[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Unsaturated Amines. IV. Structures and Reactions of the Dehydrosparteines and their Salts[1-3]

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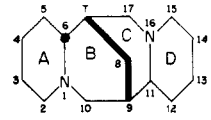
The dehydrogenation of (−)-sparteine by means of mercuric acetate leads successively to (−)-Δ^5-dehydrosparteine and (−)-$\Delta^{5,11}$-didehydrosparteine. These structures have been established by a variety of methods available for the detection of α,β-unsaturated tertiary amines (enamines). The salts corresponding to these unsaturated bases have been shown to contain the $\Delta^{1(6)}$-dehydrosparteinium and $\Delta^{1(6),11(16)}$-didehydrosparteinium cations, respectively. Advantage has been taken of the attack by nucleophilic reagents on the $>C{=}\overset{+}{N}< \longleftrightarrow >\overset{+}{C}-N<$ group present in these salts, for the preparation of 6-cyanosparteine, 6,11-dicyanosparteine, and a series of 6-alkyl- and 6-aralkylsparteines.

By a combination of methods,[5-7] it has been shown that the mild dehydrogenation of quinolizidine (I) by means of mercuric acetate results in $\Delta^{1(10)}$-dehydroquinolizidine (II), which forms salts of the $\Delta^{5(10)}$ dehydroquinolizidinium type (III).[2] With such knowledge available for this representative bicyclic system, it was of interest to return to a consideration of the mercuric acetate dehydrogenation[8] of the tetracyclic alkaloid sparteine (IV), $C_{15}H_{26}N_2$, which consists effectively of two fused quinolizidine moieties. The products, called dehydrosparteine, $C_{15}H_{24}N_2$, and α-didehydrosparteine,

I II III



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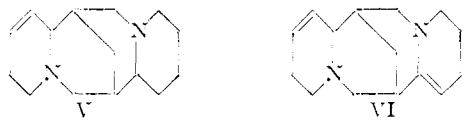


V VI

$C_{15}H_{22}N_2$, which resulted successively from the action of mercuric acetate on *l*-sparteine,[8] were assigned structures V and VI (stereochemistry not indicated) by Winterfeld and his co-workers.[9,10] A re-examination of the structures V and VI and those of their salts is facilitated by our present knowledge of the stereochemistry of the C_{15} family of lupin alkaloids.[11,12]

The placement of the second double bond introduced into the sparteine molecule at the 11,12-position is required because of the over-all change in stereochemistry at C-11 effected by catalytic hydrogenation of α-didehydrosparteine.[8-11] On the basis of the analogy of the removal of hydrogen from a tertiary carbon (C-11) during the second step of the mercuric acetate dehydrogenation of sparteine and the further analogy of the removal of the C_{10}-hydrogen from quinolizidine (I → II),[2] it would be expected that the first double bond introduced into (−)-sparteine also would appear at a tertiary carbon (C-6), making dehydrosparteine "(−)-Δ^5-dehydrosparteine" (VII) and α-didehydrosparteine "(−)-$\Delta^{5,11}$-didehydrosparteine" (VIII) (stereochemistry indicated).[11] While these structures have been regarded as correct representations of the dehydro products for some time both in

VII VIII

this Laboratory and elsewhere,[13,14] our present results offer conclusive evidence in support of VII and VIII.

To begin with, the dehydrosparteine of Winterfeld and Rauch was known to possess the same skeletal structure as its precursor, sparteine, because of the regeneration of sparteine upon catalytic hydrogenation.[8] The assignment of the entering double bond to an α,β-position with respect to nitrogen has now been reached—thus definitely ruling out structure V as a possibility—by a compelling accumulation of evidence. The infrared spectrum of the $C_{15}H_{24}N_2$ compound in chloroform showed absorption at 1650 cm.$^{-1}$, while the monoperchlorate salt in the same solvent had an intense absorption maximum at 1692 cm.$^{-1}$ (1695 cm.$^{-1}$ in Nujol mull). The shift toward higher infrared frequency in going from an unsaturated tertiary amine to its salt has been shown to be indicative of α,β-unsaturation in the amine $>C^{\beta}{=}\overset{\alpha}{C}-N<$ (IX) and the structure $>CH-C{=}\overset{+}{N}< \longleftrightarrow >CH-\overset{+}{C}-N<$ (X) in the cation of the salt.[2,6] Supporting this con-

(1) A section of this paper was presented at the 5th Summer Seminar in the Chemistry of Natural Products at the University of New Brunswick, Fredericton, N. B., Canada, August 19, 1953.

(2) Paper III in this series: N. J. Leonard, A. S. Hay, R. W. Fulmer and V. W. Gash, THIS JOURNAL, **77**, 439 (1955).

(3) This work was supported in part by a grant from the Research Board of the University of Illinois.

(4) Sinclair Refining Company Fellow in Organic Chemistry, 1953-1954. Work done under the sponsorship of the Sinclair Research Laboratories, Inc.

(5) R. Adams and J. E. Mahan, THIS JOURNAL, **64**, 2588 (1942).

(6) N. J. Leonard and V. W. Gash, *ibid.*, **76**, 2781 (1954).

(7) N. J. Leonard and D. M. Locke, *ibid.*, **77**, 437 (1955).

(8) K. Winterfeld and C. Rauch, *Arch. Pharm.*, **272**, 273 (1934).

(9) K. Winterfeld and H. E. Rönsberg, *ibid.*, **274**, 48 (1936).

(10) K. Winterfeld and H. Besendorf, *ibid.*, **282**, 33 (1944).

(11) L. Marion and N. J. Leonard, *Can. J. Chem.*, **29**, 355 (1951).

(12) Maria Przybylska and W. H. Barnes, *Acta Cryst.*, **6**, 377 (1953).

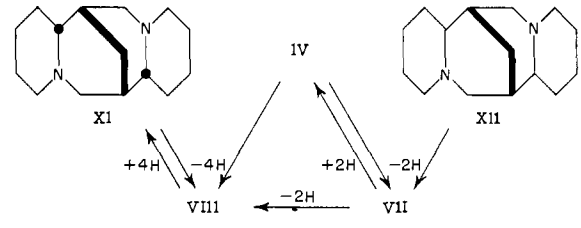
(13) Dr. Marvin Carmack, Indiana University, private communication.

(14) B. P. Moore and L. Marion, *Can. J. Chem.*, **31**, 187 (1953).

clusion is the observation that dehydrosparteine is a stronger base than sparteine, in agreement with the findings of Adams and Mahan[5] on α,β-unsaturated tertiary amines. In 66% aqueous dimethylformamide, the pK'_a values determined for *l*-sparteine diperchlorate were (1) 3.3 and (2) 11.4, and those for dehydrosparteine diperchlorate, by contrast, were (1) 5.0 and (2) 12.9. Moreover, the $C_{15}H_{24}N_2$ base (IX) was recovered unchanged from attempted reduction with lithium aluminum hydride, while the bisulfate salt (X) was converted to *l*-sparteine by the action of sodium borohydride.[2,15] The reducibility of the bisulfate salt of the $C_{15}H_{24}N_2$ base under Clemmensen conditions (also to *l*-sparteine) was further indication that the unsaturated function of the salt (or of the base in acid solution) could not be a simple carbon–carbon double bond, and therefore that the base could not be a β,γ-unsaturated amine. Positive evidence of the enamine salt structure X was obtained from the reaction of the perchlorate salt of the mercuric acetate dehydrogenation product with potassium cyanide[16] in methanol, which gave a cyanosparteine, $C_{16}H_{25}N_3$, in excellent yield. The expected proximity of the nitrile group to one of the nitrogens in this cyanosparteine was revealed by its diminished basicity, pK'_a's of (1) *ca.* 3.3 and (2) 9.4 in 66% DMF, compared with sparteine (see above). The $C_{15}H_{24}N_2$ perchlorate also reacted with Grignard reagents[2,17] to give a series of alkyl- and aralkylsparteines; the free base ($C_{15}H_{24}N_2$), by contrast, did not react with methylmagnesium iodide to give a methylated derivative.

