Bridged 1-Methylbisimidazoles as Building Blocks for Mixed Donor Bi- and Tridentate Chelating Ligands

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Abstract: Novel bi- and tridentate imidazole chelate ligands consisting of varying donor sets were prepared using an efficient one- or two-step procedure. Keto- and methylene-bridged bisimidazoles **1**, **2** served as versatile starting materials for the introduction of additional donor groups, thus allowing the facile variation of donor sets within a bisimidazole ligand framework.

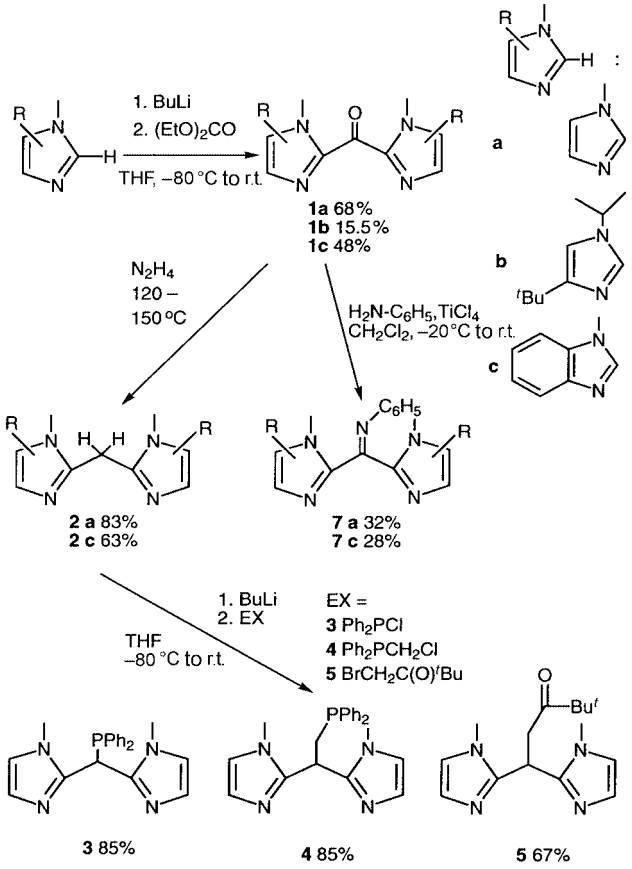
Keywords: heterocycles, imidazoles, ligands, phosphines

Industrial requirements for high performance catalysts to produce important classes of compounds have stimulated the development of a wide range of ligand systems, most of them coordinating through phosphorus. More recently the synthesis of well tailored chelating ligands containing nitrogen donors or a mixed set of donor atoms has received considerable interest in homogeneous catalysis and coordination chemistry.[1–3]

As part of our ongoing interest in functionalised ligand systems,[4] we have chosen the bridged bisimidazoles **1** and **2** (Scheme 1) as building blocks for the synthesis of novel bi- and tridentate mixed donor ligands (N^P; N^N'; N^O^N; N^P^N).

Chelate ligands derived from imidazole have found widespread application in model systems to mimic active sites of metalloenzymes.[5–11] A number of rhodium,[12,13] ruthenium,[14,15] palladium,[16–18] and platinum[19] complexes bearing polyimidazole ligands have also been reported, some of them found to be catalytically active. In the present report, we give a detailed description of the syntheses of novel chelate ligands with mixed donor atoms derived from imidazole derivatives.

A general synthesis of the new ligands is outlined in Scheme 1. Bis(1-methylimidazole-2-yl)ketone **1a**[13,14,16,20] and the methylene bridged bis(1-methylimidazoles) **2a**[13,14,16] and **2c**[12] were prepared by using modifications of previously described procedures which in the case of **2a** gave improved yields. For the ketone **1a**, we could show that prolonged exposure to water leads to decomposition. In a test experiment, **1a** was allowed to stand for one week in CH_2Cl_2/H_2O after which only 1-methylimidazole was recovered, indicating decomposition via hydrolysis and final loss of CO_2. Hence, liquid − liquid extraction of the product from aqueous solution was replaced by extracting the product with CH_2Cl_2 or $CHCl_3$ from the resulting crude oil of the reaction. After removal of the solvent, the pure product can be obtained by recrystallisation from acetone. After the initial crystallisation stage, on allowing the mother liquor to stand and slowly evaporate in air over one week further product precipitates from the oily solution.



Scheme 1

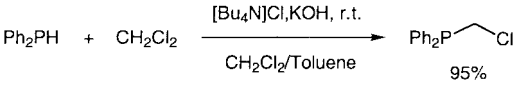
Since the steric requirements of a given ligand system may strongly influence the reactivity of its transition metal complexes, we became interested in synthesising a derivative of the ketone **1a** containing sterically demanding

substituents on the ring system. As a starting compound, we chose 1-isopropyl-4-*tert*-butylimidazole which has recently been reported by Sorell et al.[7,21] The fact that the *tert*-butyl group is linked to the imidazole ring in position 4 was crucial to our choice since it guarantees that steric bulk will be in proximity of the coordination sphere in metal complexes synthesised from the final chelate ligand. Due to its lower acidity, the starting imidazole was added to a THF solution of BuLi and warming to room temperature was necessary during the initial metallation reaction. However, after reaction with diethylcarbonate five compounds including unreacted starting material were detected (TLC) in the reaction mixture, from which **1b** could be isolated in 15.5% yield.

