

## THE CHEMISTRY OF THE WESTERN AUSTRALIAN RUTACEAE\*

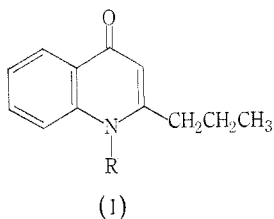
### III. THE ALKALOIDS OF BORONIA TERNATA ENDL.

By A. M. DUFFIELD† and P. R. JEFFERIES†

In Western Australia, *Boronia* (Rutaceae) is represented by about 50 species, of which a few occur in the Kimberley District, but the majority are found in regions of the South-West Province, where the annual rainfall exceeds 15 in., and with rare exception penetrate the interzone area. *Boronia ternata* Endl. is the most common exception and hence in our study of the arid and semi-arid Rutaceae we have carried out a preliminary examination of its constituents.

Extraction of the leaves with ether slowly removed an alkaloid mixture from which a base,  $C_{15}H_{17}O_3N$ , and a smaller quantity of skimmianine were obtained. The former had infrared absorption at  $1740\text{ cm}^{-1}$  (ester) and  $1640\text{ cm}^{-1}$  (conjugated carbonyl) and these results taken together with ultraviolet measurements in neutral and acidic solution suggested that the base was a 4-quinolone. To obtain more efficient extraction of the plant material methanol was used as a solvent but yielded a different base,  $C_{12}H_{13}ON$ , which behaved similarly, as a 4-quinolone, and was identified as 2-n-propyl-4-quinolone (I;  $R = H$ ) by permanganate oxidation to *N*-butyrylanthranilic acid.

The probability that (I;  $R = H$ ) was an artifact produced in the isolation procedure was supported by the observation that treatment of the original base with alkali produced formaldehyde, acetic acid, and (I;  $R = H$ ). Similarly, treatment with hydrogen chloride gave the hydrochloride of (I;  $R = H$ ). These results are consistent with the fission of an acetoxymethyl group located at positions 1 or 3 or vinyllogously. However failure to detect an active hydrogen atom excludes all possibilities except (I;  $R = CH_2OAc$ ). This structure is supported by n.m.r. measurements which were made at 60 Mc/s using tetramethylsilane as internal standard in deuterochloroform solution. A triplet centred at 9.1 ( $\tau$  scale, 3H), a multiplet at 8.3 (2H), and a triplet at 7.25 (2H) correspond



to the propyl group. The acetate group absorbs at 7.85 (3H) and the associated methylene group at 3.84 (2H). A sharp line at 3.81 (1H) may be assigned to the hydrogen at position 3. The other aromatic protons give rise to a multiplet centred at 2.50 (3H) and the proton at position 5, adjacent to the carbonyl group, an eight line signal centred at  $\sim 1.6$  with coupling constants of  $\sim 8$ ,  $\sim 2$ , and  $\sim 1$  c/s as expected for *ortho*-, *meta*-, and *para*-couplings. The signals were unaltered by the addition of deuterium oxide. As a comparison the spectrum of (I;  $R = H$ ) was

\* Manuscript received October 1, 1962.

† Chemistry Department, University of Western Australia, Nedlands, W.A.

measured and showed the expected propyl resonances together with analogous aromatic signals at 2.5 and 1.6. The acidic proton resonates as a broad band at  $\sim -3.1$ , the position varying with concentration and the assignment is confirmed by removal of the signal by exchange with deuterium oxide.

Simple quinolines, known to occur in the Rutaceae, are the minor Angostura alkaloids which include 2-methylquinoline,<sup>1</sup> and 2-n-amyl-4-methoxyquinoline.<sup>2</sup> Related substances have been obtained from culture filtrates of *Pseudomonas* spp. and of these 2-heptyl, 2-nonyl, and 2-undecyl-4-hydroxyquinoline-*N*-oxides may be mentioned.<sup>3</sup> The occurrence of the 2-n-propyl group in (I; R = H) thus completes the series of odd-numbered homologous chains up to undecyl. Cornforth and James<sup>3</sup> account for the occurrence of odd-numbered chains by biogenesis via an anthranilic ester and a  $\beta$ -ketoacid.

