(+)-9-AZA-1-METHYLBICYCLO[3,3,1]NONAN-3-ONE, A NEW ALKALOID FROM *EUPHORBIA ATOTO* FORST.

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Summary

A new alkaloid isolated from *Euphorbia atoto* Forst. has been shown to be (+)-9-aza-1-methylbicyclo[3,3,1]nonan-3-one.

Introduction

A new alkaloid, $C_9H_{15}NO$, m.p. 30°, $[\alpha]_D$ +6° in methanol, has been isolated from *Euphorbia atoto* Forst., a small procumbent sea-coast plant (1–1½ ft) of the family Euphorbiaceae. *E. atoto* is found along the northern shores of Australia and extends in range to the Pacific Islands and Eastern India.

Discussion

Spectroscopic evidence indicates that the alkaloid is (+)-9-aza-1-methylbicyclo-[3,3,1]nonan-3-one (I), and the structure has been established by comparison with the (±) form of (I), the synthesis of which had previously been described.[1] Although a variety of alkaloids have been isolated from plants belonging to the family Euphorbiaceae, there has been no previous isolation of an alkaloid of this type. The alkaloid has a close structural resemblance to pseudopelletierine (II), an alkaloid of *Punica granatum* (family Punicaceae).[2,3] The presence of the methyl substituent at C 1 provides evidence for a probable biosynthetic route to (I) from the condensation of ammonia with an acetate-derived C_{10} residue, as indicated in (III). Despite a formal resemblance to the alkaloids of the tropane group, the alkaloid (I) is more likely to be related biosynthetically to those alkaloids of general structure (IV) represented by pinidine[4] (IV; R = CH_3; R′ = $-CH{=}CH{-}CH_3$) and the *Lobelia* alkaloids.[5] In terms of biosynthetic relationships it is of interest that two imidazole alkaloids from a *Glochidion* species of the family Euphorbiaceae also have structures in which a ketodecanoic acid residue is incorporated.[6]

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[1] Alder, K., Betzing, H., and Kuth, R., *Liebigs Ann.* 1959, **620**, 73.

[2] Tanret, Ch., *C. r. hebd. Séanc. Acad. Sci., Paris*, 1879, **88**, 716.

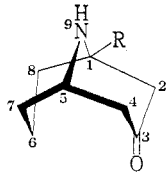
[3] Hess, K., *Ber. dt. chem. Ges.*, 1919, **52**, 1005.

[4] Tallent, W. H., Stromberg, V. L., and Horning, E. C., *J. Am. chem. Soc.*, 1955, **77**, 6361.

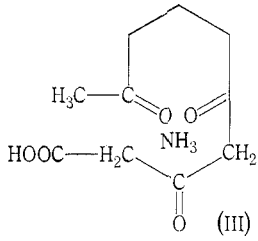
[5] Boit, H.-G., "Ergebnisse der Alkaloid-Chemie bis 1960." p. 128. (Akademie-Verlag: Berlin 1961.)

[6] Johns, S. R., and Lamberton, J. A., *Chem. Commun.*, 1966, 312.

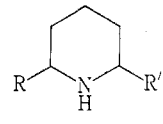
An absorption band at 1705 cm^{-1} in the i.r. spectrum of alkaloid (I) (CCl_4 solution) indicated the presence of a ketonic group, while the presence of an NH function was shown by an i.r. band at 3400 cm^{-1} and by the formation of an *N*-acetyl derivative. A *C*-methyl substituent at a tertiary carbon atom was shown to be present by a sharp three-proton singlet at δ 1·17 in the 60-Mc/s n.m.r. spectrum of (I) ($CDCl_3$ solution) and a broad one-proton multiplet at 210–230 c/s has been assigned to the single proton at the C 5 bridgehead position. The mass spectrum of (I) shows a fragmentation pattern which can be rationalized by analogy with the breakdown pattern exhibited by tropinone.[7]



(I) R = CH_3
(II) R = H



(III)



(IV)

The alkaloid (I) comprises at least 80% of the total alkaloids of *E. atoto*. The remainder was composed largely of constituents having *N*-methyl groups, as indicated by the n.m.r. spectrum of the residues recovered after the isolation of (I), but comparison by gas chromatography showed that the *N*-methyl derivative of (I) was not present in the mixture.

