DEGRADATION OF TOMATIDINE

Sir:

In view of the recent interest in tomatidine[1,2,3] we wish to report our results on the degradation of tomatidine.[4]

Our analytical data of tomatidine and derivatives agree with the empirical formula $C_{27}H_{45}NO_2$ proposed by Fontaine, *et al.*,[5] rather than $C_{27}H_{43}NO_2$, suggested tentatively by Kuhn, *et al.*[3] Tomatidine. *Anal.* Calcd. for $C_{27}H_{45}NO_2$: C, 78.02; H, 10.91; N, 3.37; for $C_{27}H_{43}NO_2$: C, 78.40; H, 10.48; N, 3.39. Found: C, 78.02; H, 10.96; N, 3.43.

Tomatidine hydrochloride. *Anal.* Calcd. for $C_{27}H_{46}ClNO_2$: C, 71.73; H, 10.26; for $C_{27}H_{44}ClNO_2$: C, 72.05; H, 9.85. Found: C, 71.83; H, 10.35.

N,O-Diacetyltomatidine.[6]—*Anal.* Calcd. for $C_{31}H_{49}NO_4$: C, 74.50; H, 9.88; for $C_{31}H_{47}NO_4$: C, 74.81; H, 9.52. Found: C, 74.66; H, 9.92.

Tomatidine forms a sparingly soluble digitonide. On treatment with sodium nitrite in acetic acid a N-nitroso derivative is obtained, m.p. 234–237°[7]; λ_{max} 233 mμ, log ε 3.87: λ_{max} 360, log ε 1.83 (ethanol). *Anal.* Calcd. for $C_{27}H_{44}N_2O_3$: N, 6.30. Found: N, 6.36.

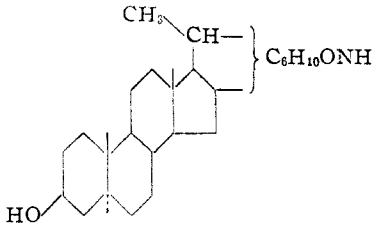
Treatment of tomatidine with acetic anhydride yielded an unsaturated triacetyl derivative (A), m.p. 105–107°. *Anal.* Calcd. for $C_{33}H_{51}NO_5$: C, 73.16; H, 9.49. Found: C, 73.12; H, 9.78.

A gave with dilute alkali a monoacetyl derivative, m.p. 210–215°. *Anal.* Calcd. for $C_{29}H_{47}NO_3$: C, 76.10; H, 10.35; N, 3.06. Found: C, 76.11; H, 10.42; N, 3.08.

Oxidation of A with chromic acid anhydride in acetic acid, and subsequent hydrolysis resulted in the formation of Δ^{16}-allopregnen-3(β)-ol-20-one, m.p. 205–206°, no depression when admixed with an authentic sample. *Anal.* Calcd. for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.55; H, 10.30.

The acetate of the compound likewise agrees well (m.p. 167–168°, mixed m.p., ultraviolet and infrared spectra) with authentic samples.[8] *Anal.* Calcd. for $C_{23}H_{34}O_3$: C, 77.05: H, 9.56. Found: C, 77.58; H, 9.80.

The isolation of the allopregnenolone establishes the structure of the steroidal moiety of tomatidine (I) and the attachment of the portion containing the secondary nitrogen, at C-20. The second point of attachment is most likely at position 16.



I

(1) Fontaine, Irving, Ma, Poole and Doolittle, *Arch. Biochem.*, **18**, 467 (1948).
(2) Kuhn and Löw, *Chem. Ber.*, **81**, 552 (1948).
(3) Kuhn, Löw and Gauhe, *ibid.*, **83**, 448 (1950).
(4) Kindly supplied to us by Dr. Thomas D. Fontaine, Bureau of Agricultural and Industrial Chemistry.
(5) Fontaine, Ard and Ma, THIS JOURNAL, **73**, 000 (1951).
(6) Purified by chromatography.
(7) All melting points were taken on the Kofler block and are uncorrected.
(8) A sample was kindly supplied to us by Dr. R. B. Wagner of Pennsylvania State College. Another generous sample was given to us by Dr. George Rosenkranz of Syntex, S. A.

NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND
YOSHIO SATO
ALFRED KATZ[9]
ERICH MOSETTIG

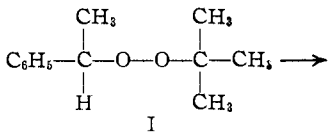
RECEIVED DECEMBER 8, 1950

(9) Organisch-chemische Anstalt, University of Basel.

