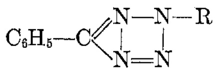
Communications TO THE EDITOR

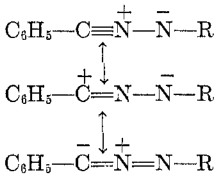
The Formation of Nitrile Imines in the Thermal Breakdown of 2,5-Disubstituted Tetrazoles

Sir:

We wish to report evidence that nitrile imines (II) are intermediates in the thermal decomposition of 2,5-disubstituted tetrazoles (I). As one might expect from the structural and electronic relationship to azides and nitrile oxides, these compounds are quite reactive and attempts to isolate them have thus far been unsuccessful. However, these intermediates can be intercepted by various reagents. These reactions are of theoretical interest because they demonstrate the existence of II and they also appear to have synthetic possibilities.



Ia. R = CH_3
Ib. R = C_6H_5

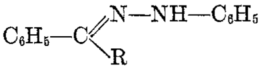


$$C_6H_5{-}C{\equiv}\overset{+}{N}{-}\overset{-}{N}{-}R \leftrightarrow C_6H_5{-}\overset{+}{C}{=}N{-}\overset{-}{N}{-}R \leftrightarrow C_6H_5{-}\overset{-}{C}{=}\overset{+}{N}{=}N{-}R$$

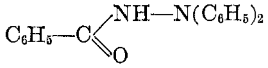
IIa. R = CH_3
IIb. R = C_6H_5

The first-order thermolysis of the 2,5-disubstituted tetrazoles (I) occurs at a convenient rate at temperatures of 150° for Ib and 200° for Ia. These compounds are less reactive than pentazoles and 5-substituted 2-acyl tetrazoles[1] but Ib undergoes ring opening faster than 1,5-disubstituted tetrazoles which are reported[2] to give carbodiimides at 220°.

When Ib is decomposed in aniline a 75% yield of IIIa is obtained. The thermal breakdown of Ib in thiophenol gives IIIb in 88% yield. Both of these reactions apparently involve a 1,3-addition to the intermediate nitrile imine IIb. The analogous reaction with phenol is followed by an O→N migration of the phenyl group to give 79% yield of benz-*N*,*N*-diphenylhydrazide IV.

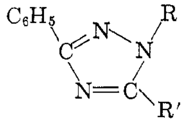


IIIa. R = $-NHC_6H_5$
IIIb. R = $-SC_6H_5$

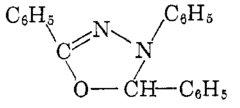


IV

Cyclic structures are formed when I is decomposed in nitriles, aldehydes or olefins with strained carbon-carbon double bonds. For example, the decomposition of Ib in benzonitrile gives 63% of 1,3,5-triphenyl-1,2,4-triazole (Va) (identified by comparison with an authentic specimen). The reaction of Ia with benzonitrile yields 1-methyl-3,5-diphenyltriazole (Vb); with *p*-chlorobenzonitrile the product is Vc. The product resulting from the decomposition of Ib in benzaldehyde (yield 75%) has analytical and spectral data indicating that it is VI. Both V and VI can be considered to arise by the 1,3-addition of a multiple bond to the intermediate nitrile imine intermediate.

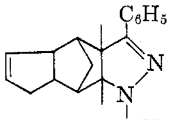


Va. R = R′ = C_6H_5
Vb. R = CH_3, R′ = C_6H_5
Vc. R = CH_3, R′ = p-ClC_6H_4

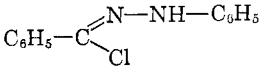


VI

The reaction of nitrile imines with olefins containing strained double bonds is apparently analogous to the reaction of azides and diazoalkanes with substances of this type.[3] The thermolysis of Ib in dicyclopentadiene gives a 68% yield of a crystalline compound which appears to be the tetracyclic product VII. This structural assignment is based on the chemical composition and the infrared spectrum. This same compound VII is obtained in 83% yield when a benzene solution of benzphenylhydrazide chloride (VIII) and dicyclopentadiene is treated with triethylamine. This alternate route to the nitrile imine intermediate by a 1,3-dehydrochlorination is probably analogous to the syntheses of nitrile oxides from hydroxamic acid chlorides.



