Supplementary Material for Chemical Communications

Catalytic phosphorylation using a bifunctional imidazole derived nucleophilic catalyst

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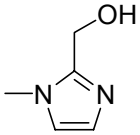
Supplementary Information – Contents

General Experimental

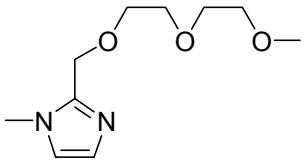
THF and diethyl ether were freshly distilled over sodium and CH_2Cl_2 was distilled over CaH_2. All reagents were used as supplied without purification unless stated. Column chromatography was carried out on Fluorochem Limited Silica Gel 40-63υ 60A and TLC on aluminium sheets coated with 0.2mm silica gel. Plates were visualised using an UV light and $KMnO_4$ and PMA with heating. 250MHz ^{1}H NMR analysis were carried out on a Bruker AC250 sample changer, 300MHz ^{1}H & ^{13}C NMR were carried out on a Bruker Advance 300 spectrometer and 500MHz ^{1}H & ^{13}C NMR were carried out on a JEOL λ500MHz spectrometer. Residual signals from the deuterated solvents were used as reference. Coupling constants were measured in Hz. Mass spectra were recorded on a VG Autospec spectrometer.

(1-Methylimidazol-2-yl) methanol 3[1]



N-Methylimidazole (10.0g, 9.6 cm^3, 0.12 mol) and paraformaldehyde (10.0 g, 0.33 mol) were refluxed at 160 ^{0}C for 1 h. The brown solution was dissolved in methanol (12 cm^3) and cooled to -78 ^{0}C and triturated to precipitate a brown solid that was filtered off. The product was recrystallized from CH_2Cl_2 / petrol (40:60) to give (1-methylimidazol-2-yl) methanol **3** (8.7 g, 0.07 mol, 63%) as a light brown solid. Mpt 115 ^{o}C (lit.[Error! Bookmark not defined.] 114 ^{o}C); δ_H (300MHz, $CDCl_3$) 6.81 (1H, d, *J* 1.2, C*H*=CH), 6.75 (1H, d, *J* 1.2, C*H*=CH), 5.45 (1H, br s, O*H*), 4.55 (2H, s, CH_2OH), 3.66 (3H, s, CH_3N); δ_C (75MHz, $CDCl_3$) 148.4, 127.0, 121.9, 56.1, 33.2. All NMR data was in accordance with the literature.

2-[2-(2-Methoxy-ethoxy)-ethoxymethyl]-1-methyl-1H-imidazole 1



NaH (0.16 g, 4 mmol) was washed with petrol (3 x 5 cm^3) and dried under vacuum. This was suspended in dry THF (10 cm^3) and stirred under N_2 for 5 mins. (1-Methyl imidazol-2-yl) methanol **3** (0.11 g, 1.0 mmol) was added and after 30 mins 1-bromo-2-(2-methoxy ethoxy)ethane[2] (0.36 g, 2.0 mmol) was added. The brown mixture was left to stir for 20 h at rt. Methanol (5 cm^3) was added followed by water (3 cm^3) to quench excess NaH. The brown solution was extracted with CH_2Cl_2 (10 × 15 cm^3). The organic layer dried over $MgSO_4$ and the solvent removed giving a crude yellow oil. Purification by column chromatography on silica gel with an eluent of CH_2Cl_2:MeOH (9.5:0.5) gave a yellow oil **1** (0.134 g, 0.65 mmol, 63%). ν_{max} cm^{-1} (film) 2878, 1654, 1501, 1453, 1096; δ_H (500MHz, $CDCl_3$) 6.86 (1H, s, CH=C*H*), 6.80 (1H, s, CH=C*H*), 4.57 (2H, s, ArCH_2O), 3.64 (3H, s, NCH_3), 3.54 (6H, m, CH_2O), 3.47 (2H, m, CH_2O), 3.30 (3H, s, OCH_3); δ_C (125MHz, $CDCl_3$) 144.5, 127.3, 122.0, 71.9, 70.4, 69.0, 65.0, 59.0, 32.8; *m/z* (EI) 215.1389 (1.4%; MH^+, $C_{10}H_{19}N_2O_3$ requires 215.1396), 199 (16), 183 (2), 169 (4), 139 (3), 125 (7), 111 (96), 95 (100).

