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| **Supporting Information** |
| **Cu(OTf)2 catalyzed synthesis of highly substituted 1-methoxy imidazoles *via* (3+2) cycloaddition between imino carbenoids and nitriles** |
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| **General Methods:** All the reactions were carried out in a flame or oven dried glassware under nitrogen atmosphere with freshly distilled dry solvents under anhydrous conditions unless otherwise indicated. Column chromatography was performed with silica gel 60 (100 – 200 mesh) or aluminium oxide. Chromatograms were visualized by fluorescence quenching with UV light at 254 nm or by staining using base solution of potassium permanganate and molybdate. NMR spectra were recorded at room temperature on 400 or 500 MHz FT NMR Spectrometer (Bruker AV III).The residual solvent signals were taken as the reference (7.26 ppm for 1H NMR spectra and 77.0 ppm for 13C NMR spectra in CDCl3) Chemical shift (δ) is reported in ppm; coupling constants (*J*) are given in Hz. The following abbreviations classify the multiplicity: s = singlet, d = doublet, t = triplet, m = multiplet dd = doublet of doublet, q = quartet and br = broad signal. |
| **Materials:** All solvents were distilled under nitrogen from the following drying agents immediately before use: acetonitrile and dichloroethane were distilled from P2O5. |
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| **General procedure for the synthesis of *α*-diazo oxime ethers from oxime ethers** |
| To a solution of *β*-oximino ester (1 eq.) and 4-toluenesulfonyl azide (1.1 eq.) in dry CH3CN at room temperature was added triethyl amine (2 eq.) followed by NaOH (2 eq.). The resulting pale yellow solution was stirred at the same temperature for 30 min. After the completion of the reaction as indicated by the TLC, the mixture was washed with water, brine, extracted with ethyl acetate and dried over anhydrous Na2SO4. The organic layer was concentrated under reduced pressure to get crude product, which was purified by column chromatography using pet ether: ethyl acetate (**7:3**) to obtain pure *α*-diazo oxime ethers. |
| **Catalyst & Solvent screening for 1-methoxy imidazole synthesis *via* (3+2) cycloaddition** |
| |  |  |  |  | | --- | --- | --- | --- | | S.No | Catalyst | Solvent | Yield b (%) | | 1 | Cu(hfacac)2c | CH2Cl2 | 56 | | 2 | CuOTf | CH2CL2 | 62 | | 3 | Cu(OTf)2 | CH2Cl2 | 89 | | 4 | CuI | CH2Cl2 | traced | | 5 | Pd(OAc)2 | CH2Cl2 | 48 | | 6 | PdCl2 | CH2Cl2 | 31 | | 7 | Rh2(OAc)4 | CH2Cl2 | 78 | | 8 | Cu(OTf)2 | THF | 55 | | 9 | Cu(OTf)2 | ClCH2CH2Cl2 | 74(e) | | 10 | Cu(OTf)2 | CHCl3 | 71 | | 11 | Cu(OTf)2 | (C2H5)2O | 43 | |
| aReaction conditions: *α*-diazo Oxime ether (1 mmol), Nitrile (1 mmol), Solvent (3 mL/1 mmol), byield corresponding to the isolated product by column chromatography, cVacuum dried, dobserved by HPLC. eYield at 90 oC using dichloroethane as solvent. |
