Supplementary Material (ESI) for Chemical Communications

Selective Functionalization of Imidazoles *via* an Iodine-Copper Exchange Reaction

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Supporting Information

General considerations

Unless otherwise indicated, all reactions were carried out with magnetic stirring and, if air or moisture sensitive, in flame-dried glassware under argon. Syringes used to transfer reagents and solvent were purged with argon prior to use. Reactions were monitored by gas chromatography (GC and GC-MS) or thin layer chromatography (TLC).
Organolithium solutions were titrated using the method of Paquette.[1]

Synthesis of $(Nphyl)_2CuLi$[2]

A 500 mL round-bottomed flask, flame dried and flushed with argon was charged with lithium metal (3.0 g, 432 mmol) and neophylchloride (14.0 mL, 86.9 mmol) in hexane (75 mL). The reaction mixture was heated under reflux overnight. After cooling to rt, the hexane was removed *in vacuo* and diethyl ether was added to the resulting mixture. The resulting mixture was stirred at rt for few mins and then kept static for another few mins. The solution was cannulated into a flame dried Schlenk tube and was centrifuged (2000 rpm, 30 min). The clear solution of neophyllithium thus obtained was titrated before use with menthol using *o*-phenantroline as indicator and could be stored at -30 °C for several days.

A 25 mL round-bottomed flask, flame dried and flushed with argon was charged with CuCN (110 mg, 1.2 mmol). THF (3 mL) was added and the suspension cooled to -78 °C. The freshly titrated solution of neophyllithium (2.4 mmol) was added and the mixture quickly warmed to rt and stirred for 10 min, till a clear yellow solution of the desired cuprate **2** was obtained.

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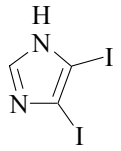
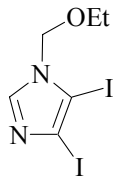
[1] Lin, H.-S.; Paquette, L. A. *Synth. Commun*. **1994**, *24*, 2503.
[2] (a) Cano, A.; Cuenca, T.; Galakov, M.; Rodríguez, G. M.; Royo, P.; Cardin, C. J.; Convery, M. A. *J. Organomet. Chem.* **1995**, *493*, 17. (b) Negishi, E.; Swanson, D. R.; Rousset, C. J. *J. Org. Chem*. **1990**, *55*, 5406.

Synthesis of 4,5-diiodo-1H-imidazole[3]



Iodine (46.0 g, 181 mmol) and potassium iodide (30.0 g, 181 mmol) were dissolved in water (250 mL) and added with a dropping funnel to a solution of imidazole (3.4 g, 50.0 mmol) and sodium hydroxide (24.0 g, 600 mmol) in water (50 mL) at rt. The resulting mixture was stirred at rt overnight. The reaction was neutralized with AcOH until the ph value is around 8. The precipitate was filtered and washed many times with water. The solid was dried in oven (60 ^{o}C) to givr desired product as a white solid (14.5 g, 90%).

Synthesis of 4,5-diiodo-1-ethoxymethyl-1H-imidazole (1a)



4,5-Diiodo-1H-imidazole (9.5 g, 29.7 mmol) was dissolved in DMF (89 mL) and NaH (1.25 g, 31.2 mmol) was added. The mixture was stirred at 0 °C for 1 h, then chloromethyl ethyl ether (2.9 mL, 31.2 mmol) was added and the mixture was let warm to rt and stirred for additional 4 h. The reaction was quenched with brine and the aqueous phase extracted with EtOAc (6 x 30 mL). The organic fractions were washed with with brine (30 mL), dried ($MgSO_4$) and concentrated in vacuo. The crude solid was recrystallized from pentane to give 54 as a light yellow solid (7.6 g, 78 %).

m.p 108 °C

IR (KBr, cm^{-1}): $\tilde{\nu}$ 3131 (w), 1495 (vs), 1478 (s), 1437 (m), 1250 (vs), 1171 (s), 1080 (s), 940 (vs), 655 (m).

