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A number of imidazole derivatives were prepared in the course of studying the limits of carbon-metal bond formation in complexes of imidazole with first-row transition metals. Seven of the compounds were new. The 4- and 5-methyl and 4,5-dimethyl derivatives of 1-(2-pyridyl)-imidazole were prepared by reaction of the appropriate imidazole with 2-bromopyridine. Alkylation of imidazole, 4,5-dimethylimidazole, and benzimidazole with 2-chloromethylpyridine gave a series of 1-(2-pyridylmethyl)imidazoles. 1-(2,3-Diaminopropyl)imidazole was prepared in six steps via a Gabriel sequence.

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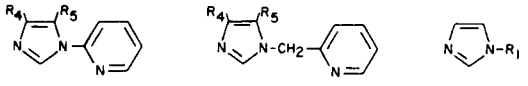
As a part of our work (1) aimed at delineating the conditions under which the imidazole ring forms carbon-bound complexes with transition metal ions, (2) a series of imidazoles which are potentially bi- or tridentate in the carbon bound mode were prepared. This note reports the preparative methods and the physical characterization of these compounds.

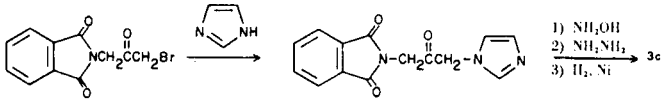


	R_4	R_5
1a	H	H
1b	CH_3	H
1c	H	CH_3
1d	CH_3	CH_3
1e	-benzo-	

	R_4	R_5
2a	H	H
2b	CH_3	CH_3
2c	-benzo-	

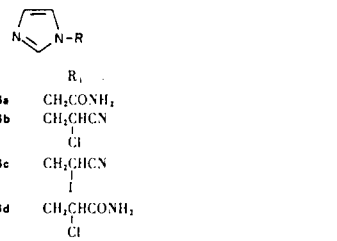
	R_1
3a	$-(CH_2)_3NH_2$
3b	$-(CH_2)_2NH_2$
3c	$-CH_2CHCH_2NH_2$ (NH₂)

Compounds **1b-1d** were prepared by a method previously reported (3) for **1a** and **1e** involving copper-catalyzed arylation by 2-bromopyridine. Compounds **2a-2c** were prepared by alkylation of the conjugate base of the appropriate imidazole in liquid ammonia using 2-chloromethylpyridine. Compounds **3a** and **3b**, were prepared by a modification of a previously reported (4,5) method via the appropriate ω-bromoalkylphthalimide. The synthesis of **3c** commenced with the known compound **4** (6) and involved alkylation of imidazole, oximation, hydrazinolysis of the phthalimide group and catalytic reduction.



4 5

The new compounds **1b-1d**, **2a-2c** and **3c** were characterized by elemental analysis and mass spectral fragmentation as reported in Table I. Salient nmr data for compounds **1a-e** and **2a-c** are reported in reference 1.



	R_1
6a	CH_2CONH_2
6b	CH_2CHCN (Cl)
6c	CH_2CHCN (I)
6d	$CH_2CHCONH_2$ (Cl)

A number of other previuosly unreported 1-substituted imidazoles (**6a-d**) were prepared by alkylation procedures in the course of ultimately unsuccessful routes to related ligands.

EXPERIMENTAL

4-Methyl-1-(2-pyridyl)imidazole (**1b**) and 5-Methyl-1-(2-pyridyl)-imidazole (**1c**).

A mixture of 4-methylimidazole (2.05 g., 25 mmoles), 4-bromopyridine (4.00 g., 25.5 mmoles), potassium carbonate (5.0 g.) and copper oxide (0.2 g.) was heated together under nitrogen for 20 hours. The crude product was separated into two components by chromatography on alumina using 20% chloroform in benzene for elution. The less polar component **1b** (1.50 g., 9.4 mmoles, 38%) was obtained as a waxy hygroscopic solid, m.p. 50-52°, after distillation (b.p. 125°/1mm) and crystallization. The more polar component **1c** (0.28 g., 1.7 mmoles, 7%) was distilled, b.p. 125°/1mm, and crystallized from ether-hexane, m.p. 65-66°. The identity of the more polar component as 5-methyl-1-(2-pyridyl)imidazole was established by X-ray diffraction (7).

Anal. Calcd. for $C_9H_9N_3$: C, 67.90; H, 5.70; N, 26.40. Found: (**1b**) C, 67.81; H, 5.75; N, 26.21; Found: (**1c**) C, 67.99; H, 5.74; N, 26.31.

