UDC 547.792.3 + 541.454

BASICITY AND STRUCTURE OF 1,2,4-TRIAZOLE DERIVATIVES

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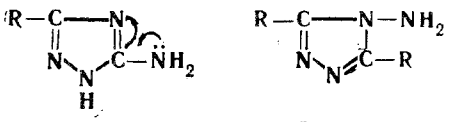
Khimiya Geterotsiklicheskikh Soedinenii, Vol. 2, No. 3, pp. 440-442, 1966

Basicity constants for a number of 1,2,4-triazole derivatives are determined. An assumed amine structure for 3-amino-1,2,4-triazoles in aqueous solution is demonstrated. It is assumed that protonization of 3- and 4-amino-1,2,4-triazoles occurs at the nitrogen in the heterocyclic ring, and not at the amino group.

Up to the present, a large number of 1,2,4-triazoles have been prepared [1], but their physicochemical properties have been insufficiently studied, and there are practically no data on the basicities of 1,2,4-triazole derivatives in the literature. Only a paper by Dedichen [2], written in 1906, gives basicity constants of 1,2,4-triazole and some of its 2-amino-3,5-dialkyl substitution products. We have now determined the basicity constants pK_B, of 1,2,4-triazole, methyl substituted derivatives, 3-amino-1,2,4-triazole, 4-amino-3,5-triazole, and its derivatives, by potentiometric titration of their salts (nitrates or hydrochlorides) (see table).

Generally, the effects of methyl, amino, and phenyl groups run parallel to their inductive effects: basicity is increased by methyl or amino groups, but decreased by the phenyl group (V, VI, and VII).

Substituents have different effects in 5(3)-amino-1,2,4-triazoles and 4-amino-1,2,4-(1H)-triazoles. The basicity of 5(3)-amino-1,2,4- triazoles is, for example, ten times that of the corresponding 4-amino-1,2,4-triazoles (V and IX). The basicity of 4-amino-1,2,4-triazoles is near to that of an unsubstituted triazole (I and IX).



A B

A possible explanation of 3-amino-1,2,4-triazoles (A) being, for example, ten times weaker bases than 4-amino-1,2,4-triazoles (A) is as follows. With the cation of 3-amino-1,2,4-triazole, the mesomeric forms C, D must be taken into account. On the whole, such a mesomeric cation functions as a weaker acid, due to conjugation of the lone electron pair of the amino group, in comparison with 4-amino-1,2,4-triazole (B), where no such conjugation obtains.

C D

Spectroscopy shows [4] that in solution, salts of 3-amino-1,2,4-triazoles are present as the amino form C, but in the solid state in the imino form D. Hence it is the form C which is involved when determining pK_B by potentiometric titration.

Comparison of compound I with IX, IV with IX, leads to the conclusion that in the case of 4-amino-1,2,4-triazoles, the salt-forming center is also one of the ring nitrogens. The preservation of the basicity order when electron-accepting groups, e.g., 2,2-dinitropropyl (see compounds IX and XIII, X and XIV, XI and V, XII and XVI), acetyl (see compounds XI and XVII with starting amine) are introduced into the amino group of 4-amino-1,2,4-triazoles, confirms this view. For comparison, it should be noted that pK_B of acetanilide is 4 units lower than for aniline (13.4 and 9.4) [5].

Since it is impossible to say definitely which ring nitrogen atom is involved in salt formation, it was not possible to correlate the basicities of the compounds with the polar constants of the substituents (Hammett's σ) for 4-amino-1,2,4-triazoles.

Potentiometric titration of salts of bicyclic aminotriazoles (XVIII-XX) showed them to be diacid bases with pK_B values differing less than by 1 unit.