The accumulated data thus require structure IX in the free base and X in its salts. The double bond, which must be α,β to one of the nitrogens, can be assigned to ring A (see IV) in Winterfeld and Rauch's dehydrosparteine, since rings B and C are excluded for steric reasons and ring D is excluded on the basis of the physical and chemical properties of their α-didehydrosparteine, which is known to contain the same double bond and an additional one at C-11 in ring D.[8-11] The infrared spectrum of α-didehydrosparteine had a strong band at 1646 cm.$^{-1}$ (10% in chloroform, 1645 cm.$^{-1}$ in Nujol mull[18]), that of the diperchlorate, a well-resolved intense band at 1690 cm.$^{-1}$ (mull). Electrometric titrations indicated a progressive increase in the first pK'_a value for sparteine (3.3), dehydrosparteine (5.0) and α-didehydrosparteine (6.8), and the second pK'_a value for α-didehydrosparteine was 13.0 in 66% DMF. That two separate enamine functions (IX) were present in the α-didehydrosparteine also was indicated by a comparison of the ultraviolet absorption spectra of the same $C_{15}H_{26}N_2$, $C_{15}H_{24}N_2$ and $C_{15}H_{22}N_2$ compounds.[7] Moreover, α-didehydrosparteine diperchlorate reacted with potassium cyanide in methanol to give a dicyanosparteine, $C_{17}H_{24}N_4$, in excellent yield. The existence of dual structures X in the salt was proved further by the proximity of one entering nitrile group to each of the nitrogens in the dicyanosparteine, as shown by the low pK'_a values for the latter (66% DMF): (1) <3.0; (2) 6.9 (compare cyanosparteine above).

With the unsaturation in Winterfeld and Rauch's dehydrosparteine limited to ring A of the sparteine tetracyclic system and to an α,β-position with respect to N-1, the only two possibilities are the Δ^2- and Δ^5-dehydro structures. Preference for the Δ^5-structure has already been indicated, and a consideration of certain dehydrogenation experiments with α-isosparteine (XI)[11,12] and β-isosparteine (XII)[11] supports this choice. It has been found by Kettelhack, Rink and Winterfeld[19] that both *l*-



sparteine (IV) and 1-α-isosparteine[20] yield the same product, α-didehydrosparteine (tentatively VIII), upon removal of four atoms of hydrogen by the action of mercuric acetate. One of the double bonds must be at C-11 to account for the identity of the products from both dehydrogenations. The other double bond in α-didehydrosparteine is placed at the same position as the sole double bond in its precursor,[8-11] dehydrosparteine (tentatively VII), which results from the removal of two atoms of hydrogen by the action of mercuric acetate on *l*-sparteine and on (*d* or *l*?)-β-isosparteine.[14,21] This double bond would have to be at C-5 to account for the identity of the products from both of these dehydrogenations of the corresponding steroisomers. A more direct proof for structures VII and VIII is to be found in the established enantiomorphic relation of the products of didehydrogenation of *l*-sparteine and of "spartalupine,"[22] which has

(15) *Cf.* H. Schmid and P. Karrer, *Helv. Chim. Acta*, **32**, 960 (1949); M. E. Herr and F. W. Heyl, THIS JOURNAL, **75**, 5927 (1953); B. Witkop, *ibid.*, **75**, 3361 (1953); B. Witkop and J. B. Patrick, *ibid.*, **75**, 4474 (1953); A. P. Gray, E. E. Spinner and C. J. Cavallito, *ibid.*, **76**, 2792 (1954); W. M. Whalley and C. N. Robinson, *ibid.*, **75**, 2008 (1953); J. J. Panouse, *Compt. rend.*, **233**, 260, 1200 (1951); O. E. Edwards, F. H. Clarke and B. Douglas, *Can. J. Chem.*, **32**, 235 (1953).

(16) For reactions of the cyanide ion with the $>C{=}N^+<$ function (conjugated) see, for example: A. Kaufmann and A. Albertini, *Ber.*, **42**, 3776 (1909); A. Kaufmann and A. Albertini, *ibid.*, **44**, 2052 (1911); A. Kaufmann, *ibid.*, **51**, 116 (1918); A. Kaufmann, *J. Chem. Soc.*, **114**, 187 (1918); A. Kaufmann and A. Albertini, *Ber.*, **42**, 1999 (1909); R. D. Haworth and W. H. Perkin, *J. Chem. Soc.*, **127**, 1434 (1925); (unconjugated), N. J. Leonard and A. S. Hay, THIS JOURNAL, in press.

(17) For reactions of Grignard reagents with the $>C{=}N^+<$ function (conjugated) see, for example: M. Freund, *Ber.*, **36**, 4257 (1903); **37**, 4666 (1904); M. Freund and H. H. Reitz, *ibid.*, **39**, 2219 (1906); M. Freund and K. Lederer, *ibid.*, **44**, 2353, 2356 (1911); E. Späth and J. Gangl, *Monatsh.*, **44**, 103 (1923); M. Freund and L. Richard, *Ber.*, **42**, 1101 (1909); M. Freund and H. Beck, *ibid.*, **37**, 4679 (1904).

(18) N. J. Leonard and R. E. Beyler, THIS JOURNAL, **72**, 1316 (1950).

(19) D. Kettelhack, Melanie Rink and K. Winterfeld, *Arch. Pharm.*, **287**, 1 (1954).

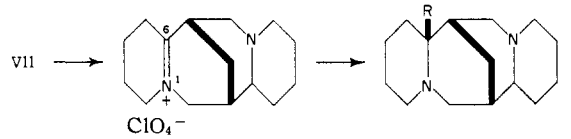
(20) L. Marion and N. J. Leonard, *Can. J. Chem.*, **29**, 297 (1951).

(21) Assumed to be the monodehydro compound—although not actually characterized in this case—since one mole equivalent of mercurous acetate was isolated in the dehydrogenation of β-isosparteine and one mole equivalent of hydrogen was taken up in the subsequent catalytic hydrogenation to sparteine.[14]

(22) E. W. Martin, Ph.D. Thesis, University of Pennsylvania, 1949; M. Carmack and E. W. Martin, Abstracts of Papers, 124th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 6-11, 1953, p. 32-O; E. W. Martin and M. Carmack, *J. Org. Chem.*, in press.

been shown to be one of the isomers of β-isosparteine.[23] The catalytic hydrogenations of (−)-Δ^5-dehydrosparteine (VII) to (−)-sparteine (IV) and (−)-$\Delta^{5,11}$-didehydrosparteine (VIII) to (−)-α-isosparteine (XI) are consistent with the stereochemical assignments in the lupin alkaloid family and the surface nature of the hydrogenation process.[11]

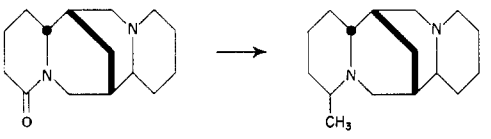
We utilized, for differentiating between Δ^5-dehydrosparteine (VII) and the less likely Δ^2-dehydrosparteine structure, a subsidiary method which depended upon a reaction of the corresponding salt form, $\Delta^{1(6)}$-dehydrosparteinium perchlorate (XIII).



