The Senecio *Alkaloids. Part XI.* The Conversion of Rosmarinine into Senecionine and the General Structure of the* Senecio *Alkaloids.*

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Rosmarinine (III) readily gives a monotoluene-*p*-sulphonate (V) which on hydrolysis gives senecic acid and *epi*rosmarinecine. Refluxing (V) with pyridine causes elimination of toluene-*p*-sulphonic acid with the formation of senecionine. The action of thionyl chloride on (III) gives anhydrorosmarinine in which water is seemingly eliminated from the acid moiety.

IN Part X * it was shown that rosmarinecine was hydroxyplatynecine and could be prepared by the hydration of retronecine by way of its epoxide. Leisegang and Warren (*J.*, 1949, 486) assigned the complete structure for retrorsine (I); and with the general structure of the acids (cf. Kropman and Warren, *J.*, 1950, 700) and bases in mind, it seemed reasonable to assume that the acids were similarly orientated in the other *Senecio* alkaloids, *e.g.*, senecionine (II), rosmarinine (III), and platyphylline (IV). This assumption received some confirmation from the observation that the trihydroxy-base rosmarinecine (cf. Part X) formed only a dibenzoyl derivative as does the dihydroxy-base platynecine. This would indicate an analogous esterification of platyphylline and rosmarinine.

To test this concept attempts were made to dehydrate rosmarinine. Use of thionyl chloride gave anhydrorosmarinine (picrate, m. p. 243—246°), which gave rosmarinecine on hydrolysis, together with, probably, anhydrosenecic acid (3-methylhepta-2 : 5-diene-2 : 5-dicarboxylic acid).

Rosmarinine (III) readily gave the toluene-*p*-sulphonate ester (V). This readily gave senecic acid on hydrolysis; but the basic fission product after acetylation gave a picrate,

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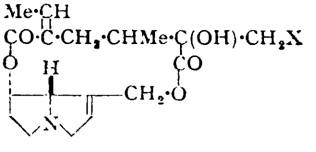
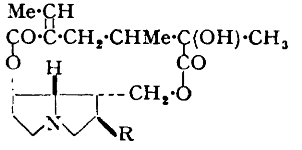
* Part X, preceding paper.

m. p. 143—144°, which was different from triacetylrosmarinecine picrate, m. p. 139—140° as well as from diacetylretronecine picrate, m. p. 143—144°. It is seemingly *epi*-rosmarinecine which would be expected from the inversion during the hydrolysis of the toluene-*p*-sulphonyl group.

Rosmarinine toluene-*p*-sulphonate in refluxing dry pyridine lost toluene-*p*-sulphonic acid, to yield the expected senecionine, m. p. 234—236°, which was characterised by identification of retronecine and senecic acid on hydrolysis as well as by comparison with an authentic specimen.



(I) : X = OH. Retrorsine (β-longilobine)
(II) : X = H. Senecionine



(III) : R = OH. Rosmarinine
(IV) : R = H. Platyphylline
(V) : R = *p*-$Me{\cdot}C_6H_4{\cdot}SO_3$

An authentic specimen of senecionine was prepared from *Senecio squalidus* (cf. Barger, *J.*, 1936, 742; Koekemoer and Warren, *J.*, 1951, 66), collected in May in North London. The plant contained 0·025% of senecionine and 0·037% of senecionine *N*-oxide, showing that our previous conclusion with regard to the occurrence of the *Senecio* alkaloids also as *N*-oxides was applicable to senecionine and to *Senecio* species growing in temperate climates.

Apart from the formation and reduction of the alkaloid *N*-oxides, the preparation of senecionine from rosmarinine is the first example of the conversion of one complete *Senecio* alkaloid into another. These results establish the structure of senecionine (II), rosmarinine (III), and platyphylline (IV). The structure of integerrimine, shown by Kropman and Warren (*J.*, 1950, 700) to be the *trans*-form of senecionine, follows, so that the structures of five *Senecio* alkaloids are now established. All occur in the plant also as their *N*-oxides (cf. Koekemoer and Warren, *loc. cit.*).

The structures advanced for the different alkaloids reveal a close similarity (cf. earlier Parts of this series). The structures of the other *Senecio* alkaloids will doubtless conform to the same general carbon skeleton.

