[CONTRIBUTION FROM THE CHEMICAL RESEARCH SECTION, PICATINNY ARSENAL]

A STUDY OF TAUTOMERISM IN THE 5-AMINOTETRAZOLES[1]

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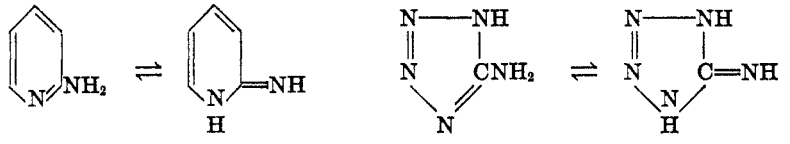
The 5-aminotetrazoles resemble the α- and γ-aminopyridines to some extent in that certain of their reactions are typical of neither aliphatic nor aromatic amines. For example, both classes of compounds react abnormally with nitrous acid (1–3), alkylate on the ring nitrogen rather than the amino group (4–6), and form primary nitramines directly upon nitration (7, 8). The possibility that these compounds may exist in either the amino- or imino-forms (I → IV) is well recognized and such tautomeric equilibria have been suggested to explain their abnormal reactions (6, 9).



I II III IV

The recent work of Angyal and his associates (3, 10) has demonstrated, however, that the α- and γ-aminopyridines do not tautomerize, but that their anomalous reactions may be explained on the basis of resonance theory. This has led us to undertake a similar study of the structure of the 5-aminotetrazoles. A number of these and related compounds were therefore prepared, and examined in the ultraviolet and rock-salt infrared regions of the spectrum.

All of the compounds examined which are capable of existing in the amino-form, regardless of the possibility of tautomerism, exhibit an absorption maximum in the ultraviolet between 218 and 232 mμ. (Table I and Figure 1). On the other hand 1,4-dimethyl-5-imino tetrazole and 1,4-dimethyl-5-methylimino-tetrazole, which are incapable of tautomerism and can only exist in the imino-form, absorb at 260 mμ and 267 mμ, respectively. The low molecular extinction values rule out the possibility that this is a simple bathochromic shift of the band at 218–232 mμ.

This would appear to indicate that the 5-aminotetrazoles exist in the amino- rather than the imino- form. Nevertheless, this evidence cannot be accepted as conclusive, especially if one considers that from examining the ultraviolet absorption spectra of the aminopyridines, different investigators had, in the past, drawn contradictory conclusions regarding the structure of these compounds (11, 12). We, therefore, extended our spectrographic study of the aminotetrazoles to the infrared region.

It may be seen (Table II) that all of the compounds examined which have a

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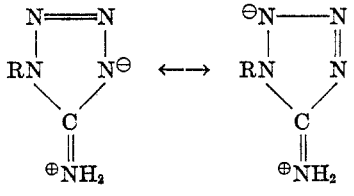
TABLE I

ULTRAVIOLET ABSORPTION OF 5-AMINOTETRAZOLES

Compound	λ_{max}, mμ	E_M
5-Aminotetrazole	218	3091
1-Methyl-5-aminotetrazole	222	2991
5-Methylaminotetrazole	225	3097
1-Methyl-5-methylaminotetrazole	227	3295
1-Methyl-5-dimethylaminotetrazole	232	3442
1-*n*-Propyl-5-aminotetrazole	222	3152
1-*i*-Propyl-5-aminotetrazole	222	3147
1-Benzyl-5-aminotetrazole	225	3719
1-Phenyl-5-aminotetrazole	229	6447
1-*o*-Tolyl-5-aminotetrazole	230	4958
1-*m*-Tolyl-5-aminotetrazole	228	14043
1-*p*-Nitrophenyl-5-aminotetrazole	217	8591
1-*m*-Nitrophenyl-5-aminotetrazole	225	11800
1-*p*-Chlorophenyl-5-aminotetrazole	226	5314
1,4-Dimethyl-5-iminotetrazole	260	1750
1,4-Dimethyl-5-methyliminotetrazole	267	1059

primary amino- group in position 5 exhibit bands in three distinct regions of the infrared, namely at about 3.0 μ, 6.0 μ, and 6.28 μ. These bands have been assigned, respectively, to the amino- and imino-stretching and amino-bending vibrations (13). Monosubstitution of the amino group, or its conversion into an imine, is accompanied by the disappearance of absorption at 6.28 μ, the bands at 3 μ and 6 μ being retained.

