TABLE I

MUTAROTATION OF α-MELIBIOSE IN WATER AT 20°

α-Melibiose (0.9798 g.) containing 3.64% water in 25 ml. of solution observed in a 4-dm. tube

t, min.	$[\alpha]^{20}_{D}$ (anhyd. basis)	$k_1 + k_2$, min., decimal logs
0	166.0 extrap.	....
1	165.6	0.0078
3	164.7	.0081
5	163.8	.0084
10	161.9	.0083
15	158.9	.0100
25	156.2	.0093
35	153.2	.0096
45	151.1	.0095
60	148.1	.0100
95	145.3	.0094
135	143.7	.0091
220	142.3	....
285	142.3	....

tion spectra of this substance and of β-melibiose dihydrate may be compared in Fig. 1. X-Ray diffraction data[17]: 8.96 (M), 7.70 (VW), 6.80 (W), 6.30 (S), 5.40 (VW), 5.13 (VS), 4.91 (VW), 4.63 (S), 4.41 (VS), 4.11 (S), 3.94 (M), 3.63 (VW), 3.46 (M), 3.35 (W), 3.27 (W), 3.19 (VW), 3.07 (M), 3.00 (W), 2.86 (W), 2.79 (M), 2.72 (VW), 2.58 (M), 2.51 (W), 2.47 (W), 2.31 (VW), 2.28 (VW), 2.22 (VW), 2.16–2.09 (W-B), 2.01–1.96 (W-B), 1.912 (VW), 1.868 (W), 1.797 (VW), 1.750 (VW).

Crystals of α-melibiose monohydrate, grown in a viscous aqueous sirup, were negative in sign and showed, n^{20}D, α = 1.524, β = 1.542, γ = 1.559, 2V = 86° and birefringence = 0.035.

Anal. Calcd. for $C_{12}H_{22}O_{11} \cdot H_2O$: C, 40.00; H, 6.71; H_2O, 5.00. Found: C, 40.17; H, 6.70; loss of wt. *in vacuo* at 100°, 4.99.

Recrystallization of 1 g. of melibiose from 100 ml. of anhydrous methanol afforded 0.35 g. of essentially anhydrous α-melibiose (0.17% loss *in vacuo* at 100°). On exposure to air this approached a monohydrate in composition.

Acetylation of α-Melibiose.—α-Melibiose (2 g.) containing 4.2% water was acetylated in the usual fashion with acetic anhydride and sodium acetate. The crystalline product (3.2 g., 82%), recrystallized from 8 parts of absolute alcohol, showed $[\alpha]^{20}$D +104.3° in chloroform (c 0.82) and melted at 177–178° either alone or in admixture with authentic β-melibiose octaacetate.

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[17] Interplanar spacing, Å.; CuK_α radiation (nickel filter); camera diameter 14.32 cm. Relative intensity estimated visually VS = very strong, S = strong, M = moderately strong, W = weak, VW = very weak and B designates broad, unresolved line or lines.

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Octahydropyrrocoline: Resolution and Configuration

BY NELSON J. LEONARD AND WILLIAM J. MIDDLETON

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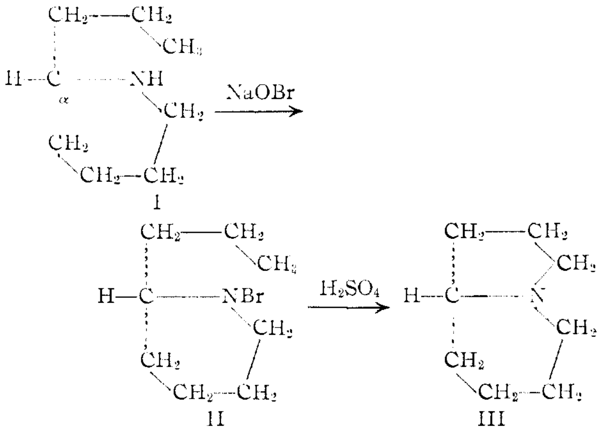
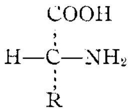
The establishment of the stereochemical configuration for (−)-octahydropyrrocoline (III)[1] is important because of the occurrence of this nucleus or moiety in many of the papilionaceous and solanaceous alkaloids. Such establishment is possible if we can be assured that the conversion by Lellmann[2] of the hemlock alkaloid (+)-coniine (I), to the N-bromo compound (II) and thence by sulfuric acid to (−)-octahydropyrrocoline proceeds