[3] Lovely, C. J.; Du, H.; Dias, H. V. R. *Heterocycles* **2003**, *60*, 1

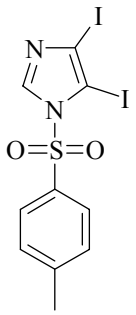
^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.74 (s, 1H), 5.33 (s, 2H), 3.51 (q, J = 7.0 Hz, 2H), 1.22 (t, J = 7.0 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 142.0, 97.5, 82.2, 78.4, 65.0, 15.1.

MS (EI, 70 eV): 378 (M^+, 100), 334, (18), 207 (40), 59 (55).

$C_6H_8I_2N_2O$	HRMS	Calcd.	377.8726
		Found	377.8706

Synthesis of 4,5-diiodo-1-(toluene-4-sulfonyl)-1H-imidazole (1b)



To a mixture of 4,5-diiodo-1H-imidazole (9.6 g, 30 mmol) and 4-methyl-benzenesulfonyl chloride (5.9 g, 31 mmol) in acetone (50 mL) at rt, Et_3N (15 mL) was added and the resulting mixture was stirred at rt for 12 h. The solvent was removed under vacuum and the residue was purified by flash chromatography (n-pentane/diethyl ether = 2/1) yielded 79b as a light yellow solid (13.4g, 94%).

mp.: 156 ^{o}C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.24 (s, 1H), 7.85-7.82 (d, J = 8.40 Hz, 2H), 7.33-7.30 (d, J = 8.40 Hz, 2H), 2.40 (s, 3H).

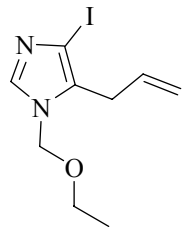
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 147.5, 142.2, 133.5, 130.7, 129.3, 103.3, 22.2.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 3126 (w), 1594 (m), 1467 (m), 1430 (w), 1379 (s), 1192 (s), 1170 (vs), 1150 (s), 1089 (vs), 1030 (m), 923 (w), 812 (w), 673 (vs), 591 (vs), 542 (m).

MS (EI, 70 ev): 474 (82) [M^+], 319 (3), 192 (4), 155 (97), 91 (100), 65 (17).

$C_{10}H_9I_2N_2O_2S$ $[M + H]^+$	HRMS (EI)	Calcd.	474.8474
		Found	474.8497

Synthesis of 5-allyl-1-ethoxymethyl-4-iodo-1H-imidazole (4a)



Typical procedure: To a solution of (4,5-diiodo-1H-1-yl)methyl ethyl ether (**1a**, 378 mg, 1.0 mmol, 1.0 equiv) in dry THF (4 mL) at –78 °C was added dropwise freshly prepared $Nphyl_2CuLi$ solution (1.2 mmol, 1.2 equiv). The resulting solution was stirred at -78 ^oC for 1 h, Dry N-methyl-2-pyrrolidinone (NMP) (1.0 mL) and allyl bromide (360 mg, 3.0 mmol, 3.0 equiv) were added successively at -78 ^oC and the resulting solution was kept stirring at rt for 0.5 h. The reaction mixture was quenched with sat. aqu. NH_4Cl solution (3 mL) and aqueous. NH_3 solution (25%, 1mL) and poured into water (10 mL). The mixture was extracted with CH_2Cl_2 (3 × 15 mL). The organic fractions were washed with brine (15 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (*n*-pentane/diethyl ether = 2/1) gave the desired product **4a** as a colorless oil (263 mg, 90% yield).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.51 (s, 1H), 5.90-5.77 (m, 1H), 5.23 (s, 2H), 5.12-4.99 (m, 2H), 3.46-3.43 (m, 2H), 3.46-3.39, (q, J = 7.07 Hz, 2H), 1.21-1.16 (t, J = 7.07 Hz, 3H).

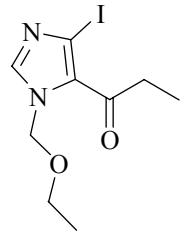
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 139.4, 133.9, 132.0, 117.1, 86.2, 64.5, 29.1, 15.0.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3369 (w), 2978 (m), 1639 (w), 1489 (m), 1425 (w), 1354 (w), 1230 (s), 1177 (s), 1102 (vs), 918 (w), 774 (w), 736 (w).

