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EUPHORBIACEAE

ALKALOIDS FROM *CROTON HUMILIS*

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Abstract—*N*-Methyltyramine, *N*-methylhomotyramine, a $C_{18}H_{27}N_3O_3$ and a $C_{35}H_{51}NO_7$ compound have been isolated from *Croton humilis* L.

INTRODUCTION

TO DATE species of *Croton* (Euphorbiaceae) have yielded alkaloids of the aporphine, proaporphine and morphinandienone groups.[1–3] Earlier preliminary investigations indicated that *C. humilis* contained alkaloids,[4] and this study has identified some of these compounds.

RESULTS AND DISCUSSION

Plant material from the Long Mountain area in Mona, Jamaica, was dried, milled and extracted in the usual way with 2% tartaric acid, and after concentration and basification, the chloroform soluble alkaloids were isolated by continuous extraction. This crude extract was then separated into phenolic and non-phenolic compounds by shaking the chloroform solution with 5% NaOH. The nonphenolic fraction was further separated by treating the brown oil obtained with acetone. A crystalline, acetone insoluble compound, $C_{18}H_{27}N_3O_3$ was separated by filtration. The acetone soluble fraction was further purified by alumina column chromatography, and subsequent vacuum distillation of the resultant oil allowed the isolation of a $C_{35}H_{51}NO_7$ alkaloid. No structural assignments have yet been proposed for these two nonphenolic compounds.

The phenolic fraction was separated into the two major alkaloids present by preparative TLC. The first compound so isolated, m.p. 127–129°, was shown to be optically inactive. From mass spectrometry, the molecular formula, $C_9H_{13}NO$, was established. The i.r. spectrum indicated the presence of a secondary amine, (3378 cm^{-1}), a hydroxy group (2900 cm^{-1}) and an aromatic system (1625 cm^{-1}). The u.v., λ_{max} 205, 227, 277 nm (ϵ 5, 192, 1550, 1416) displayed the expected bathochromic shift on the addition of NaOH. This data, taken in conjunction with the mass spectroscopic fragmentation pattern which is shown on page 2 (Fig. 1), clearly indicated that this $C_9H_{13}NO$ alkaloid was *N*-methyltyramine (I), a compound which has previously been synthesized,[5] and has been isolated from *Trichocereus schickendantzii* (Web) Br. and R.[6] The second phenolic compound, m.p. 105–108°

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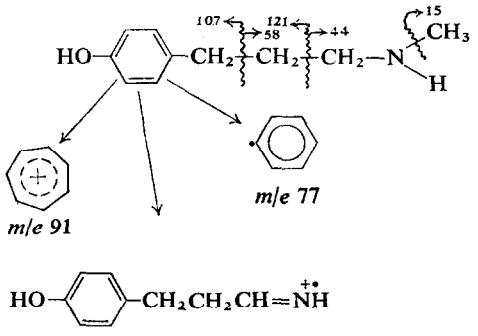
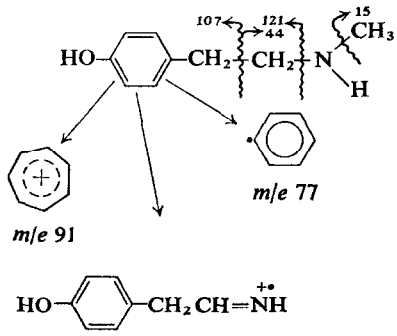
N-METHYLHOMOTYRAMINE (II)



m/e 149

m/e	Found	Calculated	Formula
165	165·1162	165·1154	$C_{10}H_{15}NO$
149	149·0841	149·0841	$C_9H_{11}NO$
121	121·0645	121·0653	C_8H_9O

N-METHYLTYRAMINE (I)



m/e 135

m/e	Found	Calculated	Formula
151	151·1003	151·0997	$C_9H_{13}NO$
121	121·0650	121·0653	C_8H_9O

FIG. 1. COMPARISON OF THE MASS SPECTRA OF *N*-METHYLHOMOTYRAMINE (II) AND *N*-METHYLTYRAMINE (I). ACCURATE MASS MEASUREMENTS WERE DETERMINED FOR THE MASSES LISTED.

was also optically inactive, and from elemental analysis and mass spectral data, a $C_{10}H_{15}NO$ molecular formula was established. The NMR spectrum showed a broad singlet at δ 8·0 (exchangeable with deuterium oxide; phenolic group), an A_2B_2 quartet ($J = 6$ Hz, four aromatic protons) appearing between δ 7·0–6·64, a three proton signal at 2·66 (*N*-methyl) a six proton signal at δ 2·36 ($—CH_2—CH_2—CH_2$) and a one proton and deuterium oxide exchangeable signal at δ 2·1 (—NH). Figure 1 shows a comparison of the mass spectral fragmentation observed for the $C_{10}H_{15}NO_3$ alkaloid and for *N*-methyltyramine. From all the available data, it is clear that the $C_{10}H_{15}NO_3$ alkaloid is the higher homologue of *N*-methyltyramine, namely *N*-methylhomotyramine (II), which to our knowledge has not previously been isolated from plants.

