TABLE III
BOND LENGTHS INVOLVING HYDROGEN ATOMS

Atoms	Bond length (A)	Atoms	Bond length (A)
N-1	None		
C-2–H-24	1.09	C-2–H-25	1.19
C-3–H-26	0.91	C-3–H-27	1.08
C-4–H-28	1.10	C-4–H-29	1.09
C-5–H-30	1.05	C-5–H-31	1.03
C-6–H-32	0.97		
C-7	None		
C-8–H-33	1.71	C-8–H-34	1.06
C-9–H-35	0.97		
C-10–H-36	1.20	C-10–H-37	0.78
C-11–H-38	1.25		
C-12–H-39	1.20	C-12–H-40	1.08
C-13–H-41	1.06	C-13–H-42	1.28
C-14–H-43	1.14	C-14–H-44	1.10
C-15–H-45	1.11	C-15–H-46	1.90
N-16–H-47	1.04		
C-17–H-48	0.98	C-17–H-49	1.11
O-18	Not located		

Estd std dev −0.1 A

The perchlorate ion, whenever found in crystal structures, seems to have associated with it an unusual amount of vibration and rotation. This can range from wide amplitudes of vibration[4] to disorder[5] to free rotation.[6] In the present structure the vibration is somewhat less, but present all the same. Correction for the rotational–vibrational effect[7] would lengthen the Cl–O bonds and result in better agreement with the accepted value[8] of 1.45 ± 0.01 A.

Registry No.—7-Hydroxy-β-isosparteine perchlorate, 10257-17-7.

Acknowledgment.—This work has been supported by a grant from the National Science Foundation (GB3807), by assistance from the Heart Research Center, Grant HE06308 from the National Heart Institute, U. S. Public Health Service, and by computer time from the Research Computation Center which is supported by Public Health Research Grant FR-00162-02.

(4) M. Sundaralingam and L. H. Jensen, *J. Am. Chem. Soc.*, **88**, 198 (1966).
(5) L. M. Trefonas, R. L. Flurry, R. Majeste, E. A. Meyers, and R. F. Copeland, *ibid.*, **88**, 2145 (1966).
(6) R. J. Prosen and K. N. Trueblood, *Acta Cryst.*, **9**, 741 (1956).
(7) D. W. J. Cruickshank, *ibid.*, **9**, 757 (1956); **14**, 896 (1961).
(8) D. W. J. Cruickshank, *J. Chem. Soc.*, 5486 (1961).

Leguminosae Alkaloids. V. Chemistry and Stereochemistry of Multiflorine[1]

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Lithium aluminum hydride reduction of the alkaloid, multiflorine, proceeds *via* the metal enolate of 4-oxosparteine stereospecifically to 4α-hydroxysparteine. The same alcohol is the sole product of hydride reduction of 4-oxosparteine. The intermediacy of 4-oxosparteine was also demonstrated in the catalytic hydrogenation of multiflorine. It was shown that the saturated ketone is both the source of 4α-hydroxysparteine and the source of the over reduction product, sparteine. Analysis of the ORD curve determined from 4-oxosparteine was found to be consistent with previous absolute configurational correlation work. The possibility that multiflorine actually possesses the β-isosparteine skeleton which undergoes isomerization to the more favorable sparteine arrangement during the reactions discussed was found to be inconsistent with the ORD curve determined from the plant alkaloid.

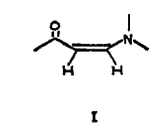
In 1955, Crow and Riggs[3] reported isolation of an alkaloid ($C_{15}H_{22}N_2O$) from the seeds and tops of *Lupinus varius* L. (now *Lupinus digitatus* Forsk.[4]) which they called Base LV-1. Preliminary structural information was determined in 1957,[5] followed by a complete structure assignment in 1959.[6] In the meantime Comin and Deulofeu,[7] studying the Argentine plant, *Lupinus multiflorus* Lam., isolated an alkaloid ($C_{15}H_{22}N_2O$) which they named multiflorine. The similarity of properties determined from multiflorine with those reported for Base LV-1 led to a direct comparison which established the identity of the two plant products.[6-8]

Examination of the spectral data determined from multiflorine led[6] to the conclusion that a vinylogous amide (I) must be present in the alkaloid. This information combined with the fact that both hydride reduction[6] and catalytic hydrogenation[6,7] of an acid solution of multiflorine were reported to result in production of sparteine (II) was taken to mean that multiflorine possesses the sparteine skeleton, and that the vinylogous amide (I) may be accommodated within II in only two ways: III and IV. Structure III was favored[6] mainly because partial reduction of multiflorine gave rise to a saturated ketone that did not possess properties of an amide, while the properties of its oxime were clearly different from those exhibited by the oxime of 13-oxosparteine.