The synthesis of bis(1-methylimidazole)methane (**2a**) has previously been reported.[12,14,16] It is formed by heating a mixture of **1a**, hydrazine hydrate and sodium hydroxide in a reaction bomb to 140−150 °C for 4 hours. We found that careful control of the temperature is crucial to the relative success of the reaction. Replacing the reaction bomb with a round bottomed flask equipped with a reflux condenser resulted in the formation of a yellow solid at 60 °C and the reaction mixture becoming clear and colourless when the temperature reached 116 °C. The reaction was kept at 120 °C for 1 hour after which time the temperature was raised to 150 °C for another 3 hours. In experiments in which the temperature was instantly raised to 150 °C, the solution became dark brown and yields were low. These observations indicate that the initial hydrazone formation has to be completed prior to the final reduction step at elevated temperature. Extraction with and recrystallisation of the crude product from acetone[14] leads to a considerable loss of product possibly due to aldol condensation between **2a** and acetone. A pure product was obtained in 83% yield by recrystallisation from THF. Under the same conditions the benzimimidazole ketone **1c**[22] could be reduced to the methylene bridged derivative **2c**[12] in 63% yield.

Metallation of **2a** at the bridging methylene group with BuLi at low temperature provides the nucleophile for further coupling reactions. The respective electrophiles were then added in situ. Canty et al. prepared a tripodal nitrogen donor ligand in a similar manner using 2-bromopyridine as an electrophile and phenyl lithium as metallating agent.[17] Slow addition of Ph_2PCl to metallated **2a** in THF at −80 °C gave the phosphinated bis(1-methylimidazole) **3** as a white air sensitive solid in 85% yield. The doublet of the methine proton was observed at 5.37 ppm ($^2J_{P\text{-}H}$ = 2.4 Hz), while the bridging carbon appears as a doublet at 39.47 ppm ($^2J_{C\text{-}P}$ = 17.7 Hz), in the ^{13}C NMR spectrum. Compared to **2a** both signals are shifted to lower field by 1.13 ppm (^1H NMR) and 12.25 ppm (^{13}C NMR), respectively.

According to the synthetic approach outlined in Scheme 1, the synthesis of the N^P^N ligand **4** requires an electrophile in which the leaving group and the diphenyl phosphine group are linked to the same carbon. We prepared the electrophile Ph_2PCH_2Cl according to a modified procedure (2−3 times the amount of KOH and n-Bu_4NCl; prolonged reaction time; GC monitoring) reported by Stelzer et al.[23] (Scheme 2). In some cases the formation of $Ph_2P(O)CH_3$ (isolated and characterised by NMR and MS) as a by-product was observed, probably resulting from initial hydrolysis of Ph_2PCH_2Cl and subsequent rearrangement.



Scheme 2

Coupling between Ph_2PCH_2Cl and metallated **2a** was carried out in the same manner as that described for **3** although the less electrophilic Ph_2PCH_2Cl required longer reaction times at room temperature. Compound **4** was isolated as a pale air sensitive viscous oil in 85% yield. The methine hydrogen displays a pseudo quartet (4.95 ppm; $^3J_{H\text{-}H}$ = 8.2 Hz) in the ^1H NMR spectrum due to coupling with the methylene protons and phosphorus. The respective bridging carbon appears as a doublet at 31.5 ppm ($^3J_{C\text{-}P}$ = 12.9 Hz) in the ^{13}C NMR spectrum.

The structurally related N^O^N ligand **5** was prepared by reacting metallated **2a** with 1-bromopinacolone and isolated as colourless crystals containing 1.5 moles H_2O in 67% yield. The methine hydrogen appears as a triplet at 4.75 ppm ($^3J_{C\text{-}H}$ = 6.9 Hz) in the ^1H NMR spectrum. The keto group gives rise to a singlet at 213.9 ppm in the ^{13}C NMR spectrum. A by-product **6** was obtained in this reaction (approx. 6%), which was identified by ^1H NMR spectroscopy (methine hydrogen: 5.81 ppm; N-CH_3: 3.64 ppm) and x-ray diffraction as the C-C coupling product between two bis(1-methylimidazole-2-yl)methane units. Single crystals of **5** and **6** suitable for x-ray diffraction were obtained by slow solvent evaporation from an ether/petrol spirit solution and a chloroform solution respectively.

5. $C_{15}H_{22}N_4O \bullet 1.5H_2O$, M = 301.4. Monoclinic, space group $P2_1/c$ (C^5_{2h}, No.14), a = 7.927(2), b = 26.269(6), c = 8.453(2) Å, β = 105.391(3)°, V = 1690(1) Å^3. D_c (Z = 4) = 1.17$_9$ g cm^{-3}. 16421 CCD area-detector absorption-corrected reflections (specimen: 0.45 × 0.40 × 0.20; $T_{min,max}$ = 0.67, 0.91) reduced to 4259 unique (R_{int} = 0.035), 3380 (= N_o) with $F > 4\sigma(F)$ considered 'observed' and used in the full matrix least squares refinement (C, N, O displacement parameters anisotropic; (x, y, z, U_{iso})$_H$ (parent molecule) refined), T *ca* 153 K; Mo-*Kα* radiation, λ = 0.71073 Å, $2\theta_{max}$ = 58°. A string of difference map residues was modelled as water molecule oxygen fragments, without associated hydrogens, site occupancies 0.5. Final R, R_w (weights: $(\sigma^2(F) + 0.0004\,F^2)^{-1}$; refinement on $|F|$): 0.061, 0.070. $|\Delta\rho_{max}|$ = 0.44(2) e Å^{-3}.

