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Physical Data of **9b–d**, **10b,d**, **11b-c**, **12b–d**, **13c–e**, **14b–e**, **19**, **22a,b**, **23a,b**, **27–29a**, **31–33**, **36–38**, **42**, **43**, **45**, **48–51a**, and **53a–55a**.

8-[(2,6-Dimethoxy-3-nitrobenzyl)oxy]-2-methylquinoline (9b). Using a similar procedure to that used for **9a**, the title compound was obtained in 90.3% yield from **7b** and **8** as yellow crystals after crystallization from MeOH: mp 194–196 °C; ^{1}H NMR ($CDCl_3$) δ 2.68 (3H, s), 3.91 (3H, s), 4.08 (3H, s), 5.40 (2H, s), 6.78 (1H, d, *J* = 8 Hz), 7.22–7.31 (2H, m), 7.37–7.46 (2H, m), 8.00 (1H, d, *J* = 8 Hz), 8.09 (1H, d, *J* = 8 Hz). Anal. ($C_{19}H_{18}N_2O_5$) C, H, N.

8-[(2-Chloro-5-nitrobenzyl)oxy]-2-methylquinoline (9c). Using a similar procedure to that used for **9a**, the title compound was obtained in 83.9% yield from **7c** and **8** as a colorless amorphous solid: ^{1}H NMR (DMSO-d_6) δ 2.69 (3H, s), 5.48 (2H, s), 7.32 (1H, d, *J* = 8 Hz), 7.43 (1H, d, *J* = 8 Hz), 7.46 (1H, d, *J* = 8 Hz), 7.53 (1H, d, *J* = 8 Hz), 7.83 (1H, d, *J* = 8 Hz), 8.22 (2H, dd, *J* = 8, 2 Hz), 8.77 (1H, d, *J* = 2 Hz). Anal. ($C_{17}H_{13}ClN_2O_3$) C, H, N.

2-Methyl-8-[(2-methyl-3-nitrobenzyl)oxy]quinoline (9d). Using a similar procedure to that used for **9a**, the title compound was obtained in 91.7% yield from **7d** and **8** as pale yellow crystals after crystallization from MeOH: mp 186–188 °C; ^{1}H NMR ($CDCl_3$) δ 2.56 (3H, s), 2.80 (3H, s), 5.48 (2H, s), 7.00 (1H, d, *J* = 8 Hz), 7.28–7.44 (4H, m), 7.74 (1H, d, *J* = 8 Hz), 7.82 (1H, d, *J* = 8 Hz), 8.04 (1H, d, *J* = 8 Hz); MS (ESI) *m/z* 309 (M + 1). Anal. ($C_{18}H_{16}N_2O_3$) C, H, N.

8-[(3-Amino-2,6-dimethoxybenzyl)oxy]-2-methylquinoline (10b). Using a similar procedure to that used for **10a**, the title compound was obtained in 63.6% yield from **9b** as pale brown crystals after crystallization from MeOH: mp 208–210 °C; ^{1}H NMR ($CDCl_3$) δ 2.27 (3H, s), 2.37 (3H, s), 2.72 (3H, s), 3.57 (2H, br s), 5.32 (2H, s), 6.67 (1H, d, *J* = 8 Hz), 6.91 (1H, d, *J* = 8 Hz), 7.18–7.31 (2H, m), 7.36–7.42 (2H, m), 8.00 (1H, d, *J* = 8 Hz); MS (ESI) *m/z* 325 (M + 1). Anal. ($C_{19}H_{20}N_2O_3$) C, H, N.

8-[(3-Amino-2-methylbenzyl)oxy]-2-methylquinoline (10d). Using a similar procedure to that used for **10c**, the title compound was obtained in 62.1% yield

from **9d** as pale brown crystals after crystallization from MeCN: mp 223–227 °C; ^{1}H NMR ($CDCl_3$) δ 2.23 (3H, s), 2.79 (3H, s), 3.66 (2H, br s), 5.41 (2H, s), 6.68 (1H, br d, J = 8 Hz), 6.92–7.05 (3H, m), 7.24–7.38 (3H, m), 8.00 (1H, d, J = 8 Hz); MS (ESI) m/z 279 (M + 1). Anal. ($C_{18}H_{18}N_2O$) C, H, N.

8-[[2,6-Dimethoxy-3-(*N*-phthalimidoacetyl)aminobenzyl]oxy]-2-methylquinoline (11b). Using a similar procedure to that used for **11a**, the title compound was obtained in 93.4% yield from **10b** and *N*-phthaloylglycyl chloride as pale pink crystals after crystallization from acetone: mp 229–231 °C; ^{1}H NMR ($CDCl_3$) δ 2.70 (3H, s), 3.79 (3H, s), 3.94 (3H, s), 4.55 (2H, s), 5.36 (2H, s), 6.66 (1H, d, J = 8 Hz), 7.22–7.30 (2H, m), 7.32–7.42 (2H, m), 7.71–7.79 (2H, m), 7.86–7.92 (2H, m), 7.99 (1H, d, J = 8 Hz), 8.08 (1H, br s), 8.19 (1H, d, J = 8 Hz); MS (ESI) m/z 512 (M + 1). Anal. ($C_{29}H_{25}N_3O_6$) C, H, N.