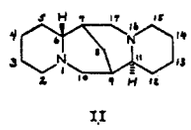
Recent phytochemical investigations of *Lupinus diffusus*[9] and of *L. westianus*[10] in this laboratory established the presence of multiflorine in these plants and provided a source of the alkaloid for further study.

In contradistinction to the report by Crow,[6] we have been unable to observe the formation of sparteine by treatment of multiflorine with lithium aluminum hydride. The only compound formed on complete reduc-

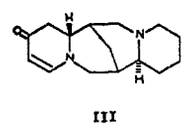
(1) It is a pleasure to acknowledge the aid received in support of this work from a National Institute of Mental Health research grant.
(2) Taken in part from the doctoral dissertation submitted in April 1966 by R. F. M. to the Graduate School, University of South Carolina, in partial fulfillment of the requirements for the Ph.D. degree.
(3) W. D. Crow and N. V. Riggs, *Australian J. Chem.*, **8**, 136 (1955).
(4) J. S. Gladstones, *J. Roy. Soc. W. Australia*, **41**, 29 (1958).
(5) W. D. Crow and M. Michael, *Australian J. Chem.*, **10**, 177 (1957).
(6) W. D. Crow, *ibid.*, **12**, 474 (1959).
(7) J. Comin and V. Deulofeu, *ibid.*, **12**, 468 (1959).
(8) Despite its obvious priority, the designation Base LV-1, which is inconsistent with traditional nomenclature practice, is avoided here in favor of the name, multiflorine, which does reflect the customary practice of relating an alkaloid to an original natural source.
(9) S. I. Goldberg and R. F. Moates, *Phytochemistry*, **6**, 137 (1967).
(10) S. I. Goldberg and M. S. Sahli, *J. Med. Chem.*, **10**, 124 (1967).



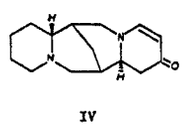
I



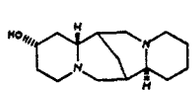
II



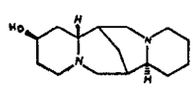
III



IV

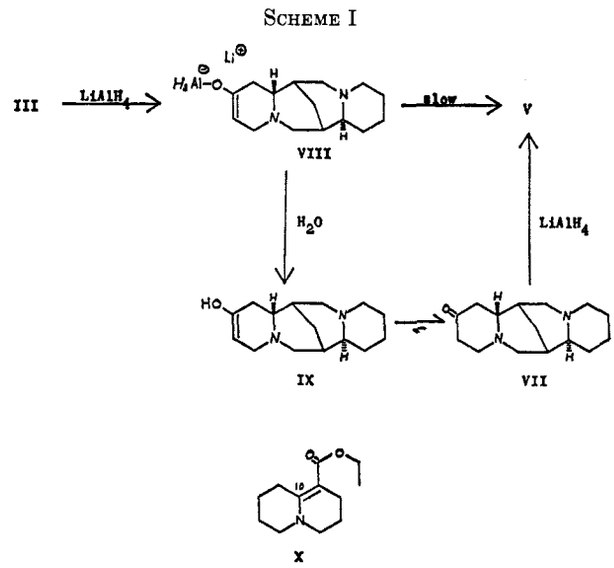


V



VI

SCHEME I



X

tion was identified as (−)-4α-hydroxysparteine (V). This substance was apparently the same product obtained by Comin and Deulofeu[7] *via* catalytic hydrogenation of multiflorine. Its formation was also observed during our catalytic hydrogenation experiments. The identification of the substance as 4α-hydroxysparteine (V) rested on the fact that the infrared spectrum determined from the base in solution was found to be superimposable upon that obtained from racemic 4α-hydroxysparteine, but found to be different from the infrared spectrum determined from the epimeric substance, racemic 4β-hydroxysparteine (VI).[11] Establishment of the structure of the alcohol as V was a key point, for this provided rigorous corroborating evidence in support of the structure assignment to multiflorine since it positively showed the C-4 position, not the C-13 position, of the sparteine skeleton to be the site of the oxygen atom.