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| **General Procedure for the synthesis of 1-methoxy imidazole**  A solution of *α*-diazo oximino ester (1 eq.) in dry CH2Cl2 was charged with 5 mol% Cu(OTf)2 catalyst followed by the addition of organo nitrile (1 eq.). The reaction mixture was refluxed for 2h. After the completion of the reaction as indicated by the TLC, the mixture was washed with water, brine, extracted with ethyl acetate and dried over anhydrous Na2SO4. The organic layer was concentrated under reduced pressure to get crude product, which was purified by column chromatography using pet ether: ethyl acetate (7:3) to obtain pure 1-methoxy imidazole. |
| **1H and 13C spectra of 1-methoxy imidazoles (3a-p)** |
| **Ethyl 1-Methoxy-2,5-dimethyl-1H-imidazole-4-carboxylate (3a)**  The title compound was prepared according to the general procedure and the product was obtained as pale yellow gum. Yield: 89% (0.201 gm); 1H NMR (400 MHz, CDCl3) δ 4.13 (q, *J* = 7.1 Hz, 2H), 3.79 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); 13C NMR (CDCl3, 125 MHz) δ 164.93, 142.97, 138.13, 126.87, 70.23, 60.70, 12.76, 12.53, 11.52; MS (EI) m/z [M+H]+: Calcd for C9H14N2O3:198.2190, Found: 198.2194. |
| **Ethyl 2-ethyl-1-methoxy-5-methyl-1H-imidazole-4-carboxylate (3b)**  The title compound was prepared according to the general procedure and the product was obtained as pale yellow gum. Yield: 77% (0.204 gm); 1H NMR (400 MHz, CDCl3) δ 4.13 (q, *J* = 7.1 Hz, 2H), 3.80 (s, 3H), 2.83 (q, *J* = 7.3 Hz, 2H), 2.40 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.13 (t, *J* = 7.3 Hz, 3H); 13C NMR (CDCl3, 125 MHz) δ 163.63, 149.20, 144.50, 65.66, 61.18, 25.67, 13.76, 13.53, 12.73; MS (EI) m/z [M+H]+: Calcd for C10H16N2O3: 212.2456, Found: 212.2452. |
| **Ethyl 1-methoxy-5-methyl-2-propyl-1H-imidazole-4-carboxylate (3c)**  The title compound was prepared according to the general procedure and the product was obtained as pale yellow gum. Yield: 78% (0.205 gm); 1H NMR (400 MHz, CDCl3) δ 4.13 (q, *J* = 7.1 Hz, 3H), 3.80 (s, 4H), 2.71 (t, *J* = 7.4 Hz, 3H), 2.33 (s, 4H), 1.84 – 1.48 (m, 3H), 1.32 (t, *J* = 7.1 Hz, 4H), 1.04 (t, *J* = 7.0 Hz, 4H); 13C NMR (CDCl3, 125 MHz) δ 163.90, 149.54, 144.37, 128.95, 65.31, 61.18, 27.73, 21.53, 13.95, 13.90, 13.58; MS (EI) m/z [M+H]+: Calcd for C11H18N2O3: 226.2722, Found: 226.2726. |
| **Ethyl 1-methoxy-5-methoxy-2-vinyl-1H-imidazole-4-carboxylate (3d)**  The title compound was prepared according to the general procedure and the product was obtained as pale yellow gum. Yield: 75% (0.188 gm); 1H NMR (400 MHz, CDCl3) δ 6.79 (dd, *J* = 17.8, 11.4 Hz, 1H), 6.29 (dd, *J* = 17.8, 1.0 Hz, 1H), 5.33 (dd, *J* = 11.4, 1.0 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 3H), 2.46 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H); 13C NMR (CDCl3, 125 MHz) δ 163.91, 148.81, 144.13, 130.06, 124.48, 121.75, 65.70, 61.62, 14.01, 13.35; MS (EI) m/z [M+H]+: Calcd for C10H14N2O3: 210.2297, Found: 210.2299. |
