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THE PREPARATION OF 5-HYDROXY-Δ^2-1,2,3-TRIAZOLINES FROM ORGANIC AZIDES AND ALIPHATIC KETONES

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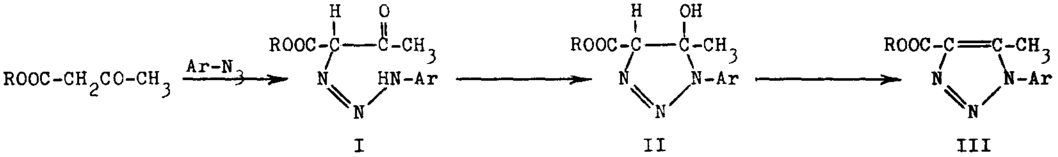
The formation of 1,2,3-triazoles from the reaction of organic azides with compounds containing an activated methylene group is well known. Thus the reaction of acetoacetic ester with aryl azides, in the presence of sodium alkoxide, yields 1,2,3-triazoles (III). The reaction probably proceeds via a triazene (I) (1) and a hydroxy triazoline (II). However, neither (I) nor (II) have been isolated.



It has now been found, that aliphatic monoketones react with organic azides in the presence of potassium <u>tert</u>. butoxide to give 5-hydroxy-Δ^2-1,2,3-triazolines (V) in good yield. The reaction is conducted in <u>tert</u>. butanol at 2o^{o} and is in many cases completed in a few min. The reaction mixture is then poured into water and the products are isolated by crystallization or by extraction with methylene chloride. Presumably the anion of the ketone reacts with the azide to give the salt of a triazene which, possibly after reaction with water, undergoes ringclosure to the 5-hydroxy-Δ^2-1,2,3-triazoline (V). The results of a number of experiments are shown in Table 1.