It is evident that the observed absorption in the double-bond (6.0 μ) region is not due to the >C=N— linkage in the ring, since this band disappears when the potentially tautomeric amino- group in position 5 is removed or replaced (14). Nor could this absorption arise from the presence of the imino-form of the molecule in tautomeric equilibrium with the amino-form. Such a tautomeric equilibrium would not only be contrary to the conclusions already inferred from the ultraviolet spectra, but would not be expected to exist under the experimental conditions, since all of the infrared spectra were obtained with the sample in the solid, crystalline state.



V VI

If resonance of the molecule among structures involving separation of charges (V and VI) were sufficient to account for the double-bond absorption, we would expect the 6.0 μ band to appear in the spectra of both 1-methyl-5-dimethylaminotetrazole and 1,4-dimethyl-5-iminotetrazole since both of these compounds,

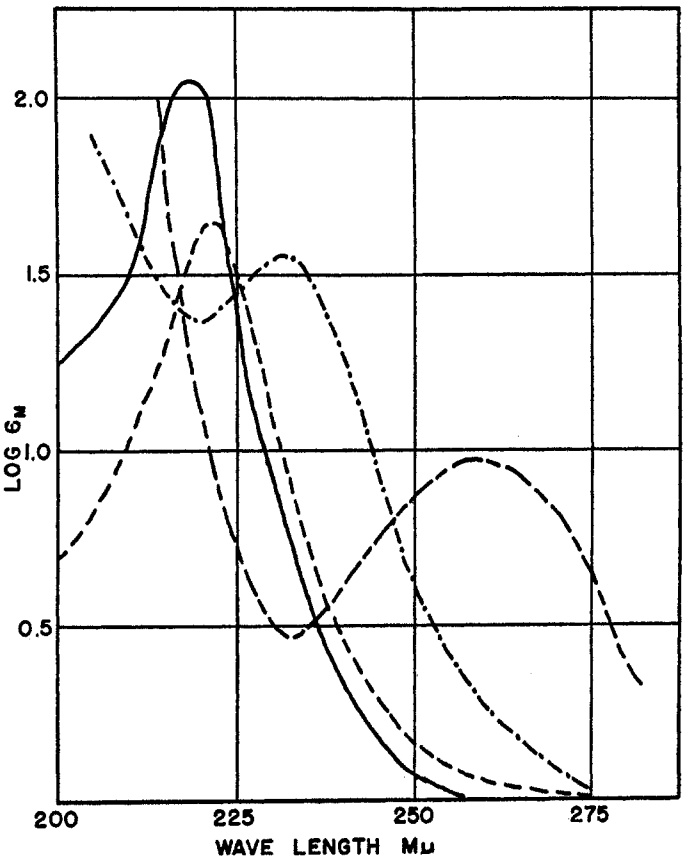


FIGURE 1. ULTRAVIOLET ABSORPTION SPECTRA OF 5-AMINO- AND 5-IMINOTETRAZOLES. Solutions 0.003% in alcohol; 2-cm cell. ————, 5-Aminotetrazole; – – – – –, 1-Methyl-5-aminotetrazole; –·–·–·–, 1-Methyl-5-diethylaminotetrazole; – — – — –, 1,4-Dimethyl-5-iminotetrazole.

although incapable of tautomerism, could nevertheless possess extreme resonating structures having the same charge separation (VII → X). Instead, these compounds exhibit only that absorption expected for the uncharged molecule (Figs. 2a and b).[3]

[3] The salts of these compounds exhibit essentially the same absorption between 6.0 and 6.28μ (Figs. 2c and d). This is to be expected, since salt formation leads in each case to the formation of the same sort of resonating guanidinium-type ion (XI → XIV).