8-[[2-Chloro-5-(*N*-phthalimidoacetyl)aminobenzyl]oxy]-2-methylquinoline (11c). Using a similar procedure to that used for **11a**, the title compound was obtained from **10c** and *N*-phthaloylglycyl chloride as colorless solid, which was directly used to the next step without further purification.

2-Methyl-8-[[2-methyl-3-(*N*-phthalimidoacetyl)aminobenzyl]oxy]quinoline (11d). Using a similar procedure to that used for **11a**, the title compound was obtained in 80.6% yield from **10d** and *N*-phthaloylglycyl chloride as pale yellow crystals after crystallization from acetone: mp 283–285 °C; ^{1}H NMR (DMSO-d_6) δ 2.27 (3H, s), 2.65 (3H, s), 4.48 (2H, s), 5.30 (2H, s), 7.20 (1H, t, J = 8 Hz), 7.26–7.34 (4H, m), 7.85–7.98 (4H, m), 8.20 (1H, d, J = 8 Hz), 9.85 (1H, br s); MS (ESI) m/z 466 (M + 1). Anal. ($C_{28}H_{23}N_3O_4$) C, H, N.

8-[[2,6-Dimethoxy-3-(*N*-methyl-*N*-phthalimidoacetyl)aminobenzyl]oxy]-2-methylquinoline (12b). Following a similar procedure to method A, the title compound was obtained in 93.4% yield from **11b** and methyl iodide as colorless crystals after crystallization from MeCN: mp 184–185 °C;

^{1}H NMR ($CDCl_3$) δ 2.70 (3H, s), 3.29 (3H, s), 3.90 (3H, s), 4.01 (3H, s), 4.22 (1H, d, J = 17 Hz), 4.32 (1H, d, J = 17 Hz), 5.44 (2H, s), 6.79 (1H, d, J = 8 Hz), 7.24–7.44 (5H, m), 7.69–7.75 (2H, m), 7.81–7.89 (2H, m), 8.00 (1H, d, J = 8 Hz); MS (ESI) *m/z* 526 (M + 1). Anal. ($C_{30}H_{27}N_3O_6$) C, H, N.

8-[[2-Chloro-5-(*N*-methyl-*N*-phthalimidoacetyl)aminobenzyl]oxy]-2-methylquinoline (12c). Following a similar procedure to method A, the title compound was obtained in 14.8% yield from **11c** and methyl iodide as colorless crystals after crystallization from diethyl ether: mp 120–124 °C; ^{1}H NMR (DMSO-d_6) δ 2.67 (3H, s), 3.18(3H, br s), 4.06 (2H, br s), 5.42 (2H, br s), 7.29 (1H, d, J = 8 Hz), 7.414–7.96 (10H, m), 8.19 (1H, d, J = 8 Hz). Anal. ($C_{28}H_{22}ClN_3O_4$) C, H, N.

2-Methyl-8-[[2-methyl-3-(*N*-methyl-*N*-phthalimidoacetyl)aminobenzyl]oxy]quinoline (12d). Following a similar procedure to method A, the title compound was obtained in 62.3% yield from **11d** and methyl iodide as pale brown crystals after crystallization from AcOEt: mp 158–161 °C; ^{1}H NMR ($CDCl_3$) δ 2.47 (3H, s), 2.80 (3H, s), 3.26 (3H, s), 3.92 (1H, d, J = 17 Hz), 4.19 (1H, d, J = 17 Hz), 5.46 (2H, s), 7.06 (1H, br d, J = 8 Hz), 7.23–7.42 (5H, m), 7.65–7.75 (3H, m), 7.81–7.89 (2H, m), 8.03 (1H, d, J = 8 Hz); MS (ESI) *m/z* 480 (M + 1). Anal. ($C_{29}H_{25}N_3O_4$) C, H, N.

8-[[5-(*N*-Aminoacetyl-*N*-methylamino)-2-chlorobenzyl]oxy]-2-methylquinoline (13c). Using a similar procedure to that used for **13b**, the title compound was obtained in 90.7% yield from **12c** as colorless crystals after crystallization from diethyl ether: mp 82–87 °C; ^{1}H NMR ($CDCl_3$) δ 2.83 (3H, s), 2.94 (2H, s), 3.19 (3H, s), 5.53 (2H, s), 6.95 (1H, d, J = 8 Hz), 7.07 (1H, br d, J = 8 Hz), 7.30–7.44 (3H, m), 7.46 (1H, d, J = 8 Hz), 7.56 (1H, d, J = 1 Hz), 8.05 (1H, d, J = 8 Hz). Anal. ($C_{20}H_{20}ClN_3O_2$) C, H, N.