EXPERIMENTAL

Formation of Toluene-p-*sulphonate Ester of Rosmarinine.*—Rosmarinine (2 g., 1 mol.) in redistilled dry pyridine (15 ml.) at 0° was added to toluene-*p*-sulphonyl chloride (2·2 g., 2 mol.) in cold pyridine (10 ml.) at such a rate that the temperature did not exceed 0°. After 72 hr. at 4° the slightly reddish solution was poured into cold 5N-ammonia (75 ml.) and extracted with ether. The extract was washed with a little water, dried (Na_2SO_4), and evaporated, to yield a white solid (2·5 g.), m. p. 114—118°. After complete removal of pyridine in a vacuum-desiccator the solid was crystallised five times from 50% ethanol to yield the *ester* as needles, m. p. 120° (Found : C, 58·8; H, 6·2; N, 2·5; S, 6·3. $C_{25}H_{33}O_8NS$ requires C, 59·1; H, 6·55; N, 2·8; S, 6·3%). Chloroform extraction failed to yield unchanged starting material.

Hydrolysis of Rosmarinine Toluene-p-*sulphonate.*—The sulphonate (1·5 g., 1 mol.), suspended in water (50 ml.), was heated with hydrated barium hydroxide (3 g.) at 100° for 2 hr., cooled and made acid to Congo-red with 2N-hydrochloric acid (7·5 ml.). Extraction with ether (5 × 40 ml.) yielded after washing, drying, etc., 0·42 g. of crude solid, which after recrystallisation from ethyl acetate had m. p. 145—147° alone or mixed with senecic acid. The acid solution remaining was basified with solid barium hydroxide and evaporated to dryness under reduced pressure. Extraction of the powdered dry residue with boiling chloroform yielded 100 mg. of hygroscopic, somewhat discoloured, base which, after acetylation, yielded an oil whose *picrate*, m. p. 143—144°, on admixture with triacetylrosmarinecine picrate, m. p. 139—140°, and diacetylretronecine picrate, m. p. 143—144°, respectively, gave large m. p. depressions (Found : C, 45·5; H, 4·2; N, 11·2. $C_{20}H_{24}O_{13}N_4$ requires C, 45·5; H, 4·6; N, 10·6%).

Senecionine from Rosmarinine Toluene-p-*sulphonate.*—The toluene-*p*-sulphonate (400 mg.) was refluxed for 3 hr. with dry pyridine (7 ml.), cooled, poured into 5N-aqueous ammonia

(50 ml.), and extracted with ether. The ether solution gave a small amount of crystalline material, m. p. 230—232°. Extraction with chloroform yielded more material of the same m. p. The combined solid residues (180 mg.), contaminated with a little gummy material, were washed with cold acetone and recrystallised twice from ethanol to yield senecionine as monoclinic prisms, m. p. 234—236° undepressed on admixture with senecionine from *Senecio squalidus* (Found : C, 64·4, 64·4; H, 7·2, 7·6; N, 4·1, 4·3. Calc. for $C_{18}H_{25}O_5N$: C, 64·5; H, 7·5; N, 4·2%). Hydrolysis of this senecionine gave senecic acid, m. p. 145—147°, and retronecine, identified as diacetylretronecine picrate, m. p. 143—144°.

Senecionine from S. squalidus.—The dried and ground *S. squalidus* (1 kg.) collected in May in North London was extracted as described by Koekemoer and Warren (*J.*, 1951, 66). The extraction gave senecionine (0·25 g.) directly and an additional quantity (0·37 g.) after reduction.

Anhydrorosmarinine.—Rosmarinine (2 g.) was treated at 0° with freshly distilled thionyl chloride (8 ml.) and then heated for 3 hr. under reflux. Excess of reagent was removed under reduced pressure, and the residue treated with cold dilute hydrochloric acid and freed from resins by extraction with chloroform. The solution was basified with sodium carbonate and extracted with chloroform; this extract gave an oil which solidified in a vacuum. This solid which was readily soluble in most organic solvents gave with picric acid, and after several crystallisations from ethanol, *anhydrorosmarinine picrate* as yellow needles, m. p. 243—246° (Found : C, 51·05; H, 4·9; N, 9·5. $C_{24}H_{28}O_{12}N_4$ requires C, 51·05; H, 5·0; N, 9·9%).

The anhydrorosmarinine (1·5 g.) was refluxed with sodium methoxide, prepared from sodium (1 g.), for 6 hr. The solution was acidified with hydrochloric acid and evaporated to dryness in a vacuum. The solid was ground with sodium carbonate and extracted (Soxhlet) with acetone to yield rosmarinecine.

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