It is significant that lithium aluminum hydride reduction of multiflorine proceeds at a relatively slow rate. This was indicated by the fact that in one of our runs the reaction mixture was worked up after a few hours reaction time instead of the usual overnight treatment, and 4-oxosparteine (VII) was found along with the alcohol V. That observation suggested that initial hydride delivery to multiflorine is at C-2, giving the enolate form VIII. Slow conversion of multiflorine to V is consistent with the intermediacy of VIII, for it is generally recognized[13] that hydride reduction of an enolate is slow. Interruption of the process by hydrolysis of the reaction mixture would lead to vinyl alcohol IX which would exist predominately as ketone VII. In support of this interpretation (Scheme I) it was shown recently,[14] by means of deuterium-labeling experiments, that C-10 in 1-carboethoxy-1(10)-dehydroquinolizidine (X) is the site of hydride delivery. It was also shown during the present investigation that lithium aluminum hydride reduction of V, prepared by partial hydrogenation of multiflorine, gave the levorotatory alcohol V exclusively. The stereospecific formation of the 4α alcohol *via* reduction of the metal enolate VIII and/or reduction of the ketone VII appears to be a consequence of the fact that in each case both steric approach control and product development control would be expected to favor formation of the more stable equatorial alcohol V. In the case of the metal enolate, the transition state leading to production of axial alcohol would possess serious nonbonded interactions between the bulky aluminoxy group and the quasi-axial hydrogens at C-2 and C-5, whereas the aluminoxy group would only be subject to interaction with the angular hydrogen at C-6 in the transition state leading to production of equatorial alcohol. Using the same argument, approach of the reagent to the ketone VII is clearly favored for the β side of the molecule, leading to axial hydride delivery and equatorial alcohol formation.

Catalytic hydrogenation of multiflorine in acidic hydroxylic solvents during the present study gave rise to II and V. While similar results were observed by Comin and Deulofeu,[7] Crow[6] reported the formation of only II. Crow[6] also reported that interruption of the hydrogenation (Pt in glacial acetic acid) provided, in addition to sparteine, a ketone which he concluded to be 4-oxosparteine (VII). The same ketone was obtained by Crow[6] from reduction of multiflorine with tin and hydrochloric acid. This material, similarly prepared during the present investigation, was confirmed as being VII since it gave V by hydride reduction and by catalytic hydrogenation. The formation of sparteine during the catalytic hydrogenation of multiflorine was of interest, and we have shown that its formation must arise from over-reduction of VII. Since partial hydrogenation of multiflorine yields 4-oxosparteine, it seems reasonably clear that the latter is the immediate product of hydrogenation of the former. In other words, the plant alkaloid is first reduced at its carbon–carbon double bond. Subsequent reduction of the ketone VII leads to the alcohol V. We have shown, however, that sparteine (II) is also formed from the ketone VII and not *via* dehydration–reduction of the alcohol V. Separate hydrogenation experiments, using the same conditions of hydro-

(11) We are indebted to Professor F. Bohlmann and to Dr. E. Winterfeldt of the Technischen Universität, Berlin, for their cooperation and generosity in supplying copies of the infrared spectra of their synthetic material.[12]

(12) F. Bohlmann, E. Winterfeldt, and H. Brackel, *Ber.*, **91**, 2194 (1958).

(13) See discussion by H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., New York, N. Y., 1965, p 28.

(14) S. I. Goldberg and I. S. Ragade, *J. Org. Chem.*, **32**, 1046 (1967).

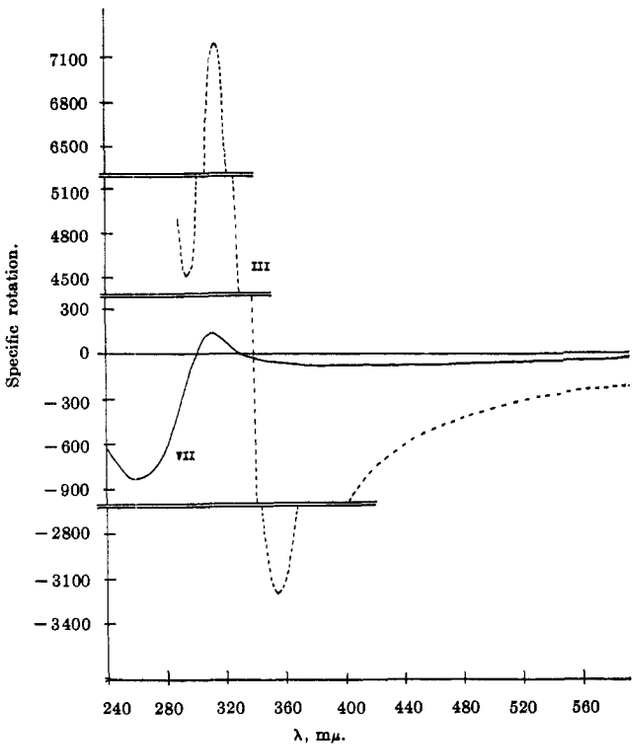
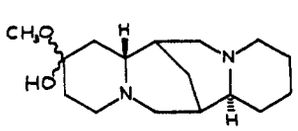


Figure 1.—ORD curves of multiflorine (III) and 4-oxosparteine (VII).

genation of multiflorine, showed that 4-oxosparteine (VII) gave rise to the mixture of V and II, while the alcohol V, in a separate experiment, was recovered unchanged. An explanation for the ability of the ketone VII to undergo the observed over-reduction was suggested by the accidental preparation of the methyl hemiketal of 4-oxosparteine monoperchlorate (XI).



