due (6.4 g, 60%) containing a mixture of *o*- and *m*-toluidine was obtained. The mixture consisted of 67% *o*-toluidine and 33% *m*-toluidine as determined by vapor phase chromatographic analysis. In addition 4.0 g (31.5%) of *o*-chlorotoluene, bp 157–159° (760 mm), was recovered.

Reaction of *o*-Chlorotoluene with Lithium Amide in Liquid Ammonia. Using the same procedure as that which was employed with sodium amide and *o*-chlorotoluene, the reaction of lithium amide (0.2 mol) and *o*-chlorotoluene (12.7 g, 0.1 mol) gave upon the removal of the solvent 0.5 g (2%) of a mixture containing 73% *o*-toluidine and 27% *m*-toluidine. In addition, 11.5 g (90.5) of *o*-chlorotoluene, bp 157–159° (760 mm), was recovered.

Reaction of Potassium Amide and *o*-Chlorotoluene in Liquid Ammonia. The reaction of potassium amide (0.20 mol) and *o*-chlorotoluene (12.7 g, 0.10 mol) gave upon removal of the solvent 6.7 g (63%) of a mixture containing 54% *o*-toluidine and 46% *m*-toluidine. Also, 3.9 g (30.7%) of *o*-chlorotoluene, bp 156.5–159° (760 mm), was recovered.

Registry No.—Lithium amide, 7782-89-0; sodium amide, 7782-92-5; potassium amide, 17242-52-3; *o*-toluidine, 95-53-4; *m*-toluidene, 108-44-1; *o*-chlorotoluene, 95-49-8.

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The Imidazole–Formaldehyde Reaction. Formation of 1-Imidazolemethanol

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Spectral,[1,2] NMR,[3] and potentiometric[4] studies have shown the formation in solution of 1-imidazolemethanol (**1**) from the reaction of imidazole and formaldehyde, although **1** was not isolated. These studies show that only one nitrogen is involved in methylol formation in basic media.[3,4] In an acid medium,[3,4] both ring nitrogens may be hydroxymethylated. Jones[5] has shown that 1-benzylimidazole forms the 2-hydroxymethyl derivative in nearly quantitative yield in a sealed tube reaction between formaldehyde and 1-benzylimidazole.

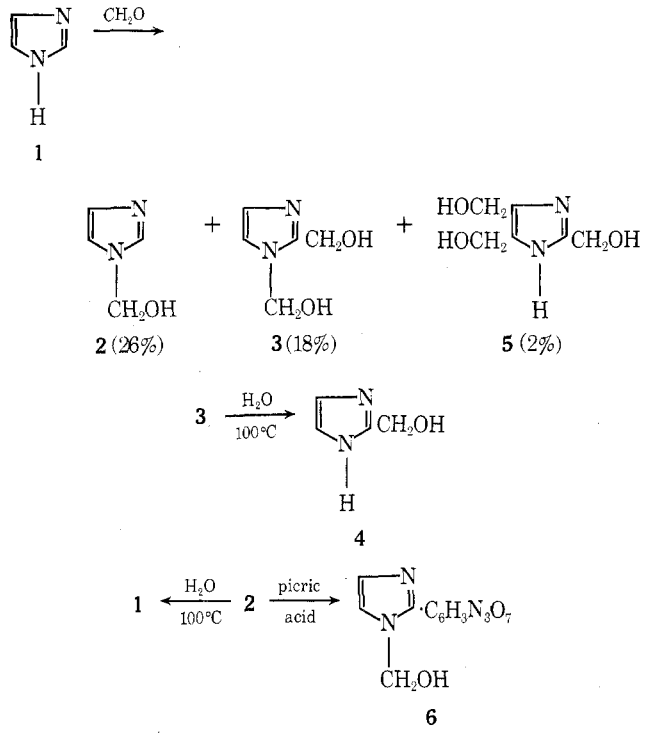
From a sealed tube reaction between imidazole and formaldehyde at 120–130°, a liquid fraction was isolated by chromatography of the crude product. This material gave a picrate derivative (**6**) corresponding to that of a methylolated imidazole. NMR data on the methylolated imidazole indicates the presence of the $-NCH_2O-$ protons by a singlet at δ 5.39 (in D_2O), in agreement with the values reported by Dunlop, Marini, Fales, Sokoloski, and Martin[3] (δ 5.40 in D_2O). Boiling this material in water yields imidazole. These data indicate that the liquid is 1-imidazolemethanol (**2**).