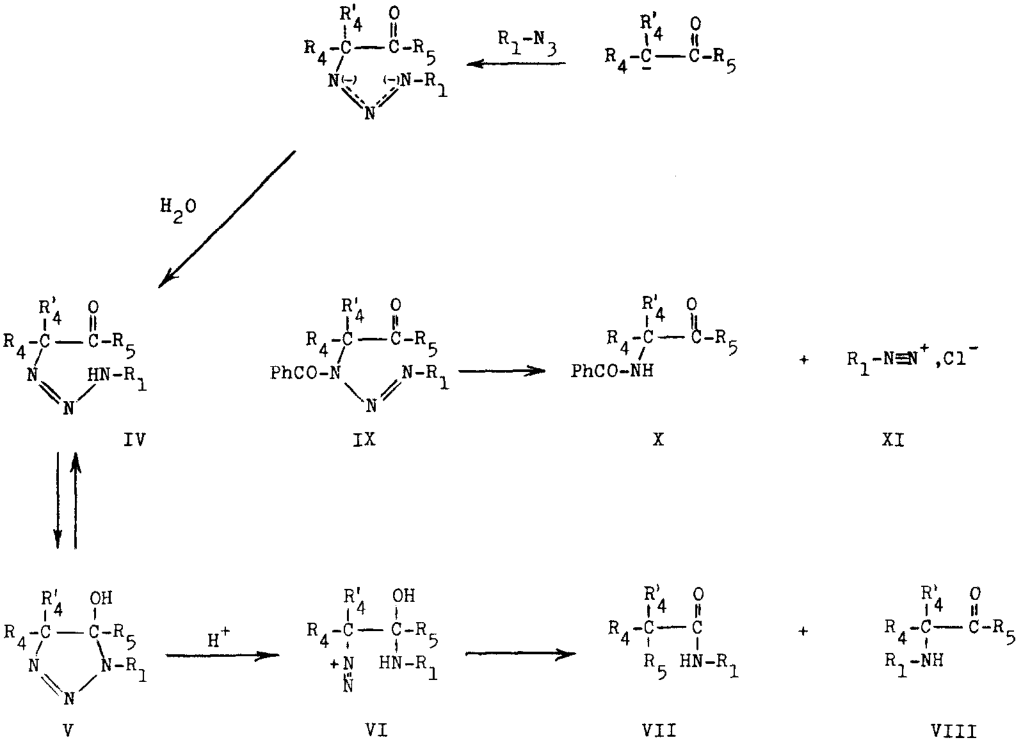


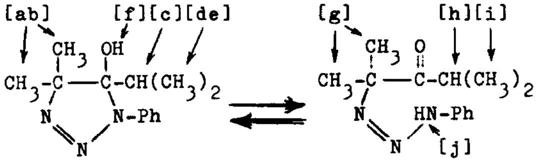
TABLE 1

5-Hydroxy-Δ^2-1,2,3-triazolines

	R_1	R_4	R'_4	R_5	m.p. °C	yield, %
a	Ph-	CH_3-	H-	CH_3-	84-85 (dec.)	72
b	Ph-	CH_3-	H-	C_2H_5-	119-120 -	85
c	$PhCH_2$-	CH_3-	H-	C_2H_5-	104-105 -	65
d	Ph-	CH_3-	CH_3-	$(CH_3)_2CH$-	65-66 -	71
e	$PhCH_2$-	CH_3-	CH_3-	$(CH_3)_2CH$-	99-102 -	91
f	p-NO_2Ph-	CH_3-	CH_3-	$(CH_3)_2CH$-	98-99 -	84
g	Tosyl-	CH_3-	CH_3-	$(CH_3)_2CH$-	not isolated	

All the products gave satisfactory analysis.

The infrared spectra of the products (V) in KBr showed no carbonyl absorption, however, infrared spectra of (Vd) and (Vf) in chloroform solution showed carbonyl bands at 1710 cm^{-1}. NMR spectra of (Vd) and (Vf) in deuteriochloroform indicated that two isomeric compounds were present (FIG. 1). This seems to indicate that the two products exist in chloroform solution as a mixture of the triazoline (V) and the triazene (IV). The NMR spectra showed the two methyl groups at C_4 as two separate signals in the triazolines (Vd and Vf) whereas in the triazenes (IVd and IVf) the two methyl groups were equivalent. Integration of the NMR spectra showed that the ratio of (Vd) to (IVd) in deuteriochloroform was 50:50. The ratio of (Vf) to (IVf) was 15:85. NMR spectra in hexadeuterio dimethyl sulphoxide (FIG. 1) and in pyridine indicated that the equilibrium was shifted towards the triazolines (Vd and Vf) in these solvents.



