(0.1 mm) (air bath)], giving a distillate (19 mg) which was shown to be VII by means of superimposability of its infrared spectrum with that determined from 4-oxosparteine prepared by partial catalytic hydrogenation of multiflorine.

Registry No.—III, 529-80-6; V, 10349-34-5; V methiodide, 10380-52-6; VII, 10349-35-6; 4-oxosparteine monoperchlorate, 10380-53-7; XI, 10349-36-7.

Senecio Alkaloids. Synthesis of Decanecic Acids

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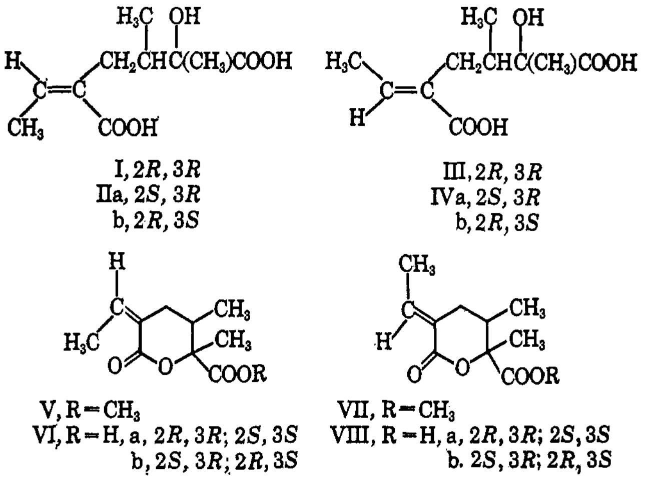
All diastereomers of senecic and integerrinecic acids have been synthesized. The physical constants of these acids are compared with those of reported necic acids assumed to be isomeric with senecic acid.

The preparation of the four racemates V and VII was recently reported[2,3] in a synthesis of senecic acid[4–7] (I) (Chart I) (*cis*-2*R*,3*R*-2-hydroxy-3-methyl-5-heptene-2,5-dicarboxylic acid) and the corresponding geometric isomer, integerrinecic acid (III). A number of decanecic acids, isomeric with senecic acid, have been reported[4] from different laboratories by the hydrolysis of various pyrrolizidine alkaloids. Some have been shown to be identical whereas others were found[8] to be mixtures, *e.g.*, hieracinecic acid. There is still some question as to the structures of platynecic and usaramoensinecic acids and formulations as diastereomers (C_2 epimers) of integerrinecic and senecic acids have been made or considered.[4,9,10] For this reason, the preparation of these stereoisomers from V and VII was carried out.

CHART I



The mixture of racemates represented by V and VII was separated[2] into three fractions, V, VIIa, and VIIb, by column chromatography. The VIIb racemate on hydrolysis yielded the diastereomeric racemate of integerrinecic acid. Since preliminary work on the resolution of this dicarboxylic acid racemate was not encouraging, it was converted to the acid lactone VIIIb, mp 154–156°, by evaporation with hydrochloric acid. This acid lactone racemate was resolved by means of brucine and the salt of the (+) isomer, mp 198–200°, gave on decomposition (+) VIIIb, mp 134–136°, $[\alpha]_D$ +10.8°. The salt of the (−) isomer, mp 187–189°, gave on decomposition (−) VIIIb, mp 134–136°, $[\alpha]_D$ −10.0°. A mixture (1:1) of these two enantiomers melted at 152–154°. These enantiomeric acid lactones, on hydrolysis, gave the corresponding dicarboxylic acids: (+) IV, mp 132–133°, $[\alpha]_D$ +26°; (−) IV, mp 132–133°, $[\alpha]_D$ −24°. A prepared mixture (1:1) of these enantiomers melted at 159–162°, reported[2] (±) IV mp 162–164°.

Because the V mixture of racemates could not be resolved by column chromatography and fractional crystallization of the dicarboxylic acid mixture formed by hydrolysis was not practical,[2] the photochemical isomerization of the accessible VII isomers was studied.

Initial experiments were made utilizing (±) VIIa and (±) VIIb. After exposure to a Hanovia lamp, separation by column chromatography gave 25–40% of the expected *cis* racemates. Hydrolysis of the two V racemates gave the corresponding dicarboxylic acid racemates (I and II) which were shown to be identical with those prepared by the fractional crystallization procedure.[2]

Pure (+) VIIIb prepared by the above resolution was converted by diazomethane to (+) VIIb. This was photochemically isomerized (44%) to (+) Vb which, on hydrolysis, gave (+) II, mp 119–120°, $[\alpha]_D$ +46.0°. In the same way (−) VIIIb was converted to (−) II, mp 119–120°, $[\alpha]_D$ −42.6°. A prepared mixture (1:1) of these two enantiomeric acids was crystallized, mp 159–160°, reported[2] (±) II mp 160–162°.

The physical constants[11,12] reported for platynecic acid were mp 133–135°, $[\alpha]_D$ −6.5°, −11°, and structure IVa was suggested.[10] The constants reported for usaramoensinecic acid were mp 170°, $[\alpha]_D$ + 6.66°,

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[1] Robert A. Welch Foundation postdoctoral fellow.

