temperature. The mass was evaporated to dryness in vacuum and the residue was recrystallized from water, giving white crystals.

Compounds **IIIb** and **IIIc** were obtained similarly.

N-(2-Hydroxy-5-iodopyrimid-4-yl)leucine (IVa). With stirring at room temperature, 0.51 g (4 mM) of iodine was added to a solution of 0.47 g (2 mM) of **Ib** in 20 ml of 1 N NaOH. After the completion of the reaction, the solution was evaporated in the water bath to small bulk and, with careful cooling, was acidified with HCl. After recrystallization from water, white crystals were obtained.

Information on compounds **I–IV** is given in the table.

REFERENCES

1. T. Ueda and J. Fox, J. Med. Chem., 6, 697, 1963.
2. H. Balweg, Ann., **673**, 153, 1964.

22 May 1967

Institute of Organic Synthesis
AS Latvian SSR, Riga

THE METALLATION OF 1, 2-DIMETHYLIMIDAZOLE

B. A. Tertov, V. V. Burykin, and I. D. Sadekov

Khimiya Geterotsiklicheskikh Soedinenii, Vol. 5, No. 3, pp. 560–562, 1969

UDC 547.78+542.957

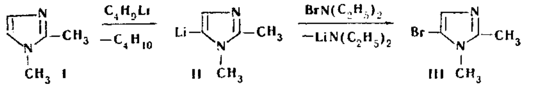
Under the action of butyllithium, 1, 2-dimethylimidazole is metallated in position 5. The reactions of 5-lithio-1, 2-dimethylimidazole with N-bromodiethylamine, benzaldehyde, benzophenone, dimethylformamide, and ω-iodophenylacetylene have been performed.

As is well known, when α-picoline, quinaldine, and 2-methylbenzothiazole react with metallating agents, the hydrogen of the methyl group is replaced by a metal [1, 2]. 2-Benzyl-4-methylthiazole behaves similarly [3]. It could be expected that 1, 2-dimethylimidazole (I) will undergo a similar reaction; however, it has been found that the action on it of butyllithium followed by N-bromoethylamine forms a compound with the composition $C_5H_7N_2Br$ differing in properties from 2-bromomethyl-1-methylimidazole. It was concluded from this that in this case the heterocyclic ring is metallated.

Table 1

Found and Calculated Values of the Dipole Moments of Imidazole Derivatives

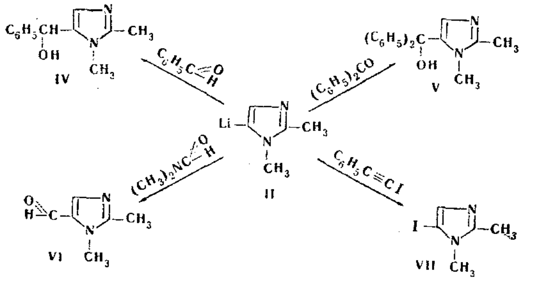
Compound	Dipole moment, D	
	found	calculated
VIII	3.81	—
I	3.74	—
IX	—	4.7
X	—	2.9
III	3.37	—



To elucidate the structure of compound **II**, we have calculated the dipole moments of 4-bromo-1, 2-dimethylimidazole (**IX**) and 5-bromo-1, 2-dimethylimidazole (**X**) by the vectorial scheme and have compared the figures obtained with the moment of compound **III** obtained experimentally. In the calculation the imidazole molecule was considered as a regular pentagon. The di dipole moments of CH_3 and Br were taken as 4.4 and 1.5 D, respectively. The direction of the vector of the dipole moment of I was determined approximately from the experimental magnitudes of the moments of 1-methylimidazole (**VIII**) and of compound **I** (Table 1).

The figures of Table 1 show that compound **II**, which is converted into the bromine derivative **III**, is 5-lithio-1, 2-dimethylimidazole.

Besides its reaction with N-bromodiethylamine, we studied the following reactions of 5-lithio-1, 2-dimethylimidazole:



EXPERIMENTAL

1, 2-Dimethylimidazole (I). This was obtained by the methylation of 2-methylimidazole with methyl iodide in liquid ammonia by analogy with Roe's work [4]. Colorless crystals with mp 35–36.5° C,

Table 2

Dipole Moment of Imidazole Derivatives

Compound	N, molar fractions	ε	*d*	P_∞, cm³	P_E, cm³	μ, *D*
VIII	0.00000	2.273	0.8737	321.8	24.3	3.81
	0.01010	2.476	0.8754			
	0.01639	2.604	0.8764			
	0.02956	2.861	0.8787			
	0.04965	3.290	0.8821			
I	0.00488	2.368	0.8744	315.9	28.9	3.74
	0.01195	2.501	0.8754			
	0.01939	2.662	0.8765			
III	0.00152	2.297	0.8752	268.7	36.6	3.37
	0.00263	2.315	0.8762			
	0.00445	2.343	0.8777			

bp 200–202° C. According to the literature [5], bp 205° C. Yield 65%. Found, %: C 62.15; H 8.44. Calculated for $C_5H_8N_2$, %: C 62.48; H 8.39. The mp of the picrate (181–182° C) corresponds to that given in the literature [5].