VII → ClO_4^- XIII → XIV

(a, R = CN; b, CH_3; c, C_2H_5; d, n-C_3H_7; e, n-C_4H_9; f, $C_6H_5CH_2$; g, p-$CH_3OC_6H_4CH_2$)

The *dl*-form of the $\Delta^{1(6)}$-dehydrosparteinium perchlorate was used, as obtained from the mercuric acetate dehydrogenation of *dl*-sparteine[18] by the same method that furnished the optically active form from *l*-sparteine. The gross structural identity of the optically inactive and active salts was confirmed by the identity of their infrared absorption spectra in chloroform solution. Treatment of *dl*-XIII with excess methylmagnesium iodide following the method employed in the preceding article in this series[2] furnished a *dl*-methylsparteine (could not be caused to solidify; dipicrate, m.p. 226–227° dec.; dichloroaurate, m.p. 159° dec., monohydrate, m.p. 170° dec. which was not identical with *dl*-2-methylsparteine (XVI) (m.p. 48–50°; dipicrate, m.p. 221°; dichloroaurate monohydrate, m.p. 178° dec.,[24] as indicated by recorded differences in physical properties, including the melting points and crystal forms of the corresponding derivatives. *dl*-2-Methylsparteine (*dl*-XVI), which was made unequivocally by Winterfeld and Hoffmann[24] by the action of methylmagnesium iodide on the alkaloid *dl*-lupanine (*dl*-XV), followed by hydrolysis, dehydration and subsequent hydrogenation, would have been the product of our Grignard sequence if the enamine salt had possessed the $\Delta^{1(2)}$-



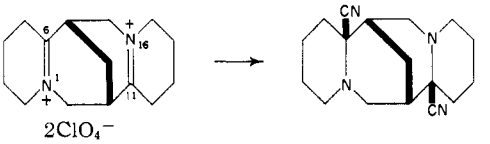
XV XVI

(and therefore the enamine, the Δ^2-structure) instead of the $\Delta^{1(6)}$-structure (XIII).

The structures of the mercuric acetate dehydrogenation products of sparteine therefore are established as Δ^5-dehydrosparteine (VII) and $\Delta^{5,11}$-didehydrosparteine (VIII), and the corresponding enamine salts as $\Delta^{1(6)}$-dehydrosparteinium perchlorate (XIII) and $\Delta^{1(6),11(16)}$-didehydrosparteinium diperchlorate (XVII).

(23) B. Douglas and M. Carmack, THIS JOURNAL, in press.

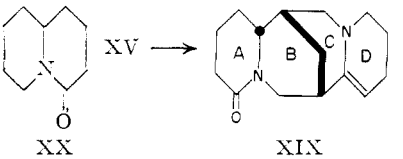
(24) K. Winterfeld and E. Hoffmann, *Arch. Pharm.*, **275**, 5 (1937).



$2ClO_4^-$ XVII XVIII

Accordingly, the $C_{16}H_{25}N_3$ product of the reaction of $\Delta^{1(6)}$-dehydrosparteinium perchlorate with potassium cyanide can be assigned the 6-cyanosparteine structure XIVa, wherein the configuration at C-6 is not decided but is suggested as having the nitrile group *cis* to the $C_{7,9}$-methylene bridge on the basis of stereochemical considerations.[11,25] Similarly, the $C_{17}H_{24}N_4$ product from $\Delta^{1(6),11(16)}$-didehydrosparteinium diperchlorate (XVII) and potassium cyanide must be 6,11-dicyanosparteine (XVIII). Nucleophilic attack of a series of Grignard reagents on $\Delta^{1(6)}$-dehydrosparteinium perchlorate gave bridgehead substitution: 6-methylsparteine (XIVb),[26] 6-ethylsparteine (XIVc), 6-n-propylsparteine (XIVd), 6-n-butylsparteine (XIVe), 6-benzylsparteine (XIVf) and 6-(p-methoxybenzyl)-sparteine (XIVg). Treatment of $\Delta^{1(6)}$-dehydrosparteinium perchlorate (XIII) with phenylmagnesium bromide or p-methoxyphenylmagnesium bromide did not give the corresponding substituted sparteines; only starting material was isolated as such or as VII.[27]

The product of mercuric acetate dehydrogenation of *d*-lupanine (XV) has been assigned the structure Δ^{11}-dehydrolupanine (XIX) on the basis of the inversion of the asymmetric center at C-11 on subsequent catalytic hydrogenation.[11] The cor-



XX XIX

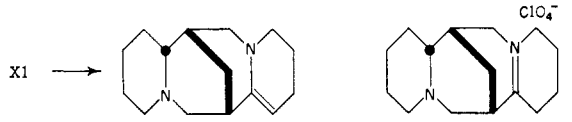
rectness of this structural assignment is indicated further by present studies on 4-ketoquinolizidine (XX) which serves as a model of rings A and B of *d*-lupanine. The action of mercuric acetate upon 4-ketoquinolizidine in dilute acetic acid solution was without visible effect, even after the application of heat, and XX was recovered unchanged from the reaction mixture, thus pointing to the introduction of α,β-unsaturation with respect to the nitrogen common to rings C and D in the parallel dehydrogenation of the alkaloid XV. The product resulting from the removal of one mole of hydrogen by the action of mercuric acetate on *l*-α-isosparteine

(25) See, for example, E. J. Corey, THIS JOURNAL, **76**, 175 (1954).

(26) In this connection, the micro-Zerewitinoff determinations on XIII and XVII were potentially misleading, not only because of the hygroscopic nature of these salts, but because in the reaction of XIII with methylmagnesium iodide on a fairly large scale, an 87% yield of 6-methylsparteine was realized and could not have resulted from a salt having the proton on nitrogen. (Δ^5-Dehydrosparteine did not react with methylmagnesium iodide.) The active methylene group at C-5 could have accounted for the observed liberation of methane in the micro-determination, similar to the gas evolution observed by B. Witkop and J. B. Patrick (*ibid.*, **73**, 1558 (1951)) upon treatment of an indolenine with ethylmagnesium bromide and its recovery after hydrolysis.

(27) By contrast, K. Winterfeld and E. Hoffmann, found *dl*-2-phenylsparteine[24] and *dl*-2-(p-methoxyphenyl)-sparteine (*Arch. Pharm.*, **275**, 526 (1937)) to be stable compounds.

(XI) can safely be assigned structure XXI, Δ^{11}-dehydrosparteine, on the basis of analogy with the



XXI XXII

dehydrogenation of *l*-sparteine and the product resulting from the removal of two moles of hydrogen from *l*-α-isosparteine.[19] Infrared evidence indicates the existence of the salts in the form indicated by XXII ($\Delta^{11(16)}$).

