

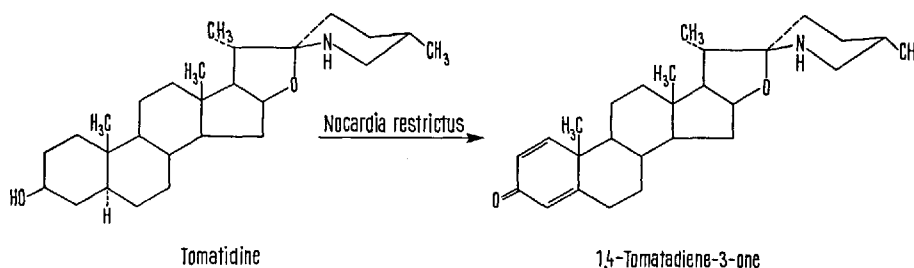
Microbiological Dehydrogenation of Tomatidine

Although the microbiological dehydrogenation of steroids has already become a well-known procedure, such dehydrogenation is scarcely known to occur with steroidal sapogenins and steroidal alkaloids¹. Diosgenin is dehydrogenated by *Fusarium solani*; the yield, however, is high only if diosgenin is previously transformed to diosgenone². Conessine can be dehydrogenated by *Gloesporium cyclaminis*³ or *Stachybotrys parvispora*⁴ to 4-conenin-3-one. Otherwise only hydroxylation

of conessine⁵⁻⁷, tomatidine⁸ and solasodine⁹ have been observed.

Our attempts at dehydrogenation of tomatidine and tomatidone by *Fusarium solani* have not been successful¹⁰. On the other hand, dehydrogenation of tomatidine by *Nocardia restrictus* has been achieved yielding 60% of 1,4-tomatadiene-3-one.

Incubation of tomatidine with *Nocardia restrictus* yielded, as the main metabolite, a crystalline substance:



¹ H. IZUKA and A. NAITO, *Microbial Transformation of Steroids and Alkaloids* (University of Tokyo Press 1967), p. 228.

² E. KONDO and T. MITSUGI, *J. Am. chem. Soc.* **88**, 4737 (1966).

³ J. DE FLINES, A. F. MARX, W. F. VAN DER WAARD and D. VAN DE SIJDE, *Tetrahedron Lett.* **1962**, 1257.

⁴ A. F. MARX, H. C. BECK, W. F. VAN DER WAARD and J. DE FLINES, *Steroids* **8**, 391 (1966).

⁵ S. M. KUPCHAN, L. J. SIH, S. KUBOTA and A. M. RAHIM, *Tetrahedron Lett.* **1963**, 1767.

⁶ E. L. PATTERSON, W. N. ANDRES and R. E. HARTMAN, *Experientia* **20**, 256 (1964).

⁷ A. F. MARX, H. C. BECK, W. F. VAN DER WAARD and J. DE FLINES, *Steroids* **8**, 421 (1966).

⁸ Y. SATO and S. HAYAKAWA, *J. org. Chem.* **29**, 198 (1964).

⁹ Y. SATO and S. HAYAKAWA, *J. org. Chem.* **26**, 4181 (1961).

¹⁰ I. BELIČ, E. PERTOT and H. SOČIČ, unpublished results.

¹¹ H. BUDZIKIEWICZ, C. DJERASSI and D. H. WILLIAMS, *Structural Elucidation of Natural Products by Mass Spectrometry* (Holden-Day Inc., San Francisco 1964), p. 21 and 91.

¹² A. I. SCOTT, *Interpretation of Ultraviolet Spectra of Natural Products* (Pergamon Press, London 1964), p. 64 and 406.

¹³ W. NEUDERT and A. RÖPKE, *Atlas of Steroid Spectra* (Springer Verlag, Berlin 1965), p. 293.

¹⁴ Acknowledgment. The authors are indebted to Dr. J. MARSEL and Eng. Chem. D. MILIVOJEVIĆ, J. Stefan Institute, Ljubljana, for the determination of the mass spectrum. The financial support of the Boris Kidrič Fund is gratefully acknowledged.

¹⁵ Taken in part from the forthcoming doctorate dissertation of H. SOČIČ.

mp 242–245°; TLC homogeneous with the solvent system cyclohexane-ethylacetate (1:2); visualized by spraying with 50% sulfuric acid. The mass spectrum showed a M^+ ion 409, corresponding to a loss of 6 hydrogen atoms from the tomatidine molecule (calc. for $C_{22}H_{30}O_2N$: 409) and, in addition, intense peaks at m/e 138 and m/e 114, typical for the unchanged tomatidine rings E and F. The presence of the peak at m/e 288 corresponding to $M-121$ points to the 1,4-diene-3-one structure of ring A¹¹. The absorption maximum at λ_{max}^{EtOH} 244 nm (ϵ 15,400)¹² and the IR-spectrum showing absorption bands at 1660 cm^{-1} (3 C=O), 1622 cm^{-1} (1:2 C=C) and 1605 cm^{-1} (4:5 C=C)¹³ are in agreement with the above structure of ring A. Therefore, the structure of the metabolite is that of 1,4-tomatadiene-3-one.

Zusammenfassung. Mit Hilfe von *Nocardia restrictus* wurde aus Tomatidin in 60% Ausbeute 1,4-Tomatadien-3-on erhalten.

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Lecithin-Chloroform Interaction as a Model for the Action of General Anesthetics

Water has been proposed by PAULING¹ and MILLER² as the primary reactant with non-hydrogen-bonding anesthetic molecules. The formation of anesthetic-water clathrates has been thought possible under physiological conditions if stabilizing agents other than the anesthetic molecule were also operating. The charged side chains of proteins were considered to act as stabilizers on the basis of their analogy with alkylammonium derivatives, which are known to form clathrates with water.

We thought³ that lecithin would have been a more suitable stabilizer, and here we present some data on the in vitro interaction between chloroform ($CHCl_3$) and synthetic lecithin, and on the stabilizing power of a number of compounds in respect to $CHCl_3$ hydrates.

The escaping tendency of $^{14}CHCl_3$ (GMBH Products) was studied in the presence of DL- α -dipalmitoyl-lecithin, glutathione, choline, phosphocholine, palmitic acid and mixtures of palmitic acid and phosphocholine (Table I). All reagents were Fluka, AG, Buchs products.

The effect of lecithin concentration (Table II) and temperature (Table III) on $^{14}CHCl_3$ evaporation were

¹ L. PAULING, *Science* **134**, 15 (1961).

² S. L. MILLER, *Proc. natn. Acad. Sci., USA* **47**, 1515 (1961).

³ L. GALZIGNA, *Abstracts 2nd Int. Meeting Int. Soc. Neurochem., Milan 1969*, p. 343.