THE BASE CATALYZED DECOMPOSITION OF A DIALKYL PEROXIDE

Sir:

We have found that bases, such as potassium hydroxide, sodium ethoxide, or piperidine, catalyze the decomposition of 1-phenylethyl-*t*-butyl peroxide (I)



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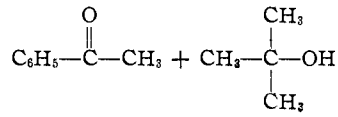
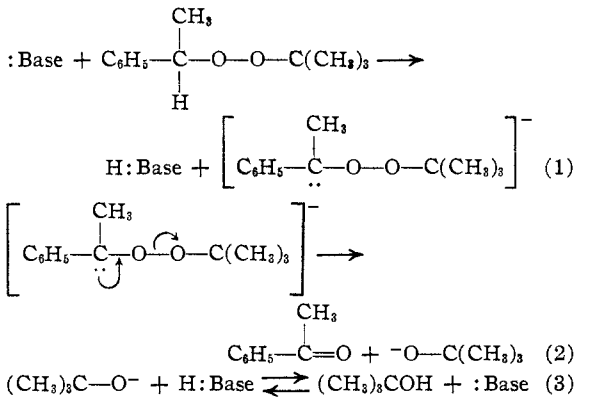


This reaction takes place smoothly at room temperature and apparently is the first demonstration of the instability of a dialkyl peroxide toward base. The facile decomposition of I contrasts sharply with the inertness of di-*t*-butyl peroxide to potassium hydroxide[1] or piperidine.

The following mechanism, which is in accord with all the known facts, emphasizes the relationship of this reaction to the well-known elimination reaction[2]; steps (1) and (2) presumably are synchronous.



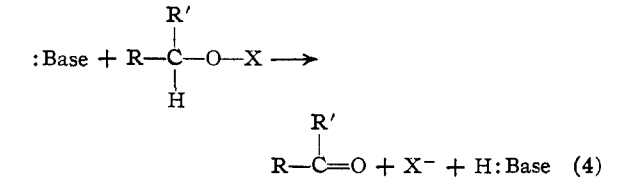
This mechanism also affords a reasonable explanation for the conversion of α-tetralin hydroperoxide (II) to α-tetralone under the influence of sodium hydroxide.

It is a consequence of this mechanism that only those dialkyl peroxides and alkyl hydroperoxides having a hydrogen on the carbon attached to the peroxide linkage will undergo base catalyzed decomposition. That the aromatic nucleus in I and II is not a necessary structural feature is indicated

(1) N. A. Milas and D. M. Surgenor, THIS JOURNAL, **68**, 205 (1946).
(2) E. D. Hughes, C. K. Ingold, *et al.*, *J. Chem. Soc.*, 2093 (1948).

by the report that isopropyl hydroperoxide, which is relatively stable to acidic and neutral solutions, under alkaline conditions rapidly gives acetone.[3] Similarly, peroxides and hydroperoxides such as *i*-propyl-*t*-butyl peroxide and cyclohexene hydroperoxide will be expected to exhibit instability toward bases.[4]

The base-catalyzed decompositions of peroxides and hydroperoxides apparently exemplify a rather general type of elimination reaction which may be anticipated for compounds in which an atom or group X, capable of giving a relatively stable anion X^-, is attached to oxygen



Thus the decomposition of nitrate esters (X = $-NO_2$) under the influence of hydroxide ion is an analogous process; $HO^- + C_6H_5CH(H)O\overset{\curvearrowright}{N}O_2 \downarrow$ $C_6H_5CH{=}O + NO_2^- + H_2O$.[5] To test the generality of reaction (4) the following suggest themselves for study: X = $C(C_6H_5)_3$, NR_2, mesitoyl, —C≡C—Aryl, etc.[6]

Peroxide I was obtained by the action of potassium *t*-butyl peroxide on 1-phenylethyl bromide; b.p. 56.3–57° (1.3 mm.); $n^{20}D$ 1.4809 (calcd. for $C_{12}H_{18}O_2$: C, 74.18; H, 9.34. Found: C, 74.35, 74.51; H, 9.18, 9.14). When I (0.08 mole) was dissolved in piperidine (0.40 mole) the temperature rose to 50° within fifteen minutes. At this point the solution was cooled to 25° and then maintained at 25° for eighty hours. Acetophenone was isolated in 79% yield; *t*-butyl alcohol, in 25% yield. When 0.05 mole I was mixed with 0.01 mole piperidine the temperature did not rise; after eighty-four hours at 25°, a 32% yield of acetophenone was obtained.

(3) S. S. Medwedew and E. Alexejewa, *Ber.*, **65**, 133 (1932).