XI

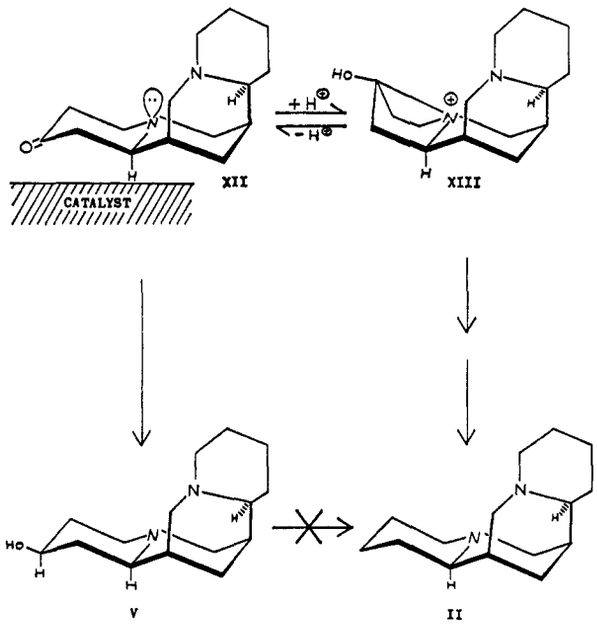
The material was obtained during attempts to recrystallize the ketone monoperchlorate from an ether–methanol mixture. The unusual ease of hemiketal formation may be accounted for by a transannular nitrogen–carbonyl interaction which may also be invoked to rationalize the conversion of VII to sparteine during catalytic hydrogenation. These ideas are illustrated in Scheme II.

Since approach of the catalyst to the β side of the ketone is clearly favored (XII) over the α side, the stereospecific formation of the α alcohol V would appear to follow directly. However, transannular interaction of the nitrogen with the carbonyl carbon along with protonation of oxygen may also give rise to a species such as XIII which may be expected to undergo hydrogenolysis to II.

The configurational correlation work of Okuda, *et al.*,[15] established the absolute configurational relationship of (−)-anagyrine with that of (+)-epilupinine whose absolute configuration was determined previously

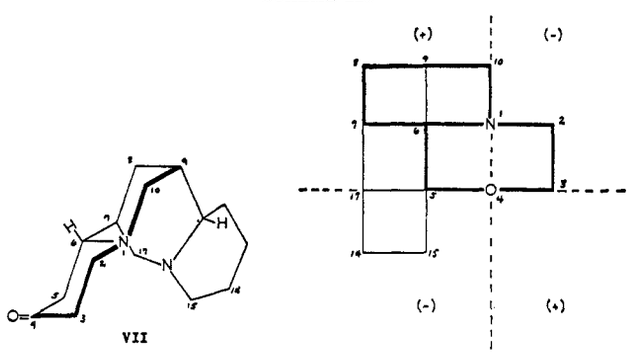
(15) S. Okuda, H. Kataoka, and K. Tsuda, *Chem. Pharm. Bull.* (Tokyo), **13**, 487, 491 (1965).

SCHEME II



by Cookson.[16] It follows from previously determined[17] relative configurations that (−)-sparteine is as shown in II and that the other compounds described in the present study also are as represented in the structures. It was of interest, therefore, to determine the rotatory dispersion curve[18] of (−)-4-oxosparteine and to examine it in terms of the tenets of the octant rule.[19] It was found that the positive Cotton effect displayed by the ketone (Figure 1) is consistent with that predicted from octant rule analysis of VII (Scheme III), but not with the mirror image of VII.

SCHEME III



Thus, the original designation by Crow[6] and by Comin and Deulofeu[7] of multiflorine as a derivative of (−)-sparteine was corroborated by the evidence obtained during the present study. However, that assignment rests solely on the fact that multiflorine gives rise to sparteine and oxygenated sparteine derivatives. It would also be consistent with the evidence to represent multiflorine as possessing the β-isosparteine skeleton XIV since it is conceivable that the various acidic and basic transformations of multi-