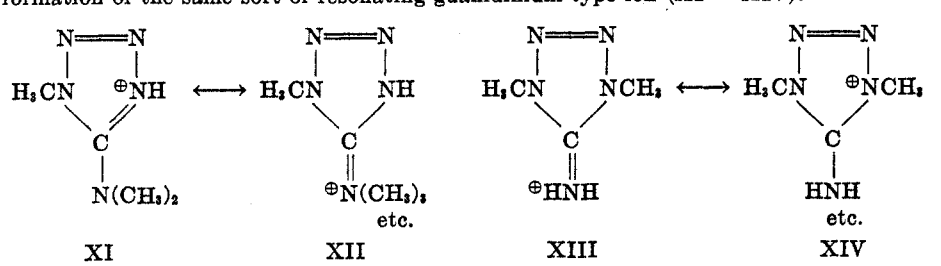


TABLE II

INFRARED ABSORPTION OF 5-AMINOTETRAZOLE IN THE 3 AND 6 MICRON REGIONS

Compound	Principal Bands, μ		
5-Aminotetrazole	3.03	6.0	6.30
1-Methyl-5-aminotetrazole	3.06	6.0	6.25
5-Methylaminotetrazole	3.05	6.0	
1-Methyl-5-methylaminotetrazole	3.10	6.15	
1-Methyl-5-dimethylaminotetrazole			6.25
1-*n*-Propyl-5-aminotetrazole	3.0	6.0	6.26
1-Isopropyl-5-aminotetrazole	3.02	6.0	6.30
1-Benzyl-5-aminotetrazole	3.05	6.0	6.28
1-Phenyl-5-aminotetrazole	3.0	6.0	6.25
1-*p*-Chlorophenyl-5-aminotetrazole	3.0	6.06	6.25
1-*m*-Chlorophenyl-5-aminotetrazole	3.02	6.02	6.27
1-*p*-Nitrophenyl-5-aminotetrazole	3.0	6.05	6.25
1-*m*-Nitrophenyl-5-aminotetrazole	3.05	6.01	6.25
1-*o*-Tolyl-5-aminotetrazole	3.07	6.02	6.26
1,4-Dimethyl-5-iminotetrazole	3.05	6.0	
1,4-Dimethyl-5-iminotetrazole•HCl		6.0	
1-Methyl-5-dimethylaminotetrazole•HCl		6.0	
1,4-Dimethyl-5-methyliminotetrazole•HCl		6.0	

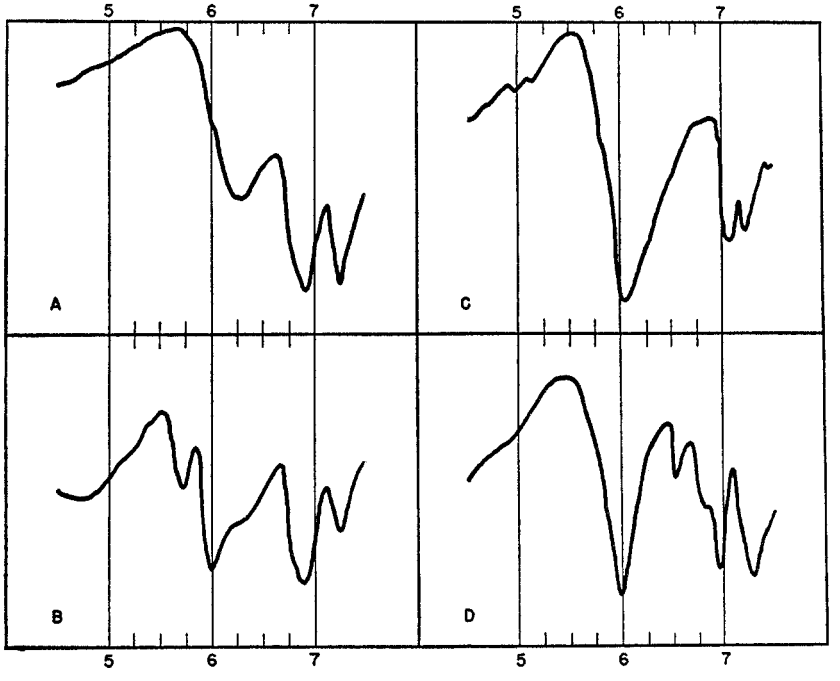


FIGURE 2. INFRARED ABSORPTION SPECTRA. a. 1-Methyl-5-dimethylaminotetrazole; b. Hydrochloride; c. 1,4-Dimethyl-5-iminotetrazole; d. Hydrochloride.