5-Bromo-1,2-dimethylimidazole (III). Over 15 min, a solution of 3 g of I in 25 ml of ether was added at −10° C to the butyllithium obtained from 0.9 g of lithium and 8.5 g of butyl bromide in 30 ml of ether [6]. The mixture was stirred at the same temperature for an hour and was then cooled to −78° C and 9 g of N-bromodiethylamine was added gradually. After 30 min, the temperature was brought to that of the room and the reaction mixture was treated with 25 ml of water and 5 ml of saturated sodium bisulfite solution, after which two layers separated. The ethereal layer was treated with 25 ml of 10% H_2SO_4, the acid extracts were combined with the aqueous layer, the solution was made alkaline with caustic soda, and compound III was extracted several times with ether. After the ether had been driven off, the residue was distilled in vacuum, a fraction being collected at 100–135° C (17 mm) which partially crystallized. After 8–10 hr the colorless crystals of III were filtered off, washed with petroleum ether, and dried. Mp 91–92° C (from a mixture of benzene and petroleum ether). Yield 1.4 g (25.6%). Found, %: C 34.62; H 3.94; N 15.85; Br 45.56. Calculated for $C_5H_7N_2Br$, %: C 34.32; H 4.03; N 16.01; Br 45.65.

1,2-Dimethylimidazol-5-yl phenyl carbinol (IV). At −15° C, a solution of 2.9 g of benzaldehyde in 5 ml of ether was added to a solution in 30 ml of ether of the II obtained from 1.6 g of I. The reaction was carried out for 1.5 hr, and then the product of the addition of benzaldehyde to II was decomposed with 5 ml of water and the carbinol was extracted with 20 ml of 10% HCl. The hydrochloric acid extract was made alkaline with caustic soda and the IV that separated was filtered off, washed with water, and dried. Yield 2 g (59.5%). Mp 173–174° C. After recrystallization from benzene containing petroleum ether, mp 177–178° C. Found, %: C 70.87; H 7.08; N 14.14. Calculated for $C_{12}H_{14}N_2O$, %: C 71.26; H 6.98; N 13.85.

1,2-Dimethylimidazole-5-diphenyl carbinol (V). This was synthesized in a similar manner to IV with a yield of 73%. Mp 186–187° C. Found, %: C 77.28; H 6.39; N 10.18. Calculated for $C_{18}H_{18}N_2O$, %: C 77.67; H 6.52; N 10.06.

5-Formyl-1,2-dimethylimidazole (VI). At −15° C, 13.5 g of dimethylformamide was added to the II obtained from 6 g of I. After 1 hr, the mixture was treated with 25 ml of 50% acetic acid and then with sodium carbonate to give a weakly alkaline reaction, and the layers were separated. The compound VI was extracted from the ethereal layer with water several times, after which it was repeatedly extracted with ether from the combined aqueous extracts, and the ethereal solution was dried with magnesium sulfate, after which the ether was driven off and the residue was distilled in vacuum, a fraction boiling at 125–135° C (15 mm) being collected. The distillate was shaken with 3 ml of saturated sodium bisulfite solution for 2 hr, and the bisulfite compound of the aldehyde was precipitated by the addition of ethanol and then ether. The bisulfite compound yielded 1.46 g (19.6%) of VI. Mp 77–78° C (from hexane). Found, %: C 57.82; H 6.54; N 22.85. Calculated for $C_6H_8N_2O$, %: C 58.05; H 6.49; N 22.57. **Oxime.** This was obtained by the action of hydroxylamine on an aqueous solution of VI in a weakly alkaline medium. Mp 226–227° C.

5-Iodo-1,2-dimethylimidazole (VII). A solution of the compound II obtained from 3 g of I was cooled to −78° C, and 14 g of iodophenylacetylene was added to it. The reaction mixture was stirred for 30 min and then the cooling mixture was removed and the reaction was continued for another 30 min at room temperature. After the end of the reaction, 20 ml of water and 30 ml of 10% HCl were added When the aqueous layer was made alkaline with caustic soda, crystals of VII separated out. Yield 3.3 g (47.5%). Mp 182–183° C (from benzene containing petroleum ether). Found, %: C 27.38; H 3.36; N 12.50; I 57.45. Calculated for $C_5H_7N_2I$, %: C 27.04; H 3.18; N 12.62; I 57.16.

Method of determining dipole moments. The measurements of the dielectric constant were carried out in benzene solutions at 25° C by the method of beats at a frequency of 5×10^5 Hz. The dipole moments were calculated from the formula: $\mu = 0.0128((P_\infty - P_E)T)^{1/2}$. The polarization at infinite dilution P_∞ was calculated from Hedestrand's equation [7]. The electronic polarization P_E was taken as equal to the molecular refraction. The atomic polarization was not taken into account. The results of the measurements and calculations are given in Table 2.

REFERENCES

1. K. Ziegler and H. Zeizer, Ann., 485, 174, 1931.
2. C. Courtot and S. Tchelicheff, C. r., 217, 231, 1943.
3. D. I. Brown, A. H. Cook, and I. Heilbron, J. Chem. Soc., S106, 1949.
4. A. M. Roe, J. Chem. Soc., 2195, 1963.
5. K. Hofmann, Imidazole and its Derivatives, Vol. 6, New York, 327, 1953.
6. H. Gilman, J. A. Beel, C. G. Brannen, M. W. Bullock, G. E. Dunn, and L. S. Miller, J. Am. Chem. Soc., 71, 1499, 1949.
7. G. Hedestrand, Z. Phys. Chem., B2, 428, 1929.

24 July 1967

Rostov-on-Don State
University