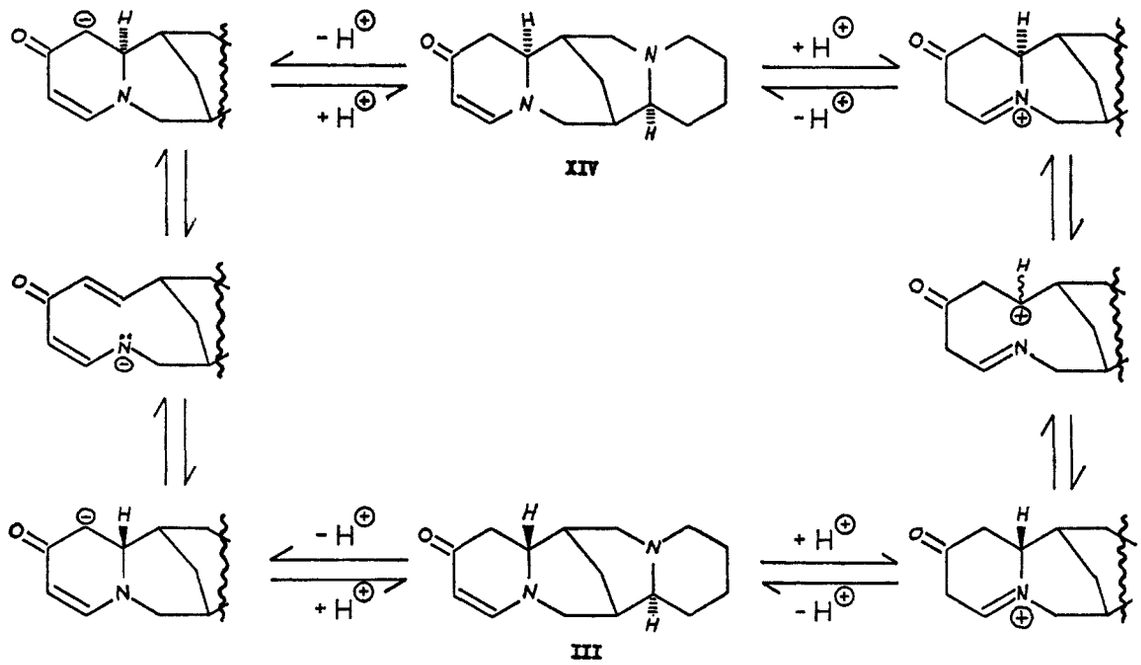
(16) R. C. Cookson, *Chem. Ind.* (London), 337 (1953).

(17) N. J. Leonard, *Alkaloids*, **3**, 119 (1953); **7**, 253 (1960).

(18) We are indebted to Dr. Herman Ziffer of the National Institute of Arthritis and Metabolic Diseases for this determination for which a Cary Model 60, recording spectropolarimeter was used.

(19) C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, Chapter 13.

SCHEME IV



florine could also promote isomerization of the less favorable *cis*-A/B ring fusion of the β-isosparteine skeleton to the more stable *trans*-A/B ring fusion found in sparteine.[20] These possibilities are represented in Scheme IV.

This point was settled by examination of the rotatory dispersion curve determined[18] from multiflorine. The long-wavelength, negative, Cotton effect (Figure 1), is, according to early empirical correlations[19] and to the recent theoretical treatment by Snatzke,[22] consistent with the (*S*) configuration at C-6 (as shown in III) but not with the (*R*) configuration at C-6 (as shown in XIV). This analysis, incidentally, provides an additional basis for rejection of 13-oxo-14,15-dehydrosparteine (IV) as the structure of multiflorine.

Experimental Section

General.—All temperatures were uncorrected. Melting points were determined in sealed, evacuated capillary tubes. Infrared spectra were obtained with a Perkin-Elmer, Model 337, grating spectrophotometer. Ultraviolet spectra were determined with a Cary, Model 14, recording spectrophotometer; and proton magnetic resonance (pmr) spectra were recorded on a Varian Associates, Model A-60, instrument at 60 Mc, near 30° in solutions (carbon tetrachloride or chloroform-*d*) containing tetramethylsilane (TMS) as internal standard. Chemical shifts were determined under the δ convention (parts per million) relative to TMS (0 ppm).

Descending paper chromatography was carried out on Whatman No. 1 paper, using a solvent system of butanol–acetic acid (10:1 v/v) saturated with water. Chromatograms were allowed to develop through a distance of about 25 cm before they were dried and sprayed with Dragendorff reagent.[23] Column elution chromatography was done with Woelm nonalkaline alumina (Brockmann grade I) with purified[24] solvents.

Combustion analyses were carried out by the Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

Reduction of Multiflorine with Lithium Aluminum Hydride.—Multiflorine[25] (131 mg, 0.53 mmole) was dissolved in 5 ml of anhydrous ether and added to a magnetically stirred slurry of lithium aluminum hydride (150 mg, 3.9 mmoles) in 20 ml of anhydrous ether. The reaction mixture, adequately protected from atmospheric moisture, was stirred continuously at room temperature overnight. Excess hydride was destroyed by the careful addition of distilled water to the cooled reaction mixture. The resulting hydrolyzate was phase separated and the two 5-ml ether washes of the aqueous phase were combined with the original ethereal phase which was dried and evaporated to obtain 123 mg of a partially solidified material.