6. (Similar procedure) $C_{18}H_{22}N_8 \bullet 2CDCl_3$, M = 591.2. Monoclinic, space group $P2_1/n$ (No. 14, variant), a = 8.766(1), b = 8.356(1), c = 17.962(2) Å,

Table Chelate Parameters for {(Tetrahedral C)$(im)_2$} Metal Chelates

Metal[Ref.]	r[c]	b[d]	θ[e]	ϕ[f]
Cu[9]	1.998(3), 2.000(2)	2.882(4)	87.7(1)	44.9(2)
Rh[a,12]	2.048(3)−2.071(3)	2.78(1)/ 2.76(1)	87.6(1)/ 87.1(1)	39.4(6)/ 38.36(6)
Fe[a,11]	2.113(5)−2.169(6)	2.812(8)/ 2.822(7)	82.1(2)/ 82.7(2)	6.3(3)/ 9.0(3)
Ru[14]	2.139(5), 2.181(5)	2.908(8)	84.7(2)	20.9(4)
H[b]	2.45(2), 2.50(2)	3.218(2)	81.1(7)	69.14(8)

[a]The Rh and Fe complexes have two ligands.
[b]This work.
[c] r = the metal-nitrogen distances (Å).
[d] b = N…N bite (Å).
[e] θ = N-M-N bite angle (°).
[f] ϕ = C_3N_2/C_3N_2 interplanar dihedral angle (°).

β = 95.737(2)°, V = 1309.0(5) Å^3. D_c (Z = 2) = 1.50$_0$ g cm^{-3}. μ_{Mo} = 6.8 cm^{-1}; specimen: 0.45 × 0.35 × 0.25; $T_{min,max}$ = 0.76, 0.93. N_t = 12455, N = 3230 (R_{int} = 0.018), N_o = 2887; R, R_w (weights: $(\sigma^2(F) + 0.0004\,F^2)^{-1}$; refinement on |$F$|): 0.038, 0.048. $|\Delta\rho_{max}|$ = 0.76(1) e Å^{-3}. (x, y, z, $U_{iso})_{H,D}$ refined throughout.

The results of 153 K single crystal X-ray structure determination* of **5** and **6** are consistent with the above formulation in terms of stoichiometry and connectivity, with stereochemistries/conformations as shown in Figure 1; the parent molecules are accompanied by residues in the lattice modelled as water molecule oxygen fragments for **5**, and as $CDCL_3$ molecules of solvation in **6**, the latter displaying significant interaction with the parent. One half of the **6**·2$CDCl_3$ array comprises the asymmetric unit of the latter structure, a crystallographic inversion centre being located at the centre of the central C-C bond. The solvent 'deuterium' approaches N(15,25) of the parent molecule symmetrically, contacting them at 2.45(2), 2.50(2) Å. The dihedral angle between the pair of *gem*-C_3N_2 planes is 69.14(8)°; C(1')-C(1)-C(n1)-N(n5) (n = 1,2) are 52.1(2), −51.8(2), *cf.* C(1')-C(1)-C(n1)-N(n2) −128.8(2), 131.6(2)°, contacts between H(1) on the central carbon and the two methyl substituents being congenially packed around van der Waals expectations, with N(15)…N(25) 3.218(2) Å, the symmetry of the aggregate putatively 2/*m*, beyond *i*. Geometries associated with similar {(tetrahedral C)$(im)_2$} arrays as ligands about a metal atom, which are structurally defined are compared with the present (regarding the deuterium as a 'pseudo-metal') in the Table. While the angles between the pair of nitrogen donor atoms lies above 80° in all cases, the remaining parameters are very variable, the ligand seemingly very flexible in response to electronic and structural vicissitudes, and, despite the appealing symmetry of the deuterium environment in the present, the interaction must be fairly weak.

By contrast, the counterpart array in **5**, without co-crystallised $CDCl_3$, is less restrained. Here C(2)-C(1)-C(n1)-N(n5) are 4.1(3), -64.3(2), and C(2)-C(1)-C(n1)-N(n2) − 176.8(2), 113.8(2)°; the C_3N_2/C_3N_2 interplanar dihedral angle is 89.85(9)° and N(15)…N(25) 3.766(3)°, a more haphazard array, devoid of any approach to intrinsic sym-