MS (EI, 70 ev): 292 (100) [M^+], 246 (21), 233 (16), 121 (26), 80 (13), 59 (71).

$C_9H_{13}IN_2O$	HRMS (EI)	Calcd.	292.0073
		Found	292.0071

Synthesis of 1-(3-ethoxymethyl-5-iodo-3H-imidazol-4-yl)-propan-1-one (4b)



Prepared according to TP from (4,5-diiodo-1H-imidazol-1-yl)methyl ethyl ether (**1a**) (378 mg, 1.0 mmol), lithium dineophylcuprate (**2**) (1.2 mmol), propionyl chloride (278 mg, 3.0 mmol) and NMP (0.5 mL). Reaction time: 1 h at -78 °C. Purification by flash chromatography (n-pentane/diethyl ether = 1/2) yielded **4b** as a colorless oil (265 mg, 86%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.63 (s, 1H), 5.60 (s, 2H), 3.52-3.45, (q, J = 7.07 Hz, 2H), 3.09-3.02, (q, J = 7.18 Hz, 2H), 1.16-1.11 (t, J = 7.07 Hz, 3H), 1.15-1.10 (t, J = 7.18 Hz, 3H).

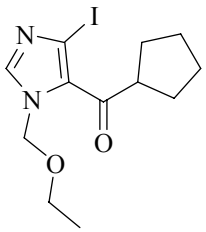
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 191.5, 141.7, 131.3, 92.6, 76.9, 64.4, 34.9, 13.9, 7.0.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3102 (w), 2977 (m), 1666 (vs), 1495 (s), 1460 (m), 1378 (m), 1235 (s), 1165 (m), 1107 (vs), 908 (w), 756 (m), 658 (w).

MS (EI, 70 ev): 308 (20) [M^+], 279 (100), 261 (6), 249 (4), 221 (15), 59 (16).

$C_9H_{13}IN_2O_2$	HRMS (EI)	Calcd.	308.0022
		Found	308.0048

Synthesis of cyclopentyl-(3-ethoxymethyl-5-iodo-3H-imidazol-4-yl)-methanone (4c)



Prepared according to TP from (4,5-diiodo-1H-imidazol-1-yl)methyl ethyl ether (**1a**) (189 mg, 0.5 mmol), lithium dineophylcuprate (**2**) (0.6 mmol), cyclopentanecarbonyl chloride (200 mg, 1.5 mmol) and NMP (0.3 mL). Reaction time: 1 h at -78 °C. Purification by flash chromatography (n-pentane/diethyl ether = 1/2) yielded **4c** as a colorless oil (141 mg, 81%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.77 (s, 1H), 5.69 (s, 2H), 4.19-4.08, (m, 1H), 3.61-3.54, (q, J = 7.07 Hz, 2H), 2.08-1.70 (m, 8H), 1.27-1.23 (t, J = 7.07 Hz, 3H).

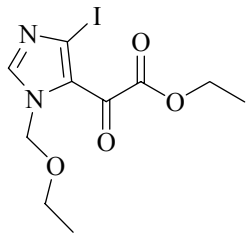
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 195.9, 143.0, 132.3, 114.0, 93.2, 78.1, 65.6, 49.0, 30.1, 26.5, 15.2.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3105 (w), 2955 (vs), 1659 (vs), 1495 (s), 1461 (w), 1384 (m), 1257 (m), 1201 (vs), 1106 (vs), 965 (w), 763 (w).

MS (EI, 70 ev): 348 (91) [M^+], 319 (100), 301 (83), 289 (24), 279 (52), 252 (23) 235 (14), 221 (34), 174 (13), 59 (75)..