IV

$$\begin{array}{c} \mathrm{COOH} \\ \vdots \\ \mathrm{H—C—NH_2} \\ \vdots \\ \mathrm{R} \end{array}$$

with retention of configuration at the asymmetric carbon. The changes involved in the conversion would not be expected to result in inversion at the α-carbon, but it seemed advisable to determine whether any appreciable racemization had occurred. The rotation reported by Lellmann[2] for the active octahydropyrrocoline obtained from (+)-coniine was −7.8°. We have resolved synthetic octahydropyrrocoline by means of dibenzoyl-D-tartaric acid and have obtained active octahydropyrrocoline of constant maximum rotation, $[\alpha]^{27}$D −7.89°. It is thus apparent that the Lellmann product was of optical purity and identical configuration with (+)-coniine. Since (+)-coniine has been related to D(+)-pipecolinic acid,[3–5] it follows that levorotatory octahydropyrrocoline has the D-configuration, wherein the designation "D" acquires meaning when represented by the projection formula III (*cf.* IV).

Experimental

Mono-(−)-octahydropyrrocoline Dibenzoyl-D-tartrate.—A solution of 112.8 g. (0.3 mole) of dibenzoyl-D-tartaric acid monohydrate[6] in 400 ml. of methanol was mixed with 37.5 g. (0.3 mole) of synthetic octahydropyrrocoline.[7] The white crystalline mass which formed a few minutes after mixing was removed by filtration and washed with cold methanol. This material was recrystallized from 4 liters of methanol. After five additional recrystallizations from methanol, 33.8 g. of large colorless prisms was obtained, m.p. 163–164° with decomposition; $[\alpha]^{27}$D −75.8° (c 0.600, methanol).

Anal. Calcd. for $C_{26}H_{29}NO_8$: C, 64.58; H, 6.05; N, 2.89. Found: C, 64.29; H, 6.16; N, 2.93.

(−)-**Octahydropyrrocoline** (III).—A slurry of 31.4 g. of mono-(−)-octahydropyrrocoline dibenzoyl-D-tartrate and 200 ml. of 3 N hydrochloric acid was shaken for 30 minutes. The oil which separated solidified on addition of a few crys-

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[1] Alternative names: (−)-δ-coniceine, piperolidine and 1-azabicyclo[4.3.0]nonane.

[2] E. Lellmann, *Ber.*, **23**, 2141 (1890).

[3] "The Alkaloids. Chemistry and Physiology," edited by R. H. F. Manske and H. L. Holmes, Academic Press, Inc., New York, N. Y., Vol. I, 1950, pp. 215, 217, 225, 226.

[4] W. Leithe, *Ber.*, **65**, 927 (1932).

[5] A. Neuberger, *Advances in Protein Chemistry*, **4**, 297 (1948).

[6] C. L. Butler and L. H. Cretcher, THIS JOURNAL, **55**, 2605 (1933).

[7] V. Boekelheide and S. Rothschild, *ibid.*, **70**, 864 (1948).

tals of dibenzoyl-D-tartaric acid monohydrate. The solid was removed by filtration, and the filtrate was cooled and made basic with cold 33% potassium hydroxide solution. The alkaline solution was extracted with ether and the ether extracts were dried. The ether was evaporated and the residue was distilled under reduced pressure, yielding 5.1 g. of (−)-octahydropyrrocoline, b.p. 58–59° (18 mm.), $n^{20}D$ 1.4712, $[\alpha]^{27}D$ −7.89°.

Anal. Calcd. for $C_8H_{15}N$: C, 76.74; H, 12.08; N, 11.19. Found: C, 76.50; H, 11.96; N, 11.40.