From this same reaction there was obtained a white, crystalline solid (mp 126–127°) which appears to be 1,2-bis(hydroxymethyl)imidazole (**3**). NMR data on this material also show the presence of an NCH_2O- methylene group (NMR peak at δ 5.47 in D_2O) as well as a methylene group (NMR peak at δ 4.75 in D_2O) at the 2 position.

A small amount of a second white, crystalline material (mp 158–159°) was also isolated. Elemental analysis and NMR data indicate that the material is 2,4,5-tris(hydroxymethyl)imidazole (**5**).

Table I summarizes the NMR data on the products of this reaction.[7] Scheme I summarizes the principal reactions.

Scheme I



Experimental Section

Ir spectra were obtained using a Beckman Model 10 grating ir spectrophotometer with potassium bromide cells. Solids were pressed into 1% KBr pellets. NMR spectra, graciously run by Dr.

Table I
Proton Chemical Shifts for Imidazole Derivatives[a-c]

Compd	Proton bands, ppm			
	C_2	C_4, C_5	$-NCH_2O-$	$-CCH_2O$
2-Imidazolemethanol[c]		7.06 (s)		4.64 (s)
1,2-Bis(hydroxymethyl)-imidazole[c]		7.05 (bs)	5.47 (s)	4.75 (s)
1-Imidazolemethanol[c]	7.70 (bs)	7.07 (bs)	5.39 (s)	
2,4,5-Tris(hydroxymethyl)-imidazole[c,d]				4.57 (bs),[c] 4.50, 4.30[d]

[a] Legend to symbols: s, singlet; bs, broad singlet. [b] All chemical shifts are reported in parts per million (δ). [c] D_2O solvent. [d] CH_3OD solvent.

James Woodyard, were recorded with a Varian A-60 spectrophotometer. The elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Melting points were taken on a Mel-Temp capillary melting point apparatus and are uncorrected. All chromatographic columns were prepared by pouring Merck reagent grade aluminum oxide, previously dried for 2 hr at 100°, onto a column filled with chloroform (reagent grade). The elutant from the column was analyzed by thin layer chromatography using microslides prepared by the method of Peifer[6] from silica gel G (according to Stahl), 1:1 ether–methanol as developing solvent, and iodine vapor for visualization of spots.

Sealed Tube Reaction between Imidazole and Formaldehyde. A solution of 13.6 g (0.20 mol) of imidazole (Sigma Chemical Co.) and 50 g of 37% aqueous formaldehyde solution in sealed Pyrex tubes was heated for 15 hr in an oil bath at 120–130° and was then evaporated in vacuo to give 17.8 g of colorless, viscous syrup. A drop of crude product treated with picric acid gave a resinous picrate derivative. The syrup was extracted with a hot mixture of 140 ml of acetone, 15 ml of methanol, and 15 ml of chloroform. After cooling, the supernatant was decanted from an insoluble syrup. This syrup was dissolved in a small volume of methanol and 35 ml of a 1:1 mixture of chloroform–acetone was added. After cooling overnight at 10° the supernatant was decanted from about 1.5 g of insoluble syrup. The solvents were evaporated from the two extracts, leaving syrupy residues: 10 g of more soluble material; 6 g of less soluble material. These two fractions were separately chromatographed on alumina.

1,2-Dihydroxymethylimidazole. The 10 g of more soluble material was dissolved in an acetone–chloroform mixture, placed on a 15.5 × 4 cm column, and eluted with six 25-ml portions of 3:1 chloroform–acetone, four 24-ml portions of chloroform–acetone mixture plus 1 ml of methanol, and three fractions with increasing amounts of methanol. By digesting the first nine fractions with acetone a total of 3.25 g of white, crystalline solid was obtained. Melting points of the different fractions ranged from 90–115° to 121–125° but all gave identical ir spectra. A sample for analysis recrystallized twice from acetone melted at 126–127°. The NMR spectrum and analysis indicated this material to be 1,2-bis(hydroxymethyl)imidazole.

Anal. Calcd for $C_5H_8N_2O_2$: C, 46.87; H, 6.29; N, 21.86. Found: C, 46.79; H, 6.16; N, 22.03.

2-Imidazolemethanol was prepared by the method of Jones;[5] purification by chromatography yielded a white, crystalline solid, mp 112–112.5° (lit.[7] mp 114–115°). The NMR sample of the 1,2-dihydroxymethylimidazole (0.1413 g) was repeatedly digested with water to remove deuterium. The final residue (72 mg after one recrystallization from acetone) melted at 108–109° and gave an ir spectrum identical with that of 2-imidazolemethanol.

The syrupy residues (2.4 g) from recrystallizations of different fractions of 1,2-dihydroxymethylimidazole were combined, boiled with water, and chromatographed, yielding 0.25 g of imidazole, mp 91–92° (identified by ir), and 1.5 g of crude 2-imidazolemethanol (identified by ir).