$C_{12}H_{17}IN_2O_3$	HRMS (EI)	Calcd.	348.0335
		Found	348.0340

Synthesis of (3-ethoxymethyl-5-iodo-3H-imidazol-4-yl)-oxo-acetic acid ethyl ester (4d)



Prepared according to TP from (4,5-diiodo-1H-imidazol-1-yl)methyl ethyl ether (**1a**) (189 mg, 0.5 mmol), lithium dineophylcuprate (**2**) (0.6 mmol), oxalyl chloride (245 mg, 1.5 mmol) and NMP (0.3 mL). Reaction time: 1 h at -78 ^{o}C. Purification by flash chromatography (n-pentane/diethyl ether = 1/2) yielded **4d** as a colorless oil (130 mg, 74%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.75 (s, 1H), 5.61 (s, 2H), 4.43-4.36, (q, J = 7.19 Hz, 2H), 3.54-3.47, (q, J = 7.07 Hz, 2H), 1.39-1.35 (t, J = 7.19 Hz, 3H), 1.17-1.12 (t, J = 7.07 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 176.9, 161.6, 143.3, 127.3, 97.9, 77.0, 64.6, 62.0, 15.1, 14.2.

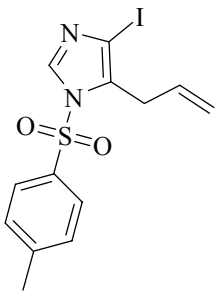
IR (film, cm^{-1}): $\tilde{\nu}$ = 3109 (w), 2980 (w), 1735 (vs), 1654 (vs), 1501 (s), 1461 (w), 1441 (w), 1349 (m), 1257 (m), 1206 (vs), 1108 (vs), 1011 (s), 960 (w), 748 (w).

MS (EI, 70 ev): 352 (30) [M^+], 279 (100), 251 (8), 235 (4), 221 (12), 59 (19).

$C_{10}H_{13}IN_2O_4$	HRMS (EI)	Calcd.	351.9920

Found 351.9928

Synthesis of 5-allyl-4-iodo-1-(toluene-4-sulfonyl)-1H-imidazole (4e)



Prepared according to TP from 4,5-diiodo-1-(toluene-4-sulfonyl)-1H-imidazole (1b) (474 mg, 1.0 mmol), lithium dineophylcuprate (**2**) (1.2 mmol), allyl bromide (360 mg, 3.0 mmol) and NMP (0.5 mL). Reaction time: 0.5 h at -78 °C. Purification by flash chromatography (n-pentane/diethyl ether = 5/1) yielded **4e** as a colorless oil (360 mg, 93%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.01 (s, 1H), 7.69-7.67 (d, J = 8.24 Hz, 2H), 7.29-7.27 (d, J = 8.24 Hz, 2H), 5.58-5.48 (m, 1H), 4.87-4.77, (m, 2H), 3.40-3.38, (dt, J = 5.80 Hz, J = 1.83 Hz, 2H), 2.38 (s, 3H).

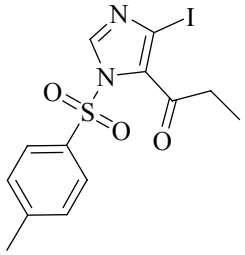
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 146.6, 138.8, 134.4, 132.1, 130.6, 130.4, 127.8, 117.0, 89.7, 29.0, 21.7.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 2921 (w), 1639 (w), 1494 (w), 1461 (m), 1383 (s), 1191 (m), 1177 (vs), 1152 (vs), 1111 (vs), 812 (m), 680 (vs), 593 (vs).

MS (EI, 70 ev): 388 (32) [M^+], 233 (23), 155 (42), 91 (100), 65 (7).

$C_{13}H_{13}IN_2OS$	HRMS (EI)	Calcd.	387.9742
		Found	387.9746

Synthesis of 1-[5-iodo-3-(toluene-4-sulfonyl)-3H-imidazol-4-yl]-propan-1-one (4f)



Prepared according to TP from 4,5-diiodo-1-(toluene-4-sulfonyl)-1H-imidazole (**1b**) (474 mg, 1.0 mmol), lithium dineophylcuprate (**2**) (1.2 mmol), propionyl chloride (278 mg, 3.0 mmol) and NMP (0.5 mL). Reaction time: 0.5 h at -78 °C. Purification by flash chromatography (n-pentane/diethyl ether = 2/1) yielded **4f** as a light yellow solid (327 mg, 81%).

mp.: 102 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.17 (s, 1H), 7.88-7.86 (d, J = 8.40 Hz, 2H), 7.33-7.30 (d, J = 8.40 Hz, 2H), 2.99-2.91, (q, J = 7.19 Hz, 2H), 2.38 (s, 3H), 1.13-1.08 (t, J = 7.19 Hz, 3H).