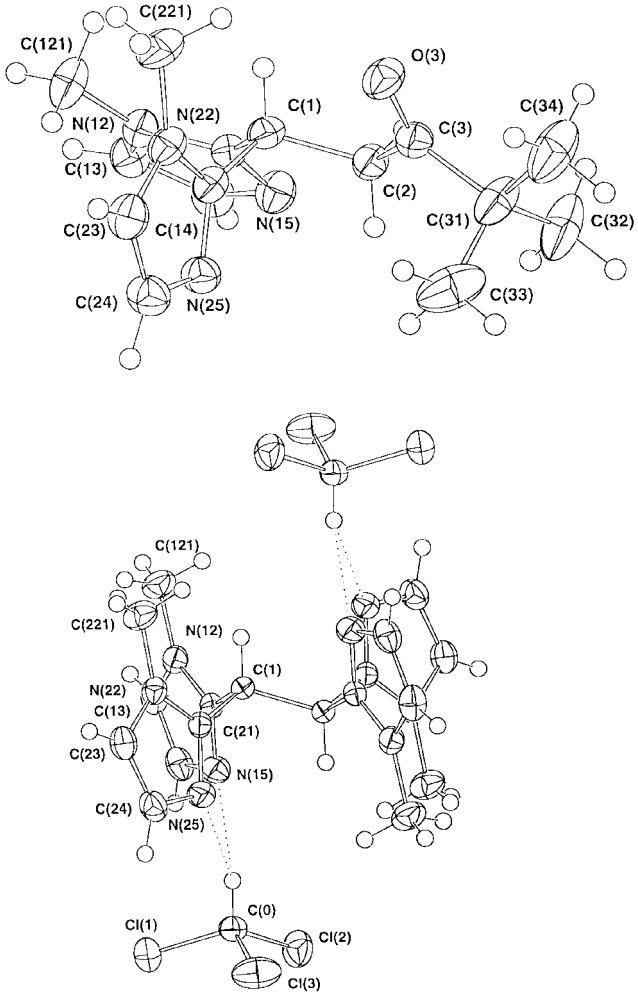


Figure 1 Projections of individual molecules of **5** and **6**, the latter in association with $CDCl_3$ solvent. 50% ellipsoids are shown for the non-hydrogen atoms, hydrogen atoms having arbitrary radii of 0.1 Å

metry. In both **5** and **6**, bond lengths and angles are generally as expected.

The compounds **1a**, **c** were also converted into the respective imines **7a**, **c**. Since initial attempts to react **1a** with aniline by using classical methods failed, we employed a method first reported by Weingarten et al.[24] Hence, **1a** was reacted with a slight excess of aniline in the presence of $TiCl_4$ (Scheme 1). After 72 hours at room temperature, a mixture of the desired product and **1a** was obtained from which the imine **7a** could be separated as yellow crystals by recrystallisation from acetone/ether in 32% yield. Under the same conditions, the benzimidazole derivative **7c** could be prepared in 28% yield from **1c**. Due to the introduction of the H_2N-C_6H_5 function, the ^1H and ^{13}C NMR spectra display two sets of signals for the inequivalent imidazole rings (Figure 2). A full assignment of all signals was obtained by gCOSY, gHMQC and gHMBC experiments.

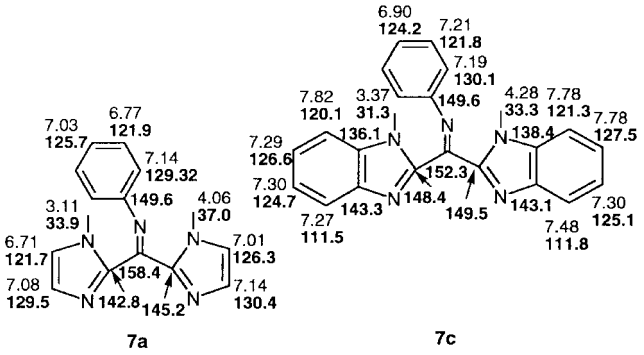


Figure 2 Assignment of ^1H and ^{13}C NMR signals for **7a** ($CDCl_3$) and **7c** (^1H: $CDCl_3$, ^{13}C: CD_3OD, 50 °C)

In conclusion, the metallation of bis(1-methylimidazole)methane (**2a**) and subsequent reaction with electrophiles is an effective method for the preparation of novel chelating ligands containing a bisimidazole backbone. Various electrophiles carrying donor functions may be readily introduced, hence providing a convenient synthetic route to ligands with various donor sets within structurally related chelate systems. Since bis(1-methylimidazole)methane (**2a**) is an important building block for many of these new ligands it is essential that it be readily available. Consequently, an improved method for its preparation was developed. Including the previously reported tris[2-(-methylimidazolyl)]methoxymethane,[6] a set of N^N^N; N^P^N and N^O^N tripodal ligands is available, thus allowing a study of the effect of varying donor sets on the properties of co-ordination compounds consisting of a structurally similar ligand environment. The mixed donor compounds **1** and **3** can also co-ordinate either in an N^O, N^P or an N^N fashion. The co-ordination chemistry of these ligands is currently under investigation by our group and will be reported elsewhere.[18]

All manipulations were carried out under an atmosphere of dry, deoxygenated N_2 using standard Schlenk techniques, unless otherwise indicated. All solvents for use in an inert atmosphere were purified by standard procedures and distilled under N_2 immediately prior to use. Mps were determined with a Gallenkamp apparatus and are uncorrected. NMR spectra were recorded on a Varian Gemini−200 NMR spectrometer and on a Varian Unity Inova 400 WB NMR spectrometer. Elemental analysis (Carlo Erba EA 1108), IR (Bruker IFS-66 FTIR), and MS (Kratos Concept ICQ) were carried out at the Central Science Laboratory (CSL), University of Tasmania. 1-Bromopinacolon, BuLi, diethylcarbonate, diphenylphosphine chloride, and 1-methylimidazole were purchased from Aldrich and used as received. Diphenylphosphine was prepared according to a published procedure.[25]

For new compounds satisfactory microanalyses were obtained: C, H, N ≤0.4% of that expected, except for **4**, which gave C −0.25, H +0.44, N −0.92%.

X-ray data: Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre, nos. CCDC-152 806 (**5**) and 152 807 (**6**). Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax +441223336033; E-mail: deposit@ccdc.cam.ac.uk).