8-[[3-(*N*-Aminoacetyl-*N*-methylamino)-2-methylbenzyl]oxy]-2-methylquinoline (13d). Using a similar procedure to that used for **13b**, the title compound was obtained in 88.4% yield from **12d** as a colorless amorphous solid: ^{1}H

NMR ($CDCl_3$) δ 2.29 (3H, s), 2.80 (3H, s), 2.90 (1H, d, J = 17 Hz), 3.13 (1H, d, J = 17 Hz), 3.24 (3H, s), 5.40 (2H, s), 7.01 (1H, br d, J = 8 Hz), 7.09 (1H, br d, J = 8 Hz), 7.21–7.43 (4H, m), 7.60 (1H, br d, J = 8 Hz), 8.03 (1H, d, J = 8 Hz); MS (ESI) *m/z* 350 (M + 1). Anal. ($C_{21}H_{23}N_3O_2$) C, H, N.

8-[[3-(*N*-Aminoacetyl)amino-2,6-dichlorobenzyl]oxy]-2-methylquinoline (13e). Using a similar procedure to that used for **13b**, the title compound was obtained in 87.7% yield from **11a** as a pale brown amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.73 (3H, s), 3.52 (2H, s), 5.62 (2H, s), 7.20–7.45 (5H, m), 8.01 (1H, d, J = 8.5 Hz), 8.51 (1H, d, J = 8.5 Hz). Anal. ($C_{19}H_{17}Cl_2N_3O_2$) C, H, N.

8-[[2,6-Dimethoxy-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methylquinoline (14b). Following a similar procedure to method B, the title compound was obtained in 85.7% yield from **13b** and (*E*)-4-(*N*-methylcarbamoyl)cinnamic acid[22] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.26 (3H, s), 2.99 (3H, d, J = 5 Hz), 3.32 (3H, s), 3.82–3.92 (7H, m), 3.98 (1H, dd, J = 17, 5 Hz), 5.31 (1H, d, J = 10 Hz), 5.47 (1H, d, J = 10 Hz), 6.28 (1H, br d, J = 5 Hz), 6.51 (1H, d, J = 15 Hz), 6.70 (1H, br t, J = 5 Hz), 6.75 (1H, d, J = 8 Hz), 7.19 (1H, d, J = 8 Hz), 7.22–7.59 (7H, m), 7.74 (2H, d, J = 8 Hz), 7.99 (1H, d, J = 8 Hz); MS (ESI) *m/z* 583 (M + 1). Anal. ($C_{33}H_{34}N_4O_6$) C, H, N.

8-[[2-Chloro-5-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methylquinoline (14c). Following a similar procedure to method B, the title compound was obtained in 79.7% yield from **13c** and (*E*)-4-(*N*-methylcarbamoyl)cinnamic acid[22] as colorless crystals after crystallization from AcOEt: mp 223–227 °C; ^{1}H NMR ($CDCl_3$–CD_3OD) δ 2.79 (3H, s), 3.00 (3H, s), 3.24 (3H, s), 3.76 (2H, s), 5.52 (2H, s), 6.52 (1H, d, J = 15 Hz), 7.03 (1H, dd, J = 8, 1 Hz), 7.19 (1H, dd, J = 8, 1 Hz), 7.33–7.44 (3H, m), 7.49–7.60 (4H, m), 7.68 (1H, d, J = 1 Hz),

7.76 (2H, d, J = 8 Hz), 8.07 (1H, d, J = 8 Hz); MS (FAB) *m/z* 557 (M + 1). Anal. ($C_{31}H_{29}ClN_4O_4$) C, H, N.

2-Methyl-8-[[2-methyl-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamidoacetyl]amino]benzyl]oxy]quinoline (14d). Following a similar procedure to method B, the title compound was obtained in 93.0% yield from **13d** and (*E*)-4-(*N*-methylcarbamoyl)cinnamic acid[22] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.32 (3H, s), 2.79 (3H, s), 3.02 (3H, d, J = 5 Hz), 3.28 (3H, s), 3.67 (1H, dd, J = 17, 5 Hz), 3.88 (1H, dd, J = 17, 4 Hz), 5.38 (1H, d, J = 10 Hz), 5.46 (1H, d, J = 10 Hz), 6.18 (1H, br d, J = 5 Hz), 6.52 (1H, d, J = 15 Hz), 6.70 (1H, br s), 7.06 (1H, dd, J = 8, 3 Hz), 7.12 (1H, br d, J = 8 Hz), 7.24–7.43 (4H, m), 7.50–7.66 (4H, m), 7.75 (2H, d, J = 8 Hz), 8.04 (1H, d, J = 8 Hz); MS (FAB) *m/z* 537 (M + 1). Anal. ($C_{32}H_{32}N_4O_4$) C, H, N.