(4) Compare V. L. Vaiser, *C. A.*, **44**, 3446 (1950); F. F. Rust, F. H. Seubold, and W. E. Vaughan, THIS JOURNAL, **72**, 338 (1950).

(5) J. W. Baker and D. M. Easty, *Nature*, **166**, 156 (1950).

(6) The base-catalyzed decomposition of hypohalites has been formulated as in eq. 4; X = Cl. Private communication from Dr. Saul Winstein.

DEPARTMENT OF CHEMISTRY
PURDUE UNIVERSITY NATHAN KORNBLUM
LAFAYETTE, INDIANA HAROLD E. DELAMARE

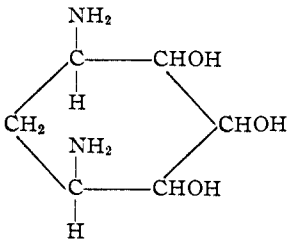
RECEIVED DECEMBER 1, 1950

STREPTOMYCES ANTIBIOTICS. XXIII. 1,3-DIAMINO-4,5,6-TRIHYDROXYCYCLOHEXANE FROM NEOMYCIN A.

Sir:

Neomycin A has been degraded to a new compound which has been established as a *meso* form of 1,3-diamino-4,5,6-trihydroxycyclohexane (I).

Hydrolysis of Neomycin A[1] by heating a solution of it in 6 *N* hydrochloric acid at 140° for sixteen hours yielded the dihydrochloride of an optically inactive diacidic base. *Anal.* Calcd. for $C_6H_{14}N_2O_3 \cdot 2HCl$: C, 30.66; H, 6.86; N, 11.93; Cl, 30.17; eq. wt., 117.5. Found: C, 30.89; H, 6.71; N, 12.19; Cl, 29.44; eq. wt., 120 (potentiometric titration). Benzoylation of this base gave a pentabenzoate. *Anal.* Calcd. for $C_6H_9N_2O_3(C_6H_5CO)_5$: C, 72.12; H, 5.02; N, 4.10. Found: C, 71.77; H, 5.05; N, 4.04. Selective oxygen-debenzoylation of the pentabenzoate with barium methoxide in methanol yielded an N,N′-dibenzoyl derivative. *Anal.* Calcd. for $C_6H_{12}N_2O_3(C_6H_5CO)_2$: C, 64.85; H, 5.99; N, 7.55. Found: C, 65.05; H, 5.90; N, 7.70.



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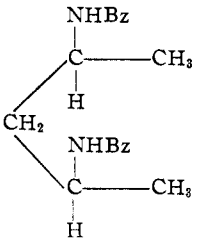
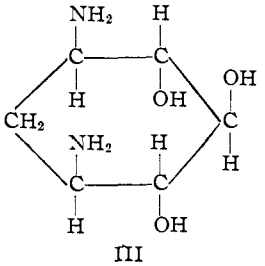


II

The original free base consumed four moles of periodate whereas its N,N′-dibenzoyl derivative utilized two moles. These combined data suggested that the structure of the base was that of a 1,3-diamino-4,5,6-trihydroxycyclohexane (I).

Confirmation of structure I was obtained by the following series of reactions and products. Periodate oxidation of the N,N′-dibenzoyl derivative yielded a dialdehyde, which was not separated, but which upon treatment with ethyl mercaptan and hydrogen chloride gave a dimercaptal; m.p. 140–141°. *Anal.* Calcd. for $C_{13}H_{28}N_2S_4(C_6H_5CO)_2$: C, 58.87; H, 6.95; N, 5.09; S, 23.3. Found: C, 58.97; H, 6.91; N, 5.40; S, 23.8. The dimercaptal was converted by hydrogenolysis with Raney nickel to an N,N′-dibenzamido-pentane (II); m.p. 197–197.5°. *Anal.* Calcd. for $C_{19}H_{22}N_2O_2$: C, 73.55; H, 7.10; N, 9.03. Found: C, 73.53; H, 6.96; N, 8.50.

The higher-melting *meso* isomer[2] of 1,3-dibenzamido-pentane was prepared by stepwise catalytic reduction and benzoylation of acetylacetone dioxime. It melted at 197.5–198°, and caused no depression of melting point upon admixture with the degradation product.



III

The nitrogen atoms of this *meso* isomer of 1,3-diamino-4,5,6-trihydroxycyclohexane must have a *cis* relationship, and if the molecule is biogenetically related to streptidine, which has an all-*trans*-

(1) Peck, Hoffhine, Gale and Folkers, THIS JOURNAL, **71**, 2590 (1949).

(2) Dippel, *Rec. trav. chim.*, **50**, 525 (1931).