### Experimental

Melting points are uncorrected. Light petroleum had b.p. 56–60°C. Ultraviolet spectra were recorded on a Unicam SP 700 recording spectrophotometer. Precise infrared frequencies were determined with a Grubb–Parsons single-beam spectrophotometer and routine spectra were recorded with a Perkin–Elmer Infracord model 137. Analyses were performed by Dr. K. W. Zimmermann, C.S.I.R.O. Microanalytical Laboratory, Melbourne. All identities were confirmed by comparison of infrared spectra.

(a) *Ether Extraction of Boronia ternata*.—Crushed leaves and terminal branches (3.9 kg) were exhausted with ether (3  $\times$  5 l.) during 5 days at room temperature. Extraction of the ethereal solution with 2N HCl, basification of the aqueous phase (NaHCO<sub>3</sub>), and isolation with ether gave a crude alkaloid fraction (2.7 g). Dissolution in benzene (30 ml), chromatography on neutral alumina (15 g), and elution with benzene and benzene–methanol (19:1; 100 ml) afforded crystalline material (1.7 g). Crystallization from benzene–light petroleum gave 1-acetoxymethyl-2-n-propyl-4-quinolone as prisms, m.p. 112°C (Found: C, 69.6; H, 6.4; N, 5.4; OAc, 17.0; Act. H, 0.06%. Calc. for C<sub>15</sub>H<sub>17</sub>NO<sub>3</sub>: C, 69.5; H, 6.6; N, 5.4; 1  $\times$  OAc, 16.6; 1  $\times$  Act. H, 0.39%). The ultraviolet absorption spectrum (methanol) had  $\lambda_{\max}$ . 208, 236, 314, 328 with shoulders at 270 and 279 m $\mu$ ; extinctions: 18,200, 28,200, 15,500, 17,400, 4300, and 4700 respectively. In the infrared (CS<sub>2</sub>) absorption bands were noted at 1740, 1640, 1360, 1300, 1260, 1240 (shoulder), 1220 (shoulder), 1210, 1190, 1150, 1070, 1040, 1020, 960, 765, 755, and 670 cm<sup>-1</sup>.

Elution with benzene–methanol (9:1; 100 ml) and crystallization from benzene–light petroleum afforded a mixture of prisms and pale yellow needles. Manual separation and crystallization of the prisms (0.032 g) from benzene–light petroleum gave 1-acetoxymethyl-2-n-propyl-4-quinolone, m.p. and mixed m.p. 112°C. Crystallization of the needles (0.015 g) from methanol gave skimmianine as pale yellow needles, m.p. 175–176°C, undepressed on admixture with an authentic sample of m.p. 177°C.

(b) *Methanol Extraction of Boronia ternata*.—Dried milled leaves and terminal branches (9 kg) were exhausted with methanol (3  $\times$  7 l.) during 2 days at room temperature. The combined extracts were concentrated to 1.5 l. and added to 2N H<sub>2</sub>SO<sub>4</sub> with vigorous stirring. The solution was filtered, the filtrate basified (NaHCO<sub>3</sub>), and the crude bases (29 g) isolated with chloroform. Dissolution in chloroform and refractionation with acid gave 2-n-propyl-4-quinolone (4 g) which crystallized from benzene–light petroleum as needles, m.p. 166–168°C. (Camps<sup>4</sup> quotes m.p. 166°C) (Found: C, 76.8; H, 6.8; N, 7.5%. Calc. for C<sub>12</sub>H<sub>13</sub>NO: C, 77.0; H, 7.0; N, 7.5%).

<sup>1</sup> Späth, E., and Pikl, J. (1930).—*Mh. Chem.* **55**: 352.

<sup>2</sup> Späth, E., and Pikl, J. (1929).—*Ber. dtsch. Chem. Ges.* **62**: 2244.

<sup>3</sup> Cornforth, J. W., and James, A. T. (1956).—*Biochem. J.* **63**: 124.

<sup>4</sup> Camps, R. (1899).—*Arch. Pharm.* **237**: 659.