8-[[3-[*N*-[(*E*)-3-(6-Acetamidopyridin-3-yl)acryloylglycyl]amino]-2,6-dichloro-benzyl]oxy]-2-methylquinoline (14e). Following a similar procedure to method B, the title compound was obtained in 15.8% yield from **13e** and (*E*)-3-(6-acetamidopyridin-3-yl)acrylic acid[22] as colorless crystals after crystallization from AcOEt: mp 274–279 °C; ^{1}H NMR (DMSO-d_6) δ 2.11 (3H, s), 2.60 (3H, s), 4.14 (2H, d, J = 5.5 Hz), 5.47 (2H, s), 6.76 (1H, d, J = 16 Hz), 7.34–7.57 (5H, m), 7.60 (1H, d, J = 9 Hz), 7.92 (1H, d, J = 9 Hz), 8.00 (1H, d, J = 9 Hz), 8.11 (1H, d, J = 9 Hz), 8.20 (1H, d, J = 9 Hz), 8.45–8.60 (2H, m), 9.80 (1H, s), 10.67 (1H, s); MS (FAB) *m/z* 578 (M + 1). Anal. ($C_{29}H_{25}Cl_2N_5O_4$) C, H, N.

8-[[2,6-Dichloro-3-(2,5-dioxolanyl)benzyl]oxy]-2-methylquinoline (19). Using a similar procedure to that used for **9a**, the title compound was obtained in 73.0% yield from **8** and **18** as colorless crystals after crystallization from AcOEt: mp 156–158 °C; ^{1}H NMR ($CDCl_3$) δ 2.74 (3H, s), 4.02–4.18 (4H, m), 5.64 (2H, s), 6.17 (1H, s), 7.21–7.45 (5H, m), 7.59 (1H, d, J = 8 Hz), 8.00 (1H, d, J = 8 Hz); MS (ESI) *m/z* 390 (M + 1). Anal. ($C_{20}H_{17}Cl_2NO_3$) C, H, N.

8-[[3-[(*Z*)-3-Aminopropenyl]-2,6-dichlorobenzyl]oxy]-2-methylquinoline (22a). Using a similar procedure to that used for **13b**, the title compound was obtained in 89.1% yield from **21a** as a pale yellow amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.73 (3H, s), 3.46 (2H, d, *J* = 7 Hz), 5.61 (2H, s), 5.92 (1H, dt, *J* = 10, 7 Hz), 6.57 (1H, br d, *J* = 10 Hz), 7.18 (1H, d, *J* = 8 Hz), 7.24–7.47 (5H, m), 8.02 (1H, d, *J* = 8 Hz); MS (ESI) *m/z* 373 (M + 1). Anal. ($C_{20}H_{18}Cl_2N_2O$) C, H, N.

8-[[3-[(*E*)-3-Aminopropenyl]-2,6-dichlorobenzyl]oxy]-2-methylquinoline (22b). Using a similar procedure to that used for **13b**, the title compound was obtained in 82.6% yield from **21b** as a pale yellow amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.74 (3H, s), 3.53 (2H, d, *J* = 5 Hz), 5.63 (2H, s), 6.29 (1H, dt, *J* = 15, 5 Hz), 6.90 (1H, br d, *J* = 15 Hz), 7.23–7.48 (6H, m), 8.00 (1H, d, *J* = 8 Hz); MS (ESI) *m/z* 373 (M + 1). Anal. ($C_{20}H_{18}Cl_2N_2O$) C, H, N.

8-[[2,6-Dichloro-3-[(*Z*)-3-[(*E*)-4-(*N*-methylcarbamoyl)cinnamido]propenyl]benzyl]oxy]-2-methylquinoline (23a). Following a similar procedure to method B, the title compound was obtained in 91.5% yield from **22a** and (*E*)-4-(*N*-methylcarbamoyl)cinnamic acid[22] as colorless crystals after crystallization from MeCN: mp 194–196 °C; ^{1}H NMR ($CDCl_3$–CD_3OD) δ 2.62 (3H, s), 2.95 (3H, br d, *J* = 5 Hz), 4.05 (2H, br d, *J* = 7 Hz), 5.53 (2H, s), 5.96 (1H, dt, *J* = 10, 7 Hz), 6.52 (1H, d, *J* = 15 Hz), 6.61 (1H, br d, *J* = 10 Hz), 6.96 (1H, br s), 7.19–7.32 (4H, m), 7.41–7.50 (3H, m), 7.54 (1H, d, *J* = 15 Hz), 7.68 (2H, d, *J* = 8 Hz), 8.08 (1H, d, *J* = 8 Hz); MS (ESI) *m/z* 560 (M + 1). Anal. ($C_{31}H_{27}Cl_2N_3O_3$) C, H, N.

8-[[2,6-Dichloro-3-[(*E*)-3-[(*E*)-4-(*N*-methylcarbamoyl)cinnamido]propenyl]benzyl]oxy]-2-methylquinoline (23b). Following a similar procedure to method B, the title compound was obtained in 52.4% yield from **22b** and (*E*)-4-(*N*-methylcarbamoyl)cinnamic acid[22] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$–CD_3OD) δ 2.65 (3H, br s), 2.94 (3H, br d, *J* = 5 Hz), 4.15 (2H, br d, *J* = 6 Hz), 5.52 (2H, s), 6.20 (1H, m), 6.61 (1H, d, *J* = 15 Hz),

6.90 (1H, br d, J = 15 Hz), 7.21–7.38 (2H, m), 7.40–7.49 (3H, m), 7.51–7.66 (4H, m), 7.79 (2H, br d, J = 8 Hz), 8.07 (1H, d, J = 8 Hz); MS (ESI) *m/z* 560 (M + 1). Anal. ($C_{31}H_{27}Cl_2N_3O_3$) C, H, N.