| **Ethyl 1-methoxy-5-methyl-2-phenyl-1H-imidazole-4-carboxylate (3e)**  The title compound was prepared according to the general procedure and the product was obtained as pale yellow gum. Yield: 76% (0.210 gm); 1H NMR (400 MHz, CDCl3) δ 4.13 (q, *J* = 7.1 Hz, 2H), 3.80 (s, 3H), 2.71 (t, *J* = 7.4 Hz, 2H), 2.33 (s, 3H), 1.73 – 1.59 (m, 2H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.04 (t, *J* = 7.0 Hz, 3H); 13C NMR (CDCl3, 125 MHz) δ 163.74, 144.18, 135.18, 132.37, 130.78, 129.06, 128.81, 128.46, 65.64, 61.81, 13.82, 13.41; MS (EI) m/z [M+H]+: Calcd for C14H16N2O3: 260.2884, Found: 260.2882. |
| **Ethyl 2-(2-chlorophenyl)-1-methoxy-5-methyl-1H-imidazole-4-carboxylate (3f)**  The title compound was prepared according to the general procedure and the product was obtained as brown gum. Yield: 77% (0.226 gm); 1H NMR (400 MHz, CDCl3) δ 7.799 (d, *J* = 6.4 Hz, 1H), 7.761(d, *J* = 8.0 Hz, 1H), 7.404 (m, 2H), 4.147 (q, *J* = 7.2, 14 Hz, 2H), 3.888 (s, 3H), 2.562 (s, 3H), 1.347 (t, *J* = 6.8 Hz, 3H); 13C NMR (CDCl3, 125 MHz) δ 160.66, 151.90, 136.49, 131.40, 129.56, 128.81, 128.40, 128.21, 127.40, 127.30, 59.77, 56.90, 14.51, 13.14; MS (EI) m/z [M+H]+: Calcd for C14H15N2O3: 294.7335, Found: 294.7333 |
| **Ethyl 2-(4-formylphenyl)-1-methoxy-5-methyl-1H-imidazole-4-carboxylate (3g)**  The title compound was prepared according to the general procedure and the product was obtained as dark yellow gum. Yield: 78% (0.224 gm); 1H NMR (400 MHz, CDCl3) δ 9.253 (s, 1H), 8.031 (d, *J* = 8 Hz, 1H), 7.927 (d, J = 1.2 Hz, 1H) 7.905 (d, *J* = 1.4 Hz, 1H), 7.759 (d, *J* = 8.4 Hz, 1H), 4.199 (q, *J* = 7.2, 14.4 Hz, 2H), 3.919 (s, 3H), 2.637 (s, 3H), 1.343 (t, *J* = 6.8 Hz, 3H); 13C NMR (CDCl3, 125 MHz) δ 190.15, 160.26, 151.50, 136.09, 135.02, 128.34, 128.02, 128.00, 125.75, 125.73, 125.41, 59.37, 56.50, 14.12, 12.74; MS (EI) m/z [M+H]+: Calcd for C15H16N2O4: 288.2985, Found: 288.2984. |
| **Ethyl-1-methoxy-2-methyl-5-phenyl-1H-imidazole-4-carboxylate (3h)**  The title compound was prepared according to the general procedure and the product was obtained as pale yellow gum. Yield: 77% (0.239 gm); 1H NMR (400 MHz, CDCl3) δ 7.56 (dd, *J* = 7.7, 1.3 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 2H), 7.36 – 7.26 (m, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 2.46 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); 13C NMR (CDCl3, 125 MHz) δ 160.69, 145.52, 139.87, 139.53, 132.43, 129.54, 129.28, 126.56, 65.64, 61.21, 14.40, 12.11; MS (EI) m/z [M+H]+: Calcd for C14H16N2O3: 260.2884, Found: 260.2887. |
| **Ethyl 2-ethyl-1-methoxy-5-phenyl-1H-imidazole-4-carboxylate (3i)**  The title compound was prepared according to the general procedure and the product was obtained as pale yellow gum. Yield: 74% (0.241 gm); 1H NMR (400 MHz, CDCl3 ) δ 7.56 (dd, *J* = 7.7, 1.3 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 2H), 7.36 – 7.27 (m, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 2.91 (q, *J* = 6.7 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 6.7 Hz, 3H); 13C NMR (CDCl3, 125 MHz) δ 164.91, 149.51, 145.47, 133.62, 127.96, 126.79, 70.14, 61.11, 25.96, 14.05, 12.79; MS (EI) m/z [M+H]+: Calcd for C15H18N2O3: 274.3150, Found: 274.3152. |