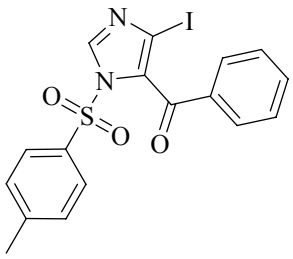
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 192.7, 146.8, 142.4, 134.6, 134.4, 130.2, 129.4, 129.3, 92.4, 36.9, 22.2, 8.3.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (vs), 1685 (vs), 1492 (m), 1375 (s), 1218 (m), 1171 (vs), 1155 (s), 1113 (vs), 813 (m), 671 (vs), 572 (m).

MS (EI, 70 ev): 388 (32) [M^+], 233 (23), 155 (42), 91 (100), 65 (7)..

$C_{13}H_{13}IN_2O_3S$	HRMS (EI)	Calcd.	403.9692
		Found	403.9711

Synthesis of [5-iodo-3-(toluene-4-sulfonyl)-3H-imidazol-4-yl]-phenyl-methanone (4g)



Prepared according to TP from 4,5-diiodo-1-(toluene-4-sulfonyl)-1H-imidazole (**1b**) (474 mg, 1.0 mmol), lithium dineophylcuprate (**2**) (1.2 mmol), benzoyl chloride (420 mg, 3.0 mmol)

and NMP (0.5 mL). Reaction time: 0.5 h at -78 °C. Purification by flash chromatography (n-pentane/diethyl ether = 2/1) yielded **4g** as a white solid (384 mg, 85%).

mp.: 96 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.12 (s, 1H), 7.90-7.89 (d, J = 8.40 Hz, 2H), 7.76-7.75 (d, J = 8.40 Hz, 2H), 7.60-7.57 (m, 1H), 7.44-7.42 (m, 2H), 7.34-7.42 (m, 2H), 2.40 (s, 3H).

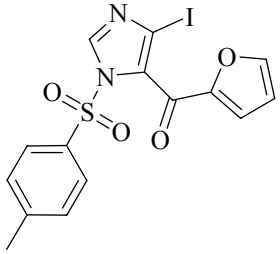
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 188.2, 147.8, 141.1, 136.6, 134.8, 134.3, 132.4, 130.9, 130.7, 129.6, 129.3, 92.4, 22.3.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3435 (w), 1660 (vs), 1596 (m), 1467 (s), 1382 (vs), 1238 (w), 1194 (vs), 1178 (vs), 1133 (vs), 1097 (s), 882 (m), 688 (vs), 586 (vs).

MS (EI, 70 ev): 452 (34) [M^+], 388 (16), 297 (12), 155 (75), 105 (7), 91 (100), 77 (21).

$C_{17}H_{13}IN_2O_3S$	HRMS (EI)	Calcd.	451.9692
		Found	451.9677

Synthesis of furan-2-yl-[5-iodo-3-(toluene-4-sulfonyl)-3H-imidazol-4-yl]-methanone (4h)



Prepared according to TP from 4,5-diiodo-1-(toluene-4-sulfonyl)-1H-imidazole (**1b**) (237 mg, 0.5 mmol), lithium dineophylcuprate (**2**) (0.6 mmol), 2-furoyl chloride (195 mg, 1.5 mmol) and NMP (0.3 mL). Reaction time: 0.5 h at -78 °C. Purification by flash chromatography (n-pentane/diethyl ether = 3/2) yielded **4h** as a white solid (157 mg, 71%).

mp.: 102 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.08 (s, 1H), 7.89-7.87 (d, J = 8.16 Hz, 2H), 7.68-7.67 (m, 1H), 7.33-7.32 (d, J = 8.16 Hz, 2H), 7.22-7.21 (d, J = 3.22 Hz, 1H), 6.58-6.57 (dd, J = 3.22 Hz, J = 1.50 Hz, 1H), 2.39 (s, 3H).