8-[[3-(2-Cyanophenyl)-2,6-dimethylbenzyl]oxy]-2-methylquinoline (27). Following a similar procedure to that used for **9a**, the title compound was obtained in 89.9% yield from **8** and **26** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.33 (3H, s), 2.55 (3H, s), 2.73 (3H, s), 5.40 (1H, d, J = 12 Hz), 5.46 (1H, d, J = 12 Hz), 7.13 (1H, d, J = 8 Hz), 7.18 (1H, d, J = 8 Hz), 7.23–7.48 (6H, m), 7.63 (1H, t, J = 8 Hz), 7.74 (1H, d, J = 8 Hz), 8.02 (1H, d, J = 8 Hz); MS (ESI) *m/z* 379 (M + 1). Anal. ($C_{26}H_{22}N_2O$) C, H, N.

8-[[3-(2-Aminomethylphenyl)-2,6-dimethylbenzyl]oxy]-2-methylquinoline (28). Following a similar procedure to that used for **40**, the title compound was obtained in 50.4% yield from **27** as a brown oil, , which was used for the next step without further purification.

8-[[2,6-Dimethyl-3-[2-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamide]phenyl]benzyl]oxy]-2-methylquinoline (29a). Following a similar procedure to method B, the title compound was obtained in 15.3% yield from **28** and (*E*)-4-(*N*-methylcarbamoyl)cinnamic acid[22] as a pale yellow amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.10 (3H, s), 2.20 (3H, s), 2.55 (3H, s), 3.00 (3H, d, J = 6 Hz), 4.29 (1H, dd, J = 16, 6 Hz), 4.48 (1H, dd, J = 16, 6 Hz), 5.30 (2H, s), 6.45 (1H, d, J = 16 Hz), 6.55 (1H, br s), 6.88–7.78 (6H, m), 8.23 (1H, d, J = 8 Hz); MS (ESI) *m/z* 570 (M + 1). Anal. ($C_{37}H_{35}N_3O_3$) C, H, N.

1-(*tert*-Butyldiphenylsiloxymethyl)-2,6-dimethyl-3-[3-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamido]phenyl]benzene (31). Following a similar procedure to method B, the title compound was obtained in 81.6% yield from **30** and (*E*)-4-(*N*-methylcarbamoyl)cinnamic acid[22] as pale yellow crystals after crystallization from MeCN: mp 245–247 °C; ^{1}H NMR (DMSO-d_6) δ 1.01 (9H, s), 2.12 (3H, s), 2.21 (3H, s), 2.79 (3H, d, J = 5 Hz), 4.79 (2H, s), 6.88–6.98 (2H, m), 7.01–7.11 (2H, m), 7.30–

7.52 (7H, m), 7.59–7.75 (11H, m), 7.90 (2H, d, J = 8 Hz), 8.51 (1H, br d, J = 5 Hz); MS (ESI) m/z 653 (M + 1). Anal. ($C_{42}H_{44}N_2O_3Si$) C, H, N.

2,6-Dimethyl-1-hydroxymethyl-3-[3-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamido]phenyl]benzene (32). Following a similar procedure to the preparation of **26**, the title compound was obtained in 86.3% yield from **31** as colorless crystals after crystallization from AcOEt: mp 272–277 °C; ^{1}H NMR (DMSO-d_6) δ 2.28 (3H, s), 2.40 (3H, s), 2.80 (3H, d, J = 5 Hz), 4.57 (2H, d, J = 6 Hz), 4.78 (1H, t, J = 6 Hz), 6.87–7.10 (4H, m), 7.38 (1H, t, J = 8 Hz), 7.57–7.74 (5H, m), 7.89 (2H, d, J = 8 Hz), 8.50 (1H, br d, J = 5 Hz); MS (ESI) m/z 415 (M + 1). Anal. ($C_{26}H_{26}N_2O_3$) C, H, N.

1-(*tert*-Butyldiphenylsiloxymethyl)-2,6-dimethyl-3-(2-cyanothiophen-3-yl)benzene (34). Following a similar procedure to the preparation of **25**, the title compound was obtained in 29.0% yield from **24** and 3-bromo-2-cyanothiophene as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 1.04 (9H, s), 2.13 (3H, s), 2.25 (3H, s), 4.76 (2H, s), 7.00–7.08 (2H, m), 7.13 (1H, d, J = 8 Hz), 7.32–7.48 (6H, m), 7.56 (1H, d, J = 6 Hz), 7.69 (4H, br d, J = 8 Hz); MS (ESI) m/z 482 (M + 1). Anal. ($C_{30}H_{31}NOSSi$) C, H, N.