| **Ethyl 1-methoxy-5-phenyl-2-propyl-1H-imidazole-4-carboxylate (3j)**  The title compound was prepared according to the general procedure and the product was obtained as pale yellow gum. Yield: 76% (0.255 gm); 1H NMR (400 MHz, CDCl3) δ 7.56 (dd, *J* = 7.7, 1.3 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 2H), 7.36 – 7.27 (m, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 2.93 (t, *J* = 6.5 Hz, 2H), 1.91 – 1.78 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.04 (t, *J* = 6.6 Hz, 3H); 13C NMR (CDCl3, 125 MHz) δ 161.79, 149.50, 145.47, 139.85, 128.83, 128.74, 128.32, 65.39, 61.28, 27.72, 21.59, 14.63, 13.98; MS (EI) m/z [M+H]+: Calcd for C16H20N2O3: 288.3416, Found: 288.3418. |
| **Ethyl 1-methoxy-5-phenyl-2-vinyl-1H-imidazole-4-carboxylate (3k)**  The title compound was prepared according to the general procedure and the product was obtained as yellowish gum. Yield: 74% (0.222 gm); 1H NMR (400 MHz, CDCl3) δ 7.61 – 7.54 (m, 2H), 7.50 – 7.34 (m, 3H), 6.29 (ddd, *J* = 19.1, 17.6, 6.2 Hz, 2H), 5.37 (dd, *J* = 10.9, 1.5 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.88 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H); 13C NMR (CDCl3, 125 MHz) δ 161.68, 148.81, 145.47, 139.45, 131.46, 128.27, 128.13, 127.25, 125.78, 120.70, 65.66, 61.27, 14.03; MS (EI) m/z [M+H]+: Calcd for C15H16N2O3: 272.2991, Found: 272.2993. |
| **Ethyl 1-methoxy-2,5-diphenyl-1H-imidazole-4-carboxylate (3l)**  The title compound was prepared according to the general procedure and the product was obtained as yellowish gum. Yield: 70% (0.245 gm); 1H NMR (400 MHz, CDCl3) δ 7.69 – 7.43 (m, 10H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.94 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); 13C NMR (CDCl3, 125 MHz) δ 161.68, 145.47, 139.45, 135.12, 132.46, 132.03, 130.42, 129.28, 128.79, 128.27, 128.13, 126.78, 65.66, 61.23, 14.09; MS (EI) m/z [M+H]+: Calcd for C19H18N2O3: 322.3578, Found: 322.3575. |
| **Ethyl 2-(2-ethoxy-2-oxoethyl)-1-methoxy-5-phenyl-1H-imidazole-4-carboxylate (3m)**  The title compound was prepared according to the general procedure and the product was obtained as pale yellow gum. Yield: 76% (0.256 gm); 1H NMR (400 MHz, CDCl3) δ 7.56 (dd, *J* = 7.6, 1.2 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 2H), 7.31 (ddd, *J* = 8.4, 2.7, 1.4 Hz, 1H), 4.27 (s, 2H), 4.14 (qd, *J* = 7.1, 2.8 Hz, 4H), 3.85 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.15 (t, *J* = 7.1 Hz, 3H); 13C NMR (CDCl3, 125 MHz) δ 171.51, 161.66, 152.91, 130.61, 129.41, 128.93, 128.67, 126.73, 125.00, 60.77, 60.65, 57.89, 32.54, 14.12; MS (EI) m/z [M+H]+: Calcd for C19H18N2O3: 332.3511, Found: 332.3514. |
| **Benzyl 1-methoxy-2,5-dimethyl-1H-imidazole-4-carboxylate (3n)**  The title compound was prepared according to the general procedure and the product was obtained as pale yellow gum. Yield: 80% (0.242 gm); 1H NMR (400 MHz, CDCl3) δ 7.55 – 7.28 (m, 5H), 5.14 (s, 2H), 3.79 (s, 3H), 2.37 (s, 3H), 2.33 (s, 3H); 13C NMR (CDCl3, 125 MHz) δ 164.99, 139.94, 138.74, 135.28, 130.96, 130.73, 128.21, 127.78, 127.44, 65.29, 57.11, 11.39; MS (EI) m/z [M+H]+: Calcd for C14H16N2O3: 260.2884, Found: 260.2880. |