In conclusion,[28] an advance has been made in our knowledge of the behavior of mercuric acetate as a dehydrogenating agent on the tetracyclic system present in the C_{15}-lupin alkaloids, and the enamine salts thus made available have been employed advantageously in representative syntheses.

Experimental[29]

4-Ketoquinolizidine (XX).—Prepared essentially by the method of Boekelheide and Rothchild,[30] the compound, b.p. 83–85° (0.6 mm.), $n^{28}D$ 1.5055, exhibited an infrared absorption maximum at 1638 cm.$^{-1}$. **The perchlorate** was prepared by adding 65% perchloric acid to a methanolic solution of the lactam until the solution was acid to congo red. This useful derivative for identification crystallized as colorless needles from ethyl acetate, m.p. 170–171°.

Anal. Calcd. for $C_9H_{16}ClNO_5$: C, 42.61; H, 6.36. Found: C, 42.71; H, 6.32.

4-Ketoquinolizidine was recovered unchanged under the same mercuric acetate dehydrogenation conditions that converted quinolizidine to $\Delta^{1(10)}$-dehydroquinolizidine.[2]

Sodium Hydrobromide Dehydrogenation of Quinolizidine.—The procedure was modelled after that used by Winterfeld and Schirm[31] for the dehydrogenation of sparteine. Freshly distilled quinolizidine,[30] 7.7 g. (0.051 mole), was dissolved in 20 ml. of water by dropwise addition of sulfuric acid until a clear solution resulted. The solution was poured into a 500-ml., three-necked flask equipped with a loosely fitted stirrer and two dropping funnels. From one funnel was added, at a rapid dropping rate, a solution of 27.2 g. (0.17 mole) of bromine in 277 ml. of 3.7% sodium hydroxide and simultaneously from the second funnel, an approximately 1 *N* solution of sodium hydroxide (120 ml.) at about one-tenth the rate of the former. The reaction mixture was decolorized until the end of the addition, at which time it assumed an amber coloration. After filtration, the solution was made strongly alkaline with concentrated sodium hydroxide and extracted with ether. The ether was removed from the dried extracts by evaporation *in vacuo*, leaving a dark oil which was distilled through a Holzman column, b.p. 30–33° (1 mm.). The clear oil was unstable in air, consequently it was kept under a nitrogen atmosphere on Dry Ice.

A portion of the base was dissolved in absolute ethanol and 65% perchloric acid added until the solution was just acid to congo red paper. The precipitated perchlorate was recrystallized several times from ethanol to give colorless plates, m.p. 234–235° dec.

Anal. Calcd. for $C_9H_{16}ClNO_4$: C, 45.48; H, 6.79; N, 5.89. Found: C, 45.65; H, 7.01; N, 5.85.

The perchlorate had an identical infrared spectrum (mull) with that of $\Delta^{5(10)}$-dehydroquinolizidinium perchlorate[2] and mixtures of the two samples were not depressed in melting decomposition point.

The presence of unchanged quinolizidine in the final mixture (above) was determined by the formation of a picrate, m.p. 194–195° dec., yellow plates from ethanol, which was identical with quinolizidine picrate.

$\Delta^{1(6)}$-Dehydrosparteinium Perchlorate (XIII) from (−)-Sparteine.—The mercuric acetate dehydrogenation procedure was that of Winterfeld and Rauch,[3] with slight modifications. A solution of 56 g. (0.132 mole) of *l*-sparteine sulfate pentahydrate (Inland Alkaloid Co., Tipton, Indiana) in a small amount of water was basified with 20% aqueous potassium hydroxide and extracted five times with ether. The combined ether extracts were shaken with four 100-ml. portions of 5% aqueous acetic acid. To the combined acetic acid extracts was added 169 g. (0.528 mole) of mercuric acetate, and the resulting mixture was stirred for 24 hours at 25°. The precipitated mercurous acetate was the theoretical amount that would result from the removal of one mole equivalent of hydrogen. The filtrate was saturated with hydrogen sulfide and the insoluble mercuric sulfide was removed by centrifugation. To the decanted solution was added 26 g. of 36 *N* sulfuric acid, and the whole was evaporated to about 100 ml. under reduced pressure. The concentrate was made strongly basic with potassium hydroxide, the mixture was extracted with ether and the ether extracts were combined and dried. The ethereal solution was concentrated to small volume *in vacuo*, 75 ml. of absolute ethanol was added and the resulting solution was rendered slightly acidic by 72% perchloric acid, then adjusted to *p*H 8 with concentrated ammonium hydroxide. The solid which was collected by filtration was recrystallized from absolute ethanol as colorless needles, m.p. 160–161° dec., $[\alpha]^{20}D$ 52.0 ± 1.0° (*c* 6.1 in chloroform), yield 14 g. (45%).

Anal. Calcd. for $C_{15}H_{25}ClN_2O_4$: C, 54.13; H, 7.57; N, 8.42. Found: C, 54.02; H, 7.75; N, 8.38.

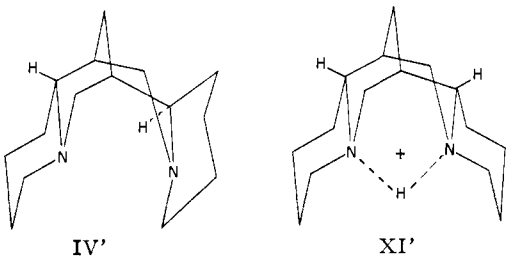
The infrared spectrum of a 10% solution in chloroform had an intense band at 1692 cm.$^{-1}$; of a Nujol mull, at 1695 cm.$^{-1}$. The perchlorate of *l*-sparteine was transparent in this region. Active hydrogen: calcd. for one active hydrogen, 0.30%; for two active hydrogens, 0.60%; found: 0.43%[32] (1.4 active hydrogens).[33]

$\Delta^{1(6)}$-Dehydrosparteinium Diperchlorate.—A solution of the monoperchlorate in methanol was treated with 72% perchloric acid until acid to congo red. The solid which separated upon cooling was recrystallized as nearly colorless prisms from water, m.p. 239–240° dec. The same diperchlorate was obtained directly from the free base (above) by similar treatment. The diperchlorate was insoluble in chloroform.

Anal. Calcd. for $C_{15}H_{26}Cl_2N_2O_8$: C, 41.58; H, 6.05; N, 6.47. Found: C, 41.57; H, 6.09; N, 6.39.

The infrared spectrum of a Nujol mull exhibited a peak at 1680 cm.$^{-1}$ and one at 3160 cm.$^{-1}$. Active hydrogen:

(28) Of incidental interest is a comparison of the base strengths of the alkaloids *l*-sparteine (IV'), and *l*-α-isosparteine. The pK'_a values for α-isosparteine diperchlorate were determined in 66% DMF as (1) <2.5 and (2) 12.1; those for sparteine diperchlorate (also given above), as (1) 3.3 and (2) 11.4. The indication is that the +1 ion (XI') of the free base α-isosparteine has greater stabilization than that related to sparteine. This enhanced stabilization of the +1 ion with respect to both the +2 ion and the free base can be explained by the favorable steric situation in α-isosparteine for intramolecular hydrogen bonding between N-1 and N-16 (XI').