Paper chromatographic examination of the residue revealed only one spot whose R_f value did not correspond to that of the starting material, multiflorine, or that of sparteine when all three were run on the same papergram. The formation of only one product, different from multiflorine and sparteine, by lithium aluminum hydride treatment of the former was also the case in three other experiments. In a fourth experiment a second product was obtained, but it was 4-oxosparteine (VII), produced by incomplete reduction of multiflorine.

The crude reaction product was dissolved in 10 ml of boiling *n*-hexane. On cooling, the *n*-hexane solution deposited thin, white, needle-shaped crystals which, after recrystallization from *n*-hexane, melted at 77–80°: $[\alpha]^{26}D$ −34.5 ± 0.5° (*c* 2.50, methanol); infrared, $\nu_{max}^{CHCl_3}$ 3620 (OH stretch),[26] 2780, 2800 cm^{-1} (*trans*-quinolizidine).[26] Combustion analysis of the crystalline material indicated it to be hydrated. In order to obtain a water-free sample for analysis a portion of the material was molecularly distilled in a modified Späth bulb [100–120° (0.10 mm) (air bath)]. The distillate, a colorless, viscous oil, was directly sealed, under reduced pressure, in a capillary tube receiver and submitted for analysis.

Anal. Calcd for $C_{15}H_{26}N_2O$: C, 71.95; H, 10.74; N, 11.19. Found: C, 71.75; H, 10.78; N, 10.91.

A portion of the crystalline material (32 mg, 0.13 mmole) was added to methyl iodide (2.2 g, 15.5 mmoles), dissolved in 15 ml of acetone, and the resulting mixture was heated under reflux during 3 hr. The solvent was then evaporated under reduced pressure, and the semisolid residue was dissolved in 3 ml of ethanol. Ether was added dropwise until the solution became

(20) An example of this type of ring fusion isomerization may be seen in Oppenhauer oxidation of 13-hydroxylupanine which gave rise to 13-oxo-α-isolupanine.[21]

(21) F. Bohlmann, E. Winterfeldt, O. Schmidt, and W. Reusche, *Chem. Ber.*, **94**, 1767 (1961).

(22) G. Snatzke, *Tetrahedron*, **21**, 413 (1965).

(23) R. Munier, *Bull. Soc. Chim. Biol.*, **35**, 1225 (1935).

(24) J. A. Riddick and E. E. Toops, Jr., "Technique of Organic Chemistry," Vol. VII, A. Weissberger, Ed., Interscience Publishers, Inc., New York, N. Y., 1955.

(25) The multiflorine used in this work was isolated from *Lupinus diffusus Nutt.*[9] and from *L. westianus* Small.[10]

(26) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1958; K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962.

cloudy, and after standing several hours at room temperature crystalline material was deposited. The crude methiodide was recrystallized from ethanol–ether solvent to yield material which melted at 256–258°.

It is fairly certain that this lithium aluminum hydride reduction product is the same substance which Comin and Deulofeu[7] obtained *via* catalytic hydrogenation of multiflorine, and which we have identified (see below) as 4α-hydroxysparteine (V). The properties of the "hydroxysparteine" which they reported are $[\alpha]^{29}D$ −32.5° (*c* 0.3, ethanol), methiodide mp 258–260°.

This same compound was obtained during the present investigation *via* other reduction procedures which are described below. We have shown the material to be (−)-4α-hydroxysparteine (V) by means of the fact that its infrared spectrum ($CHCl_3$) was found to be superimposable upon that obtained from (±)-4α-hydroxysparteine, but not superimposable upon the infrared spectrum determined from (±)-4β-hydroxysparteine.[11]

In one of our lithium aluminum hydride reduction experiments, carried out as described above except for the fact that it was run under shorter reaction time, the reaction product gave rise to an infrared spectrum which possessed a strong absorption band at 1720 cm^{-1}, indicating the presence of 4-oxosparteine, a substance whose preparation is described below. The indication was strengthened by the fact that the material was converted to 4α-hydroxysparteine by reduction with lithium aluminum hydride.

Reduction of (−)-4-Oxosparteine (VII) by Lithium Aluminum Hydride.—4-Oxosparteine (99 mg, 0.40 mmole), dissolved in 15 ml of anhydrous ether, was added to a stirred slurry of lithium aluminum hydride (98 mg, 2.6 mmoles) in 20 ml of ether at room temperature. The reaction mixture was stirred overnight before the excess hydride was destroyed by careful addition of water. The hydrolyzate was phase separated, and the ethereal solution was dried and evaporated to a residue which was dissolved in 10 ml of warm hexane. The hexane solution was kept in the refrigerator where it deposited a crop of white crystals. This material was recrystallized twice from hexane: mp 67–72°. Its infrared spectrum showed it to be the same substance (V) as was obtained from hydride reduction of multiflorine.