[2] J. D. Edwards, Jr., T. Hase, C. Hignite, and T. Matsumoto, *J. Org. Chem.*, **31**, 2282 (1966).

[3] The structures listed here as Va, Vb, VIIa, and VIIb were referred to in the previous paper[2] as *cis*-VA, *cis*-VB, *trans*-VA, and *trans*-VB.

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[5] C. C. J. Culvenor and T. A. Geissman, *J. Am. Chem. Soc.*, **83**, 1647 (1961).

[6] J. Fridrichsons, A. McL. Mathieson, and D. J. Sutor, *Acta Cryst.*, **16**, 1075 (1963).

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[8] R. Adams and M. Gianturco, *J. Am. Chem. Soc.*, **78**, 398 (1956).

[9] A. G. Gonzalez and A. Calero, *Anales Real. Soc. Espan. Fis. Quim.* (Madrid), **54B**, 223 (1958); *Chem. Abst.*, **54**, 19740 (1960).

[10] R. Adams and B. L. Van Duuren, *J. Am. Chem. Soc.*, **75**, 4631 (1953); R. Adams and M. Gianturco, *ibid.*, **79**, 174 (1957).

[11] A. V. Danilova and R. A. Konovalova, *Dokl. Akad. Nauk SSSR*, **73**, 315 (1950).

[12] In a recent private communication from Dr. Danilova, she states that because of work done after 1950 she and Professor Konovalova considered platynecic acid, originally reported as an individual compound, to be a mixture of senecic and integerrinecic acid. Professor Leonard also suggested that this was the case when he evaluated[4] the data on platynecic acid and its degradation products relative to similar studies on senecic acid.

with IIa suggested[10] as a possible structure. These names should now be dropped from the necic acid list.

Since (±)-integerrinecic acid has not been reported, hydrolysis of (±) VIIa was carried out and gave this racemate, mp 178–180°. The cesium salt of (+)-integerrinecic acid lactone also was prepared and crystallized, mp 204–206°, $[\alpha]_D$ +33.8°.

Experimental Section[13]

(±) VIIIb.—A solution of 20 mg of (±) IV in 5.0 ml of 5% hydrochloric acid was evaporated on a steam bath and the residue was recrystallized from ether–petroleum ether (bp 30–60°) to give 12.8 mg of colorless crystals, 154–156°. A mixture melting point determination with (±) IV (mp 162–164°) was 130–138°.

Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.55; H, 7.19.

Resolution of (±) VIIIb.—To a hot solution of 151.5 mg of brucine in 3.0 ml of ethyl acetate there was added 76 mg of (±) VIIIb. After cooling to room temperature, the solution was kept in a refrigerator for 24 hr. The colorless crystals, 93.9 mg, mp 194–197°, were filtered and washed with ethyl acetate. Recrystallization from ethyl acetate gave 91.8 mg of crystals, mp 198–200°, $[\alpha]_D$ +21.1° (*c* 1.40, ethanol).

Anal. Calcd for $C_{33}H_{40}N_2O_8$: C, 66.87; H, 6.80; N, 4.73. Found: C, 66.63; H, 6.88; N, 4.78.

The above filtrate was evaporated to dryness under vacuum and the residue was recrystallized first from ethyl acetate–ligroin (bp 60–90°) and then from acetone–ligroin to give 71.3 mg of colorless crystals, mp 187–189°, $[\alpha]_D$ −24.8° (*c* 1.98, ethanol). A mixture melting point determination with the above (+)-brucine salt was 175–180°.

Anal. Calcd for $C_{33}H_{40}N_2O_8$: C, 66.87; H, 6.80; N, 4.73. Found: C, 66.45; H, 6.88; N, 4.96.

(+) VIIIb.—To 5.0 ml of 5% sulfuric acid there was added 91.0 mg of the above (+)-brucine salt (mp 198–200°). The solution was extracted five times with ether and after washing with water and drying over sodium sulfate, the ether was evaporated under vacuum. The residue (27.9 mg) was recrystallized from ether–petroleum ether to give 27.1 mg of colorless crystals, mp 134–136°, $[\alpha]_D$ +10.8° (*c* 1.19 ethanol).

Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.58; H, 6.96.

(−) VIIIb.—This compound was prepared in the same way as (+) VIIIb from 37.9 mg of the (−)-brucine salt (mp 187–189°) and 7.5 mg of colorless crystals was obtained, mp 134–136°, $[\alpha]_D$ −10.0° (*c* 2.40, ethanol).

Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.41; H, 7.03.

(+) IV.—A mixture of 14.6 mg of (+) VIIIb, 63 mg of barium hydroxide octahydrate, and 2.4 ml of water was refluxed for 1.5 hr. After acidification to congo red paper with dilute hydrochloric acid, the solution was extracted four times with ether. The combined ether extracts were washed with water, dried, and evaporated under vacuum. The residue was recrystallized from ether–petroleum ether to give 9.7 mg of colorless crystals, mp 132–133°, $[\alpha]_D$ +26° (*c* 0.5, ethanol). A mixture melting point with (+) VIIIb was 105–110°.

Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46. Found: C, 55.71; H, 7.35.

(−) IV.—In the same way as with (+) VIIIb, 24.0 mg of (−) VIIIb was hydrolyzed to give 19.5 mg of colorless crystals, mp 132–133°, $[\alpha]_D$ −24° (*c* 0.5, ethanol). A mixture melting point with (−) VIIIb was 105–108°.

Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46. Found: C, 55.74; H, 7.44.

(±)-Integerrinecic Acid.—The hydrolysis of 110 mg of (±) VIIa with barium hydroxide was carried out as that for (+) IV to give, after crystallization from ether–petroleum ether, 91.3 mg of colorless crystals, mp 178–180°. A mixture melting point with (±) IV (mp 162–164°) was 153–157°.

Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46. Found: C, 55.93; H, 7.42.

Ultraviolet Irradiation Studies. A. (±) VIIa.—A solution of 143 mg of (±) VIIa in 3.0 ml of ethanol in a stoppered silica spectrophotometer cell was irradiated 6 in. from an unscreened Hanovia ultraviolet 325-w lamp for 3 hr. After evaporation under vacuum, the residue was recrystallized from ether–petroleum ether to give[14] 36.3 mg of (±) VIIa. The filtrate was evaporated to dryness under vacuum and the residue was chromatographed on a column of 30 g of silica gel (E. Merck AG, 0.08 mm) and eluted with purified chloroform[15] containing 3% dry ether. Fraction 1 (145 ml) was discarded; fractions 2 and 3 (50 ml) on evaporation under vacuum gave 57.1 mg (oil) of (±) Va. Fractions 4–6 (60 ml) were primarily[14] recovered (±) VIIa (46.5 mg). Hydrolysis of (±) Va with barium hydroxide as above and crystallization from ether–petroleum ether gave a 70% yield of colorless crystals, mp 163–165°. This was shown by mixture melting point to be identical with (±)-senecic acid.[2]

B. (±) VIIb.—In the same way, 63 mg of (±) VIIb gave 16.0 mg of (±) Vb and a recovery of 35.6 mg of starting material.[14] Hydrolysis of (±) Vb (oil) with barium hydroxide and recrystallization from ether–petroleum ether, gave[2] a 73% yield of (±) II, mp 160–162°.

Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46. Found: C, 55.40; H, 7.28.

C. (+) VIIb.—To a solution of 44.7 mg of (+) VIIIb in 3.0 ml of ether immersed in an ice bath, there was added dropwise with stirring, an ethereal solution of diazomethane (10% excess). After standing at this temperature for 15 min the solution was evaporated to dryness, dissolved in ethanol, and irradiated. The solvent was removed and chromatography as above gave 20.0 mg of (+) Vb and a recovery[14] of 24 mg of (+) VIIb. After the usual hydrolysis, recrystallization from ether–petroleum ether gave a 78% yield of (+) II acid, mp 119–120°, $[\alpha]_D$ +46.0° (*c* 0.433, ethanol).

D. (−) VIIb.—Treatment of (−) VIIIb with diazomethane gave (−) VIIb and on irradiation and chromatography yielded 25% of (−) Vb. Hydrolysis and crystallization from ether–petroleum ether gave a 70% yield of (−) II, mp 119–120°, $[\alpha]_D$ −42.6° (*c* 0.99, ethanol).

Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46. Found: C, 55.89; H, 7.52.

Cesium Salt of Integerrinecic Acid Lactone.—A solution of 12.1 mg of integerrinecic acid lactone in 1.5 ml of 50% aqueous ethanol was neutralized with 0.1 *N* cesium hydroxide. The solution was evaporated to dryness under vacuum and the residue was recrystallized from ethanol–acetone to give 12.5 mg of colorless crystals, mp 204–206°, $[\alpha]_D$ +33.8° (*c* 1.57, ethanol).

Registry No.—I, 6582-63-4; (+) II, 10407-68-8; (−) II, 10407-69-9; (±) II, 10407-70-2; III, 10407-71-3, (+) IV, 10407-72-4; (−) IV, 10407-73-5; (+) VIIIb, 10407-74-6, (−) VIIIb, 10407-75-7; (±) VIIIb, 10407-76-8; (+)-brucine salt of VIIIb, 10407-77-9; (−)-brucine salt of VIIIb, 10421-81-5; cesium salt of (+) VIIIb, 10414-78-5.

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[13] All elemental analyses were done by Huffman Laboratories, Inc., Wheatridge, Colo. Melting points are uncorrected and were obtained on a Fisher-Johns apparatus. Rotations of the dicarboxylic acids were taken on a Perkin-Elmer Model 141 polarimeter. The authors are indebted to Dr. John R. Dice, Parke Davis and Co., Ann Arbor, Mich., and to Dr. Harold P. Smith, Perkin-Elmer Corp., Norwalk, Conn., for these determinations.

[14] By infrared analysis.

[15] L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1955, p 283.