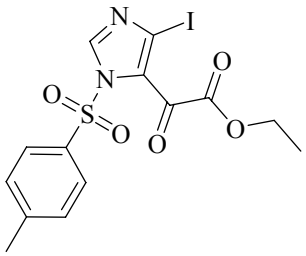
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 171.3, 150.4, 147.7, 146.0, 139.5, 132.8, 130.2, 129.1, 127.9, 122.2, 112.2, 89.0, 20.8.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (w), 1646 (vs), 1563 (w), 1457 (s), 1388 (vs), 1262 (w), 1194 (m), 1178 (vs), 1147 (s), 1104 (s), 849 (m), 671 (vs), 584 (s).

MS (EI, 70 ev): 442 (24) [M^+], 378 (21), 288 (8), 155 (63), 106 (7), 91 (100), 65 (11).

$C_{15}H_{11}IN_2O_4S$	HRMS (EI)	Calcd.	441.9484
		Found	441.9447

Synthesis of [5-iodo-3-(toluene-4-sulfonyl)-3H-imidazol-4-yl]-oxo-acetic acid ethyl ester (4i)



Prepared according to TP from 4,5-diiodo-1-(toluene-4-sulfonyl)-1H-imidazole (**1b**) (237 mg, 0.5 mmol), lithium dineophylcuprate (**2**) (0.6 mmol), ethyl oxayl chloride (205 mg, 1.5 mmol) and NMP (0.3 mL). Reaction time: 0.5 h at -78 °C. Purification by flash chromatography (n-pentane/diethyl ether = 2/1) yielded **4i** as a colorless oil (170 mg, 76%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.22 (s, 1H), 7.89-7.87 (d, J = 8.24 Hz, 2H), 7.33-7.31 (d, J = 8.24 Hz, 2H), 4.38-4.33 (q, J = 7.32 Hz, 2H), 2.39 (s, 3H), 1.36-1.32 (t, J = 7.32 Hz, 3H).

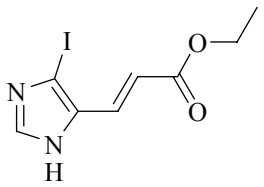
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 176, 161, 147.1, 143.6, 133.5, 1130.1, 129.8, 129.1, 98.4, 63.4, 21.8, 13.8.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3436 (w), 1741 (vs), 1686 (vs), 1592 (w), 1487 (s), 1386 (vs), 1303 (m), 1247 (m), 1193 (s), 1134 (s), 1081 (vs), 1023 (s), 921 (w), 815 (w), 673 (vs), 591 (vs).

MS (EI, 70 ev): 448 (5) [M^+], 375 (100), 221 (9), 155 (66), 91 (70), 65 (8).

$C_{14}H_{13}IN_2O_5S$	HRMS (EI)	Calcd.	447.9590
		Found	447.9590

Synthesis of 3-(5-iodo-3H-imidazol-4-yl)-acrylic acid ethyl ester (4j)



Prepared according to TP 6 from 4,5-diiodo-1-(toluene-4-sulfonyl)-1H-imidazole (**1b**) (237 mg, 0.5 mmol), lithium dineophylcuprate (**2**) (0.6 mmol), ethyl propiolate (147 mg, 1.5 mmol) and NMP (0.3 mL). Reaction time: 0.5 h at -78 ^{o}C. Purification by flash chromatography (n-pentane/diethyl ether = 1/4) yielded **4j** as colorless oil (79 mg, 54%).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.75-7.73 (d, J = 13.97 Hz, 1H), 7.60 (s, 1H), 7.29 (s, 1H), 5.99-5.97 (d, J = 13.97 Hz, 1H), 4.22-4.18 (q, J = 7.09 Hz, 2H), 1.27-1.25 (t, J = 7.09 Hz, 3H).

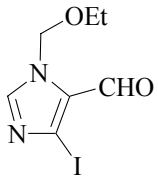
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 164.5, 138.0, 134.1, 120.8, 107.1, 84.8, 60.1, 13.2.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3436 (w), 1701 (vs), 1652 (vs), 1487 (s), 1372 (w), 1277 (m), 1221 (m), 1204 (vs), 1184 (vs), 1103 (w), 1028 (w), 960 (w), 609 (w).

