The Structure of Tazettine

By E. Wenkert, Ames, Iowa

The chemistry of tazettine, a minor alkaloid of the Amaryllidaceae, was investigated first by Späth, who had isolated the natural product from the bulbs of Narcissus tazetta L. The compound was found to contain a tertiary nitrogen, a methylenedioxy, a hydroxy, and one anthridine, while permanganate oxidation produced stage Hoffmann degradation, however, yielded a crystalline base VIII, one of the minor alkaloids isolated from Lycoris radiata Herb., and with ungerine, obtained by Orehoff from the bulbs of Ungerinia Sewertzowii (Rgl.) Fedisch, established the identity of the three compounds. Orehoff's few experiments supplemented those of Späth. Thus the hydrogenatability of the alkaloid pointed definitely to the presence of unsaturation in the molecule, while the isolation of compound I both from a single-stage Hoffmann degradation and from a vigorous base treatment of the alkaloid itself indicated the general lability of the natural product toward alkali.

In a recent series of six papers, Kondo and coworkers, a H. Kondo, T. Ikeda, and J. Taga, ibid. 3, 30 (1952); b H. Kondo, T. Ikeda, and N. Okuda, Ann. Reports Itsuu Lab. 1, 21 (1960); c H. Kondo and T. Ikeda, ibid. 5, 18 (1951); d H. Kondo, T. Ikeda, and K. Takeda, ibid. J, 24 (1953); e H. Kondo, T. Ikeda, and J. Taga, ibid. J, 30 (1952); f H. Kondo, T. Ikeda, and J. Taga, ibid. 4, 30 (1953). The compound was found to contain a N-methyl but no C-methyl group, and on Hoffmann degradation, preceded by methylation, yielded a host of mainly non-nitrogenous products (see Table I), including 6-phenylpiperonyl alcohol (I). Whereas none of the structures of these compounds; and it should be pointed out that intravenous injections, in connection with convulsions or other motor disorders, must be made with great care until more is known about the central effects of the drug.

C. G. Bernhard and E. Bohm

Physiological Department II, Karolinska Institutet and Neurotraumatological Clinic, Serafimerlasaretet, Stockholm, May 26, 1954.

Zusammenfassung

Es hat sich gezeigt, dass kleine intravenöse Dosen von Xylocain im Versuch an der Katze die zentralen epileptiformen Nacherregungen und die poststimulatorischen Krämpfe blockieren können, und in Analogie hierzu zeigte eine préliminäre Untersuchung am Menschen, dass epileptische Anfälle durch intravenöse Injectionen von Xylocain abgebrochen werden können.

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part formulas (II and VIII) of tazettine, whose side-chain appears at C-9. This inconsistency, added to the fact that many of Kondo's tazettine degradation products were formulated as fractional hydrates (see the empirical formulas in parentheses in Table I), called for a reevaluation of Kondo's chemical, especially analytical, data.

Recalculation of Kondo's reported analytical values for compound $D^*$, the major Hoffman degradation product, reveals that $C_{20}H_{18}O_4$ is the most acceptable (non-hydrated) empirical formula (see italicized formulas in Table I). The fact that this compound was oxidizable to a mixture of aldehyde $V$ and acid $VI$ and was hydrogenatable to $F$, whose corrected empirical structure is $C_{19}H_{14}O_3$, with a concomitant loss of an oxygen atom limits its structural formula to the benzyl alcohol $X$ and consequently that of its hydrogenolysis product $F$ to XII. These formulations are strengthened by the fact the "des-N-base" $D$, now compound XI, had been reported to be acetylable to a product which on alkaline hydrolysis reverted to the starting material. Whereas, $C_{19}H_{18}O_5 \cdot 1/2H_2O$ was the assigned formula for this acetate, a recalculation showed that $C_{17}H_{14}O_5$ fitted the analytical values best and hence established the already-predictable structure XIII for this compound. Coincidentally, the latter also must be the structure of "des-N-base" $C$ since its empirical formula as well as melting point, 87-89°, agree with those of the acetate (m.p. 89-90°). As a final confirmation for the above arguments it must be mentioned that Kondo's ultraviolet absorption spectra* for compounds XI, XII, and XIII are essentially superposable as would be expected for an identical diphenyl chromophoric system in all three degradation products.

$B$, the only nitrogenous Hoffman product, has been assigned correctly formula $C_{18}H_{19}O_5N$ and has been reported to possess no methoxy group*$. The structure of this compound can be envisaged to be XIV mainly on the basis of it having to possess a dimethylamino group in the position of the methylimino function in the original phenanthridine nucleus. The ultraviolet spectra of $B$ confirms the presence of a diphenyl system although its absorption characteristics are different than those of the above Hoffman degradation products and thus in agreement with a shift of chromophores, i.e. p-methoxy to o-dimethylamino. The oxygen atoms, other than those associated with the ever-recurring methylenedioxy linkage, were assigned their function as acetate for reasons that will become obvious below although one immediate reason for considering only this structure is the fact that their only other logical position, i.e. somewhere in the newly created benzene ring, would most likely affect the chromophore of the system more drastically than the spectra would warrant. Compound $E$, $C_{18}H_{20}O_7$, was

* See footnote pag. 476.