1-(*tert*-Butyldiphenylsiloxymethyl)-2,6-dimethyl-3-[2-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidomethyl]thiophen-3-yl]benzene (36). Following a similar procedure to method B, the title compound was obtained in 82.0% yield from **35** and (*E*)-4-(*N*-methylcarbamoyl)cinnamic acid[22] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 1.05 (9H, s), 2.05 (3H, s), 2.28 (3H, s), 3.02 (3H, d, J = 6 Hz), 4.49 (2H, br s), 4.77 (2H, s), 6.00 (1H, br s), 6.29 (1H, br s), 6.35 (1H, d, J = 16 Hz), 6.85 (1H, d, J = 6 Hz), 7.02 (2H, br s), 7.25 (1H, d, J = 8 Hz), 7.33–7.90 (15H, m); MS (ESI) m/z 673 (M + 1). Anal. ($C_{41}H_{44}N_2O_3SSi$) C, H, N.

2,6-Dimethyl-1-hydroxymethyl-3-[2-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidomethyl]thiophen-3-yl]benzene (37). Following a similar procedure to the preparation of **26**, the title compound was obtained

in 90.3% yield from **36** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$–CD_3OD) δ 1.94 (1H, s), 2.23 (3H, s), 2.44 (3H, s), 3.00 (3H, s), 4.50 (2H, s), 4.80 (2H, s), 6.31 (1H, d, *J* = 16 Hz), 6.41 81H, br s), 6.88 (1H, d, *J* = 6 Hz), 7.02 (1H, d, *J* = 8 Hz), 7.08 (1H, d, *J* = 8 Hz), 7.26 (1H, m), 7.50 (2H, d, *J* = 8 Hz), 7.55 (1H, d, *J* = 16 Hz), 7.74 (2H, d, *J* = 8 Hz); MS (ESI) *m/z* 435 (M + 1). Anal. ($C_{25}H_{26}N_2O_3S$) C, H, N.

8-[[2,6-Dimethyl-3-[2-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidomethyl]thiophen-3-yl]benzyl]oxy]-2-methylquinoline (38). Following a similar procedure to the preparation of **9a**, the title compound was obtained in 74.5% yield from **8** and **37** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.22 (3H, s), 2.50 (3H, s), 2.62 (3H, s), 2.99 (3H, d, *J* = 6 Hz), 5.35 (2H, s), 6.08 (1H, br s), 6.37 (1H, d, *J* = 16 Hz), 6.87 (1H, d, *J* = 6 Hz), 7.04 (1H, br s), 7.17 (2H, br s), 7.20–7.34 (4H, m), 7.42–7.60 (6H, m), 8.07 (1H, d, *J* = 8 Hz); MS (ESI) *m/z* 578 (M + 1). Anal. ($C_{35}H_{33}N_3O_3S$) C, H, N.

8-[[2,6-Dichloro-3-[2-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidomethyl]pyrrol-1-yl]benzyl]oxy]-2-methylquinoline (42). Following a similar procedure to method B, the title compound was obtained in 87.4% yield from **41** and (*E*)-4-(*N*-methylcarbamoyl)cinnamic acid[22] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.59 (3H, s), 2.95 (3H, d, *J* = 5 Hz), 4.27 (1H, br dd, *J* = 16, 4 Hz), 4.47 (1H, br dd, *J* = 16, 4 Hz), 5.48 (1H, br d, *J* = 10 Hz), 5.54 (1H, br d, *J* = 10 Hz), 6.26 (1H, dd, *J* = 3, 2 Hz), 6.32 (1H, br s), 6.37 (1H, d, *J* = 16 Hz), 6.48 (1H, br s), 6.56 (1H, br s), 6.39 (1H, br s), 7.16 (1H, d, *J* = 8 Hz), 7.21–7.49 (8H, m), 7.56 (2H, d, *J* = 8 Hz), 8.02 (1H, d, *J* = 8 Hz); MS (ESI) *m/z* 599 (M + 1). Anal. ($C_{33}H_{28}Cl_2N_4O_3$) C, H, N.

8-[[2,6-Dichloro-3-[2-[(*E*)-4-(*N*, *N*-dimethylcarbamoyl)cinnamamidomethyl]pyrrol-1-yl]benzyl]oxy]-2-methylquinoline (43). Following a similar procedure to method B, the title compound was obtained in 82.0% yield from **41** and (*E*)-4-(*N*, *N*-dimethylcarbamoyl)cinnamic acid[22] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ

2.63 (3H, s), 2.92 (3H, br s), 3.09 (3H, br s), 4.30 (1H, br dd, J = 16, 4 Hz), 4.47 (1H, br dd, J = 16, 4 Hz), 5.52 (1H, br d, J = 10 Hz), 5.60 (1H, br d, J = 10 Hz), 6.24–6.37 (4H, m), 6.67 (1H, br s), 7.13–7.30 (6H, m), 7.30–7.51 (5H, m), 8.02 (1H, d, J = 8 Hz); MS (ESI) *m/z* 613 (M + 1). Anal. ($C_{34}H_{30}Cl_2N_4O_3$) C, H, N.