Catalytic Hydrogenation of Multiflorine.—Multiflorine (50 mg, 0.20 mmole), dissolved in 2 ml of 2 *N* aqueous hydrochloric acid, was added to 8 ml of 2 *N* aqueous hydrochloric acid containing 10 mg of reduced platinum oxide catalyst. The mixture was magnetically stirred while it was left in contact with hydrogen (1 atm) at room temperature during 19 hr. The total, corrected hydrogen uptake was 2.8 equiv. After the catalyst was collected in a filter, and the filtrate was made strongly basic by addition of aqueous sodium hydroxide solution, the latter was extracted with four successive, 10-ml portions of ether. Paper chromatographic examination of the basic material present in the combined ethereal extracts showed only the presence of sparteine (R_f 0.49) and 4α-hydroxysparteine (R_f 0.31). These identifications were indicated by the fact that authentic sparteine and 4α-hydroxysparteine gave parallel respective spots when all were run on the same papergram. The identifications were corroborated by determinations of the infrared spectra of the individual reaction components and comparison of each with the infrared spectra of the authentic compounds. The reaction components were separated by careful elution chromatography: sparteine eluted with hexane containing 2% (v/v) ether, and 4α-hydroxysparteine eluted with ether.

Similar results were obtained from the hydrogenation of multiflorine in 95% aqueous ethanol containing 15% (v/v) 1 *N* aqueous hydrochloric acid.

It was found, however, that in ethanolic perchloric acid, the hydrogenation of multiflorine could be interrupted to yield 4-oxosparteine. Thus, multiflorine (150 mg, 0.65 mmole), dissolved in 10 ml of 95% aqueous ethanol, was treated with 0.5 ml of concentrated perchloric acid, and the entire solution was added to 10 ml of 95% aqueous ethanol containing 20 mg of reduced platinum oxide catalyst. The mixture was stirred at room temperature while it was kept in contact with hydrogen (1 atm). After 4.9 hr the corrected uptake of hydrogen amounted to 1.35 equiv, and the catalyst was separated from the reaction mixture by filtration. After the solvent was evaporated from the filtrate, the residue was taken up in 15 ml of 1 *N* hydrochloric acid, made strongly basic with concentrated sodium hydroxide solution, and extracted with five successive 10-ml portions of chloroform. The combined chloroform extracts were dried over anhydrous sodium sulfate, filtered, and evaporated to a residue which was taken up in a minimum volume of absolute ethanol and titrated with 14% ethanolic perchloric acid to pH 6.5–7.0 (external indicator). After the solution had remained in the refrigerator for several hours, a crop of white crystalline material was formed. This material, later shown to be 4-oxosparteine monoperchlorate had mp 199–200°, lit.[6] mp 203–205°. Attempts to purify the salt by recrystallization from methanol–ether solvent resulted in the formation of the **methyl hemiketal of 4-oxosparteine monoperchlorate (XI)**: mp 166–168°; infrared, ν_{max}^{KBr} 3450 (OH),[26] 3040 ($^+$NH),[26] and 620 cm^{-1} (ClO_4^-).[26]

Anal. Calcd for $C_{16}H_{29}ClN_2O_6$: C, 50.45; H, 7.68; Cl, 9.31; N, 7.36. Found: C, 50.43; H, 7.78; Cl, 9.13; N, 7.44.

A portion of the methyl hemiketal perchlorate was dissolved in water, made basic by addition of aqueous sodium hydroxide, and extracted with ether. The combined and dried ether extracts were evaporated to a residue that gave rise to two signals in its nmr spectrum [δ^{CDCl_3} 3.16 (3 H) and 3.21 (3 H)] with chemical shifts consistent for a mixture of epimeric methyl hemiketals.

Another sample of the hemiketal was dissolved in 1 *N* aqueous perchloric acid and allowed to remain at room temperature for 3 hr. The solution was then made strongly basic with aqueous sodium hydroxide and extracted with ether. Evaporation of the ether left a residue which gave, upon molecular distillation in a Späth bulb [100–110° (0.03 mm) (air bath)], **(−)-4-oxosparteine (VII)**: $[\alpha]^{26}D$ −26.3 ± 0.9° (*c* 0.66 95% aqueous ethanol); infrared, ν_{max}^{neat} 2810, 2770 (*trans*-quinolizidine), 1725 cm^{-1} (carbonyl).[26] This material could be crystallized as a hydrate of uncertain composition and with an indefinite melting point. A sample was prepared for analysis by molecular distillation, with the distillate sealed in a capillary tube.

Anal. Calcd for $C_{15}H_{24}N_2O$: C, 72.54; H, 9.74. Found: C, 72.77; H, 9.66.