MS (EI, 70 ev): 292 (100) [M^{+}], 247 (17), 220 (6), 166 (5), 137 (11), 109 (8), 65 (4).

$C_8H_9IN_2O_2$	HRMS (EI)	Calcd.	291.9709
		Found	291.9728

Synthesis of 1-(ethoxymethyl)-4-iodo-1H-imidazole-5-carbaldehyde (4k)



In a dried and argon flushed two necked 100 mL flask, equipped with a reflux condenser, **1a** (3.5 g, 9.3 mmol) was dissolved in THF (10 mL) at rt. EtMgCl (5.4 mL, 10.7 mmol, 2 M solution in THF) was added slowly and the mixture was heated to reflux for 1 h. Dry DMF (1.0 mL, 11.0 mmol) was then added and after one additional hour the reaction was quenched

with saturated, aqueous NH_4Cl (60 mL). The aqueous phase was extracted with EtOAc (6 × 30 mL). The organic fractions were washed with brine (30 mL), dried ($MgSO_4$) and concentrated in vacuo. Purification by flash chromatography (penatne/diethyl ether 1:1) yielded **4k** as a light yellow oil (1.7 g, 66%).

IR (film, cm^{-1}): $\tilde{\nu}$ 3112 (m), 1698 (vs), 1528 (w), 1455 (m), 1427 (s), 1399 (vs), 1345 (s), 954 (m), 790 (vs).

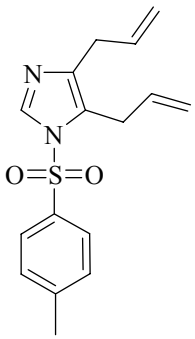
^1H NMR ($CDCl_3$, 300 MHz): δ 9.60 (s, 1H), 7.75 (s, 1H), 5.62 (s, 2H), 3.51 (q, J = 7.2 Hz, 1H), 3.41 (q, J = 7.2 Hz, 1H), 1.14 (t, J = 7.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 181.5, 144.7, 129.7, 101.5, 76.2, 65.8, 15.2.

MS (EI, 70 eV): 280 (M^+, 30), 251 (100), 221 (10), 59 (25).

$C_7H_9IN_2O_2$	HRMS	Calcd.	279.9709
		Found	279.9685

Synthesis of 4,5-diallyl-1-(toluene-4-sulfonyl)-1H-imidazole (5a)



Prepared according to TP from 5-allyl-4-iodo-1-(toluene-4-sulfonyl)-1H-imidazole (**4e**) (388 mg, 1.0 mmol), lithium dineophylcuprate (**2**) (1.2 mmol) and allyl bromide (360 mg, 3.0 mmol). Reaction time: 1 h at -78 °C. Purification by flash chromatography (n-pentane/diethyl ether = 2/1) yielded **5a** as a colorless oil (214 mg, 71%).

^1H-NMR ($CDCl_3$, 300 MHz): δ = 7.63-7.60 (d, J = 8.51 Hz, 2H), 7.28-7.28 (d, J = 8.51 Hz, 2H), 6.58 (s, 1H), 6.06-5.93 (m, 1H), 5.86-5.74 (m, 1H), 5.11-5.01, (m, 4H), 3.70-3.68, (dt, J = 6.60 Hz, J = 1.30 Hz, 2H), 3.41-3.38, (dt, J = 6.74 Hz, J = 1.30 Hz, 2H), 2.38 (s, 3H).

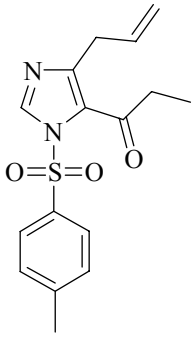
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 149.7, 146.2, 136.4, 133.8, 133.4, 132.5, 130.6, 127.7, 127.3, 118.3, 118.0, 34.7, 31.0, 22.1.

