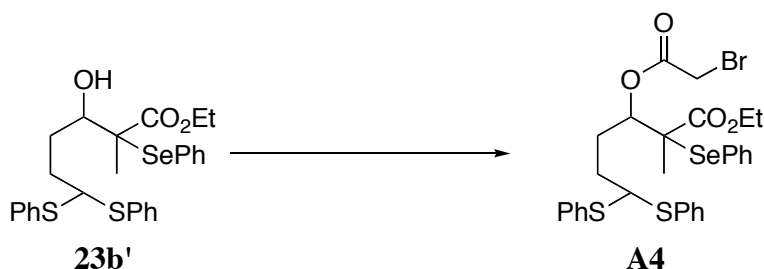
6-Methoxycarbonyl-2-(methoxymethyl)heptanedioic Acid Dimethyl Ester (XX), 6-Methoxycarbonyl-2-methylhept-2-enedioic Acid Dimethyl Ester (YY) and 2-Methoxycarbonyl-6-methyleneheptanedioic Acid Dimethyl Ester (ZZ).



DBU (22.6 mg, 0.15 mmol) was added into a stirred solution of **49** and **53** (3:1, 20.2 mg, 0.074 mmol) in MeOH (0.2 mL). Stirring at room temperature was continued for 41 h and the mixture was filtered through a pad (ca 5 cm) of silica gel in a Pasteur pipette, using EtOAc. Evaporation of the filtrate and flash chromatography of the residue over silica gel (0.7 x 7 cm), using 1:5 EtOAc-hexane and then 4:5 EtOAc-hexane, gave 6-methoxycarbonyl-2-(methoxymethyl)heptanedioic acid dimethyl ester (**XX**) (ca 2.4 mg, 11%) and what we assume [^1H NMR on the ester exchanged (OMe in place of OEt) starting materials] to be 6-methoxycarbonyl-2-methylhept-2-enedioic acid dimethyl ester (**YY**) and 6-methoxycarbonyl-2-methylenehept-1-enedioic acid dimethyl ester (**ZZ**) (8 mg, 42%) as an oil:

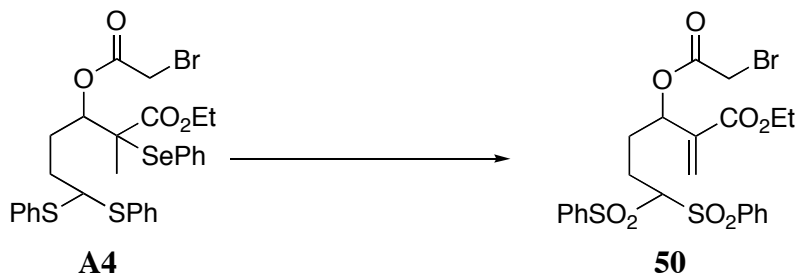
6-Methoxycarbonyl-2-(methoxymethyl)heptanedioic acid dimethyl ester (**XX**) had: FTIR (CDCl_3 cast) 2955, 2870, 1737, 1436 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.33 (quintet J = 8.0 Hz, 2 H), 1.49-1.67 (m, 2 H), 1.87-1.94 (m, 2 H), 2.66 (dddd, J = 5.4, 5.4, 2.6, 2.6 Hz, 1 H), 3.32 (s, 3 H), 3.35 (t, J = 7.6 Hz, 1 H), 3.43 (dd, J = 9.2, 5.2 Hz, 1 H), 3.57 (dd, J = 9.2, 8.0 Hz, 1 H), 3.70 (s, 3 H), 3.74 (s, 6 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 25.0 (t), 28.4 (t), 28.6 (t), 45.7 (d), 51.4 (q), 51.7 (d), 52.5 (q), 59.0 (q), 73.3 (t), 169.7 (s), 174.7 (s); exact mass (electrospray) m/z calcd for $C_{13}H_{22}NaO_7$ 313.1258, found 313.1258.

3-Bromoacetoxy-2-methyl-2-(phenylseleno)-6,6-bis(phenylthio)hexanoic Acid Ethyl Ester (A4).