Experimental

E. atoto was collected by the shore at Red Island Point on Cape York, northern Queensland. The milled dried leaves and stems (2 kg) were extracted with ethanol at 40°, and the alkaloid fraction separated by the method previously described.[8] The crude alkaloid fraction (2·1 g) was a light brown liquid, and was shown by gas chromatography to have one major component (*c.* 80%). The major alkaloid was conveniently separated as a sparingly soluble picrate, m.p. 240° (dec.) after crystallization from ethanol (Found: C, 47·2; H, 4·8; N, 15·2. Calc. for $C_9H_{15}NO,C_6H_3N_3O_7$: C, 47·1; H, 4·8; N, 14·7%). The free base was recovered from the picrate and after purification by sublimation in vacuum was obtained as colourless crystals, m.p. 30°, $[\alpha]_D$ +3°, (*c*, 2·0 in $CHCl_3$), $[\alpha]_D$ +6° (*c*, 2·0 in methanol), ν 3400, 1705 cm^{-1} in CCl_4 solution. The 60-Mc/s n.m.r. spectrum ($CDCl_3$ solution, tetramethylsilane δ 0·00) showed a three-proton singlet at δ 1·17 (*C*-CH_3), a one-proton multiplet at 210–230 c/s (C**H**–NH), a four-proton multiplet at 130–160 c/s (–CH_2–CO–CH_2–), and a multiplet from 80–110 c/s (all other protons). The mass spectrum of (I) showed peaks at *m/e* 153 (25% of base peak), 111 (25), 110 (base peak, 100%), 96 (40), 95 (20), 94 (20), 93 (36), 83 (26), 82 (32), 68 (16), 66 (18), 58 (21), 43 (94), 42 (27), and 41 (21).

Identical spectroscopic properties were observed for the (±) form of (I), which was synthesized by the condensation of 2,3-dihydro-2-methoxy-6-methylpyran with acetonedicarboxylic acid and ammonium chloride by the method described.[1] 2,3-Dihydro-2-methoxy-6-methylpyran was used instead of the corresponding -2-ethoxy compound, and it was prepared by thermal condensation of methyl vinyl ketone and methyl vinyl ether according to the method used for preparing the -2-ethoxy compound.[9]

[7] Budzikiewicz, H., Djerassi, C., and Williams, D. H., "Interpretation of Mass Spectra of Organic Compounds." p. 92. (Holden-Day: San Francisco 1964.)
[8] Johns, S. R., Lamberton, J. A., and Sioumis, A. A., *Aust. J. Chem.*, 1966, **19**, 2331.
[9] Smith, C. W., Norton, D. G., and Ballard, S. A., *J. Am. chem. Soc.*, 1951, **73**, 5267.

The *N*-acetyl derivative of (I) prepared by heating (I) in a solution of acetic anhydride and pyridine at 100° was obtained as a colourless gum (ν 1705, 1665 cm^{-1} in CCl_4 solution). The n.m.r. spectrum of the *N*-acetyl compound showed a three-proton singlet at δ 1·72 (*C*-CH_3), a three-proton singlet at δ 2·17 (*N*-$COCH_3$), and a one-proton multiplet at 260–280 c/s (H 5).

N-Methylation of a sample of synthetic (I) by the Clarke–Eschweiler method[10] afforded an *N*-methyl derivative which was characterized by its mass spectrum (molecular ion at *m/e* 167 and corresponding fragment ions) and n.m.r. spectrum (*N*-methyl signal at δ 2·56). Comparative gas chromatograms showed that the *N*-methyl derivative did not coincide in retention time with any of the minor constituents of the *E. atoto* alkaloids.

[10] Clarke, H. T., Gillespie, H. B., and Weisshaus, S. Z., *J. Am. chem. Soc.*, 1933, **55**, 4571.