VII



VIII

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[1] Phenylpentazole gives a quantitative yield of phenyl azide and nitrogen at 0° in methanol with a half-life of 13 min. 5-Substituted tetrazoles react rapidly with carboxylic acid chlorides or imino chlorides in pyridine at 50–90° to give 1,3,4-oxadiazoles and 1,2,4-triazoles, respectively. It is noteworthy that these compounds represent substances which are highly aromatic in the sense that there is substantial resonance stabilization, but nonetheless are very reactive. See R. Huisgen and I. Ugi, *Chem. Ber.*, **90**, 2914 (1957); I. Ugi and R. Huisgen, *Chem. Ber.*, **91**, 531 (1958); I. Ugi, H. Perlinger, and L. Behringer, *Chem. Ber.*, **91**, 2324 (1958); R. Huisgen, J. Sauer, and H. J. Sturm, *Angew. Chem.*, **70**, 272 (1958); R. Huisgen, J. Sauer, and M. Seidel, *Chem. and Ind.* (*London*,) 1114 (1958).

[2] P. A. S. Smith and E. Leon, *J. Am. Chem. Soc.*, **80**, 4647 (1958); J. Vaughan and P. A. S. Smith, *J. Org. Chem.*, **23**, 1909 (1958).

[3] K. Alder and G. Stein, *Ann.*, **485**, 211 (1931); **501**, 1 (1933); K. Ziegler, H. Sauer, L. Bruns, H. Froitzheim-Kohlhorn, and I. Schneider, *Ann.* **589**, 122 (1954).

The addition reactions involving the nitrile imines and their formation by thermolysis of I and dehydrochlorination of VIII are novel in that they represent examples of 1,3-addition and elimination reactions. Apparently, the only nitrile imine described previously is "isodiazomethane,"[4] prepared by de- and reprotonation of diazomethane.

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Received March 30, 1959

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[4] E. Müller and W. Kreutzmann, *Ann.*, **512**, 264 (1934); E. Müller and D. Ludsteck, *Ber.*, **87**, 1887 (1954); **88**, 921 (1955); E. Müller and W. Rundel, **90**, 2673 (1957).

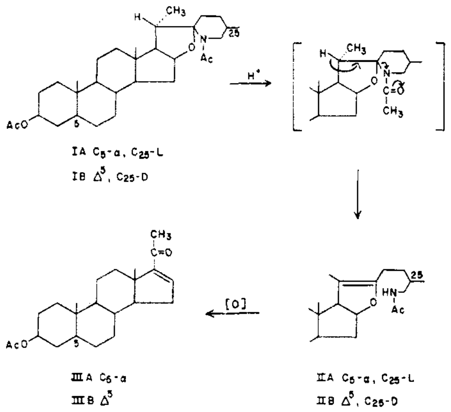
Improvement in the Preparation of 3β-Acetoxy-5α-pregn-16-en-20-one and 3β-Acetoxypregna-5,16-dien-20-one from the Steroidal Alkaloids, Tomatidine and Solasodine

Sir:

The degradation of the steroidal alkaloids, tomatidine and solasodine into 3β-hydroxy-5α-pregn-16-en-20-one[1] (yield: *ca.* 60%) and 3β-acetoxypregna-5,16-dien-20-one[2,3] (yield: *ca.* 10%) has been previously reported. A recent article,[4] using a modification of the original method, reports a marked improvement in the yield of pregnadienolone from solasodine. We wish to report our findings on the conversion of the steroidal alkaloids which lead to a further substantial increase in the production of allopregnenolone and pregnadienolone from tomatidine and solasodine, respectively.