IR (film, cm^{-1}): $\tilde{\nu}$ = 3080 (w), 1642 (w), 1597 (m), 1374 (vs), 1194 (vs), 1182 (s), 1156 (vs), 1106 (vs), 993 (m), 920 (m), 813 (m), 672 (vs), 598 (vs), 546 (vs).

MS (EI, 70 ev): 302 (97) [M^+], 237 (3), 147 (87), 91 (100), 65 (17).

$C_{16}H_{18}N_2O_2S$	HRMS (EI)	Calcd.	302.1089
		Found	302.1054

Synthesis of 1-[5-allyl-3-(toluene-4-sulfonyl)-3H-imidazol-4-yl]-propan-1-one (5b)



Prepared according to TP from 1-[5-iodo-3-(toluene-4-sulfonyl)-3H-imidazol-4-yl]- propan-1-one (**4f**) (155 mg, 0.38 mmol), lithium dineophylcuprate (**2**) (0.42 mmol), allyl bromide (137 mg, 1,1 mmol) and NMP (0.2 mL). Reaction time: 0.5 h at -78 °C. Purification by flash chromatography (n-pentane/diethyl ether = 2/1) yielded **5b** as a white solid (73 mg, 60%).

mp.: 123 °C

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.24 (s, 1H), 7.86-7.84 (d, J = 8.51 Hz, 2H), 7.31-7.28 (d, J = 8.51 Hz, 2H), 5.93-5.82 (m 1H), 5.08-4.96 (m, 2H), 3.47-3.45 (m, 2H), 2.74-2.67, (q, J = 7.18 Hz, 2H), 2.37 (s, 3H), 1.09-1.04 (t, J = 7.19 Hz, 3H).

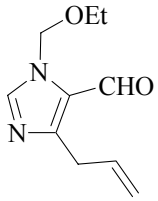
^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 192.4, 147.6, 146.2, 141.5, 135.5, 134.2, 130.0, 129.4, 129.0, 117.6, 35.9, 34.3, 22.2, 8.3.

IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3434 (w), 1676 (vs), 1539 (m), 1464 (m), 1374 (vs), 1224 (s), 1182 (vs), 1177 (vs), 1089 (vs), 989 (m), 924 (m), 815 (m), 667 (vs), 579 (vs), 545 (s).

MS (EI, 70 ev): 318 (47) [M^+], 303 (100), 289 (45), 275 (8), 261 (7), 163 (18), 139 (21), 91 (84), 65 (11).

$C_{16}H_{18}N_2O_3S$	HRMS (EI)	Calcd.	318.1038
		Found	318.1039

Synthesis of 4-allyl-1-(ethoxymethyl)-1H-imidazole-5-carbaldehyde (5c)



Prepared according to TP from 1-(ethoxymethyl)-4-iodo-1H-imidazole-5-carbaldehyde (**4k**) (280 mg, 1.0 mmol), lithium dineophylcuprate (**2**) (1.2 mmol), allyl bromide (360 mg, 3.0 mmol) and NMP (0.2 mL). Reaction time: 1 h at -78 °C. Purification by flash chromatography (n-pentane/diethyl ether = 1/1) yielded **5c** as a light yellow (126 mg, 65%).

IR (film, cm^{-1}): $\tilde{\nu}$ 3083 (m), 1672 (vs), 1520 (w), 1463 (m), 1420 (s), 1385 (vs), 1350 (s), 966 (m), 790 (vs).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.83 (s, 1H), 7.70 (s, 1H), 6.03-5.90 (m, 1H), 5.66 (s, 2H), 5.10 (m, 2H), 3.59 (d, J = 6.2 Hz, 2H), 3.49 (q, J = 6.9 Hz, 2H), 1.13 (t, J = 6.9 Hz, 3H).
^{13}C-NMR ($CDCl_3$, 75 MHz): δ 179.4, 155.0, 143.1, 135.4, 126.2, 121.2, 74.1, 64.0, 34.8, 13.9.

MS (EI, 70 eV): 194 (M^+, 33), 165 (30), 149 (27), 135 (70), 120 (100), 107 (18), 80 (30), 59 (88), 53 (28).

$C_{10}H_{14}N_2O_2$	HRMS	Calcd.	194.1055
		Found	194.1050