8-[[2,6-Dichloro-3-[2-[(*E*)-3-(6-ethoxycarbonylpyridin-3-yl)acryloylaminomethyl]pyrrol-1-yl]benzyl]oxy]-2-methylquinoline (45). Following a similar procedure to method B, the title compound was obtained in 85.7% yield from **41** and (*E*)-3-(6-ethoxycarbonylpyridin-3-yl)acrylic acid[22] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 1.43 (3H, t, J = 7 Hz), 2.61 (3H, s), 4.41–4.53 (4H, m), 5.54 (1H, d, J = 10 Hz), 5.62 (1H, d, J = 10 Hz), 6.28 (1H, m), 6.33 (1H, m), 6.45 (1H, br t, J = 3 Hz), 6.59 (1H, d, J = 16 Hz), 6.68 (1H, m), 7.25 (1H, m), 7.39 (1H, d, J = 8 Hz), 7.42–7.54 (4H, m), 7.60 (1H, dd, J = 8, 2 Hz), 7.76 (1H, d, J = 8 Hz), 8.04 (1H, d, J = 8 Hz), 8.67 (1H, d, J = 2 Hz); MS (ESI) *m/z* 615 (M + 1). Anal. ($C_{33}H_{28}Cl_2N_4O_4$) C, H, N.

8-[[2,6-Dichloro-3-[2-[(*E*)-4-(2-oxo-pyrrolidin-1-yl)cinnamamidomethyl]pyrrol-1-yl]benzyl]oxy]-2-methylquinoline (48). Following a similar procedure to method B, the title compound was obtained in 59.3% yield from **41** and (*E*)-4-(2-oxo-pyrrolidin-1-yl)cinnamic acid[22] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.10–2.24 (2H, m), 2.63 (2H, t, J = 7.5 Hz), 2.67 (3H, s), 3.83 (1H, t, J = 7.5 Hz), 4.28 (1H, br d, J = 17 Hz), 4.47 (1H, br d, J = 17 Hz), 5.51 (1H, br d, J = 10 Hz), 5.60 (1H, br d, J = 10 Hz), 6.16–6.31 (3H, m), 6.35 (1H, br s), 6.68 (1H, br s), 7.17 (1H, br d, J = 8 Hz), 7.20–7.30 (3H, m), 7.33–7.55 (7H, m), 8.05 (1H, d, J = 8 Hz); MS (ESI) *m/z* 625 (M + 1). Anal. ($C_{35}H_{30}Cl_2N_4O_3$) C, H, N.

8-[[2,6-Dichloro-3-[2-[(*E*)-3-[6-[(*E*)-2-(pyridin-4-yl)vinyl]pyridin-3-yl]acryloylaminomethyl]pyrrol-1-yl]benzyl]oxy]-2-methylquinoline (49). Following a similar procedure to method B, the title compound was obtained in 58.0% yield from **41** and 3-[6-[(*E*)-2-(4-pyridinyl)ethenyl]pyridin-3-yl]acrylic acid[24] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.63 (3H, s), 4.32 (1H, br dd, J = 17, 4

Hz), 4.50 (1H, br dd, J = 17, 4 Hz), 5.54 (1H, d, J = 10 Hz), 5.60 (1H, d, J = 10 Hz), 6.28 (1H, m), 6.35 (1H, br s), 6.45 (1H, d, J = 16 Hz), 6.58 (1H, br t, J = 4 Hz), 6.68 (1H, br d, J = 2 Hz), 7.02 (1H, d, J = 8 Hz), 7.17–7.27 (3H, m), 7.35–7.57 (9H, m), 8.03 (1H, d, J = 8 Hz), 8.53 (1H, d, J = 2 Hz), 8.60 (2H, d, J = 6 Hz); MS (ESI) *m/z* 646 (M + 1). Anal. ($C_{37}H_{29}Cl_2N_5O_2$) C, H, N.

8-[[2,6-Dichloro-3-[2-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidomethyl]pyrrol-1-yl]benzyl]oxy]-2-methylquinoline Hydrochloride (50a). Following a similar procedure to method C, the title compound was obtained in 89.1% yield from **42** as a colorless amorphous solid: ^{1}H NMR (DMSO-d_6) δ 2.79 (3H, d, J = 5 Hz), 2.85 (3H, s), 4.25 (1H, br dd, J = 15, 3 Hz), 4.46 (1H, br d, J = 15 Hz), 5.51 (1H, br d, J = 10 Hz), 5.60 (1H, br d, J = 10 Hz), 6.20–6.28 (2H, m), 6.60 (1H, d, J = 16 Hz), 6.85 (1H, br s), 7.32 (1H, d, J = 16 Hz), 7.53–7.62 (3H, m), 7.62–7.97 (7H, m), 8.40–8.53 (2H, m). Anal. ($C_{33}H_{28}Cl_2N_4O_3$•HCl) C, H, N.