Bis(1-methylimidazol-2-yl)ketone (1a)

A modification of the method described by Elgafi and coworkers was used in this work.[14] A solution of 1-methylimidazole (10.7 g, 0.13 mol) in dry THF (100 mL) was cooled to −45 °C and *n*-BuLi (1.6 M in hexane) (81.2 mL, 0.13 mol) was slowly added. The yellow solution was stirred at −45 °C for 30 min and then cooled to −80 °C. Diethylcarbonate (7.7 g, 0.065 mol) was then added dropwise. The solution changed colour from pale yellow to purple and thickened. The reaction mixture was allowed to warm to −20 °C over 5 h and was then quenched by addition of H_2O (10 mL). After warming to r.t., THF was removed in vacuo and the residue extracted with CH_2Cl_2 (3 × 50 mL). The CH_2Cl_2 layers were pooled, dried ($NaSO_4$), filtered, and evaporated to give a brown orange oil. The pure product was obtained as colourless crystals after recrystallisation from acetone, and from the resulting mother liquor after slow evaporation in air; yield: 8.4 g (68%); mp 154−155 °C (Lit.[14] mp 154−155.5 °C).

IR (KBr): ν = 1632 (C=O) cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.23 (s, 1H, H_{imid}), 7.04 (s, 1H, H_{imid}), 3.94 (s, 3H, NCH_3).

^{13}C NMR (200 MHz, $CDCl_3$): δ = 174.31 (C=O), 143.3 (C=N), 130.8 (C_{imid}), 127.2 (C_{imid}), 36.4 (NCH_3).

Bis(1-isopropyl-4-*tert*-butylimidazol-2-yl)ketone (1b)

A solution of 1-isopropy-4-*tert*-butylimidazole[21] (2.1 g, 12.6 mmol) in THF (10 mL) was slowly added to a solution of *n*-BuLi (1.6 M in hexane) (8.1 mL, 13 mmol) in THF (30 mL) at −80 °C. The solution was stirred at this temperature for 1 h and was then allowed to warm to r.t. over 1 h. The orange red solution was cooled to −80 °C and diethylcarbonate (0.75 g, 6.3 mmol) in THF (10 mL) was added dropwise. The solution was stirred for 3 h at −60 °C to −45 °C, allowed to warm to 5 °C over 15 min, and then quenched with H_2O (10 mL). THF was removed in vacuo and the oily residue extracted with Et_2O (3 × 30 mL). The pooled Et_2O extracts were washed with brine (2 × 10 mL), dried ($NaSO_4$), filtered, and concentrated. Cooling of the Et_2O solution to −20 °C resulted in precipitation of **1b** as an off-white solid. A second crop could be obtained from the concd mother liquor. A pure product was obtained after washing with a small amount of petroleum spirit and drying in a high vacuum; yield: 0.35 g (15.5%); mp 124−125 °C.

IR (KBr): ν = 1635 (C=O) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.99 (s, 1H, H_{imid}), 5.14 [sept, 1H, $^3J_{H-H}$ = 6.8 Hz, $NCH(CH_3)_2$], 1.47 [d, 6H, $^3J_{H-H}$ = 6.7 Hz, $CH(CH_3)_2$], 1.31 (s, 9H, *t*-Bu).

^{13}C NMR (200 MHz, $CDCl_3$): δ = 176.11 (C=O), 153.52 [C_{imid}(*t*-Bu)], 143.3 (C=N), 115.09 (C_{imid}), 49.39 [$NCH(CH_3)_2$], 32.55 [$C(CH_3)_3$], 30.66 [CH_3(*t*-Bu)], 24.39 [CH_3(*i*-Pr)].

MS: *m/z* (%) = 358 (62) [M^+], 343 (38) [$M - CH_3^+$], 315 (100) [$M - i\text{-}Pr^+$].

Bis(1-methylimidazol-2-yl)methane (2a); Typical Procedure

Compound **1a** (4 g, 21.04 mmol) and ground KOH (4 g, 71.3 mmol) were placed into a Schlenk flask. Hydrazine hydrate (35 mL, 0.72 mol) was added and the flask immersed into an oil bath. On heating a yellow solid began to form at 60 °C. The reaction mixture became clear and almost colourless between 110 °C and 120 °C. Stirring at 120 °C was continued for 1 h. The temperature was then raised to 150 °C and stirring was continued for 3 h at this temperature. Some white solid precipitated at the end of this period. The reaction mixture was allowed to cool to r.t. during which a white waxy solid formed. At this point all following operations were carried out in air; CH_2Cl_2 (40 mL) was added and the solution transferred to a separatory funnel. The CH_2Cl_2 layer was separated and the remaining light brown liquid extracted with CH_2Cl_2 (2 × 40 mL). The pooled CH_2Cl_2 extracts were washed twice with H_2O (2 × 15 mL) to remove excess hydrazine hydrate. The combined H_2O extracts were then repeatedly extracted with CH_2Cl_2 (12 × 20 mL; crucial to obtain good yields). The pooled CH_2Cl_2 extracts were dried (Na_2SO_4), filtered, and rotary evaporated to give an off-white solid (3.37 g, almost pure product by ^{1}H NMR). The product was recrystallised from THF (36 mL), and colourless rhombic crystals separated on cooling to r.t.. The light yellow THF solution was decanted, the crystals washed with a few mL of THF and dried under vacuum (1st crop 2.65 g). A second (0.35 g) and a third crop (0.08 g) were collected after concentration of the mother liquor and cooling to −20 °C; yield: 3.08 g (83%); mp 154−156 °C (Lit.[14] mp 152−154 °C).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.90 (d, 2H, $^3J_{H-H}$ = 1.58 Hz, =CH), 6.78 (d, 2H, $^3J_{H-H}$ = 1.58 Hz, =CH), 4.24 (s, 2H, CH_2), 3.66 (s, 6H, NCH_3).