IV' XI'

(29) All melting points are corrected. We are indebted to Mrs. Esther Fett, Mrs. Lucy Chang and Mr. Joseph Nemeth for microanalyses, and to Miss Helen Miklas and Mr. James Brader for determination of the infrared absorption spectra, using a Perkin-Elmer automatic recording infrared spectrometer, model 21.

(30) V. Boekelheide and S. Rothchild, THIS JOURNAL, **71**, 879 (1949).

(31) K. Winterfeld and M. Schirm, *Arch. Pharm.*, **276**, 544 (1938).

(32) Zerewitinoff active hydrogen determinations by the Clark Microanalytical Laboratory, Urbana, Ill.

(33) The compound was hygroscopic so that the found value is likely in error on the high side. Other salts of this dehydrosparteine have been found to be hygroscopic.[4]

calcd. for two active hydrogens, 0.46%; found, 0.48%. pK'_a (in 66% dimethylformamide): (1) 5.0; (2) 12.9.[34]

(−)-Δ^5-**Dehydrosparteine (VII).**—The base[8] was obtained from either $\Delta^{1(6)}$-dehydrosparteinium mono- or diperchlorate by treatment of an aqueous solution of the salt with potassium hydroxide, followed by ether extraction and evaporation of the dried ether extracts *in vacuo*. The residual oil was distilled through a Holzman column, b.p. 98° (0.2 mm.) (reported[8,35] 110–112° (1 mm.)). The infrared spectrum (10% in chloroform) showed a strong maximum at 1650 cm.$^{-1}$ which sparteine did not possess.

(−)-Δ^5-Dehydrosparteine was reduced to (−)-sparteine under the following conditions: (a) hydrogenation in ethanol using palladium-on-strontium carbonate[8]; (b) hydrogenation in 20% hydrochloric acid using platinum oxide catalyst. (−)-Δ^5-Dehydrosparteine was recovered unchanged from attempted reduction with lithium aluminum hydride or with sodium and liquid ammonia. The attempted sodium and ethanol reduction was not conclusive. Attempted isomerization of Δ^5-dehydrosparteine under alkaline conditions (aq. NaOH alone) similar to those used in the dehydrogenation of (−)-sparteine with sodium hypobromite[31] was not successful.

Trial Reduction of 1-Ethyl-2-methyl-Δ^2-tetrahydropyridine with Formic Acid.—The procedure used in all formic acid reductions was that of deBenneville.[36,37] To 0.73 g. (15.8 millimoles) of 98–100% formic acid at 60° was added 1.76 g. (14.1 millimoles) of freshly distilled 1-ethyl-2-methyl-Δ^2-tetrahydropyridine prepared by the method of Ladenburg.[38] Evolution of carbon dioxide was vigorous. After one hour at 60°, the reaction mixture was cooled, rendered basic with 40% aqueous sodium hydroxide solution, and extracted with ether. The residue obtained on evaporation of the ether extracts was distilled, b.p. 145–146° (reported for 1-ethyl-2-methylpiperidine,[39] 145–147°), $n^{25}D$ 1.4478, yield 1.40 g. (78%). **The picrate**, prepared in ether and recrystallized as gold-colored plates from ethanol, melted at 189–190° (reported for 1-ethyl-2-methylpiperidine picrate,[39] 188–189°).

Anal. Calcd. for $C_{14}H_{20}N_4O_7$: C, 47.19; H, 5.66; N, 15.72. Found: C, 47.27; H, 5.84; N, 15.66.

Reduction of (−)-Δ^5-Dehydrosparteine with Formic Acid.—To 2.0 g. (44 millimoles) of 98–100% formic acid at 60° was added dropwise 6.58 g. (28.3 millimoles) of freshly distilled Δ^5-dehydrosparteine while the system was swept continually with a stream of nitrogen. Heating was continued until the evolution of carbon dioxide ceased (*ca.* 2 hours), the reaction mixture was then added to 20 ml. of 18% hydrochloric acid and extracted with ether. The aqueous layer was basified and the amine recovered by ether extraction was distilled through a Holzman column, b.p. 113° (0.5 mm.), yield 5.0 g. (75%). The derivatives were identical with those of (−)-sparteine; monoperchlorate, m.p. 170–171° dec. (reported[40] 173°); dihydrobromide, m.p. 194–197° (reported[41] 194–195°).

Clemmensen Reduction of $\Delta^{1(6)}$-Dehydrosparteinium Bisulfate.—A solution of 4.75 g. (11.2 millimoles) of this salt, m.p. 224–226° dec. (reported[8,35] 225–226°), prepared from (−)-Δ^5-dehydrosparteine, in 20 ml. of 12 *N* hydrochloric acid, was added cautiously to zinc amalgam made from 18 g. of mossy zinc and 2 g. of mercuric chloride. After the initial vigorous reaction had subsided, the mixture was heated under reflux for 12 hours. At intervals of 3 hours, 5-ml. portions of hydrochloric acid were added. The product was isolated in the usual manner and distilled through a Holzman column, b.p. 110–113° (1 mm.), yield 2.2 g. (84%); **monoperchlorate**, m.p. 170–171° dec.; **dipicrate**, m.p. 207° dec. The derivatives were identical with those of (−)-sparteine.

Sodium Borohydride Reduction of $\Delta^{1(6)}$-Dehydrosparteinium Bisulfate.—A solution of 5.0 g. (11.8 millimoles) in 100 ml. of methanol was treated cautiously with 8.0 g. (0.21 mole) of sodium borohydride added in small portions. When the vigorous reaction had subsided, the reaction mixture was heated at reflux for 2 hours, then concentrated to about 40 ml. and poured into 200 ml. of 5% aqueous sodium hydroxide solution. The residual oil that resulted from ether extraction was distilled through a Holzman column; b.p. 110° (0.5 mm.), $n^{20}D$ 1.5295, yield 2.2 g. (80%). The monoperchlorate and dipicrate were identified as derivatives of (−)-sparteine.

The Diperchlorate of (−)-Sparteine.—To a solution of *l*-sparteine in absolute methanol was added 72% perchloric acid in excess, and the clear solution was allowed to cool; colorless plates, m.p. 252–254° dec.

Anal. Calcd. for $C_{15}H_{28}Cl_2N_2O_8$: C, 41.31; H, 6.48; N, 6.44. Found: C, 41.35; H, 6.39; N, 6.30.

Active hydrogen: calcd. for two active hydrogens, 0.46%; found, 0.42% (1.8 active hydrogens). The finding on the monoperchlorate of (−)-sparteine, m.p. 170–171° dec., was as follows: calcd. for one active hydrogen, 0.30%; found, 0.32% (1.07 active hydrogens). pK'_a (66% DMF): (1) 3.3; (2) 11.4.

$\Delta^{1,(6),11(16)}$-Didehydrosparteinium Diperchlorate (XVII) from (−)-Sparteine.—An ethanol solution of α-didehydrosparteine, m.p. 105–106° dec., prepared by the mercuric acetate dehydrogenation of *l*-sparteine,[8,18] was treated with 72% perchloric acid until acid to congo red. Recrystallization of the precipitated salt was accomplished from water containing a few drops of perchloric acid, m.p. 270° dec. (reported 257°[8] (no analysis), 262–263°[19]).