8-[[2,6-Dichloro-3-[2-[(*E*)-4-(*N*,*N*-dimethylcarbamoyl)cinnamamidomethyl]pyrrol-1-yl]benzyl]oxy]-2-methylquinoline Hydrochloride (51a). Following a similar procedure to method C, the title compound was obtained in 79.5% yield from **43** as a colorless amorphous solid: ^{1}H NMR (DMSO-d_6) δ 2.89 (3H, s), 2.91 (3H, br s), 2.98 (3H, br s), 4.22 (1H, br dd, J = 16, 3 Hz), 4.49 (1H, br dd, J = 16, 4 Hz), 5.53 (1H, d, J = 10 Hz), 5.62 (1H, d, J = 10 Hz), 6.20–6.29 (2H, m), 6.58 (1H, d, J = 15 Hz), 6.85 (1H, d, J = 3 Hz), 7.31 (1H, d, J = 15 Hz), 7.43 (2H, d, J = 8 Hz), 7.50–7.62 (3H, m), 7.68 (1H, d, J = 8 Hz), 7.73–8.02 (4H, m), 8.49 (1H, t, J = 7 Hz), 8.99 (1H, br s);. Anal. ($C_{34}H_{30}Cl_2N_4O_3$•HCl) C, H, N.

8-[[2,6-Dichloro-3-[[(*E*)-3-[6-(*N*-methylcarbamoyl)pyridin-3-yl]acryloylaminomethyl]pyrrol-1-yl]benzyl]oxy]-2-methylquinoline Hydrochloride (53a). Following a similar procedure to method C, the title compound was obtained in 85.8% yield from **48** as a colorless amorphous solid: ^{1}H NMR (DMSO-

d_6) δ 2.81 (3H, d, J = 6 Hz), 2.90 (3H, s), 4.21 (1H, m), 4.50 (1H, m), 5.56 (1H, d, J = 10 Hz), 5.65 (1H, d, J = 10 Hz), 6.23 (1H, m), 6.27 (1H, m), 6.73 (1H, d, J = 16 Hz), 6.85 (1H, m), 7.41 (1H, d, J = 16 Hz), 7.60 (1H, d, J = 8 Hz), 7.69 (1H, d, J = 8 Hz), 7.79–7.93 (3H, m), 7.96 (1H, br s), 8.03 (1H, d, J = 8 Hz), 8.08 (1H, dd, J = 8, 2 Hz), 8.58 (1H, br s), 8.73 (1H, br s), 8.77 (1H, br s), 8.77 (1H, br s), 9.01 (1H, br s). Anal. ($C_{32}H_{27}Cl_2N_5O_3$•2HCl) C, H, N.

8-[[2,6-Dichloro-3-[2-[(*E*)-4-(2-oxo-pyrrolidin-1-yl)cinnamamidomethyl]pyrrol-1-yl]benzyl]oxy]-2-methylquinoline Hydrochloride (54a). Following a similar procedure to method B, the title compound was obtained in 59.3% yield from **41** and (*E*)-4-(2-oxo-pyrrolidin-1-yl)cinnamic acid[22] as a colorless amorphous solid: ^{1}H NMR (DMSO-d_6) δ 2.00–2.14 (2H, m), 2.48–2.58 (2H, m), 2.85 (3H, s), 3.83 (1H, t, J = 7 Hz), 4.20 (1H, br dd, J = 17, 3 Hz), 4.44 (1H, br s), 5.51 (1H, br d, J = 10 Hz), 5.62 (1H, br d, J = 10 Hz), 6.19–6.27 (2H, m), 6.45 (1H, d, J = 16 Hz), 6.85 (1H, d, J = 2 Hz), 7.24 (1H, d, J = 16 Hz), 7.50 (2H, d, J = 8 Hz), 7.58 (1H, d, J = 8 Hz), 7.62–7.95 (7H, m), 8.37 (1H, br s), 8.93 (1H, br s). Anal. ($C_{35}H_{30}Cl_2N_4O_3$•HCl) C, H, N.

8-[[2,6-Dichloro-3-[2-[(*E*)-3-[6-[(*E*)-2-(pyridin-4-yl)vinyl]pyridin-3-yl]acryloylaminomethyl]pyrrol-1-yl]benzyl]oxy]-2-methylquinoline Trihydrochloride (55a). Following a similar procedure to method C, the title compound was obtained in 91.6% yield from **49** as a colorless amorphous solid: ^{1}H NMR (DMSO-d_6) δ 2.81 (3H, s), 4.22 (1H, br dd, J = 17, 4 Hz), 4.39 (1H, br s), 5.52 (1H, br d, J = 10 Hz), 5.60 (1H, br d, J = 10 Hz), 6.19–6.30 (2H, m), 6.72 (1H, d, J = 16 Hz), 6.85 (1H, br d, J = 2 Hz), 7.40 (1H, d, J = 16 Hz), 7.60 (1H, d, J = 8 Hz), 7.64–7.83 (7H, m), 7.87 (1H, d, J = 16 Hz), 8.00 (1H, d, J = 16 Hz), 8.04 (1H, br dd, J = 8, 2 Hz), 8.23 (2H, d, J = 6 Hz), 8.51 (1H, br t, J = 4 Hz), 8.79–8.89 (3H, m); MS (ESI) m/z 646 (M + 1). Anal. ($C_{37}H_{29}Cl_2N_5O_2$•3HCl) C, H, N.