The ultraviolet absorption spectrum (methanol) had  $\lambda_{\text{max}}$ , 215, 236, 317, and 330 with a shoulder at 282  $\text{m}\mu$ ; extinctions: 24,800, 31,100, 11,800, 11,200, and 3900 respectively. The *hydrochloride* prepared in chloroform solution crystallized from chloroform-light petroleum as needles, m.p. 214–216°C (Found: C, 64.8; H, 6.3; N, 6.0; Cl, 15.1%. Calc. for  $\text{C}_{12}\text{H}_{14}\text{NOCl}$ : C, 64.4; H, 6.3; N, 6.3; Cl, 15.8%). The chloroplatinate crystallized from water as orange needles, m.p. 226–227°C (decomp.) (Camps<sup>4</sup> quotes m.p. 228°C (decomp.)). 2-n-Propyl-4-quinolone was methylated with diazomethane in ether-methanol overnight. The product was characterized by the preparation of its picrate which crystallized from ethanol as *yellow needles*, m.p. 195°C (Found: C, 53.1; H, 4.3; N, 12.9%. Calc. for  $\text{C}_{19}\text{H}_{18}\text{N}_4\text{O}_8$ : C, 53.0; H, 4.2; N, 13.0%).

*Permanganate Oxidation of 2-n-Propyl-4-quinolone*

2-n-Propyl-4-quinolone (0.5 g) was dissolved in water (50 ml) containing KOH (0.7 g) and  $\text{KMnO}_4$  (1.5 g) added. The reaction mixture was heated on the steam-bath during 4 hr, cooled, acidified, and reduced with sodium metabisulphite. Extraction with chloroform and fractionation with 8%  $\text{NaHCO}_3$  solution afforded *N-butyrylanthranilic acid* (0.15 g) which crystallized from benzene-light petroleum as needles, m.p. 117–118°C (Found: C, 63.8; H, 6.2; N, 6.9%. Calc. for  $\text{C}_{11}\text{H}_{13}\text{NO}_3$ : C, 63.8; H, 6.3; N, 6.8%). *N-Butyrylanthranilic acid* was synthesized from *n*-butyryl chloride (0.12 g) in ether (10 ml) and addition of anthranilic acid (0.25 g). After standing at room temperature for 20 min the precipitate (0.145 g) was collected and crystallized from benzene-light petroleum as needles, m.p. 117–118°C, undepressed on admixture with the same described above from oxidation of 2-n-propyl-4-quinolone.

(c) *Hydrolysis of 1-Acetoxyethyl-2-n-propyl-4-quinolone*.—(i) *Alkaline Hydrolysis*. 1-Acetoxyethyl-2-n-propyl-4-quinolone (0.250 g) was dissolved in water (30 ml) containing KOH (1 g). Distillation into a solution of dimedone (0.1 g) in water (50 ml) precipitated formaldehyde dimedone (0.08 g) which crystallized from aqueous methanol as fine needles, m.p. and mixed m.p. 187°C. The reaction solution was acidified, distilled, and the distillate made alkaline and concentrated to approximately 1 ml, and the *p*-bromophenacyl ester prepared in the usual manner. Crystallization from aqueous ethanol gave *p*-bromophenacyl acetate as plates, m.p. and mixed m.p. 85°C. The reaction mixture was basified with  $\text{NaHCO}_3$  and the precipitate (0.13 g) crystallized from aqueous methanol as needles, m.p. 166–168°C, undepressed on admixture with the sample of 2-n-propyl-4-quinolone described in (b).

1-Acetoxyethyl-2-n-propyl-4-quinolone (0.026 g) in methanol (4 ml) was treated with 8%  $\text{NaHCO}_3$  solution (1 drop) during 16 hr at room temperature. After dilution with water the product (0.017 g) was isolated with chloroform and crystallized from aqueous methanol as needles, m.p. 165–166°C, undepressed on admixture with an authentic sample of 2-n-propyl-4-quinolone of m.p. 166–168°C.

(ii) *Acid Hydrolysis*. A solution of 1-acetoxyethyl-2-n-propyl-4-quinolone (0.082 g) in ether (15 ml) at 0°C was saturated with dry HCl. Crystallization of the precipitate (0.098 g) from methanol-acetone gave needles, m.p. 211–213°C, undepressed on admixture with an authentic sample of 2-n-propyl-4-quinolone hydrochloride of m.p. 214–216°C.

We wish to thank Mr. C. A. Gardner and Mr. R. D. Royce for identification of the plant sample and Dr. J. N. Shoolery of Varian Associates for the n.m.r. spectrum of 1-acetoxyethyl-2-n-propyl-4-quinolone.