TABLE III

MELTING POINTS OF REPRESENTATIVE AMINOTETRAZOLES

Compound	M.P., °C.
1-Methyl-5-aminotetrazole	232
1-Methyl-5-methylaminotetrazole	172
1,4-Dimethyl-5-iminotetrazole	107
1-Methyl-5-dimethylaminotetrazole	<100[a]
1,4-Dimethyl-5-methyliminotetrazole	<100
1-Phenyl-5-aminotetrazole	160
1-Phenyl-5-methylaminotetrazole	133.5–136.5[b]
1-Phenyl-5-dimethylaminotetrazole	110–111[b]

[a] B.p. 114–116° @ 3 mm. Finnegan, Henry, and Lieber, *J. Org. Chem.*, **18**, 779 (1953) report m.p. 43–44°. [b] Finnegan, Henry, and Lieber, *J. Org. Chem.*, **18**, 779 (1953).

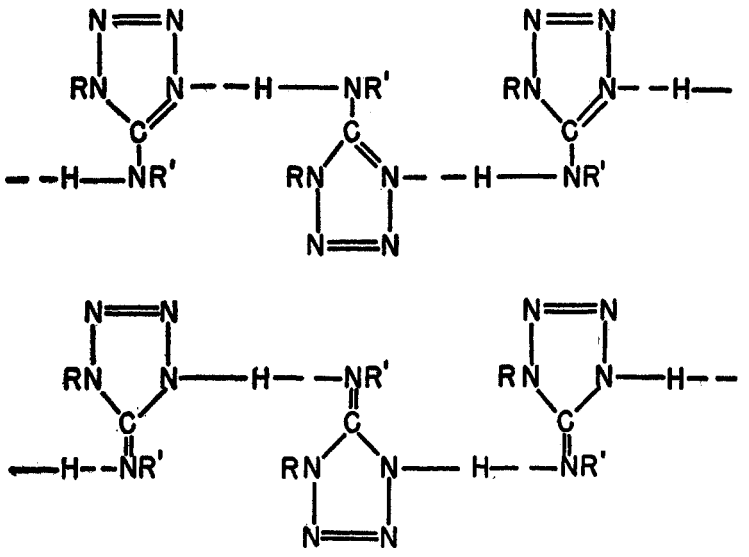
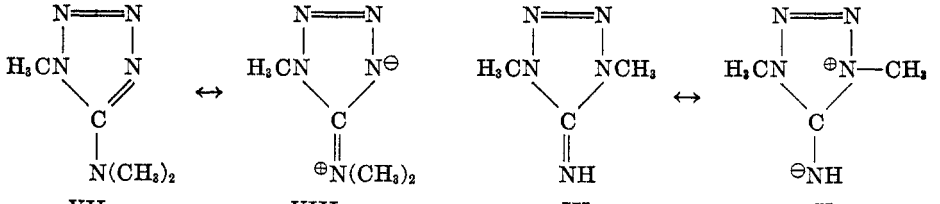


FIGURE 3. R and R′ = H, Ar, or Alk

The problem presented by the infrared absorption spectra may be clarified by a consideration of the melting points of these compounds (Table III). The



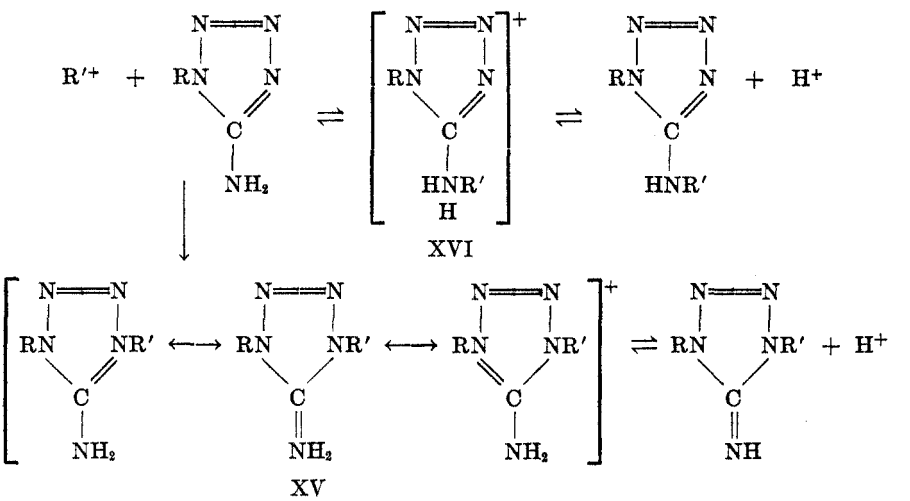
VII VIII IX X

5-aminotetrazoles are, without exception, relatively high-melting, crystalline solids (9); those with large, bulky substituents in the ring generally melting

a few degrees below those substituted with smaller groups. Further substitution of the molecule causes a progressive lowering of the melting point, the effect being most pronounced when either a second substituent has entered the ring or both amino hydrogens have been replaced.