^{13}C NMR (200 MHz, $CDCl_3$): δ = 143.91 (C=N), 127.57 (C_{imid}), 122.02 (C_{imid}), 33.69 (NCH_3), 27.25 (CH_2).

MS: *m/z* (%) = 176 (100) [M^+], 95 (43.5) [1,2-dimethylimidazole + H^+].

Bis(1-methylbenzimidazole-2-yl)methane (2c)

The reaction was carried out as described for **2a**: **1c**[22] (0.35 g, 1.2 mmol), KOH (0.3 g, 4.1 mmol), hydrazine hydrate (2 mL, 41.2 mmol).

Observations: the colour of the suspension began to fade above 44 °C and further solid formed between 65 °C and 90 °C; at 110 °C the reaction mixture became yellow; on cooling to r.t. a light brown waxy solid formed. Work up: addition of CH_2Cl_2 (10 mL) to the reaction mixture at r.t.; after separation of the CH_2Cl_2 layer the remaining light brown liquid was extracted with CH_2Cl_2 (2 × 5 mL); washing of the combined CH_2Cl_2 extracts with H_2O (2 × 5 mL); extraction of the combined aqueous extracts with CH_2Cl_2 (12 × 20 mL). 0.28 g off-white solid (almost pure product by ^{1}H NMR) was obtained after drying (Na_2SO_4) of the pooled CH_2Cl_2 extracts, filtration, and rotary evaporation. The product was recrystallised from THF (6 mL). Colourless crystals separated on cooling to r.t. (0.18 g) and a second crop (0.03 g) was obtained from the mother liquor; yield: 0.21 g (63%); mp 205−207 °C (Lit.[12] mp 206.5−208.5 °C).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.74 (m, 2H, H_{arom}), 7.28 (m, 6H, H_{arom}), 4.69 (s, 2H, CH_2), 3.90 (s, 6H, NCH_3).

^{13}C NMR (200 MHz, $CDCl_3$): δ = 149.65 (C=N), 142.77, 136.64, 123.24, 122.66, 119.96, 109.8 (C_{arom}), 30.9 (NCH_3), 29.2 (CH_2).

MS: *m/z* (%) = 276 (100) [M^+], 261 (21) [$M - CH_3^+$], 145 (62) [M − 1-methylbenzimidazole$^+$], 131 (40) [1-methylbenzimidazole].

Chloromethyl Diphenylphosphine

A solution of KOH (3 g 53.5 mmol) in H_2O (2.5 mL) was mixed with a solution of *n*-$BuNCl_4$ hydrate (0.5 g 1.8 mmol) in CH_2Cl_2 (30 mL) and toluene (5 mL). Freshly distilled diphenylphosphine (2 g, 10.7 mmol) dissolved in CH_2Cl_2 (5 mL) was then added to the emulsion under vigorous stirring over 2 h. The reaction mixture was stirred for 14 h at r.t., washed with H_2O (3 × 10 mL), and the organic layer separated. Evaporation of the solvent and drying in a high vacuum gave the pure product as a clear oil. Any $Ph_2P(O)CH_3$ that formed could be separated by addition of H_2O (15 mL) to the oil, extraction of the product into petroleum spirit (3 × 7 mL), and removal of the solvent in vacuo; yield: 2.4 g (95%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.35−7.6 (m, 10H, H_{arom}), 4.08 (d, 2H, $^2J_{H-P}$ = 5.1 Hz, CH_2).

^{13}C NMR (200 MHz, $CDCl_3$): δ = 134.6 (d, $^2J_{C-P}$ = 17.1 Hz, *ipso* C), 133.5 (d, $^3J_{C-P}$ = 19.1 Hz, *ortho* C), 129.9 (s, *para* C), 129.2 (d, $^4J_{C-P}$ = 11.2 Hz, *meta* C), 41.3 (d, $^3J_{C-P}$ = 28.4 Hz, CH_2).

^{31}P NMR (400 MHz, $CDCl_3$): δ = −10.86.

2-[(Diphenylphosphino)(1-methyl-1*H*-imidazol-2yl)methyl]-1-methyl-1*H*-imidazole (3)

A solution of **2a** (1 g, 5.7 mmol) in THF (35 mL) was cooled to −80 °C. *n*-BuLi (1.6 M in hexane; 3.65 mL, 5.8 mmol) was added slowly. The yellow solution was stirred at −80 °C to −45 °C for 1.5 h and then re-cooled to −80 °C. A solution of diphenylphosphine chloride (1.25 g, 5.7 mmol) in THF (10 mL) was added dropwise. A white precipitate formed. The reaction mixture was allowed to warm to −30 °C and then quenched with degassed H_2O (30 mL). After warming to r.t., the solvent was removed in vacuo and the residue extracted with CH_2Cl_2 (3 × 15 mL). The CH_2Cl_2 layers were pooled and evaporated to dryness giving the product as a white solid. If partial oxidation of the product occurs, it can be purified by washing with Et_2O (3 × 5 mL); yield: 1.74 g (85%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.20−7.35 (m, 10H, H_{arom}), 6.83 (s, 2H, H_{imid}), 6.65 (s, 2H, H_{imid}), 5.37 (d, 1H, $^2J_{H-P}$ = 2.4 Hz, CH), 3.63 (s, 6H, NCH_3).