Anal. Calcd. for $C_{15}H_{24}Cl_2N_2O_8$: C, 41.77; H, 5.61; N, 6.50. Found: C, 41.63; H, 5.42; N, 6.35.

The infrared spectrum of a Nujol mull had an intense band at 1690 cm.$^{-1}$. Active hydrogen: calcd. for one active hydrogen, 0.23%; found, 0.25%. pK'_a (66% DMF): (1) 6.8; (2) 13.0.

(−)-$\Delta^{5,11}$-**Didehydrosparteine (VIII).**—The amine, obtained from the perchlorate above by basification and ether extraction, was sublimed at 100–110° (0.5 mm.), m.p. 105–107°, $[\alpha]^{25}D$ −698° (*c* 1.96 in benzene) (reported for α-didehydrosparteine, $[\alpha]D$ −647°,[8] −627°[19]). The infrared spectrum of a 10% solution in chloroform had a strong band at 1646 cm.$^{-1}$ (previously reported for the mull,[18] 1645 cm.$^{-1}$). The ultraviolet absorption spectrum in ether has been reported previously,[7] and the statement in ref. 18, p. 1322, referred to the absence of a maximum, in ethanol solution,[42] typical of C=C—C=C—N (*e.g.* 281 mμ).[43]

(−)-$\Delta^{5,11}$-Didehydrosparteine was recovered unchanged from attempted reduction with lithium aluminum hydride, sodium and liquid ammonia, and sodium and ethanol.

Reduction of (−)-$\Delta^{5,11}$-Didehydrosparteine with Formic Acid.—To 0.87 g. (3.8 millimoles) of $\Delta^{5,11}$-didehydrosparteine was added dropwise 0.74 g. (16 millimoles) of 98–100% formic acid. From this point, the reaction mixture was treated as that from Δ^5-dehydrosparteine and formic acid. The product, m.p. 102–108°, was identified by direct comparison as (−)-α-**isosparteine** (*l*-α-isosparteine)[8,18]; dipicrate, m.p. 220–221° dec.; bisulfate, m.p. 264° dec.; diperchlorate, m.p. 255–257° dec.[44] pK'_a (66% DMF): (1) <2.5; (2) 12.1.

$\Delta^{11(16)}$-Dehydrosparteinium Diperchlorate from (−)-α-Isosparteine.—A solution of 2.90 g. (12.4 millimoles) of (−)-α-isosparteine in 35 ml. of 5% aqueous acetic acid and 15.3 g. (48.0 millimoles) of mercuric acetate were stirred at 25° for 5 hours. The precipitated mercurous acetate amounted to slightly more than theoretically necessary for removal of one mole equivalent of hydrogen. The filtrate was saturated with hydrogen sulfide and the precipitated mercuric sulfide was removed by filtration. After 2.54 g. of 1.84 sp. gr. sulfuric acid was added to the filtrate, the solution was concentrated to small volume under reduced pressure, basified with potassium hydroxide and extracted with ether. The ether extracts were concentrated to small volume, diluted with ethanol, and then made acid to congo red by the addition of 72% perchloric acid. Recrystallization of the precipitate from water gave nearly colorless

(34) We are indebted to Mrs. Helen Arndt and Dr. Harold E. Boaz, both of Eli Lilly and Company, Indianapolis, Ind., for the electrometric titrations and for aid in their interpretation.

(35) K. Winterfeld, *Arch. Pharm.*, **266**, 299 (1928).

(36) P. L. deBenneville and J. H. Macartney, THIS JOURNAL, **72**, 3073 (1950).

(37) P. L. deBenneville, U. S. Patent 2,578,787, Dec. 18, 1951.

(38) A. Ladenburg, *Ann.*, **304**, 54 (1899).

(39) C. F. Winans and H. Adkins, THIS JOURNAL, **54**, 306 (1932).

(40) L. Marion, N. J. Leonard and B. P. Moore, *Can. J. Chem.*, **31**, 181 (1953).

(41) J. F. Couch, THIS JOURNAL, **59**, 1469 (1937).

(42) M. E. Herr and F. W. Heyl, *ibid.*, **74**, 3627 (1952) (footnote 5), have indicated recently that ethanol is *not* the solvent of choice in detecting enamine groupings.

(43) E. A. Braude, *Ann. Repts. Chem. Soc.*, **42**, 105 (1945).

(44) L. Marion and W. F. Cockburn, *Can. J. Chem.*, **29**, 13 (1951).

TABLE I

SUBSTITUTED SPARTEINES

Compound	Yield, %	M.p., °C.	B.p., °C.	B.p., Mm.	$[\alpha]_D$	Character. infrared absorp., max., cm.$^{-1}$ [a]	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
(−)-6-Methylsparteine (XIVb)	87	80–81[b]			−12.5 ± 0.8°[b]	1363	$C_{16}H_{28}N_2$	77.36	77.19	11.36	11.58	11.28	11.49
(−)-6-Ethylsparteine (XIVc)	65	61–63	105	0.5	−16.2 ± 1.0[c]	1367, 1486	$C_{17}H_{30}N_2$					10.68	10.73
(−)-6-*n*-Propylsparteine (XIVd)	56		95	0.4	−19.2 ± 0.8[d]	1367, 1483	$C_{18}H_{32}N_2$	78.20	78.33	11.67	11.60	10.13	10.34
(−)-6-*n*-Butylsparteine (XIVe)	65		93	0.3[e]			$C_{19}H_{34}N_2$						
(+)-6-Benzylsparteine (XIVf)	66	115[f]			30.6 ± 1.0°[f,g]	1501, 1608	$C_{22}H_{32}N_2$	81.43	81.28	9.94	10.03	8.63	8.82
(+)-6-(*p*-Methoxybenzyl)-sparteine (XIVg)	74	...[h]	..	..[h]			$C_{23}H_{34}N_2O$						

	Perchlorates[i] M.p., °C.[j]	Crystal form[k]	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found		Hydriodides[r] M.p., °C.[j]	Crystal form	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
XIVb	207–208	Plates	$C_{16}H_{29}ClN_2O_4$[l]	55.08	54.83	8.38	8.11	8.03	8.15	XIVb	246–247	Needles	$C_{16}H_{29}IN_2$	51.06	51.14	7.77	7.68	7.45	7.39
XIVc	187.5	Needles	$C_{17}H_{31}ClN_2O_4$	56.26	56.13	8.61	8.69	7.72	7.52	XIVc	263–264	Needles	$C_{17}H_{31}IN_2$	52.30	52.05	8.01	7.99	7.18	7.27
XIVd	160–161	Plates	$C_{18}H_{33}ClN_2O_4$	57.36	57.46	8.82	8.83	7.43	7.40	XIVd	243–244	Microcrystals	$C_{18}H_{33}IN_2$	53.46	53.16	8.23	8.23	6.93	7.01
XIVe	153[m]	Plates	$C_{19}H_{35}ClN_2O_4$[n]	58.37	58.34	9.02	8.96	7.17	7.03	XIVe	258	Prisms	$C_{19}H_{35}IN_2$	54.54	54.22	8.43	8.37	6.70	6.65
XIVf	265	Prisms	$C_{22}H_{33}ClN_2O_4$[o]	62.18	62.25	7.83	7.81	6.59	6.62				Hydrobromides[r]						
XIVg	234–235[p]	Plates	$C_{23}H_{35}ClN_2O_5$[q]	60.71	60.93	7.75	7.78	6.16	5.97	XIVf	280	Prisms	$C_{22}H_{33}BrN_2$	65.17	64.87	8.02	7.99	6.91	6.76
										XIVg	300	Needles	$C_{23}H_{35}BrN_2O$	63.44	63.34	8.10	7.80	6.43	6.28