Pyridine (20.6 mg, 0.26 mmol) and BrCH₂COBr (44.4 mg, 0.22 mmol) were added sequentially to a stirred and cooled (0 °C) solution of **23b'** (40 mg, 0.073 mmol) in CH₂Cl₂ (1 mL). Stirring at 0 °C was continued for 10 min, the cold bath was removed and stirring was continued for 3 h. The mixture was diluted with water (5 mL) and acidified with hydrochloric acid (1 M, 1 mL). The aqueous phase was extracted with CH₂Cl₂ (3 x 5 mL) and the combined organic extracts were washed with brine, dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (0.7 x 15 cm), using 1:6 EtOAc-hexane, gave 3-bromoacetoxy-2-methyl-2-(phenylseleno)-6,6-bis(phenylthio)hexanoic acid ethyl ester (**A4**) (28.3 mg, 58%) as an oil: FTIR (CH₂Cl₂ cast) 3057, 2981, 2934, 1726, 1582, 1476, 1439 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 1.05 (t, *J* = 7.2 Hz, 3 H), 1.54 (s, 3 H), 1.82-1.98 (m, 3 H), 2.62-2.68 (m, 1 H), 3.56 (AB q, *J* = 12.5 Hz, Δ*v*_{AB} = 12.1 Hz, 2 H), 3.86 (dq, *J* = 10.7, 7.1 Hz, 1 H), 4.00 (dq, *J* = 10.7, 7.1 Hz, 1 H), 4.50 (dd, *J* = 6.1, 6.1 Hz, 1 H), 5.40 (dd, *J* = 10.0, 2.0 Hz, 1 H), 7.25-7.41 (m, 10 H), 7.50-7.57 (m, 5 H); ¹³C NMR (CDCl₃, 125 MHz) δ 13.7 (q), 17.4 (q), 25.4 (d), 27.6 (d), 32.2 (d), 52.4 (s), 57.7 (d), 61.4 (t), 77.1 (d), 126.0 (s), 127.87 (d), 127.93 (d), 129.0 (d), 129.8 (d), 132.9 (d), 133.0 (d), 133.8 (s), 138.0 (d), 165.8 (s), 171.5 (s); exact mass (electrospray) *m/z* calcd for C₂₉H₃₁⁷⁹BrNaO₄S₂⁸⁰Se 688.9905, found 688.9908.

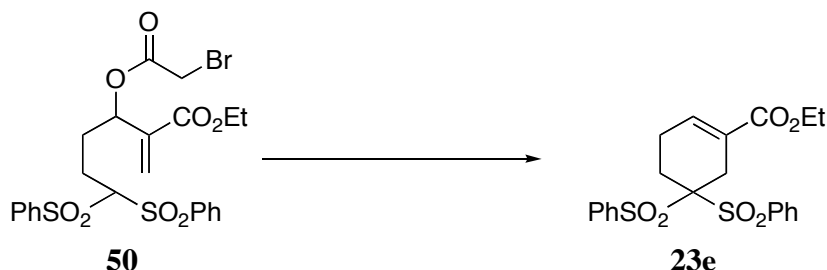
2-[4,4-Bis(benzenesulfonyl)-1-(bromoacetoxy)butyl]acrylic Acid Ethyl Ester (50).



m-CPBA (70-75%, 60.3 mg, 0.25 mmol) was added to a stirred solution of 3-bromoacetoxy-2-methyl-2-(phenylseleno)-6,6-bis(phenylthio)hexanoic acid ethyl ester (**A4**) (16.3 mg, 0.025 mmol) in CH₂Cl₂ (1 mL), and the mixture was stirred at 40 °C for 24 h, cooled