The decrease in melting point with increased substitution points towards the existence of intermolecular forces in the crystal, operating through hydrogen bonding, perhaps as shown in Figure 3. The replacement of both amine hydrogens, or the introduction of a second substituent into the ring, by rendering hydrogen bonding impossible, would, in such a case, greatly reduce the attractive force between the molecules, and bring about the observed lowering of the melting point. This phenomena bears close resemblance to the mesohydric tautomerism described by L. Hunter (18).

This picture of the molecule serves adequately to explain why, in the absence of tautomerism, these compounds, dispersed in the solid state, should exhibit bands in the infrared corresponding to both the imino- and amino-forms.



The possibility that the intermediate ion XV is stabilized by resonance to a greater extent than would be the alternative intermediate XVI, can be taken as the reason why the 5-aminotetrazoles alkylate preferentially in the ring.

Acknowledgment. We wish to thank Dr. Ronald Henry of the Naval Ordnance Testing Station for his helpful assistance.

EXPERIMENTAL

1-Alkyl- and aryl-5-aminotetrazoles. These compounds were prepared, as described elsewhere in the literature (9, 15), by the reaction between hydrazoic acid and the appropriate nitrile in the presence of sulfuric acid.

1,2-Dimethyl-3-aminoguanidinium iodide. Fifty grams (10.2 moles) of 1,2,3-trimethyl isothiouronium iodide (16) was suspended in about 400 ml. of absolute alcohol. Then 12 g. of an 85% solution of hydrazine hydrate (equivalent to 6.5 g., 0.2 mole of hydrazine) was added, and the mixture was boiled gently under an air condenser until evolution of methanethiol was complete. The mixture then was cooled and the product was filtered off and

washed with a little alcohol. Yield, 39.6 g. (85%) of white needles which did not melt up to 260°.

Anal. Calc'd for $C_3H_{11}IN_4$: C, 15.7; H, 4.8; N, 24.4.
Found: C, 15.4; H, 4.9; N, 24.2.

1,1,2-Trimethyl-3-aminoguanidinium iodide. 1,1,2,3-Tetramethyl isothiouronium iodide (12) (52.4 g., 0.2 mole) and 12 g. of 85% hydrazine hydrate solution were boiled gently under an air condenser for four hours. The solution was evaporated at reduced pressure to a volume of 100 ml. After filtering the solution to remove insoluble material, 800 ml. of absolute ether was added, and the mixture was allowed to stand overnight. The product separated as an oil, which soon crystallized. It was filtered, washed with a little alcohol and ether, and air-dried. The first crop weighed 24.2 g. Addition of more ether to the mother liquor gave a second crop of 2.8 g. Yield, 27 g. (54.5%), m.p. 89–91°.

Anal. Calc'd for $C_4H_{13}IN_4$: N, 23.0. Found: N, 22.9.

1-Methyl-5-methylaminotetrazole. 1,2-Dimethyl-3-aminoguanidinium iodide (25 g., 0.11 mole) was dissolved in 250 ml. of warm water. The solution was acidified with a few drops of nitric acid and treated with one equivalent of 50% silver nitrate solution. Any excess silver ion was precipitated with a few drops of hydrochloric acid, and the silver iodide was removed by filtration. Then 15 ml. of concentrated hydrochloric acid was added to the filtrate, which was cooled to 5° and treated with a slight excess of 30% sodium nitrite solution. The cold solution then was saturated with sodium carbonate and evaporated to dryness on a water-bath at reduced pressure. The dry residue was extracted for 14 hours with 600 ml. of benzene in a Soxhlet apparatus. The benzene extract then was cooled and filtered and the product was washed with a little fresh benzene. Yield, 5.6 g. (51.5%) of fine, colorless needles, m.p. 171–172°.

