dose of 60γ. (*Anal.* Calcd. for $C_{43}H_{66}N_{12}O_{11}S_2$: C, 52.1; H, 6.71; N, 17.0; mol.wt., 991. Found: C, 52.1; H, 6.83; N, 16.9; mol. wt.[14] 940).

From these data we can conclude that the phenolic hydroxyl group of oxytocin contributes strongly to the activity of the hormone but is not essential for biological activity.[15,16]

Acknowledgements.—The authors wish to thank Mr. Joseph Albert for the microanalyses, Mr. David De Peter for the determination of the molecular weight, Miss Dade Tull for the biological assays, and Mr. David N. Reifsnyder for technical assistance.

(14) E. V. Baldes, *Biodynamica* **No. 46**, 1 (1939).

(15) As the experiments reported here were completed, we learned at a lecture delivered by Dr. R. A. Boissonnas that the same analog of oxytocin was prepared and studied in his laboratory simultaneously but independently from our work.

(16) After this communication was submitted for publication, Professor H. B. van Dyke found that 2-phenylalanine oxytocin shows milk ejecting activity of about 60 units per mg.

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EVIDENCE OF A 1,4-METHYL MIGRATION DURING A FISCHER REACTION

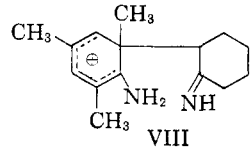
Sir:

An investigation of the structure of a compound isolated some years ago[1] as its picrate from the product of the action of boiling acetic acid on cyclohexanone mesitylhydrazone (I) has now disclosed that the compound is not "1,2,3,4-tetrahydro-6,8,12-trimethylisocarbazole" (III),[1] but is instead 6,7,8-trimethyl-1,2,3,4-tetrahydrocarbazole (II).

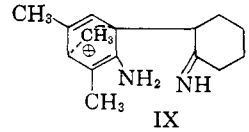
Mesitylhydrazine, m.p. 60–61° (N_2), was prepared by a new synthetic method based on the addition of mesitylene to ethyl azodicarboxylate.[2] The adduct, m.p. 159–160° (Found: C, 61.67; H, 7.61; N, 9.57[3]) was converted to mesitylhydrazine by boiling ethanolic potassium hydroxide. I, m.p. 45–47° (N_2), from mesitylhydrazine and cyclohexanone in the absence of solvent, was too unstable to analyze. Under nitrogen, boiling acetic acid converted I to II, isolated as its picrate, m.p. 171–172° (d.), as reported.[1] (Found: C, 57.61; H, 5.00; N, 12.87.) The tetrahydrocarbazole, from the picrate and sodium hydroxide, was extremely air-sensitive, m.p. 92–98° (N_2), insufficiently stable to analyze. Chloranil in xylene under nitrogen converted II to 1,2,3-trimethylcarbazole, m.p. 127.5–128.5°. (Found: C, 85.32; H, 7.37; N, 6.85); infrared and ultraviolet curves very similar to those of carbazole. Exposure in ether solution of II to air produced 11-hydroperoxy-6,7,8-trimethyl-1,2,3,4-tetrahydrocarbazolenine IV, m.p. 134° (d.). (Found: C, 72.46; H, 7.81; N, 5.77), which isomerized in ethanol solution to 9,10,11-trimethyl-1-benzazonidine-2,7-dione V, m.p. 171–172°. (Found: C, 73.08; H, 7.90; N, 5.55). The latter was converted by acid hydrolysis to δ-(2-amino-3,4,5-trimethylbenzoyl)-valeric acid VI, m.p. 146-149°. (Found: C, 68.56; H, 7.84; N, 5.50), and by alkali to 2,3-trimethylene-6,7,8-trimethyl-4-quinolone VII, darkens above 300°. (Found: C, 80.90; H, 7.64; N, 5.86). These transformations of II through IV and V to VI or VII parallel a precisely analogous series of reactions starting with tetrahydrocarbazole.[4] The ultraviolet and infrared spectra of V–VII are notably similar to those of the lower homologs derived from tetrahydrocarbazole.

The location of the methyl groups in the structure II and those of its derivatives was proven by synthesis of II from hemimellitene. The latter afforded an adduct with ethyl azodicarboxylate, m.p. 151–152° (Found: C, 60.10; H, 7.62; N, 9.60), which was converted to 2,3,4-trimethylphenylhydrazone, m.p. 105–106° (N_2), too unstable to analyze. The structure of this compound was demonstrated by its hydrogenation over Raney nickel to 2,3,4-trimethylaniline, characterized as its N-acetyl derivative. Cyclohexanone 2,3,4-trimethylphenylhydrazone, oily solid, too unstable to analyze, when boiled in acetic acid under nitrogen, afforded II, isolated as its picrate, m.p. and mixed m.p. 171–172°(d.). From this picrate II itself and from the latter 1,2,3-trimethylcarbazole and IV, V, VI and VII were prepared. Their m.pts. mixed m.pts. and spectroscopic properties identified them with samples obtained from I as starting material.

Although it is possible to rationalize the formation of II from I by means of a series of three consecutive 1,2 methyl shifts, along with the required accompanying reactions, a single 1,4 shift of methyl, although to our knowledge unprecedented, seems to us to offer a superior explanation. In either instance the shift would start with an intermediate VIII, a homolog of one for which evidence has been offered previously.[5] A single 1,4 shift of methyl, through transition state IX, would yield a second intermediate from which II could be formed by previously suggested routes.[6]



VIII



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(1) C. S. Barnes, K. H. Pausacker and W. E. Badcock, *J. Chem. Soc.*, 730 (1951).

(2) R. Huisgen, F. Jacob, W. Siegel and A. Cadus, *Ann.*, **590**, 1 (1954).

(3) Sample first prepared by Dr. Robert J. Laufer.

(4) B. Witkop and J. B. Patrick, THIS JOURNAL, **73**, 2188, 2198 (1951).

(5) R. B. Carlin and D. P. Carlson, *ibid.*, **79**, 3605 (1957).

(6) See R. B. Carlin, W. O. Henley, Jr. and D. P. Carlson, *ibid.*, **79**, 5712 (1957).

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RECEIVED DECEMBER 24, 1958

AMINO ACID INCORPORATION INTO LIPOIDAL MATERIAL BY CELL-FREE LIVER PREPARATIONS

Sir:

The incorporation of amino acids into cellular constituents via adenosine triphosphate–amino acid activation has been studied by many workers,