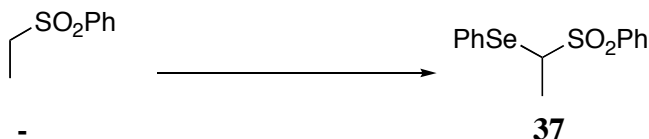
to room temperature and evaporated. Flash chromatography of the residue over silica gel (0.7 x 7 cm), using 1:2 EtOAc-hexane, gave **50** (5.3 mg, 52%) as a viscous oil: FTIR (CDCl₃ cast) 3066, 2982, 2928, 1721, 1634, 1584, 1448 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.32 (t, *J* = 7.2 Hz, 3 H), 2.04-2.15 (m, 1 H), 2.22-2.32 (m, 3 H), 3.83 (AB q, *J* = 12.2 Hz, Δ*v*_{AB} = 14.1 Hz, 2 H), 4.248 (q, *J* = 7.2 Hz, 1 H), 4.253 (q, *J* = 7.2 Hz, 1 H), 4.53 (dd, *J* = 5.6, 5.6 Hz, 1 H), 5.64 (dd, *J* = 8.0, 2.8 Hz, 1 H), 5.83 (s, 1 H), 6.34 (s, 1 H), 7.56-7.60 (m, 4 H), 7.68-7.72 (m, 2 H), 7.94-7.96 (m, 4 H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.1 (q), 21.4 (t), 25.5 (t), 31.7 (t), 61.3 (t), 76.5 (d), 82.5 (d), 125.9 (s), 129.1 (d), 129.6 (d), 134.6 (d), 137.6 (s), 137.7 (s), 138.3 (t), 164.6 (s), 166.0 (s); exact mass (electrospray) *m/z* calcd for C₂₃H₂₅⁷⁹BrNaO₈S₂ 595.0066, found 595.0064.

5,5-Bis(benzenesulfonyl)cyclohex-1-enecarboxylic Acid Ethyl Ester (23e) from 50.



Cs₂CO₃ (3.3 mg, 0.01 mmol) was added to a stirred solution of **50** (2.9 mg, 0.005 mmol) in THF (0.5 mL). Stirring at room temperature was continued for 1 h, the solid was filtered off through a pad of Celite, using CH₂Cl₂ as a rinse, and the filtrate was evaporated. The ¹H NMR spectrum of the residue showed only unreacted **50** and the ICD product **23e** in a 1:2 ratio.

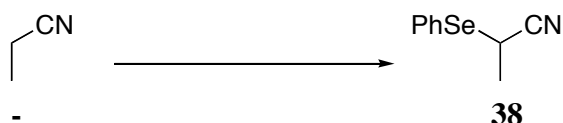
[[1-(Phenylseleno)ethyl]sulfonyl]benzene (37).¹¹



n-BuLi (1.6 M in hexane, 9.3 mL, 14.89 mmol) was added dropwise to a stirred and cooled (-78 °C) solution of (ethanesulfonyl)benzene (2.53 g, 14.89 mmol) in THF (150 mL). Stirring at -78 °C was continued for 1 h, and a solution of PhSeCl (1.34 g, 7.00 mmol) in THF (20 mL) was added rapidly in one portion. Stirring at -78 °C was continued for 3 h and the mixture was quenched with saturated aqueous NH₄Cl (40 mL). The cold bath was removed, stirring was continued for 15 min and the mixture was diluted with water (100 mL) and extracted

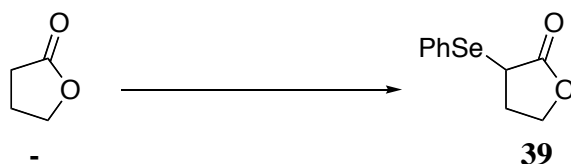
with EtOAc (3 x 40 mL). The combined organic extracts were washed with brine (50 mL), dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (3 x 15 cm), using 3:20 EtOAc-hexane, gave **37** (1.91 g, 85%) as an oil: ^1H NMR (CDCl_3 , 400 MHz) δ 1.67 (d, J = 7.2 Hz, 3 H), 4.26 (q, J = 7.2 Hz, 1 H), 7.22-7.27 (m, 2 H), 7.30-7.34 (m, 1 H), 7.51-7.55 (m, 4 H), 7.62-7.66 (m, 1 H), 7.91-7.93 (m, 2 H).