| **Ethyl 1-methoxy-2-methyl-5-(4-nitrophenyl)-1H-imidazole-4-carboxylate (3o)**  The title compound was prepared according to the general procedure and the product was obtained as yellowish crystals. Yield: 75% (0.249 gm); 1H NMR (400 MHz, CDCl3) δ 8.25 (dd, *J* = 8.8, 5.3 Hz, 2H), 7.56 (dd, *J* = 8.8, 5.3 Hz, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.90 (s, 3H), 2.54 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); 13C NMR (CDCl3, 125 MHz) δ 165.04, 147.20, 139.54, 131.60, 128.92, 127.47, 127.27, 125.12, 124.73, 124.58, 60.14, 57.21, 14.24, 12.08; MS (EI) m/z [M+H]+: Calcd for C14H15N3O5: 305.2865, Found: 305.2861. |
| **Methyl 1-methoxy-2,5-dimethyl-1H-imidazole-4-carboxylate (3p)** |
| The title compound was prepared according to the general procedure and the product was obtained as pale yellow gum. Yield: 78% (0.143 gm); 1H NMR (400 MHz, CDCl3) δ 3.801 (s, 3H), 3.734 (s, 3H), 2.364 (s, 3H), 2.330 (s, 3H); 13C NMR (CDCl3, 125 MHz) δ 164.27, 139.71, 137.49, 129.41, 57.90, 51.88, 15.50, 10.99; MS (EI) m/z [M+H]+: Calcd for C8H12N2O3: 184.1924, Found: 184.1920. |
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| **Ethyl 1-Methoxy-2,5-dimethyl-1*H*-imidazole-4-carboxylate (3a)**  EAA-ACN |
| **Ethyl 2-ethyl-1-methoxy-5-methyl-1*H*-imidazole-4-carboxylate (3b)**  EAA-PN |
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| **Ethyl 1-methoxy-5-methyl-2-propyl-1*H*-imidazole-4-carboxylate (3c)** |
| EAA-butytonitrile |
| **Ethyl 1-methoxy-5-methoxy-2-vinyl-1*H*-imidazole-4-carboxylate (3d)**  EAA-Acrylonitrile |
| **Ethyl 1-methoxy-5-methyl-2-phenyl-1*H*-imidazole-4-carboxylate (3e)**  EAA-benzonitrile |
| **Ethyl 2-(2-chlorophenyl)-1-methoxy-5-methyl-1*H*-imidazole-4-carboxylate (3f)**  **EAA-NH2Ome-N2+2-chloro benzonitrile.jpg** |
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| **Ethyl 2-(4-formylphenyl)-1-methoxy-5-methyl-1*H*-imidazole-4-carboxylate (3g)**  **EAA-NH2Ome-N2+p-cyano benzaldehyde.jpg** |
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| **Ethyl-1-methoxy-2-methyl-5-phenyl-1*H*-imidazole-4-carboxylate (3h)**  EBA-ACN |
| **Ethyl 2-ethyl-1-methoxy-5-phenyl-1*H*-imidazole-4-carboxylate (3i)**  EBA-PN |
| **Ethyl 1-methoxy-5-phenyl-2-propyl-1*H*-imidazole-4-carboxylate (3j)**  EBA-butyronitrile |
| **Ethyl 1-methoxy-5-phenyl-2-vinyl-1*H*-imidazole-4-carboxylate (3k)**  EBA-Acrylonitrile |
| **Ethyl 1-methoxy-2,5-diphenyl-1*H*-imidazole-4-carboxylate (3l)**  EBA-Benzonitrile |
| **Ethyl 2-(2-ethoxy-2-oxoethyl)-1-methoxy-5-phenyl-1*H*-imidazole-4-carboxylate** (**3m**)  EBA-NH2OMe-N2+ECA |
| **Benzyl 1-methoxy-2,5-dimethyl-1*H*-imidazole-4-carboxylate (3n)**  BAA-ACN |
| **Ethyl 1-methoxy-2-methyl-5-(4-nitrophenyl)-1*H*-imidazole-4-carboxylate (3o)**  4-nitrophenyl-ACN |
| **Methyl 1-methoxy-2,5-dimethyl-1*H*-imidazole-4-carboxylate (3p)**  MAA-ACN |
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