^{13}C NMR (200 MHz, $CDCl_3$): δ = 144.02 (d, $^2J_{C-P}$ = 11 Hz, C = N), 136.7 (d, $^2J_{C-P}$ = 16.6 Hz, *ipso* C), 133.64 (d, $^3J_{C-P}$ = 20 Hz, *ortho* C), 129.49 (s, *para* C), 128.9 (d, $^4J_{C-P}$ = 6.9 Hz, *meta* C), 127.6 (s, C_{imid}), 122.3 (s, C_{imid}), 39.5 (d, $^2J_{C-P}$ = 17.7 Hz, CH), 34.4 (d, $^4J_{C-P}$ = 7.4 Hz, NCH_3).

^{31}P NMR (400 MHz, $CDCl_3$): δ = −12.82 (s).

MS: *m/z* (%) = 361 (50) [MH^+], 176 (100) [**2a**$^+$].

2-[2-(Diphenylphosphino)-1-(1-methyl-1*H*-imidazol-2yl)ethyl]-1-methyl-1*H*-imidazole (4)

A solution of **2a** (1 g, 5.7 mmol) in THF (50 mL) was cooled to −80 °C. *n*-BuLi (1.6 M in hexane) (3.64 mL, 5.8 mmol) was added slowly. The yellow solution was allowed to warm to −45 °C, stirred for 30 min, and then cooled to −70 °C. A solution of diphenylphosphinemethane chloride (1.4 g, 5.96 mmol) in THF (5 mL) was added dropwise. On warming to r.t. a white solid formed and the lemon yellow reaction mixture was stirred for another 48 h. Degassed H_2O was then added until almost all solid had dissolved (3−4 mL). THF was removed in vacuo and degassed H_2O (15 mL) was added to the pale yellow residue. The product was extracted with Et_2O (3 × 10 mL). The combined Et_2O extracts were evaporated giving the product as a pale oil; yield: 1.83 g (85%).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.28−7.52 (m, 10H, H_{arom}), 6.94 (d, 2H, $^2J_{H-H}$ = 1.25 Hz, H_{imid}), 6.69 (d, 2H, $^2J_{H-H}$ = 1.25 Hz, H_{imid}), 4.95 (pseudo q, 1H, $^3J_{H-H}$ = 8.2 Hz, CH), 3.41 (s, 6H, NCH_3), 3.12 (d, 2H, $^3J_{H-H}$ = 8.3 Hz, CH_2P).

^{13}C NMR (200 MHz, $CDCl_3$): δ = 146.3 (d, $^3J_{C-P}$ = 6.5 Hz, C=N), 138.3 (d, $^2J_{C-P}$ = 13.4 Hz, *ipso* C), 133.4 (d, $^3J_{C-P}$ = 19.1 Hz, *ortho* C), 129.1 (s, *para* C), 128.8 (d, $^4J_{C-P}$ = 6.7 Hz, *meta* C), 127.5 (s, C_{imid}), 122.5 (s, C_{imid}), 36.4 (d, $^2J_{C-P}$ = 21.1 Hz, CH_2), 33.3 (s, NCH_3), 31.5 (d, $^3J_{C-P}$ = 12.9 Hz, CH).

^{31}P NMR (400 MHz, $CDCl_3$): δ = −22.38.

MS: *m/z* (%) = 374 (1.6) [M^+], 297 (100) [$M - C_6H_5^+$], 189 (24) [$M - P(C_6H_5)_2^+$].

4,4-Dimethyl-1,1-bis(1-methyl-1*H*-imidazol-2-yl)pentan-3-one (5)

A solution of **2a** (1.7 g, 9.7 mmol) in dry THF (140 mL) was cooled to −70 °C. *n*-BuLi (1.6 M in hexane; 6.21 mL, 9.94 mmol) was added slowly. The yellow solution was allowed to warm to −40 °C over 1 h and kept at −40 °C for about 10 min. The solution was then cooled to −75 °C and 1-bromopinacolon (1.727 g, 9.7 mmol) was added causing the reaction mixture to become cloudy. The lemon yellow mixture was stirred for 3.5 h at −70 °C to −45 °C and kept at −20 °C overnight. The now white suspension was allowed to warm to 10 °C and quenched with H_2O (5 mL) until almost all solid material had dissolved. At this stage, exclusion of air is no longer required. THF was removed under reduced pressure, CH_2Cl_2 (45 mL) was added, followed by H_2O (15 mL), and the mixture was transferred to a separatory funnel. The CH_2Cl_2 layer was separated and washed with brine (15 mL). The pooled aqueous layers were extracted with CH_2Cl_2 (3 × 5mL). Drying of the combined CH_2Cl_2 extracts (Na_2SO_4), filtration, and rotary evaporation gave 2.82 g of a light brown oil. On treatment with Et_2O (20 mL) the by-product **6** precipitated as a fluffy solid (0.21 g), which was separated by filtration through a frit. Addition of brine (8 mL) to the yellow Et_2O solution resulted in the formation of three layers from which the Et_2O layer was separated. After addition of further brine (8 mL) to the remaining two layers, the aqueous layer and the brown oil layer were extracted with Et_2O (3 × 15 mL). The combined Et_2O layers were dried (Na_2SO_4), filtered, and allowed to slowly evaporate in air. The pure product separated as colourless crystals. The mother liquor was decanted, the product washed with a small amount of Et_2O, and dried under vacuum. The total amount of product was collected by repeated crystallisation of the combined mother liquors and Et_2O washings; yield: 1.78 g (67%); mp 52−54 °C.