2-(Phenylseleno)propionitrile (**38**).¹²



n-BuLi (1.6 M in hexane, 8.9 mL, 14.3 mmol) was added dropwise to a stirred and cooled ($-78\text{ }^\circ\text{C}$) solution of *i*-Pr₂NH (1.52 g, 15.0 mmol) in THF (150). Stirring at $-78\text{ }^\circ\text{C}$ was continued for 45 min, and EtCN (826.0 mg, 15.0 mmol) was added dropwise. Stirring at $-78\text{ }^\circ\text{C}$ was continued for 1 h, and a solution of PhSeCl (1.27 g, 6.6 mmol) in THF (10 mL) was added rapidly in one portion. Stirring at $-78\text{ }^\circ\text{C}$ was continued for 1.5 h, and the mixture was quenched with hydrochloric acid (1 M, 10 mL). The cold bath was removed, stirring was continued for 15 min and the mixture was diluted with water (250 mL) and extracted with EtOAc (3 x 100 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 12 cm), using 7:100 EtOAc-hexane, gave **38** (830 mg, 60%) as a oil: FTIR (CHCl_3 cast) 3058, 2927, 2931, 2870, 2233, 1578, 1477, 1448 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 1.66 (d, J = 7.2 Hz, 3 H), 3.71 (q, J = 7.2 Hz, 1 H), 7.35-7.40 (m, 2 H), 7.44 (tt, J = 7.2, 1.2 Hz, 1 H), 7.71-7.75 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 19.2 (q), 19.4 (d), 120.7 (s), 125.8 (s), 129.4 (d), 129.6 (d), 136.4 (d); exact mass m/z calcd for $\text{C}_{16}\text{H}_9\text{N}^{80}\text{Se}$ 210.9900, found 210.9896.

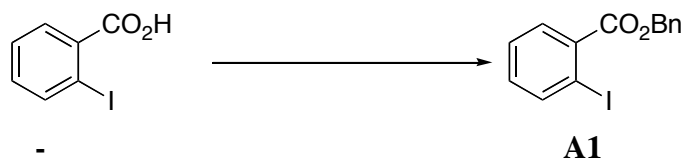
3-(Phenylseleno)dihydrofuran-2-one (**39**).¹³



n-BuLi (1.6 M in hexane, 3.9 mL, 6.27 mmol) was added dropwise to a stirred and cooled ($0\text{ }^\circ\text{C}$) solution of *i*-Pr₂NH (634.0 mg, 6.27 mmol) in THF (60). Stirring at $0\text{ }^\circ\text{C}$ was

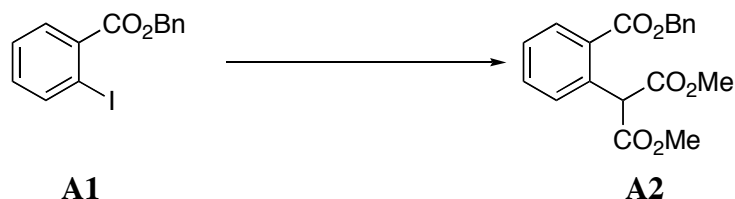
continued for 15 min, the mixture was cooled to $-78\text{ }^{\circ}\text{C}$ and γ -butyrolactone (540.0 mg, 6.27 mmol) was added dropwise. Stirring at $-78\text{ }^{\circ}\text{C}$ was continued for 1 h, a solution of PhSeCl (600 mg, 3.13 mmol) in THF (5 mL) was added rapidly in one portion. Stirring at $-78\text{ }^{\circ}\text{C}$ was continued for 1 h, and the mixture was quenched with saturated aqueous NH_4Cl (5 mL). The cold bath was removed, stirring was continued for 15 min and the mixture was diluted with water (200 mL) and extracted with EtOAc (3 x 60 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 12 cm), using 1:5 EtOAc-hexane, gave **39** (580 mg, 77%) as a oil: FTIR (CHCl_3 cast) 3056, 2989, 2912, 1765, 1578, 1478, 1438 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 2.28 (dddd, $J = 13.9, 7.2, 4.4, 4.0$ Hz, 1 H), 2.71 (dddd, $J = 13.8, 8.5, 8.3, 8.3$ Hz, 1 H), 3.93 (dd, $J = 8.5, 4.4$ Hz, 1 H), 4.12 (ddd, $J = 9.2, 8.3, 7.2$ Hz, 1 H), 4.26 (ddd, $J = 9.2, 8.4, 4.0$ Hz, 1 H), 7.31-7.41 (m, 3 H), 7.67-7.70 (m, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 30.5 (t), 35.8 (d), 66.8 (t), 126.5 (s), 129.1 (d), 129.3 (d), 135.8 (d), 176.0 (s); exact mass m/z calcd for $\text{C}_{10}\text{H}_{10}\text{O}_2^{80}\text{Se}$ 241.9846, found 241.9843.