4,5-Dimethyl-1-(2-pyridyl)imidazole (**1d**).

The same procedure as above on a 50 mmole scale provided, after distillation and recrystallization from benzene-hexane **1d** in 63% yield. Recrystallization from benzene-hexane gave pure material, m.p. 92-94°.

Anal. Calcd. for $C_{10}H_{11}N_3$: C, 69.34; H, 6.40; N, 24.26. Found: C, 69.34; H, 6.42; N, 24.20.

1-(2-Pyridylmethyl)imidazole (**2a**).

About 350 ml. of ammonia was condensed into a 500 ml. flask equipped with a Dry Ice-acetone condenser and sodamide was prepared by the addition of small pieces of sodium (5.0 g., 0.22 g.-atom) in the presence of ferric nitrate. Imidazole (6.80 g., 0.100 mole) was added followed by cautious portionwise addition of solid 2-chloromethylpyridine hydrochloride. The solution was then stirred for 0.5 hour before the cold-finger condenser was removed and the ammonia was allowed to evaporate overnight. The residual solid was triturated with a methanol-chloroform mixture and after evaporation of the solvent the product was eluted from alumina using ether-chloroform-methanol. The product was finally distilled at 120°/2 mm giving **2a** (9.3 g., 0.058 mole, 58%) as a yellow oil which rapidly solidified to nearly colorless crystals m.p. 68-70°.

Anal. Calcd. for $C_9H_9N_3$: C, 67.92; H, 5.66; N, 26.42. Found: C, 67.64; H, 5.84; N, 26.30.

TABLE I

Principal Mass Spectral Peaks

1a	145(100), 118(43), 117(63), 91(33), 78(53), 64(28)
1d	173(100), 158(19), 145(27), 143(15), 131(19), 95(30), 78(56)
1e	195(100), 169(48), 140(6), 84(10), 78(19), 67(15)
2a	159(100), 145(15), 131(72), 105(54), 104(27), 91(90), 64(70)
2b	187(52), 173(8), 147(14), 145(19), 131(12), 93(100)
2c	209(100), 131(42), 118(96), 91(36)
6a	125(100), 82(46), 81(69), 54(39)
6b	157(32), 155(100), 120(22), 93(14), 81(45)
6c	247(63), 194(24), 134(21), 120(47), 119(65), 92(63), 81(100)
6d	175(22), 173(67), 138(100), 119(38), 81(53), 68(58)

1-(2-Pyridylmethyl)-4,5-dimethylimidazole (**2b**).

A similar procedure was followed to provide **2b**, m.p. 77-79° after sublimation.

Anal. Calcd. for $C_{11}H_{13}N_3$: C, 70.59; H, 6.95; N, 22.46. Found: C, 70.34; H, 7.03; N, 22.55.

1-(2-Pyridylmethyl)benzimidazole (**2c**).

A similar procedure provided **2c** in 24% yield on a 200 mmole scale, m.p. 112-114° after recrystallization from toluene-hexane.

Anal. Calcd. for $C_{13}H_{11}N_3$: C, 74.64; H, 5.26; N, 20.10. Found: C, 74.65; H, 5.27; N, 20.06.

1-(2-Aminoethyl)imidazole (**3a**).

N-(2-Bromoethyl)phthalimide (42.5 g., 0.17 mole) and imidazole (23.1 g., 0.34 mole) were refluxed in acetone (100 ml.) for 4 hours. The solvent was evaporated, water was added and the solution was made alkaline with aqueous sodium hydroxide. The crude product was isolated by filtration. The product was dissolved in ethanol and treated with 3 equivalents of hydrazine and the solution refluxed for 2 hours. Refrigeration overnight resulted in precipitation of phthalhydrazide.

The residue was distilled in a short path still at 1 mm. The distillate was isolated as a dihydrochloride salt by dissolving in concentrated hydrochloric acid and evaporating to dryness.

1-(3-Aminopropyl)imidazole (**3b**).

This compound was prepared in a manner analogous to **3a** from *N*-(3-bromopropyl)phthalimide.

1-(2,3-Diaminopropyl)imidazole (**3c**).

N-(3-Bromo-2-hydroxypropylphthalimide was prepared and oxidized to the bromoketone **4** following the known procedure (6). The bromoketone (1.00 g., 3.2 mmoles) and imidazole (6.8 g., 10.0 mmoles) were dissolved in acetone and refluxed for 4 hours. Precipitation occurs as reaction proceeds. The solution was concentrated to one half the original volume and the precipitate was isolated by filtration. The yield of **5** was 94%. An analytical sample was prepared by recrystallization from methanol-water, m.p. 233°.

