Tetrahedron Letters No.43, pp. 4549-4551, 1968. Pergamon Press. Printed in Great Britain.

CONVERSION OF RHOEAGENINEDIOL TO COPTISINE

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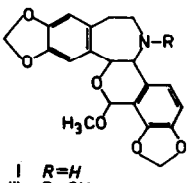
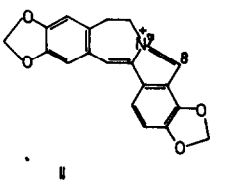
(Received in UK 19 July 1968; accepted for publication 30 July 1968)

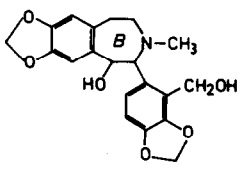
A short time back structure II was elucidated and assigned (1) to the so-called red substance which arises on treatment of papaverrubine A (I) (2,3) with hydrochloric acid.



I R=H
III R=CH3



II
V 7-Methyl-7,8-dihydro-II

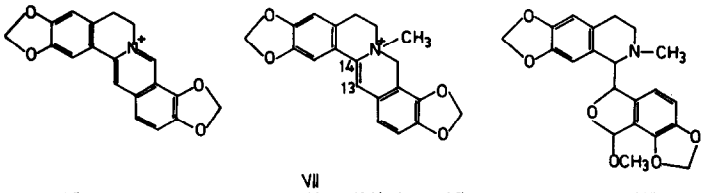


IV

We assumed the existence of a simple reaction process proceeding from rhoeadine (III) (4) via rhoeageninediol (IV) (4) to the substances of type II. On boiling rhoeageninediol (IV) for several hours with an excess of thionyl chloride in dry chloroform, cyclization and simultaneous dehydrohalogenation afforded a quarternary compound. It was designated as substance R (m.p. 175-180°C with decomposition; ultraviolet: λ_{max} 215, 255, 306, 343^{sh}, 357, and 375 nm (log ε 4.42, 3.84, 3.88, 4.26, 4.39, and 4.33), λ_{min} 244, 274, 314, and 367 nm (log ε 3.81, 3.41, 3.85, and 4.30)), and ascribed the tentative structure V. However, N-demethylation of the substance R with sodium p-toluylthiolate (5,6) gave (on boiling in a solution of butanone-2) the alkaloid coptisine (VI)*.

* Obviously, this is not the primary product of the reaction; it arises during isolation of 7,8-dihydrocoptisine by its oxidation with atmospheric oxygen. A similar behaviour was observed earlier in an analogous substance of narcotine type (6).

This indicates, however, that structure VII and not the assumed structure V has to be assigned to substance R. From this follows that either rhoeadine has to be ascribed the earlier suggested structure VIII (7,8) or that rearrangement takes place at some stage of the reaction process. The structure VIII for rhoeadine had to be excluded for the reasons given in paper (4). The most conclusive evidence is that oxyrhoeagenine and the alkaloid bicuculine are not identical (4). Consequently, an acceptable explanation is the rearrangement of the seven membered ring B of rhoeagenine-diol (IV) into a six membered ring either during cyclization by the action of thionyl chloride or during N-demethylation of the substance R.



VI VII IX 13,14-dihydro-VII VIII

Therefore, by hydrogenation of the substance R (in the presence of Adams' catalyst in methanol) its dihydroderivative (m.p. 264-268°C with decomposition; ultraviolet: λ_{max} 212, 242, and 291 nm (log ε 4.28, 3.79, and 3.77), λ_{min} 227 and 261 nm (log ε 3.67 and 3.00)) was prepared whose ultraviolet and infrared spectra are identical with those of the tetra-hydrocoptisine methiodide. From this follows that the hydrogenated substance R has to be assigned the structure IX and the substance R the structure VII.

The substance having the structure VII and designated as isoprotopine chloride was obtained earlier by Perkin (9) by treatment of protopine with phosphorylchloride. Reproduction of Perkin's procedure afforded a substance which showed to be identical with our substance R (VII).

From the results obtained it is concluded that rearrangement of the seven membered ring B into a six membered ring takes place during cyclization of rhoeageninediol (IV) through thionyl chloride. The investigation

of the reaction mechanism of the rearrangement under discussion forms the subject of further studies.

References

1. D. Walterová and F. Šantavý, Collection Czechoslov. Chem. Commun. 33, 1623 (1968).
2. A. Němečková and F. Šantavý, ibid., 27, 1210 (1962); ibid., 32, 461 (1967).
3. S. Pfeifer and S.K. Banerjee, Arch. Pharm., 298, 385 (1965).
4. F. Šantavý, J.L. Kaul, L. Hruban, L. Dolejš, V. Hanuš, K. Bláha, and A.D. Cross, Collection Czechoslov. Chem. Commun., 30, 335 (1965); ibid., 30, 3479 (1965).
5. M. Shamma, N.C. Deno, and J.F. Remar, Tetrahedron Letters, 1375 (1966).
6. V. Šimánek, V. Preininger, and F. Šantavý, Collection Czechoslov. Chem. Commun., in the press.
7. F. Šantavý, M. Maturová, A. Němečková, and M. Horák, ibid., 24, 3493 (1959); ibid., 25, 1901 (1960).
8. W. Awe and W. Winkler, Arch. Pharm., 291, 642 (1958); Arzneimittel-Forsch., 9, 773 (1959); Naturwiss., 47, 107 (1960).
9. W.H. Perkin, Jr., J. Chem. Soc., 109, 815 (1916).