General procedure for the kinetic evaluation of the catalyst for the phosphorylation of cyclohexanol in CH_2Cl_2

Et_3N (4.0 cm^3, 4.72 mmol from a stock solution in dry CH_2Cl_2) and cyclohexanol (4.0 cm^3, 4.72 mmol from a stock solution in dry CH_2Cl_2) were stirred under nitrogen for 15 min with or without catalyst (4.0 cm^3, 0.472 mmol from a stock solution in dry CH_2Cl_2) and with or without MPF_6 (0.472 mmol) as appropriate. Diphenyl chlorophosphate (4.0 cm^3, 4.72 mmol from a stock solution in dry CH_2Cl_2) was added and stirred for 24 h at 30 ^{0}C. Samples (1 cm^3) were removed at timed intervals and quenched with water (10 cm^3) and extracted with CH_2Cl_2 (10 cm^3). The organic layer

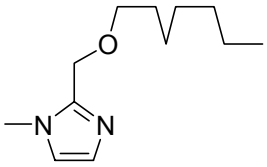
was separated, washed with water (2 × 5 cm^3) and dried with $MgSO_4$. The solvent was removed and the crude oil was dried under vacuum. The samples were analysed by ^1H NMR spectroscopy.

Data from kinetic plots (Figure 2)

Time (min)	Product 6 (%)[a]			
	No Cat 1 Or KPF_6	KPF_6	Cat 1	Cat 1 + KPF_6
0	0	0	0	0
5	4 (2)	3 (4)	44 (43)	69 (71)
15	10 (8)	10 (9)	65 (72)	84 (87)
30	9 (13)	11 (11)	70 (78)	91 (86)
60	21 (24)	21 (20)	87 (80)	86 (89)
120	27 (21)	24 (27)	95 (91)	94 (91)
540	37 (34)	30 (31)	89 (85)	91 (87)
1440	46 (49)	46 (50)	87 (89)	92 (91)

[a] Amount of product determined from comparison of the integrals of the ^1H nmr spectrum. Figures in parenthesis refer to results obtained in a duplicate experiment to validate the data.

2-Heptyloxymethyl-1-methyl-1*H*-imidazole 4

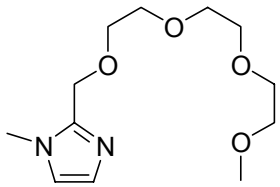


KH (0.11 g, 2.5 mmol) was suspended in dry THF (10 cm^3) and stirred under N_2 for 5 mins. (1-Methyl imidazol-2-yl) methanol **3** (0.28 g, 2.5 mmol) was added and after 30 mins 1-heptyl *p*-toluene sulphonate[3] (0.67g, 2.5mmol) was added. The mixture was left to stir for 20 h at rt and ethanol (5 cm^3) was added followed by water (3 cm^3) to quench excess KH. The brown solution was extracted with CH_2Cl_2 (10 × 15cm^3). The organic layer was dried over $MgSO_4$ and the solvent removed giving a crude yellow oil. Purification by column chromatography on silica gel eluting with CH_2Cl_2:MeOH (9.5:0.5) gave a yellow oil **4** (0.29 g, 1.38 mmol, 55%). ν_{max} cm^{-1} (film) 2929, 2857, 1500, 1457, 1095; δ_H (250 MHz, $CDCl_3$) 6.93 (1H, s, CH=C*H*), 6.86 (1H, s, CH=C*H*), 4.56 (2H, s, ArCH_2O), 3.69 (3H, s, NCH_3), 3.41 (2H, t, *J* 6.6, OCH_2), 1.61 (2H, m, CH_2), 1.35─1.19 (10H, m, CH_2), 0.78 (3H, t, *J* 6.6, C$H_3$$CH_2$); δ_C (63 MHz, $CDCl_3$) 144.8, 127.2, 121.8, 70.2, 64.7, 32.7, 31.7, 29.5, 29.0, 26.0, 22.5, 14.0; *m/z* (EI) 210.1736 (8%; M^+, $C_{12}H_{22}N_2O$ requires 210.1732), 112 (21), 111 (34), 96 (100), 95 (58), 81 (13), 57 (6), 54 (23).