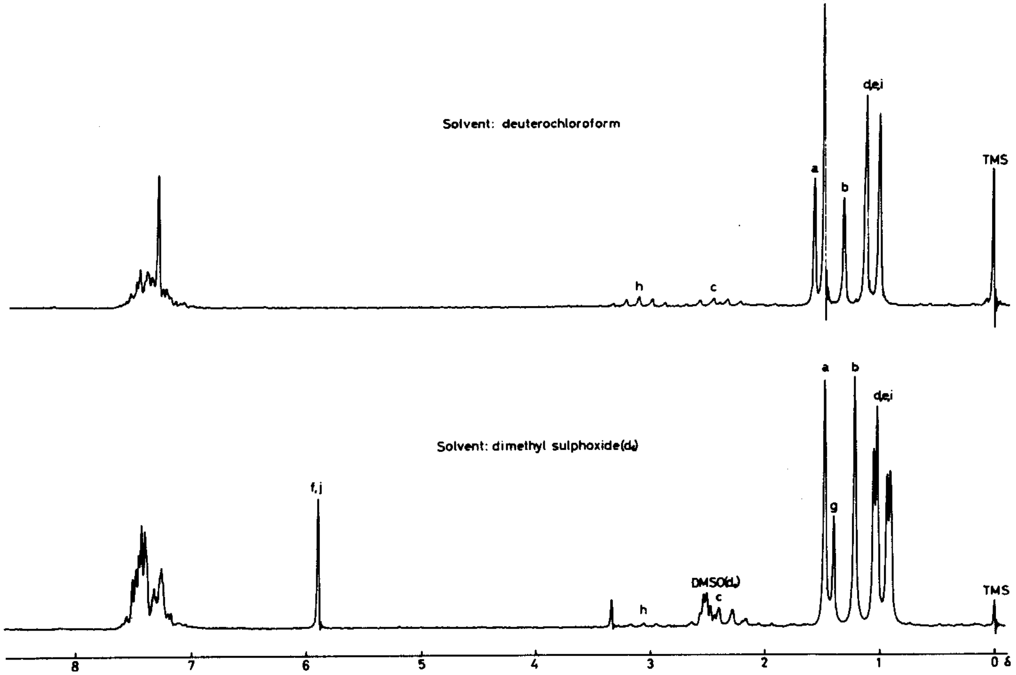


FIG. 1

NMR spectra of Vd ⇄ IVd in $CDCl_3$ and DMSO(d_6). (60 Mc).

The infrared spectra of compounds (Va, b, c, and e) dissolved in chloroform showed no carbonyl absorption and these compounds are therefore assumed to have the triazoline structure (V) almost entirely. In agreement herewith the NMR spectra of (Vb, c, and e) dissolved in $CDCl_3$ showed the presence of one product only. The NMR spectrum of (Va) indicated that two products were present in a 30:70 ratio; these two products are probably the diastereomeric forms of (Va).

Whereas the 5-hydroxy-Δ^2-1,2,3-triazolines are relatively stable under neutral or alkaline conditions they are extremely acid labile. Thus all the products described in TABLE 1 decomposed with nitrogen evolution in the course of a few minutes when treated with a trace of aqueous acid at room temperature. The products obtained (TABLE 2) were the amides (VII) and in some cases (d, e, and f) the α-aminoketones (VIII) in addition to the amides. These products were identified through infrared and NMR spectra or by comparison with authentic samples. Both the amides (VII) and the α-aminoketones (VIII) are presumably formed via the diazonium ion (VI) by the loss of nitrogen followed by a 1,2-shift.

The acid catalyzed decomposition of the 5-hydroxy-Δ^2-1,2,3-triazolines described here is analogous to reactions observed with Δ^2-1,2,3-triazolines containing a <u>tert.</u> aminogroup (2) or an alkoxy group (1) at C_5. The reaction of arylsulphonyl azides with enamines (3), enolethers (1), or with compounds containing an activated methylene group (4) is considered to proceed via triazolines which, however, are too unstable to be isolated. In agreement herewith the reaction of tosyl azide with diisopropyl ketone in the presence of potassium <u>tert</u>. butoxide gave the amide (VIIg) and the aminoketone (VIIIg), presumably with an unstable triazoline (Vg) as an intermediate.

TABLE 2

Acid catalyzed decomposition of 5-hydroxy-Δ^2-1,2,3-triazolines

Product		Triazoline (V)						
		a	b	c	d	e	f	g
VII	yield, %	93	97	100	47	32	40	63
	m.p. °C	102-103(5)	108-109(6)	45-46(7)	78-79(8)	44-45	119-120	160-164
VIII	yield, %				31	62	36	7
	m.p. °C				65-66	liq.	163-164	155-156

When the triazoline (Vb) was boiled with methanolic potassium hydroxide for 2 h a 7 % yield of 1-phenyl-4-methyl-5-ethyl-1,2,3-triazole (m.p. of picrate 143-144° (9)) was obtained. Under the same conditions the benzyl triazoline (Vc) gave a 7o % yield of 1-benzyl-4-methyl-5-ethyl-1,2,3-triazole isolated as its picrate (m.p.96-97°).

Several of the triazolines (V) have been benzoylated. Thus treatment of (Vd) with benzoyl chloride in pyridine gave a 78 % yield of a benzoyl derivative (m.p.67-68° dec.) to which the structure (IXd) was assigned. Treatment of this compound with hydrogen chloride in ether gave a 9o % yield of the benzoylated aminoketone (Xd) (m.p. 12o-121°) and phenyl diazonium chloride (XId). The latter was identified through its reaction with β-naphthol.

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