Anal. Calc'd for $C_3H_7N_5$: C, 31.8; H, 6.2, N, 61.9.
Found: C, 31.9; H, 6.2; N, 62.1.

1-Methyl-5-dimethylaminotetrazole. 1,1,2-Trimethyl-3-aminoguanidinium iodide (10 g.) was dissolved in 40 ml. of water and treated with one equivalent of 50% silver nitrate solution. The solution was filtered and acidified with 6 ml. of concentrated hydrochloric acid. It then was treated with a slight excess of 30% sodium nitrite solution at 5°. Anhydrous sodium carbonate then was added to form a paste which was thoroughly extracted with about 500 ml. of benzene in several small portions. The benzene extracts were combined, dried over sodium sulfate, and evaporated in a warm place. Yield, 3 g. (57.7%) of oil which soon crystallized. Purification was effected by distilling the product at 114–116° at 3 mm. pressure.

Anal. Calc'd for $C_4H_9N_5$: C, 37.8; H, 7.1; N, 55.1.
Found: C, 37.9; H, 6.8; N, 55.2.

The *hydrochloride*, white powder, m.p. 152–154°, was obtained by dissolving the free base in isopropyl alcohol, saturating with dry hydrogen chloride, and adding ether.

Anal. Calc'd for $C_4H_{10}ClN_5$: C, 29.4; H, 6.1; N, 42.8.
Found: C, 29.4; H, 6.1; N, 42.9.

1,4-Dimethyl-5-iminotetrazole. This compound was synthesized according to the method described by Herbst, *et al.* for the methylation of 1-ethyl-5-aminotetrazole (9). From 2.54 g. (0.026 mole) of 1-methyl-5-aminotetrazole, and 3.28 g. (0.026 mole) of dimethyl sulfate, there was obtained a yield of 2 g. (69%) of crude product. The 1,4-dimethyl-5-iminotetrazole was obtained after distillation at 122° and 32 mm., as small white crystals, m.p. 106.4–107.4°.

Anal. Calc'd for $C_3H_7N_5$: C, 31.8; H, 6.2.
Found: C, 31.1; H, 6.2.

The *hydrochloride* and *picrate* of this compound decompose at 241° and 207°, respectively. These compare with the decomposition points reported for the hydrochloride (d. 241°) and picrate (d. 203°) of the dimethyl derivative formed by heating 5-aminotetrazole in a sealed tube with excess methyl iodide (17).

1,4-Dimethyl-5-methyliminotetrazole. This compound was prepared in the same manner

as the dimethyl derivative. From 1.96 g. (0.017 mole) of crude 1,4-dimethyl-5-iminotetrazole and 2.19 g. (0.017 mole) of dimethyl sulfate, was obtained a crude yield of 0.5 g. (23%) of oil, which gradually formed deliquescent crystals. The product was isolated as the *hydrochloride* by dissolving the oil in a small amount of cold isopropyl alcohol and saturating with dry hydrogen chloride. After recrystallization from isopropyl alcohol the hydrochloride melted at 202–203°.

Anal., Calc'd for $C_4H_{10}ClN_5$: C, 29.4; H, 6.1.
Found: C, 29.0; H, 6.0.

When this compound was mixed with the hydrochloride prepared by methylating 1-methyl-5-methylaminotetrazole in the same fashion (m.p. 201–203°), the melting point was not depressed.

Absorption spectra. Infrared spectra were obtained using a Perkin-Elmer double-beam infrared spectrophotometer equipped with a rock-salt prism. A mineral oil mull was used between 6.0–6.6μ. Hexachlorobutadiene was used as the mulling agent between 2.0–6.0μ. Ultraviolet absorption spectra were determined with a Cary recording spectrophotometer, using 95% alcohol as solvent.

SUMMARY

The ultraviolet and infrared absorption spectra of a number of substituted 5-aminotetrazoles have been obtained. From an examination of these spectra it is concluded that the aminotetrazoles do not exist as a tautomeric equilibrium of amino- and imino- forms. The relative stabilities of the intermediate ions is suggested as the reason why the 5-aminotetrazoles alkylate in the ring rather than the amino group.

DOVER, NEW JERSEY

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