

## QUATERNARY AMMONIUM SALTS DERIVED OF (—) LUPININE

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Two levorotatory N-epimeric N-ethoxycarbonylmethyl lupininium iodides were prepared from (—) lupinine. One of them underwent further isomerisation to a third, dextrorotatory compound. Configurations thereof should be established later on.

A new method to establish configurations of N-trisubstituted amino alcohols has been outlined by one of us (G. F.) and his co-workers [1], [2] involving addition of ethyl iodoacetate followed by cyclisation which may lead either to a lactone or to the quaternary salt of the corresponding N-acetic acid.

It was attempted to extend this method to the field of C<sub>1</sub>-epimeric lupinines. The absolute configuration of (—) lupinine at the methylol-bearing carbon was determined by its unambiguous correlation with (—) 4-methylnonane [3]. However, the configuration of CH<sub>2</sub>OH with respect to nitrogen has been assigned to the epimers mainly by interpreting their chemical interconversions in terms of conformational analysis [4] or based upon infrared spectra [5] and dipole moment data [6] but no supporting chemical evidence has been presented yet at the beginning of our experiments.

(—) Lupinine formed on the action of ethyl iodoacetate two N-ethoxycarbonylmethyl lupininium iodides of different m. p.'s and optical rotatory data  $[\alpha]_D^{24} = -49,1^\circ$  and  $-84,8^\circ$ , resp.), depending upon quaternisation

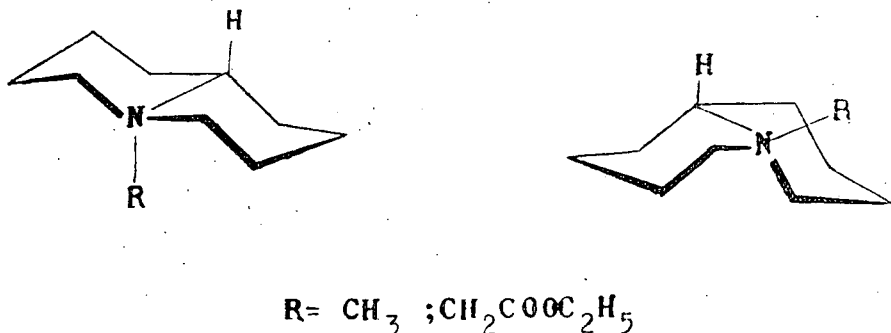


Fig. 1

performed at 25° or at 80°. These obviously represent the two N-(9)-epimeric *cis* and *trans* mono-aza decaline derivatives (Fig. 1). The formation of both

theoretically possible N-epimeric methiodides has been recorded earlier by SCHÖPF and his co-workers in the case of 1<sup>1</sup>,1-diphenyl-lupinine [7].

The salt of lower rotatory value underwent further change when the aqueous solution was heated in a sealed tube at 100° for several hours affording a third quaternary ester salt  $[\alpha]_D^{24} = +16,7^\circ$  [8].

These ester salts have been converted into the betaines and treated, in turn, with hydriodic and hydrobromic acid resp., furnishing the ammonium halides of the appropriate N-acetic acids but no lactonisation of the latter occurred.

At this stage of the work it has been anticipated by GALINOVSKY and NESVADBA [9] who succeeded in rearranging O-tosyl lupinine into the tricyclic quaternary tosylate of an azetidine derivative, supporting thereby the *cis*-relationship of CH<sub>2</sub>OH-group to nitrogen in the natural lupinine molecule. This statement seems to be consistent with physico-chemical evidence. Accordingly, attempts to lactonise any of the N-carboxymethyl-lupinium salts in order to allot a configuration to the carbon no. 1. with respect to nitrogen have considerably lost in interest.

The determination of configurations of the nitrogen atom in these quaternary salts, on the other hand, belongs to and has to be fitted in with the frames of a different research plan being in progress [1], [2], [10] in this Laboratory since a few years.

### Experimental

#### *N*-ethoxycarbonylmethyl-1-hydroxymethyl (8H)-pyridocolinium iodides

(a) *At room temperature.* 1,07 g (0,006 mole) (—) lupinine was dissolved in 3 ml dry benzene and 1,284 g (0,006 mole) ethyl iodoacetate added. Separation of the ammonium salt set in instantaneously, while on standing for 62 hours at room temperature the mixture solidified. The crystals were filtered by suction and washed with dry ether. M. p. 154°.  $[\alpha]_D^{24} = -49,06$  (H<sub>2</sub>O, *c* = 1,591). Found: C 43,6; J- 32,9. C<sub>14</sub>H<sub>26</sub>O<sub>3</sub>NJ requires: C 43,8; H 6,8; J- 33,2%.

(b) *At 95°.* (—) Lupinine (0,354 g, 0,002 mole) was dissolved in dry ethanol (1 ml), benzene (3 ml) and 0,428 g (0,002 mole) ethyl iodoacetate added, to be heated, in turn, to 95° in a sealed tube for 22 hours. After standing for 43 hours at room temperature, the brownish coloured solution was evaporated to dryness; the residue triturated with dry acetone, the crystals filtered and washed. M. p. 148°—150°.  $[\alpha]_D^{24} = -84,76$  (H<sub>2</sub>O; *c* = 1,05). (Found: C 44,47; H 7,35; J- 33,2%.)

*Conversion of the iodide (a) into the »third« epimeric ammonium ester salt (c).*

0,15 g of lupinium salt (a), dissolved in 10 ml water was heated in a sealed tube to 95° for 24 hours. The faintly yellow coloured solution was evaporated to dryness to furnish a yellowish oil. On dissolving in dry ethanol it afforded after cooling nearly colourless needles, m. p.: 150°—152°.  $[\alpha]_D^{24} = +16,67^\circ$  (H<sub>2</sub>O; *c* = 1,5).

*N*-carboxymethyl-lupinium betaine (a). 1,532 g (0,004 mole) of the salt obtained from lupinine at room temperature was dissolved in 25 ml water. After addition of excess alkali-free silver oxide the mixture was shaken for 2 hours, filtered, decolourized (charcoal), the solution refluxed for 5 hours and

then evaporated to dryness. Recrystallisation of the remainder afforded hygroscopic needles, m. p.: 244°.  $[\alpha]_D^{25} = +9,91$  (H<sub>2</sub>O; c = 1,029). (Found: C 62,0; H 9,1. C<sub>12</sub>H<sub>21</sub>O<sub>3</sub>N requires: C 63,5; H 9,2%)

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This work represents a part of the research activity of this Institute outlined by one of us (G. F.) at the Annual Meeting of the German Chemical Society (Leipzig, October 23, 1954; cf. Tagungsber. 1954, pp. 138—157) and granted by the Hungarian Academy of Sciences.

Microanalyses have been performed by Misses K. LÁNG and R. MINÁROVICS.

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