2,4,5-Trihydroxymethylimidazole. After fractions 10–13 were extracted from the above chromatography with acetone, the combined acetone-insoluble residues were dissolved in methanol. White, crystalline solid slowly separated from solution and after cooling overnight at 10°, 0.2 g of solid, mp 154–155°, was separated by filtration. After one recrystallization from methanol–acetone, a sample for analysis melted at 158–159°.

Anal. Calcd for $C_6H_{10}N_2O_3$: C, 45.57; H, 6.37; N, 17.71. Found: C, 46.14, 45.99; H, 6.52, 6.60; N, 18.26, 18.16.

A sample (50 mg) for NMR analysis was dissolved in 0.3 ml of D_2O. Only two adsorptions occurred at δ 4.81 (HOD) and 4.57. The integration data showed a ratio of HOD to $-CH_2$ of 1:1.48. The recovered sample, after boiling with water to remove deuterium, was identical in melting point and mixture melting point with the original sample and gave an identical ir spectrum. This indicates this material to be 2,4,5-trihydroxymethylimidazole.

The remaining materials from this column were divided into 6.5 g of an acetone-soluble residue and a small amount of acetone-insoluble syrup residue.

1-Imidazolemethanol. The above acetone-soluble residue was rechromatographed. The first eight fractions, eluted with 3:1 chloroform–acetone, showed only one component on TLC slides with the major amounts in fractions 2 and 3. The residue from fractions 2–4 (identical ir spectra) weighed 5.2 g and was a colorless liquid. The NMR spectrum of this material in D_2O solution indicates it is 1-imidazolemethanol. No attempt was made to purify this material. Treatment of 0.5 g of this liquid with a saturated alcoholic solution of picric acid yielded 0.49 g of crystalline picrate (**6**), mp 201–202°. A sample recrystallized for analysis from absolute alcohol melted at 202–203°.

Anal. Calcd for $C_{10}H_9N_5O_8$: C, 36.71; H, 2.77; N, 21.40. Found: C, 36.57; H, 2.64; N, 21.47.

Fractions 9 and 10 contained 1.35 g of the proposed 1,2-dihydroxymethylimidazole.

From chromatography of the 6 g of less soluble material from the second extraction of the original reaction mixture only 0.3 g of 1,2-dihydroxymethylimidazole and 0.34 g of 2,4,5-trihydroxymethylimidazole were obtained and the remainder of the material from the column remained unresolved.

Action of Water on 1-Imidazolemethanol. 1-Imidazolemethanol (0.5 g) was digested repeatedly with water. After the final evaporation of water, the residue, a syrup (0.3625 g), was dissolved in acetone and chromatographed, yielding 0.1834 g of imidazole (identified by ir), mp 79–85°.

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Registry No.—**1**, 288-32-4; **2**, 51505-76-1; **3**, 54986-29-7; **4**, 3724-26-3; **5**, 54986-27-5; **6**, 54986-28-6; formaldehyde, 50-00-0.

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A New Synthesis of 3-Substituted 1-Methylnaphthalenes via Ring Expansion of 1-Methylindenes[1]

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Specifically substituted 3-aryl-1-methylnaphthalenes and their derivatives can be synthesized by a convenient and productive reaction sequence,[2] which, however, is suitable for 3-aryl substitution only. A different approach, now reported, was required for the preparation of naphthalenes with other 3 substituents.

Since specifically substituted 1-methylindenes could be prepared easily from 3-arylbutanoic acids, ring expansion to the title compounds offered a convenient route. Parham and his group[3] obtained only 2-chloro-1-methylnaphthalene from attempts to prepare 3-chloro-1-methylnaphthalene by treating 1-methylindene with potassium *tert*-butoxide and chloroform, and they doubted the stability of the indene. Others[4–8] showed that 1-methylindene is stable under neutral or mild acidic conditions at room temperature and that it isomerized rapidly to 3-methylindene in base. We confirmed the stability of 4,6-dichloro-1-methylindene (**6b**) at room temperature under acidic conditions and isomerized it to 5,7-dichloro-3-methylindene (**8b**) by exposure to a small amount of pyridine.[9]

Carried out under neutral conditions, e.g., by carbene generation from phenyl(tribromomethyl)mercury,[10] ring expansion yielded the desired 3-bromo-1-methylnaphthalenes; e.g., 4,6-dichloro-1-methylindene (**6b**) gave 3-bromo-5,7-dichloro-1-methylnaphthalene (**7b**) (Scheme I