Compound number	Compound	Mp °C (crystallizing solvent)	Method of synthesizing the triazole (literature reference)	pK_{B_1}	pK_{B_2}
I*	1,2,4-Triazole nitrate	137 (water)	6	11.02	—
II	3-Me-1,2,4-triazole nitrate	120 (water)	7	10.32	—
III	1-Me-1,2,4-triazole nitrate	148 (EtOH-Et_2O)	8	10.80	—
IV	4-Me-1,2,4-triazole nitrate	69 — 70 (water)	—	10.60	—
V	5-NH_2-1,2,4-triazole nitrate	179 (EtOH-Et_2O)	10	9.50	—
VI	3-Me-5-NH_2-triazole nitrate	175 (EtOH-Et_2O)	11	9.32	—
VII**	3-Ph-5-NH_2-1,2,4-triazole hydrochloride	215 (water)	12	10.07	—
VIII	1-Me-5-NH_2-1,2,4-triazole nitrate	130 (EtOH-Et_2O)	13	9.80	—
IX*	4-NH_2-1,2,4-triazole hydrochloride	151—152 (water)	14	10.77	—
X*	4-NH_2-3,5-$Me_2$1,2,4-triazole nitrate	113—114 (water)	15	10.34	—
XI	4-NH_2-3,5-Et_3-1,2,4-triazole nitrate	114—115 (water)	15	9.87	—
XII	4-NH_2-3,5-di-Pr-1,2,4-triazole nitrate	101—102 (water)	15	9.70	—
XIII	4-(2',2'-Dinitropropyl)amino-3,5-Me_2-1,2,4-triazole nitrate	110—112 (water)	16	10.78	—
XIV	4-(2',2'-Dinitropropyl) amino-3,5-Me_2-1,2,4-triazole nitrate	152—153 (water)	16	10.40	—
XV	4-(2',2'-Dinitropropyl)amino-3,5-Et_2-1,2,4-triazole nitrate	134—134,5 (water)	16	10.43	—
XVI	4-(2',2'-Dinitropropyl)amino-3,5-Pr_2-1,2,4-triazole nitrate	137—138 (water)	16	10.15	—
XVII	4-Acetylamino,3,5-Et_2-1,2,4-triazole hydrochloride	140—142 (EtOH-Et_2O)	—	10.70	—
XVIII	Bis-3(5,5'-diaminotriazolyl-1,2,4) nitrate	270 (water)	17	10.06	10.94
XIX	Bis [3-(5,5'-diaminotriazolyl-1,2,4)]methane nitrate	227 (water)	17	9.45	10.70
XX	1,2-Bis 3-(5,5'-diaminotriazolyl-1,2,4)]ethane nitrate	250 (water)	17	9.14	10.30

*The following values were previously [2] given for these compounds: I—11.7; IX—11.75; X—9.85; XI—9.77.

** pK_B was also determined spectroscopically for this compound, when it was found that pK_B = 10.11. The determination was made by I. N. Shokhor and E. A. Lipatova.

Experimental

The salts of the triazoles were prepared by dissolving the starting triazoles in ethanol, and then adding 60% HNO_3 or passing in HCl gas.

4-Acetamido-3,5-Et_2-1,2,4-triazole hydrochloride. This was prepared by refluxing 1.4 g 4-NH_2-3,5-Et_2-1,2,4-triazole and 1.18 g AcOCl in 100 ml dry benzene. The benzene was vacuum-distilled off, and the solid residue recrystallized from Et_2O-EtOH, yield 1.6 g (73.5%). Found: Cl 16.30; N 25.75%. Calculated for $C_8H_4N_4O \cdot HCl$: Cl 16.24; N 25.63%.

4-Me-1,2,4-triazole. A mixture of 35 g N,N-diformylhydrazine [9] and 100 g dry $MeNH_2$ was heated in an autoclave for 24 hr at 200° C. The reaction products were distilled and a cut bp 175°–178° C (8–9 mm) taken, yield 10 g (33%), mp 90° C [1].

The potentiometric titrations were carried out with a LP-58 potentiometer, and glass and calomel elctrodes. Potentiometer readings were checked by buffer solutions: potassium diphalate, acetate buffer, and a solution of borax. 0.1 N NaOH was used for titrating, the concentration of the substance titrated being ~ 10^{-3} mole/l. pK_A was

determined from the half-equivalence point. For the salts of diamines (XVIII–XX in the table), pK_{A1} and pK_{A2} were calculated by Simms's method [18].

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12 December 1964

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