Anal. Calcd. for $C_{14}H_{11}N_3O_3$: C, 62.45; H, 4.09; N, 15.61. Found: C, 62.36; H, 4.10; N, 15.53.

The ketone (2.0 g.) was suspended in 30 ml. of 50% aqueous ethanol and 3.0 g. of hydroxylamine hydrochloride was added. When the solution was clear, sodium carbonate (3.0 g.) was added in small portions over 0.5 hour. Then stirring was continued for 1 hour. During this time the oxime precipitated and was isolated by filtration. The oxime was dissolved in absolute ethanol and a four-fold excess of hydrazine was added. The solution was refluxed for 2 hours. The solution was cooled and phthalhydrazide was removed by filtration. The amino-oxime was used immediately. Hydrogenation was carried out at 100 atmospheres of hydrogen at 100° for 24 hours over Raney nickel W5. The cooled solution was filtered through Celite filter-aid and hydrogen sulfide was then bubbled through the solution, resulting in the precipitation of nickel sulfide. The solution was again filtered through Celite and excess concentrated hydrochloric acid was added to the filtrate. The solution was evaporated to dryness at reduced pressure to give a trihydrochloride salt in 50% yield. The solid residue was recrystallized from a minimum amount of hot water.

Anal. Calcd. for $C_6H_{12}N_4 \cdot 3HCl$: C, 28.63; H, 6.01; N, 22.72. Found: C, 28.85; H, 5.99; N, 22.44.

Imidazole-1-acetamide (**6a**).

A solution of the imidazolate anion in DMSO was prepared by dissolving potassium hydroxide (3.3 g.) and imidazole (3.4 g.) in DMSO (60 ml.). To this solution there was added 9.24 g. of iodoacetamide and the solution was maintained at 60-70° for 8 hours. Most of the DMSO was removed by distillation and the oily residue was diluted with chloroform giving a precipitate of crude product mixed with potassium iodide. The product was placed in a Soxhlet extractor. Extraction with chloroform gave 3.30 g. (52%) of **6a**. An analytical sample was prepared by recrystallization from ethanol-chloroform, m.p. 182-183°.

Anal. Calcd. for $C_5H_7N_3O$: C, 47.99; H, 5.64; N, 33.58. Found: C, 47.98; H, 5.68; N, 33.65.

1-(2-Chloro-2-cyanoethyl)imidazole (**6b**).

Imidazole (3.4 g., 0.05 mole) was dissolved in tetrahydrofuran (30 ml.) and 2-chloroacrylonitrile (4.38 g., 0.05 mole) was added dropwise. After stirring 3 hours the solvent was removed yielding an oil which soon solidified and was recrystallized from chloroform-ether to give **6b** (5.22 g., 75%), m.p. 80-81°.

Anal. Calcd. for $C_6H_6ClN_3$: C, 46.32; H, 3.88; N, 27.00. Found: C, 46.47; H, 3.95; N, 26.90.

1-(2-Cyano-2-iodoethyl)imidazole (**6c**).

A mixture of 1-(2-chloro-2-cyanoethyl)imidazole (1.0 g., 6.4 mmoles) and potassium iodide (2.11 g., 12.7 mmoles) in acetone (75 ml.) was refluxed for 24 hours. The solvent was removed and the residue was triturated several times with hot chloroform. Evaporation of the chloroform gave crude **6b**, m.p. 93-97° (0.547 g., 34%) which was recrystallized from chloroform-ether giving pure **6c**, m.p. 103-104°.

Anal. Calcd. for $C_6H_6IN_3$: C, 29.17; H, 2.44; N, 17.00. Found: C, 29.14; H, 2.53; N, 17.09.

3-(1-Imidazolyl)-2-chloropropanamide (**6d**).

A solution of 1-(2-chloro-2-cyanoethyl)imidazole (7.8 g., 0.050 mole) was added dropwise to a solution of sodium cyanide (2.45 g.) in water (10 ml.) and ethanol (20 ml.). The mixture was stirred for 14 hours at room temperature. The solution was then filtered and the solvent removed. The residue was triturated with hot chloroform. The residue remaining from evaporation of the chloroform was chromatographed on neutral alumina. Benzene-chloroform eluted 3-(1-imidazolyl)-2-chloropropanamide (**6d**) (2.84 g., 32%), m.p. 129-130°.

Anal. Calcd. for $C_6H_8ClN_3O$: C, 41.51; H, 4.64; N, 24.20. Found: C, 41.42; H, 4.69; N, 24.30.

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