

ISOLATION OF METHYL HOMOHYGRINATE FROM *SOLANUM STURTIANUM* (SOLANACEAE)

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Abstract

Methyl homohygrinate has been isolated from the tops of *Solanum sturtianum* F. Muell.

The genus *Solanum* contains 1225 species¹ of which 60–70 are endemic to Australia,² and 26 of the latter have been recorded in Western Australia.³ *Solanum sturtianum* F. Muell. is a small shrub which grows in the Northern and Ereman Provinces of this State. No steroidal alkaloids, which are characteristic constituents of the genus,⁴ have yet been isolated from the plant but a low yield of an ether-soluble base was obtained.

The base was isolated as the picrate, m.p. 135–136°, which analysed for $C_8H_{15}NO_2$, $C_6H_3N_3O_7$, and was weakly dextrorotatory. The n.m.r. and infrared spectra of the base suggested that it was the methyl ester of either an *N*-methylpiperidinecarboxylic acid or of an *N*-methylpyrrolidineacetic acid.

Of the possible structures, methyl *N*-methylisonipecotate (1) was rejected, as the picrate of this substance has been reported⁵ to melt at 151–153°. However, methyl *N*-methylnipecotate (2) could not be eliminated in this way for the picrate of this substance has been reported by different authors^{6,7} to melt at 132° and 141–143°. The picrates of methyl *N*-methylpipecolate (3) and methyl homohygrinate (4) do not appear to have been prepared previously.

The picrates of methyl *N*-methylnipecotate (2) and methyl *N*-methylpipecolate (3) were prepared by standard methods⁸ but neither of these substances was identical with the picrate of the base isolated from *S. sturtianum*.

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¹ Willis, J. C., "A Dictionary of the Flowering Plants and Ferns," 6th Edn (University Press: Cambridge 1960).

² Burbidge, N. T., "Dictionary of Australian Plant Genera" (Angus & Robertson: Sydney 1963).

³ Beard, J. S. (Ed.), "Descriptive Catalogue of West Australian Plants" (King's Park Board: Perth).

⁴ Willaman, J. J., and Schubert, B. G., Tech. Bull. U.S. Dep. Agric., 1961, No. 1234; Willaman, J. J., and Li, H.-L., *Lloydia*, 1970, **33** (3A), 1.

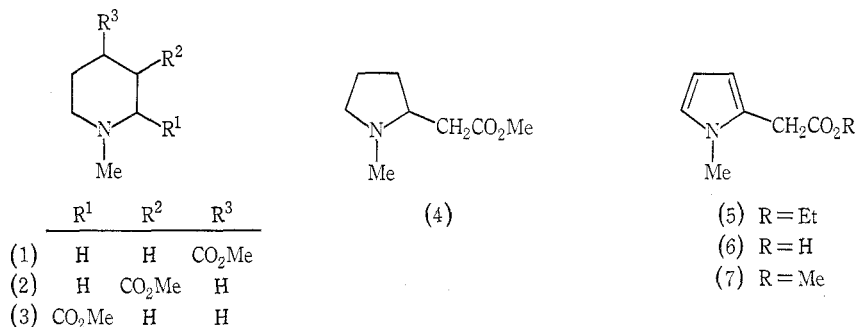
⁵ Grob, C. A., and Renk, E., *Helv. chim. Acta*, 1954, **37**, 1672.

⁶ Stoll, A., Rutschmann, J., and Schlientz, W., *Helv. chim. Acta*, 1950, **33**, 375.

⁷ Okumura, K., Tanaka, T., Saito, S., Kugita, H., and Sugimoto, N., *Chem. Abstr.*, 1959, **53**, 10214.

⁸ Sperber, N., Sherlock, M., Papa, D., and Kender, D., *J. Am. chem. Soc.*, 1959, **81**, 704.

Methyl homohygrinate was prepared by an adaptation of the method used by Sohl and Shriner⁹ to obtain the corresponding ethyl ester. Treatment of *N*-methylpyrrole with ethyl diazoacetate afforded (5) which was hydrolysed to (6).¹⁰ Re-esterification of (6) with diazomethane then yielded (7). Although treatment of *N*-methylpyrrole with methyl diazoacetate would presumably yield (7) directly, the circuitous route was chosen because methyl diazoacetate has been reported¹¹ to be much more likely to explode than the ethyl ester. Reduction of (7) then yielded racemic (4), the picrate of which proved to be virtually identical with the picrate of the base obtained from *S. sturtianum*.



Experimental

General experimental procedures which have been described previously¹² also apply to the present work. Voucher specimens (JRC 620515) of the plant material have been lodged in the Western Australian Herbarium, Perth.