2-Iodobenzoic Acid Benzyl Ester (A1).⁴⁵



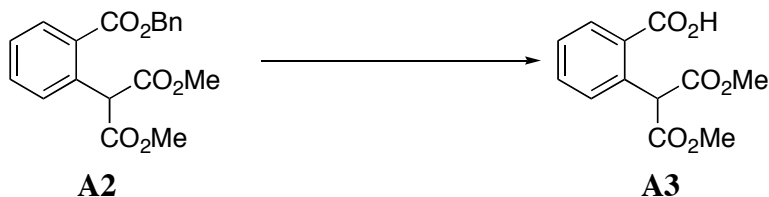
K_2CO_3 (8.90 g, 64.5 mmol) was added to a stirred solution of BnCl (4.90 g, 38.7 mmol), 2-iodobenzoic acid (8.0 g, 32.3 mmol) and Bu_4NI (1.19 g, 3.23 mmol) in THF (180 mL), and the mixture was refluxed for 6 h. The mixture was cooled to room temperature and the solid was filtered off. The filtrate was diluted with water (200 mL) and the aqueous phase was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic extracts were washed with aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (5%, 30 mL) and brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (5 x 15 cm), using 1:20 EtOAc-hexane, gave 2-iodobenzyl benzoate (**A1**) (10.81 g, 99%) as a liquid: FTIR (CDCl_3 cast) 3064, 3033, 2953, 2890, 1727, 1583, 1562, 1498, 1455, 1429 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 5.83 (s, 2 H), 7.15 (td, $J = 7.7, 1.7$ Hz, 1 H), 7.33-7.42 (m, 4 H), 7.46-7.49 (m, 2 H), 7.82 (dd, $J = 7.8, 1.7$ Hz, 1 H), 7.99 (dd, $J = 7.9, 1.1$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 67.4 (t), 94.2 (s), 127.9 (d), 128.4 (d), 128.5 (d), 128.6 (d), 131.0 (d), 132.7 (d), 135.0 (s), 135.5 (s), 141.3 (d), 166.3 (s); exact mass m/z calcd for $\text{C}_{14}\text{H}_{11}\text{IO}_2$ 337.9804, found 337.9802.

2-[(2-Benzyloxycarbonyl)phenyl]malonic Acid Dimethyl Ester (A2).



Dimethyl malonate (2.34 g, 17.8 mmol) was added slowly to a stirred suspension of NaH (0.71 g, 17.8 mmol) in 1,4-dioxane (80 mL) (N_2 atmosphere). Stirring at room temperature was continued for 15 min, and CuBr (4.24 g, 29.6 mmol) was added. Stirring at room temperature was continued for 15 min, and a solution of 2-iodobenzoyl benzoate (**A1**) (5.0 g, 14.8 mmol) in 1,4-dioxane (20 mL) was added dropwise. The mixture was refluxed for 48 h, cooled to room temperature, acidified with hydrochloric acid (1 M, 20 mL) and diluted with water (200 mL). The aqueous phase was extracted with EtOAc (3 x 80 mL) and the combined organic extracts were washed brine, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (3 x 15 cm), using 1:3 EtOAc-hexane, gave 2-[(2-benzyloxycarbonyl)phenyl]malonic acid dimethyl ester (**A2**) (1.18 g, 73%) as a white solid: mp 71-72 °C; FTIR ($CDCl_3$ cast) 3034, 3004, 2954, 2844, 1758, 1738, 1716, 1602, 1680, 1498, 1455, 1436 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) δ 3.76 (s, 6 H), 5.35 (s, 2 H), 5.84 (s, 1 H), 7.33-7.47 (m, 7 H), 7.55 (td, J = 7.6, 1.4 Hz, 1 H), 8.08 (dd, J = 7.9, 1.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 52.7 (q), 54.5 (d), 66.8 (t), 128.0 (d), 128.1 (d), 128.2 (d), 128.4 (d), 129.2 (s), 129.9 (d), 130.9 (d), 132.5 (d), 134.2 (s), 135.5 (s), 166.4 (s), 168.7 (s); exact mass (electrospray) m/z calcd for $C_{19}H_{18}NaO_6$ 365.0996, found 365.0998.