EXPERIMENTAL

M.ps are uncorrected. Mass spectral data on the phenolic compounds were obtained on a CEC 21-110B spectrometer and the mass spectral data of the non-phenolic compound on an AEI MS-9 spectrometer. NMR data were obtained on a Varian A-60 instrument in $CDCl_3$ with TMS as internal standard. U.v. spectra were determined in methanol and i.r. in nujol.

Extraction of Plant Material

In a typical experiment, 3 kg of dried and milled plant material from *Croton humilis* which was collected on Long Mountain, Mona, Jamaica in August 1967, was percolated with 2% tartaric acid until the resulting extract (20 l.) gave no precipitate with Mayer's reagent. The acid extract was concentrated on a Towers cyclic evaporator to about 600 ml, basified with 25% NH_4OH and continuously extracted with $CHCl_3$ (60 hr). The crude alkaloid so obtained was 0·4% by wt. of the dried plant material.

Separation of Phenolic Compounds from Non-phenolic

The crude alkaloid (12·5 g) was dissolved in 200 ml $CHCl_3$ and extracted with 250 ml 5% NaOH. The $CHCl_3$ layer was washed with water (3 × 50 ml) and the washings added to the alkali solution. Removal of $CHCl_3$ under *vacuo* gave 2·7 g of non-phenolic material. The phenolic compounds present in the alkali solution were extracted into $CHCl_3$ after first adjusting the solution to pH 3 with HCl and then to pH 7 with NH_4OH. Removal of the organic solvent gave 3·9 g of phenolic alkaloids.

Separation of Phenolic Alkaloids

The alkaloid mixture (1 g) was separated on silica TLC plates with $CHCl_3$–MeOH (1:1, v/v). The alkaloid bands were detected by using the side strip spraying technique with the reagent platinum iodide as the detecting reagent. The separated bands were scraped off and continuously extracted with methanol to recover the alkaloidal material.

N-Methylhomotyramine

The major band yielded 108 mg of light brown crystals. These were purified on a short alumina column eluted with EtOAc. This produced white crystals (14·1 mg), m.p. 105–108°, ν_{max}3400, 1610 cm^{-1}, λ_{max}205, 222 and 277 nm (ϵ 5, 030, 7, 019 and 1, 856). M^+ = 165·1162. Calculated for $C_{10}H_{15}NO_3$:165·1154. (Found: C, 72·48; H, 9·18; N, 8·73; O, 9·80. $C_{10}H_{15}NO$ requires C, 72·69; H, 9·15; N, 8·48; O, 9·68%.)

N-Methyltyramine

The second largest band from the TLC separation gave crystals from $CHCl_3$ m.p. 127–129°. (Literature, m.p. 130°.)[5] The u.v., λ_{max} 205, 227, 277 (ϵ 5, 192, 7, 550, 1, 416). M^+ = 151·1003. Calculated for $C_9H_{13}NO_3$. 151·0997.

Separation of Non-phenolic Alkaloids

$CHCl_3$ (10 ml) was added to the non-phenolic fraction (0·5 g) and a waxy solid separated out and was filtered off. The $CHCl_3$ was removed, and acetone (25 ml) added to the brown gum. A white crystalline material remaining undissolved had m.p. 198–200° and was optically inactive, λ_{max}209 nm (ϵ 7, 770), ν_{max}3401, 1661, and 1616 cm^{-1}. The mass spectrum showed (M^+) = 333·204. Calculated for $C_{18}H_{27}N_3O_3$:333·205. The base peak appeared at *m/e* 213, and other major peaks at *m/e* 316, 302, 259, 188 and 104. (Found: C, 63·84; H, 8·16; O, 14·40; N, 12·60. $C_{18}H_{27}N_3O_3$ requires C, 63·92; H, 8·09; O, 14·66; N, 12·91%). The acetone soluble brown gum was further purified on an alumina column packed in EtOAc. The first four fractions which were eluted with EtOAc–$CHCl_3$ (3:1, v/v) showed a single spot on TLC in several systems and were combined. The oil so obtained was distilled at 163° under reduced pressure and the product analysed. (Found: C, 70·55; H, 8·82; N, 2·44; O, 18·67. $C_{35}H_{51}NO_7$ requires C, 70·32; H, 8·6; N, 2·34; O, 18·74%).

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LABIATAE

ISOLATION AND IDENTIFICATION OF ALKANES FROM THREE TAXA OF *MONARDA*

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Abstract—Nine *n*-alkanes were isolated and identified from the herb of *Monarda punctata* var. *maritima*, seven from *Monarda punctata* var. *fruticulosa*, and five from *Monarda fistulosa* var. *mollis*. These alkanes ranged from $C_{27}H_{56}$ to $C_{35}H_{72}$. In all three taxa, the odd numbered alkanes were generally present in larger amount than the even numbered ones.