General procedure for the preparation of catalysts 7 and 8

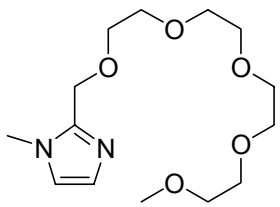
NaH (4 eq.) was washed with petrol (3 × 5 cm^3) and dried under vacuum. This was suspended in dry THF (10 cm^3) and stirred under N_2 for 5 mins. (1-Methyl imidazol-2-yl) methanol **3** (1 eq) was added and after 30 mins the appropriate polyether bromide (2 eq.) was added. The brown mixture was left to stir for 20 h at rt. After such time the reaction was quenched with methanol (5 cm^3), followed by water (3 cm^3). The brown solution was extracted with CH_2Cl_2 (5 × 15 cm^3), the organic layer dried over $MgSO_4$ and the solvent removed giving a crude product. This was purified by column chromatography on silica gel with an eluent of CH_2Cl_2:MeOH (9.5:0.5) to give the desired product.

2-{2-[2-(2-Methoxy-ethoxy)-ethoxy]-ethoxymethyl}-1-methyl-1H-imidazole 7



Catalyst **7** was obtained as a yellow oil (68%) using 1-[2-(2-bromo-ethoxy)-ethoxy]-2-methoxy-ethane[4] in accordance with the general procedure. ν_{max} cm^{-1} (film) 2876, 1648, 1501, 1454, 1103; δ_H (500 MHz, $CDCl_3$) 6.86 (1H, s, ArC*H*), 6.80 (1H, s, ArC*H*), 4.57 (3H, s, CH_3N), 3.50–3.58 (10H, m, 5 × CH_2O), 3.46 (2H, m, CH_2), 3.29 (3H, s, OCH_3); δ_C (126 MHz, $CDCl_3$) 144.3, 127.0, 121.9, 71.7, 70.3, 70.2, 70.1, 68.9, 64.8, 58.7, 32.6; *m/z* (EI) 258.1589 (12%, M^+ $C_{12}H_{22}N_2O_4$ requires 258.1579), 258 (12), 183 (7), 155 (9), 139 (13), 111 (100), 95 (84), 81 (7), 59 (42).

2-(2-{2-[2-(2-Methoxy-ethoxy)-ethoxy]-ethoxy}-ethoxymethyl)-1-methyl-1H-imidazole 8



Catalyst **8** was obtained as a yellow oil (71%) using 1-{2-[2-(2-bromo-ethoxy)-ethoxy]-ethoxy}-2-methoxy-ethane[5] in accordance with the general procedure. ν_{max} cm^{-1} (film) 2874, 1500, 1453; 1104; δ_H (250MHz, $CDCl_3$) 6.84 (1H, s, ArC*H*), 6.79 (1H, s, ArC*H*), 4.54 (2H, s, ArCH_2), 3.62 (3H, s, CH_3N), 3.52–3.56 (14H, m, 7 × CH_2O), 3.45 (2H, m, CH_2O), 3.28 (3H, s, CH_3O); δ_C (63MHz,

$CDCl_3$) 144.5, 127.3, 122.0, 71.8, 70.5, 70.4, 70.2, 69.0, 64.9, 58.9, 32.8; *m/z* (ES) 303.1911 (100%; MH^+, $C_{14}H_{27}N_2O_5$ requires 303.1920), 325 (M^++Na), 493; *m/z* (EI) 302 (6%), 257 (4), 227 (4), 199 (3), 139 (10), 111 (100), 95 (93), 59 (44).

References

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