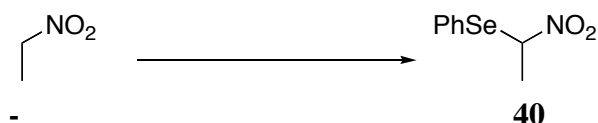
2-(2-Carboxyphenyl)malonic Acid Dimethyl Ester (A3).²⁷



Pd/C (10%, 0.32 g) was added to a solution of 2-[(2-benzyloxycarbonyl)phenyl]malonic acid dimethyl ester (**A2**) (3.23 g, 9.44 mmol) in THF (35 mL) (N_2 atmosphere). The flask was capped with a septum and the solution was degassed by being placed under house vacuum, and the flask was then filled with H_2 . This process was repeated three times, and the mixture was

stirred under H₂ (balloon) at room temperature for 24 h, and then filtered through a pad of Celite, using CH₂Cl₂ (100 mL) as a rinse. Evaporation of the filtrate gave pure (¹H NMR) 2-(2-carboxyphenyl)malonic acid dimethyl ester (**A3**) (2.38 g, 100%) as a white solid: mp 115-118 °C; FTIR (CDCl₃ cast) 3400-2500, 3007, 2956, 1737, 1602, 1780, 1493, 1437, 1411 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 3.79 (s, 6 H), 5.85 (s, 1 H), 7.44-7.48 (m, 2 H), 7.61 (td, *J* = 7.9, 1.5 Hz, 1 H), 8.16 (dd *J* = 8.1, 1.5 Hz, 1 H), ¹³C NMR (CDCl₃, 100 MHz) δ 52.9 (q), 54.6 (d), 128.1 (s), 128.3 (d), 130.3 (d), 132.0 (d), 133.5 (d), 135.0 (s), 168.9 (s), 171.6 (s); exact mass *m/z* calcd for C₁₂H₁₂O₆ 252.0634, found 252.0631.

[(1-Nitroethyl)seleno]benzene (40).^{8c}



n-BuLi (1.6 M in hexane, 8.3 mL, 13.2 mmol) was added dropwise to a stirred and cooled (-78 °C) solution of EtNO₂ (1.02 g, 13.6 mmol) in THF (120 mL). Stirring at -78 °C was continued for 1 h, and a solution of PhSeCl (1.2 g, 6.3 mmol) in THF (20 mL) was added rapidly in one portion. Stirring at -78 °C was continued for 2 h and the mixture was quenched with saturated aqueous NH₄Cl (20 mL). The cold bath was removed, stirring was continued for 15 min and the mixture was diluted with water (100 mL) and extracted with EtOAc (3 x 40 mL). The combined organic extracts were washed with brine (50 mL), dried (Na₂SO₄) and evaporated. Flash chromatography of the residue over silica gel (4 x 15 cm), using 1:20 EtOAc-hexane, gave **40** (1.17 g, 81%) as a liquid: FTIR (CDCl₃ cast) 3059, 2959, 2932, 2885, 1548, 1477, 1439 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.82 (d, *J* = 6.9 Hz, 3 H), 5.69 (q, *J* = 6.9 Hz, 1 H), 7.34-7.38 (m, 2 H), 7.41-7.46 (m, 1 H), 7.60-7.63 (m, 2 H); ¹³C NMR (CDCl₃, 100 MHz) δ 19.6 (q), 78.7 (d), 125.8 (s), 129.4 (d), 129.8 (d), 136.2 (d); exact mass *m/z* calcd for C₈H₉NO₂⁷⁸Se 228.9806, found 228.9813.

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