[a] Selected maxima not present in the analogous spectrum of (−)-sparteine (10% solution in chloroform). [b] Colorless needles from acetone; $[\alpha]^{25}D$ for *c* 7.58, ethanol. [c] $[\alpha]^{20}D$ for *c* 7.22, ethanol. [d] n_D^{28} 1.5209; $[\alpha]^{20}D$ for *c* 7.05, ethanol. [e] n_D^{27} 1.5338. [f] Colorless prisms from absolute methanol; $[\alpha]^{20}D$ for *c* 3.51, ethanol. [g] $[\alpha]^{20}D$ 9.9 ± 0.5° (*c* 6.38, chloroform). [h] Did not solidify at Dry Ice temperature and partially decomposed on attempted distillation. [i] Prepared by dropwise addition of 65% perchloric acid to a solution of the substituted sparteine in ethanol, adjustment to *p*H 8 with ammonium hydroxide. [j] With decomposition. [k] Colorless, from ethanol. [l] Characteristic infrared maximum at 1362 cm.$^{-1}$ for a 10% solution in chloroform. [m] $[\alpha]^{25}D$ −3.5 ± 0.5° (*c* 6.9, chloroform). [n] Infrared maxima at 1319, 1335, 1370, 1395, 1416, 1460, 1488 cm.$^{-1}$ for a 10% solution in chloroform. [o] Infrared maxima at 1500 and 1608 cm.$^{-1}$ for a Nujol mull. [p] $[\alpha]^{20}D$ 11.9 ± 1.0° (*c* 6.3, acetone). [q] Infrared maxima at 1038, 1143, 1258, 1521, 1619 cm.$^{-1}$ for a Nujol mull. [r] Colorless, from ethanol–ether or ethanol.

prisms, m.p. 275–276° dec., yield 1.69 g. (32%), of $\Delta^{1(16)}$-dehydrospartеinium (or $\Delta^{1(6)}$-dehydro-α-isosparteinium) diperchlorate.

Anal. Calcd. for $C_{15}H_{28}Cl_2N_2O_8$: C, 41.58; H, 6.05; N, 6.47. Found: C, 41.26; H, 5.90; N, 6.48.

The infrared spectrum of a Nujol mull exhibited a peak at 1687 cm.$^{-1}$ and one at 3045 cm.$^{-1}$.

$\Delta^{1(16)}$-Dehydrospartеinium Perchlorate (XXII).—A portion of the diperchlorate (above) was converted to the amine, and to an ether–ethanol solution of the amine was added 72% perchloric acid until the solution was almost neutral to *p*Hydrion paper. The salt which separated upon cooling was recrystallized from ether–ethanol as colorless plates, m.p. 128°, $[\alpha]_D$ 33.0 ± 0.5° (*c* 6.38 in chloroform).

Anal. Calcd. for $C_{15}H_{29}ClN_2O_4$: C, 54.13; H, 7.57; N, 8.42. Found: C, 54.26; H, 7.72; N, 8.28.

The infrared spectrum of a 10% solution in chloroform showed a strong band at 1696 cm.$^{-1}$.

***dl*-$\Delta^{1(6)}$-Dehydrospartеinium Perchlorate (*dl*-XXIII).**—*dl*-Sparteine monoperchlorate,[18] m.p. 131–132.5°, 1.90 g., equivalent to 1.31 g. (5.67 millimoles) of *dl*-sparteine, was dissolved in a small quantity of water, basified with concentrated aqueous sodium hydroxide and extracted with ether. The total ethereal solution was then extracted with three 5-ml. portions of 5% aqueous acetic acid solution. The resulting *dl*-sparteine acetate solution was stirred at 25° for 24 hours with 7.25 g. (22.7 millimoles) of mercuric acetate. The amount of precipitated mercurous acetate was that theoretically required for the removal of one mole equivalent of hydrogen from the amine. The product was isolated by following the method used for the optically active $\Delta^{1(6)}$-dehydrospartеinium perchlorate. The *dl*-$\Delta^{1(6)}$-dehydrospartеinium perchlorate was crystallized from ethanol–ether as prisms, slightly hygroscopic, m.p. 138–139° dec., yield 0.35 g. (19%).

Anal. Calcd. for $C_{15}H_{25}ClN_2O_4$: C, 54.13; H, 7.57. Found: C, 54.28; H, 7.60.

The infrared spectra for the optically inactive and active salts in 10% chloroform solution were identical within experimental error. The maximum recorded for the *dl*-salt in the $>C{=}\overset{+}{N}<$ region was at 1690 cm.$^{-1}$.

Reaction of $\Delta^{1(6)}$-Dehydrospartеinium Perchlorate with Potassium Cyanide. (−)-6-Cyanosparteine (XIVa).—To a solution of 2.5 g. (7.5 millimoles) of $\Delta^{1(6)}$-dehydrospartеinium perchlorate (XIII) in 30 ml. of methanol was added 0.7 g. (10.7 millimoles) of potassium cyanide. The resulting mixture was heated at the reflux for 30 minutes, cooled and the precipitated potassium perchlorate was removed by filtration. The filtrate was evaporated to dryness *in vacuo* and the residue was taken up in ether. The last traces of organic salts were removed by a second filtration. When the ether was removed, the residue solidified, m.p. 75–76°, yield 1.7 g. (88%), soluble in methanol, ether, low boiling petroleum ether and acetone. Two recrystallizations from acetone gave colorless prisms, m.p. 78°, $[\alpha]^{20}D$ −19.4 ± 1.0° (*c* 7.73 in absolute ethanol).

Anal. Calcd. for $C_{16}H_{25}N_3$: C, 74.08; H, 9.72; N, 16.20. Found: C, 74.05; H, 9.46; N, 16.14.

The infrared spectrum of a 10% solution in chloroform had a band of low intensity at 2220 cm.$^{-1}$, characteristic of the nitrile group. pK'_a (66% DMF): (1) 9.4; (2) *ca.* 3.3 (initial *p*H 11.6).

The perchlorate was prepared by adding 72% perchloric acid to a solution of (−)-6-cyanosparteine in absolute ethanol until the solution was neutral to *p*Hydrion paper. The precipitated salt was recrystallized from methanol as long colorless needles, m.p. 196–197° dec.

Anal. Calcd. for $C_{16}H_{25}ClN_2O_4$: C, 53.40; H, 7.28; N, 11.68. Found: C, 53.17; H, 7.04; N, 11.47.

The hydriodide was prepared by adding 48% hydriodic acid dropwise to a solution of (−)-6-cyanosparteine in absolute ethanol until the solution was just neutral to *p*Hydrion paper. Upon dilution with an equal portion of anhydrous ether, a solid separated which was recrystallized from absolute ethanol as colorless needles, m.p. 201° dec.