Extraction of *S. sturtianum*

Tops were collected from flowering shrubs growing 63 miles south of Onslow in May 1962. The milled, air-dried plant (3 kg) was extracted exhaustively with methanol at room temperature, the extracts were concentrated under reduced pressure, and the residue (c. 500 ml) was partitioned between ether (1.5 l.) and water (1.0 l.). Only a trace (25 mg) of basic residue was isolated from the ether extract. The aqueous layer was basified with aq. NH₃ (*d* 0.88) and shaken exhaustively with chloroform. The chloroform solution was extracted with 5% aq. HCl. The acid extracts were basified and re-extracted with chloroform, whereupon the crude alkaloid was obtained as a reddish resin (19.7 g). A portion (13.8 g) of this product was extracted with ether (6 × 30 ml). Evaporation of the extract afforded a brown gum (5.5 g) which was redissolved in ether and applied to a column of neutral alumina (120 g, activity II). Elution of the column with ether afforded the alkaloid as an oil (0.41 g). When a solution of this product in methanol was treated with a saturated methanolic solution of picric acid the *picrate* of methyl homohygrinate was obtained as yellow plates, m.p. 135–136° (Found: C, 43.7; H, 4.7; N, 14.4. C₁₄H₁₈N₄O₉ requires C, 43.5; H, 4.7; N, 14.5%). [α]_D²⁰ + 1° (*c*, 1.3 in acetone).

Decomposition of the *picrate* with aq. NH₃ and extraction with chloroform afforded methyl homohygrinate as an oil. $\nu_{\max}$ (CHCl₃): 1735s cm⁻¹ (ester CO). N.m.r. spectrum (CDCl₃): two prominent singlet signals at δ 3.70 (OCH₃) and 2.34 (NCH₃); the remainder of the spectrum was composed of a complex multiplet from δ 3.20 to 1.23.

⁹ Sohl, W. E., and Shriner, R. L., *J. Am. chem. Soc.*, 1933, **55**, 3828.

¹⁰ Nenitzescu, C. D., and Solomonica, E., *Ber. dt. chem. Ges.*, 1931, **64**, 1924.

¹¹ Searle, N. E., *Org. Synth.*, 1963, Coll. Vol. IV, 424.

¹² Cannon, J. R., Joshi, K. R., Meehan, G. V., and Williams, J. R., *Aust. J. Chem.*, 1969, **22**, 221.

Methyl N-Methylnipecotate (2) and Methyl N-Methylpipecolate (3)

(i) Methyl *N*-methylnipecotate (2) was prepared by reductive methylation of methyl nicotinate.⁸ The picrate of methyl *N*-methylnipecotate crystallized from ethanol as yellow needles, m.p. 129–130° (lit.⁶ 132°; lit.⁷ 141–143°). The mixed m.p. with the picrate of the base isolated from *S. sturtianum* was depressed to 110–115° (Found: C, 43.6; H, 4.7; N, 14.6. Calc. for $C_{14}H_{18}N_4O_9$: C, 43.5; H, 4.7; N, 14.5%).

(ii) Methyl *N*-methylpipecolate (3) was prepared by reductive methylation of methyl picolinate.⁸ The picrate of methyl *N*-methylpipecolate crystallized from ethanol as yellow needles, m.p. 158–159°. The mixed m.p. with the picrate of the base isolated from *S. sturtianum* was depressed to 124–135° (Found: C, 43.7; H, 4.7; N, 14.5. $C_{14}H_{18}N_4O_9$ requires C, 43.5; H, 4.7; N, 14.5%).

Methyl Homohygrinate (4)

Ethyl *N*-methyl-2-pyrrolyacetate⁹ (5) was converted into *N*-methyl-2-pyrrolyacetic acid (6) which crystallized from ether–light petroleum as needles, m.p. 113–114° (lit.¹⁰ 112°). A solution of diazomethane (c. 1.5 g) in ether (25 ml) was added to a solution of *N*-methyl-2-pyrrolyacetic acid (3.5 g) in ether. The solution was evaporated and the residue was distilled whereupon methyl *N*-methyl-2-pyrrolyacetate was obtained as an oil (2.8 g), b.p. 80–85°/2 mm (Found: C, 62.7; H, 7.1. $C_8H_{11}NO_2$ requires C, 62.7; H, 7.2%).

A solution of methyl *N*-methyl-2-pyrrolyacetate (2.8 g) in ethanol (20 ml) containing acetic acid (2 ml) was hydrogenated in the presence of a platinum catalyst (0.15 g) at 1200 p.s.i. at room temperature. The solution was then filtered and evaporated under reduced pressure. The residue was treated with saturated aq. K_2CO_3 solution and extracted with ether. Distillation then afforded methyl homohygrinate (4) as an oil (2.0 g), b.p. 80–85°/7 mm (Found: C, 61.2; H, 9.4; N, 8.7. $C_8H_{15}NO_2$ requires C, 61.1; H, 9.6; N, 8.9%). The picrate of methyl homohygrinate crystallized from ethanol as yellow plates, m.p. 135–136° which was not depressed on admixture with the picrate of the base obtained from *S. sturtianum*. The infrared spectra (KBr) of the two samples were identical (Found: C, 43.7; H, 4.7; N, 14.8. $C_{14}H_{18}N_4O_9$ requires C, 43.5; H, 4.7; N, 14.5%).

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