O,N-Diacetyltomatidine[5] (IA) and *O,N*-diacetylsolasodine[6] (IB) in an acidic medium undergo a remarkably facile prototropic rearrangement to yield the unsaturated *O,N*-diacetyl derivatives IIA and IIB. Thus, O,N-diacetyltomatidine (IA) can be converted in an almost quantitative manner (95–98%) to IIA, m.p. 128–132°,[7] $[\alpha]_D^{20}$ +1.5°, λ_{max}^{chlf} 2.89, 2.97μ (N—H); 5.78μ (3-acetoxy); 5.99, 6.59μ (NH-acetyl) (*Anal.* Calcd. for $C_{31}H_{49}O_4N$: C, 74.51; H, 9.88. Found: C, 74.66; H, 10.02), by the treatment of IA with a solution of mineral acid in acetic acid at room temperature or more conveniently by the direct introduction of IA into boiling acetic acid followed by brief refluxing (15 min.). The partially hydrolyzed alcohol of IIA has been previously obtained by the alkaline hydrolysis of the so-called unsaturated triacetyltomatidine.[8]

Upon carefully controlled oxidation of IIA with chromic acid in acetic acid and subsequent cleavage of the side chain moiety with acetic acid[9] 3β-acetoxy-5α-pregn-16-en-20-one (IIIA) is obtained in excellent yields (*ca.* 80% based on IA), m.p. 165–167°, $[\alpha]_D^{20}$ + 42° ($CHCl_3$), λ_{max} 239 mμ, log ε 3.98, (*Anal.* Calcd, for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 77.32; H, 9.58). It agreed in all properties with an authentic sample of allopregnenolone.



In a similar manner the treatment with acetic acid of *O,N*-diacetylsolasodine (IB) yielded IIB (95–98%), m.p. 135–138°, $[\alpha]_D^{20}$ −23°, λ_{max}^{chlf} 2.90, 2.98μ (N—H); 5.78μ (3-acetoxy); 5.98, 6.60μ (NH-acetyl), (*Anal.* Calcd. for $C_{31}H_{47}O_4N$: C, 74.81; H, 9.52. Found: C, 75.09; H, 9.36) which has also been previously obtained from the alumina chromatography of the unsaturated triacetylsolasodine[3] (pseudosolasodine A). Oxidation and removal of the consequent 16β-ester side chain of IIB resulted in a good yield (75–80% based on IB) of 3β-acetoxypregna-5,16-dien-20-one (IIIB) m.p. 173–175.5°, $[\alpha]_D^{20}$ −35°, λ_{max} 239 mμ, log ε 4.0, (*Anal.* Calcd. for $C_{23}H_{32}O_3$: C, 77.49; H, 9.05. Found: C, 77.45; H, 9.11), identical in all respects with an authentic specimen. In a continuous operation from solasodine without isolation and purification of intermediates, an over-all yield of 65% of IIIB was obtained.

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[1] Y. Sato, A. Katz, and E. Mosettig, *J. Am. Chem. Soc.*, **73**, 880 (1951); **74**, 538 (1952).

[2] Y. Sato, H. K. Miller, and E. Mosettig, *J. Am. Chem. Soc.*, **73**, 5009 (1951).

[3] Y. Sato, H. G. Latham, Jr., and E. Mosettig, *J. Org. Chem.*, 22, 1496 (1957).

[4] N. N. Suvorov, L. V. Sokolova, L. M. Morozovskaya, and V. S. Murasheva, *Khim Nauka i Prom.*, **3**, 281 (1958).

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[7] Melting points were taken on the Kofler block and are uncorrected. Micro analyses were performed by the Analytical Service Laboratory under the direction of Dr. William C. Alford.

[8] Y. Sato and H. G. Latham, Jr., *J. Am. Chem. Soc.*, **78**, 3150 (1956).

[9] A. F. B. Cameron, K. M. Evans, J. C. Hamlet, J. S. Hunt, P. C. Jones, and A. G. Long, *J. Chem. Soc.*, 2807 (1955).