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Partition Studies. VIII. Silver Complexes of Aromatic Amines

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Silver ion reacts like a generalized acid with a variety of olefinic[1,2] and aromatic compounds[3–5] according to the equations

$$Ag^+ + B \overset{K_1}{\rightleftarrows} AgB^+ \tag{1}$$

$$Ag^+ + AgB^+ \overset{K_2}{\rightleftarrows} Ag_2B^{++} \tag{2}$$

With nitrogen bases, complexes of the 1:2 type, AgB_2^+, rather than Ag_2B^{++}, are formed.[6,7] This observation was based upon electrometric measurements of solutions in which the ratio $(Ag^+)_{total}/(B)_{total}$ was usually less than unity. For a high value of this ratio, it seemed likely that aromatic amines would form 2:1 complexes because of the possibility that a second silver ion could coördinate with the aromatic nucleus. It was of interest, therefore, to study the argentation of aniline and its methyl-substituted homologs by the distribution method[1,5] in which a high $(Ag^+)_t/(B)_t$ ratio can be conveniently maintained.

To apply the distribution method, partition coefficients were determined in the presence and in the absence of the complexing agent. The k' values recorded in Table I are the partition coefficients for distribution of aniline and its methyl-substituted homologs between cyclohexane and aqueous silver nitrate solutions in which ionic strength was maintained at unity by addition of appropriate amounts of potassium nitrate. The k-values are the partition coefficients of the amines for distribution between cyclohexane and 1 molar potassium nitrate solution.

In all distributions, the silver ion concentration was much greater than the total concentration of amine (0.005 *M*). Under these conditions, the equilibrium constant, K, for the formation of a 1:1 complex exclusively (equation 1) can be calculated by the equation[5]

$$K = (k/k' - 1)/(Ag^+)_t \tag{3}$$

On the other hand, if the complexing action proceeds partly to the 2:1 stage (equation 2), K is not independent of $(Ag^+)_t$ and equation 4 applies.[2]

$$K = K_1 + K_1K_2(Ag^+)_t \tag{4}$$

As indicated in Table I, the calculated K values show a marked increase with silver ion concentration, and K was a linear function of the silver ion concentration for all compounds investigated; this was in accordance with equation 4. From the intercepts and slopes of these straight lines, K_I and K_2[8] were evaluated and are summarized in Table II, together with the known acidic dissociation constants (pK_a values) of the bases.

TABLE I

DISTRIBUTION OF ANILINES BETWEEN CYCLOHEXANE AND WATER IN THE PRESENCE OF SILVER NITRATE AT 25.0°

$(Ag^+)_t$, moles/liter	k	k'	K	k	k'	K	k	k'	K	k	k'	K
	Aniline			*o*-Toluidine			*m*-Toluidine			*p*-Toluidine		
0.00	1.36			5.73			4.84			4.62		
.05		0.54	30.4									
.10		.33	31.2		1.22	37.0		1.10	34.0		0.90	41.3
.20		.17	35.0									
.25		.13	37.9		0.48	43.8		0.43	41.1		.35	48.8
.35		.088	41.2		.32	48.3		.28	46.5		.24	52.2
.50		.054	48.4		.20	55.2		.17	53.3		.15	59.6
.75											.08	71.0
	N-Methylaniline			3,5-Xylidine			2,6-Xylidine					
0.00	25.2			22.0			34.7					
.05												
.10		12.54	10.2		3.77	48.4		5.58	52.2			
.20												
.25		6.50	11.5		1.54	53.1		1.95	67.2			
.35		4.77	12.3					1.22	78.4			
.50		3.28	13.4		0.65	65.7		0.73	93.0			
.75		1.97	15.7		0.37	78.0						

The observed trends in the K_1 and K_2 values appear to be most consistent with the assumption that the first silver ion coördinates with the amino nitrogen and the second with the aromatic nucleus.

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[1] S. Winstein and H. J. Lucas, THIS JOURNAL, **60**, 836 (1938).

[2] F. R. Hepner, K. N. Trueblood and H. J. Lucas, *ibid.*, **74**, 1333 (1952).

[3] L. J. Andrews and R. M. Keefer, *ibid.*, **72**, 3113 (1950); **72**, 5034 (1950); **73**, 5733 (1951).

[4] P. L. Nichols, *ibid.*, **74**, 1091 (1952).

[5] C. Golumbic and S. Weller, *ibid.*, **74**, 3739 (1952).

[6] J. Bjerrum, "Metal Ammine Formation in Aqueous Solution," P. Haase and Son, Copenhagen, 1941, p. 298.

[7] R. J. Bruehlman and F. H. Verhoek, THIS JOURNAL, **70**, 1401 (1948).

[8] For a discussion of the relation between these constants and the true thermodynamic equilibrium constants see ref. 2.