Anal. Calcd. for $C_{16}H_{25}IN_2$: C, 49.61; H, 6.77; N, 10.85. Found: C, 49.71; H, 6.80; N, 10.87.

If care is not taken in the preparation of this salt, $\Delta^{1(6)}$-dehydrosparteinium iodide results (no peak at 2220 cm.$^{-1}$, $>C{=}\overset{+}{N}<$ absorption at 1687 cm.$^{-1}$).

Reaction of $\Delta^{1(6),11(16)}$-Dehydrosparteinium Diperchlorate with Potassium Cyanide. (−)-6,11-Dicyanosparteine (XVIII).—To a slurry of 5.0 g. (11.6 millimoles) of $\Delta^{1(6),11(16)}$-didehydrosparteinium diperchlorate (XVII) in 60 ml. of methanol was added 2.2 g. (34 millimoles) of potassium cyanide. The mixture was stirred on the steam-bath until all of the diperchlorate was dissolved and then for an additional 30 minutes. The precipitated potassium perchlorate (3.2 g., 99%) was removed by cooling followed by filtration, and the filtrate was evaporated to dryness *in vacuo*. The organic material was taken up in ether, and a second filtration and evaporation of the filtrate afforded 3.0 g. (91%) of organic solid. The product was very soluble in acetone, methanol, 2-propanol and benzene, practically insoluble in ligroin and cyclohexane, and slightly soluble in low boiling petroleum ether. Recrystallization was effected by solution in 20 ml. of methanol followed by storage in the ice-box overnight. Three recrystallizations gave elongated prisms, m.p. 165–166° dec., $[\alpha]^{20}D$ −65.8 ± 1.0° (*c* 5.88 in chloroform). It was noted that methanolic solutions of the dicyanosparteine were only weakly basic to *p*Hydrion paper.

Anal. Calcd. for $C_{17}H_{24}N_4$: C, 71.79; H, 8.51; N, 19.70. Found: C, 71.91; H, 8.13; N, 20.00.

The infrared spectrum of a 10% solution in chloroform had a band at 2220 cm.$^{-1}$. pK'_a (66% DMF): (1) 6.9; (2) <3.0 (initial *p*H 11).

A perchlorate salt could not be obtained even by careful neutralization with perchloric acid. When a solution of (−)-6,11-dicyanosparteine in methanol was made acid to congo red with 72% perchloric acid, followed by cooling, an amorphous solid separated. Recrystallization from water containing a few drops of perchloric acid furnished pure **$\Delta^{1(6),11(16)}$-didehydrosparteinium diperchlorate,** identified by infrared spectral comparison, determination of melting points of mixtures with an authentic sample, and analysis.

Anal. Calcd. for $C_{15}H_{24}Cl_2N_2O_4$: C, 41.77; H, 5.61; N, 6.50. Found: C, 41.89; H, 5.67; N, 6.50.

Reaction of $\Delta^{1(6)}$-Dehydrosparteinium Perchlorate with Grignard Reagents.[45] **(−)-6-Methylsparteine (XIVb).**—To a solution of 41 millimoles of methylmagnesium iodide in 50 ml. of anhydrous ether, prepared from 1.0 g. of magnesium turnings and 5.8 g. of methyl iodide, was added 5.50 g. (16.4 millimoles) of finely powdered $\Delta^{1(6)}$-dehydrosparteinium perchlorate by means of a spatula. A grayish solid separated which adhered to the walls of the flask. The reaction mixture was heated under reflux for one hour without stirring, then for one hour with stirring. The excess Grignard reagent was decomposed with saturated aqueous ammonium chloride, 100 ml. of a saturated solution of sodium fluoride was added to the separated aqueous layer,[2] and the precipitated magnesium fluoride was removed by centrifugation. The supernatant was decanted into a separatory funnel, made strongly basic with sodium hydroxide, and the mixture was extracted five times with ether. The combined ether extracts and the original ether layer were dried, and the ether was removed to leave colorless crystals. 6-Methylsparteine was found to be soluble in ethanol, chloroform, benzene and ethyl acetate and moderately soluble in acetone. The properties of the base and its salts are given in Table I, along with those of the other substituted sparteines made by the use of the corresponding Grignard reagents.

When the Grignard reagent (CH_3MgI) was brought together with (−)-Δ^5-dehydrosparteine instead of $\Delta^{1(6)}$-dehydrosparteinium perchlorate under the same conditions, no (−)-6-methylsparteine was obtained and at least 54% of the Δ^5-dehydrosparteine could be recovered and identified by the usual derivatives.

The action of phenylmagnesium bromide and of *p*-methoxyphenylmagnesium bromide upon $\Delta^{1(6)}$-dehydrosparteinium perchlorate failed to produce the corresponding 6-substituted sparteines. The starting material was recovered, either as $\Delta^{1(6)}$-dehydrosparteinium perchlorate or as Δ^5-dehydrosparteine, converted to this salt for identification.

Reaction of *dl*-$\Delta^{1(6)}$-Dehydrosparteinium Perchlorate with Methylmagnesium Iodide. *dl*-6-Methylsparteine.—To 2.0 millimoles of methylmagnesium iodide, prepared from 48 mg. of magnesium powder and 285 mg. of methyl iodide in 20 ml. of anhydrous ether was added 223 mg. (0.67 millimole) of *dl*-$\Delta^{1(6)}$-dehydrosparteinium perchlorate. The reaction conditions and the isolation procedure were those used in the preparation of the optically active form. The oil which was obtained could not be induced to solidify even at −60°; moreover, an acetone solution of the amine did not yield crystals upon cooling in acetone–Dry Ice or upon spontaneous evaporation of the solvent. (Winterfeld and Hoffmann[24] reported m.p. 48–50° for *dl*-2-methylsparteine.) The amine was converted to the derivatives given in Table I.

The dipicrate was made from the base dissolved in absolute ethanol by the addition of ethanolic picric acid until precipitation was complete. The picrate, m.p. 211° dec., was removed by filtration and recrystallization twice from acetone–methanol (2:1) as tiny yellow prisms, m.p. 226–227° dec. (Winterfeld and Hoffmann[24] reported rosettes of short needles, m.p. 221°, for *dl*-2-methylsparteine dipicrate.)

Anal. Calcd. for $C_{28}H_{34}N_8O_{14}$: C, 47.59; H, 4.85. Found: C, 47.29; H, 4.81.

The dichloroaurate was prepared from the base in 18% hydrochloric acid and excess chloroauric acid. The solid which separated upon concentration of the solution was collected and recrystallized from 18% hydrochloric acid to which a few drops of chloroauric acid had been added; yellow prisms of the hydrate were obtained, m.p. 170° dec. Drying over phosphorus pentoxide at 100° (1 min.) for three hours gave a tan amorphous solid, m.p. 159° dec. (Winterfeld and Hoffmann[24] reported m.p. 178° dec. for the dichloroaurate monohydrate of *dl*-2-methylsparteine, yellow needles.)

Anal. Calcd. for $C_{16}H_{30}Au_2Cl_8N_2$: C, 20.70; H, 3.26; N, 3.02; Au, 42.48. Found: C, 21.07; H, 3.52; N, 3.36; Au, 41.97.

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(45) These reactions were carried out under an atmosphere of nitrogen.