Catalytic Hydrogenation of 4-Oxosparteine.—(−)-4-Oxosparteine (VII) (50 mg, 0.20 mmole), dissolved in 10 ml of aqueous 2 *N* hydrochloric acid, was added to 10 ml of 2 *N* aqueous hydrochloric acid containing 10 mg of reduced platinum oxide catalyst. The mixture was hydrogenated at atmospheric pressure and room temperature (corrected hydrogen uptake, 1.3 equiv). After the catalyst was collected in a filter, the filtrate was made strongly basic (aqueous sodium hydroxide) and exhaustively extracted with ether. Paper chromatographic examination of the residue (42 mg) obtained after evaporation of the ether revealed the presence of two components whose R_f values, 0.31 and 0.48, matched that of 4α-hydroxysparteine and sparteine, respectively. The identification was confirmed by separation of each component and determination of the infrared spectra. In each case the spectrum obtained was found to be superimposable upon that obtained from the corresponding authentic material.

Absence of Hydrogenolysis of 4α-Hydroxysparteine.—4α-Hydroxysparteine (71 mg, 0.27 mmole), dissolved in 4 ml of 2 *N* aqueous hydrochloric acid, was added to 15 ml of 2 *N* hydrochloric acid containing 10 mg of reduced platinum oxide catalyst. The mixture was stirred while it was contained in an atmosphere of hydrogen under ambient conditions during 72 hr. The reaction mixture was separated from the catalyst, made basic, and extracted with chloroform. Evaporation of the combined and dried chloroform extracts left a residue (59 mg) which gave rise to an infrared spectrum identical with that determined from the starting material, 4α-hydroxysparteine.

Reduction of Multiflorine with Tin and Hydrochloric Acid.—Granular tin (650 mg, 5.5 mmoles) was added to a solution of multiflorine (52 mg, 0.21 mmole) in 12 ml of 5 *N* aqueous hydrochloric acid, and the mixture was heated in a hot water bath for 1 hr. The mixture was allowed to cool to room temperature, and the supernatant was decanted. The unreacted tin was washed with two 5-ml portions of water, and the washings were combined with the original reaction solution which was then made basic by addition of 5 ml of 50% aqueous sodium hydroxide solution. The basic solution was then exhaustively extracted (difficult emulsion) with chloroform. Evaporation of the dried chloroform extracts gave a residue whose infrared spectrum indicated the presence of unreacted starting material: ν_{max}^{neat} 1590, 1640, and 1720 cm^{-1}. The material was, therefore, resubmitted to the tin and hydrochloric acid treatment for 1 additional hr in a boiling-water bath and worked up as before. This time the infrared spectrum determined from the reaction product did not contain the absorption bands due to multiflorine. The crude product was chromatographed on alumina, using anhydrous ether solvent. The material obtained from the ether eluates was then submitted to molecular distillation in a Späth bulb [80–90°

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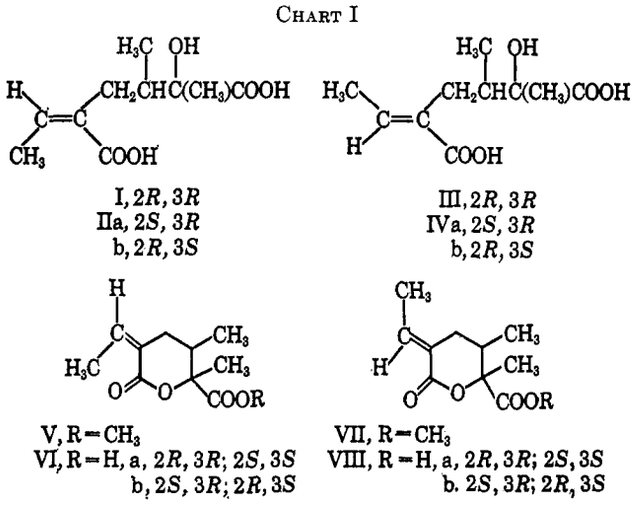
All diastereomers of senecic and integerrinecic acids have been synthesized. The physical constants of these acids are compared with those of reported necic acids assumed to be isomeric with senecic acid.

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

CHART I



I, 2*R*, 3*R*
IIa, 2*S*, 3*R*
b, 2*R*, 3*S*

III, 2*R*, 3*R*
IVa, 2*S*, 3*R*
b, 2*R*, 3*S*

V, R = CH_3
VI, R = H, a, 2*R*, 3*R*; 2*S*, 3*S*
b, 2*S*, 3*R*; 2*R*, 3*S*

VII, R = CH_3
VIII, R = H, a, 2*R*, 3*R*; 2*S*, 3*S*
b. 2*S*, 3*R*; 2*R*, 3*S*

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.

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°,

(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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(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.