IR (KBr): ν = 1704 (C=O) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.67 (d, 2H, $^3J_{CH}$ = 1.2 Hz, H_{imid}), 6.55 (d, 2H, $^3J_{CH}$ = 1.2 Hz, H_{imid}), 4.75 (t, 1H, $^3J_{C-H}$ = 6.9 Hz, CH), 3.35 (d, 2H, $^3J_{C-H}$ = 6.9 Hz, CH_2), 3.32 (s, 6H, NCH_3), 2.3 (s, 3H, H_2O), 0.92 (s, 9H, ^{t}Bu).

^{13}C NMR (200 MHz, $CDCl_3$): δ = 213.9 (C=O), 146.6 (C=N), 127.6 (C_{imid}), 122.1 (C_{imid}), 44.6 (CH_2), 40.1 (CH), 33.3 (NCH_3), 32.6 [$C(CH_3)_3$], 26.8 (^{t}Bu).

MS: *m/z* (%) = 275 (3) [MH^+], 217 (57) [$M - t$-Bu^+], 189 (100) [$M - C(O)t$-Bu^+], 175 (39) [$M - CH_2C(O)t$-Bu^+].

N-[Bis(1-methyl-1*H*-imidazol-2-yl)methylene]-*N*-phenylamine (7a); Typical Procedure

Compound **1a** (3 g, 15. 8 mmol) was placed in a 250 mL round bottom Schlenk flask. CH_2Cl_2 (40 mL) was added and the flask immersed into a cooling bath set to −20 °C. Aniline (4.85 g, 52.0 mmol) was added neat under stirring and the glass wall rinsed with CH_2Cl_2 (5 mL). A 1 M solution of $TiCl_4$ in CH_2Cl_2 (8.7 mL, 8.7 mmol) was added to the rapidly stirred solution over 0.5 h via a dropping funnel. The reaction mixture immediately turned orange red, a precipitate formed, and the colour deepened during the course of the reaction. After the addition was completed, the dropping funnel was rinsed with CH_2Cl_2 (2 × 5mL) and stirring was continued for 1 h at −20 °C, after which the reaction mixture was allowed to warm to r.t. The mixture became yellow overnight. Stirring was continued for 48 h when the contents were filtered through Celite. The reaction flask was rinsed with CH_2Cl_2 (3 × 10 mL), the light yellow solid that was collected on the frit was extracted with CH_2Cl_2 (100 mL), and the combined CH_2Cl_2 extracts were evaporated leaving a orange yellow oil. At this stage, exclusion of air is no longer necessary. NaOH (10%, 20 mL) was added followed by H_2O (40 mL) and the solution extracted with Et_2O/petroleum spirit (5:2) (4 × 28 mL). Light yellow needles (0.23 g) of **7a** separated upon slow evaporation in air at r.t. and after concentration and cooling (−20 °C) of the mother liquor (0.2 g). Additional product was obtained by extraction of the remaining aqueous phase (contains some white solid material, TiO_2) with CH_2Cl_2 (4 × 25 mL). The pooled CH_2Cl_2 extracts were washed with brine (3 × 20 mL), dried (Na_2SO_4), filtered, and evaporated to a yellow sticky solid (1.13 g). The crude product was recrystallised from boiling Et_2O/acetone (2:1). A first crop of **7a** (0.8 g) separated as light yellow needles upon cooling to r.t. and storage at −20 °C. A second crop (0.12 g) was isolated after concentration of the mother liquor and storage at −20 °C. A third crop consisted of a mixture of **1a** and **7a** (1.5:1); yield 1.35 g (32.4%); mp 131−133 °C.

MS: *m/z* (%) = 264 (100) [$M - H^+$].

N-[Bis(1-methyl-1*H*-benzimidazol-2yl)methylene]-*N*-phenylamine (7c)

The reaction was carried out as described for **7a**: **1c** (0.282 g, 0.97 mmol), aniline (0.3 g, 3.2 mmol), $TiCl_4$ 1 M in CH_2Cl_2 (0.54 mL, 0.54 mmol), CH_2Cl_2 (10 mL).

Workup: CH_2Cl_2 was removed under reduced pressure and the green yellow solid washed with Et_2O, taken up in CH_2Cl_2 (50 mL) and poured into H_2O (25 mL) upon which some white solid material formed (TiO_2). H_2O (25 mL) was added, the CH_2Cl_2 layer separated and washed with H_2O (2 × 10 mL). The pooled H_2O washings were extracted with CH_2Cl_2 (15 mL). The combined CH_2Cl_2 layers were dried (Na_2SO_4), filtered, and rotary evaporated. The obtained green yellow solid consisted of a mixture of **1c** and **7c** (2:1, ^{1}H NMR) from which **1c** was separated by washing with acetone (2 × 3 mL). Drying in air and recrystallisation from EtOAc afforded **7c** as a light yellow solid; yield 0.1 g (28%); mp 270 °C (dec.).

MS: *m/z* (%) = 365 (100) [M^+], 350 (19) [$M - CH_3^+$].

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