The Magneto-optic Rotations of Two Ephedrine Isomers and Their Hydrochlorides in Solution.

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The volume fraction rule and the partial volume fraction mixture rule, described in the preceding paper, have been used to calculate the Verdet constants of two ephedrine isomers and their hydrochlorides. The higher Verdet constant for (–)-ephedrine suggests that the bonding forces between the molecules of this isomer are less than those between the molecules of ψ-ephedrine. This is in agreement with the differences of melting point, solubility, and volatility of the isomers.

THIS paper records the study of the magnetic rotations of (—)- and ψ-ephedrine in ethanol, and of the hydrochlorides of these bases in water. The Verdet constants of the solutes have been calculated according to two of the mixture rules previously described (*loc. cit.*), *viz.*, the volume fraction rule and the apparent volume fraction rule. For the purposes of the former rule the density of the solute was determined by the expression $\Sigma q/s = 1$, where q is the concentration of a component in g./c.c., and s is its corresponding density.

EXPERIMENTAL

Materials.—Commercial (–)-ephedrine hemihydrate was purified by recrystallisation from 70% ethanol, and dehydrated by vacuum-distillation; the distillate was allowed to crystallise in a vacuum to prevent the uptake of carbon dioxide and water vapour. The anhydrous base was further recrystallised from dry ether (Na dried).

ψ-Ephedrine was also purified by recrystallisation from dry ether, and its m. p. agreed with that quoted by Henry ("Plant Alkaloids," Churchill, London, 1949, p. 638). Commercial (−)-ephedrine hydrochloride was recrystallised from water until its m. p. agreed with that quoted by Henry (*op. cit.*, p. 636), and was assayed by using a strong anion-exchange column (Saunders, Elworthy, and Fleming, *J. Pharm. Pharmacol.*, 1954, **6**, 32). ψ-Ephedrine hydrochloride was recrystallised from ethanol and its m. p. agreed with that quoted by Henry (*op. cit.*, p. 638).

TABLE 1. (−)-*Ephedrine in ethanol.*

N_2	$10^4\delta_D^{25}$	$10^4\delta_2$ (ii)	$10^4\delta_2$ (iv)	d_4^{25}	ψ_2	N_2	$10^4\delta_D^{25}$	$10^4\delta_2$ (ii)	$10^4\delta_2$ (iv)	d_4^{25}	ψ_2
0·0188	118·3	215·9	217·4	0·7995	153·5	0·1316	151·8	242·1	229·6	0·8736	146·7
0·0475	128·8	224·4	258·0	0·8204	153·3	0·2052	169·9	243·6	244·7	0·9042	156·8
0·0762	136·3	238·1	233·3	0·8387	154·6	0·2068	170·6	246·2	246·2	0·9069	155·9
0·1116	145·9	239·5	239·5	0·8597	155·4	0·2459	177·6	243·9	246·9	0·9237	149·4
							Mean	237·0	239·5		
0·0379	124·6	232·2	232·9	0·8118	154·9	0·1182	147·0	241·7	241·7	0·8753	156·1
0·0705	132·7	228·1	226·6	0·8291	158·3	0·1663	158·8	244·7	244·7	0·8795	156·3
							Mean	236·6	236·6		

Results.—In Table 1, N_2 is the mole-fraction of (−)-ephedrine; δ_D^{25} is the Verdet constant of the solution at 25° and for the Na-*D* line; δ_2 (ii) and δ_2 (iv) are the Verdet constants of (−)-ephedrine calculated respectively according to the volume fraction and the apparent volume fraction rule; d_4^{25} is the density of the solution and ψ_2 is the apparent molar volume of (−)-ephedrine in solution. The first eight solutions were made with (−)-ephedrine hemihydrate and for the purposes of calculation these were assumed to be ternary mixtures of (−)-ephedrine, water, and ethanol. The last four were made with anhydrous (−)-ephedrine and were treated as a binary mixture. An experimental variation of 0·4% in the measurement of the Verdet constant of the solution causes a variation of 2·5% in the derived Verdet constant, δ_2 (ii) and δ_2 (iv).

The Verdet constants of (−)-ephedrine in the ternary system, and in the binary system are listed below, together with the standard errors of the mean.

	10^4 × Verdet constant:	
	for ternary system	for binary system
Volume fraction rule (ii)	237·0 ± 3·7	236·6 ± 3·7
Apparent volume fraction rule (iv)	239·5 ± 4·4	236·6 ± 3·7

In Table 2 is recorded ψ_2, the apparent molar volume of ψ-ephedrine in alcohol, and there is good agreement between the values of the Verdet constant calculated according to either of the above rules.

TABLE 2. ψ-*Ephedrine in ethanol.*

N_2	$10^4\delta_D^{25}$	$10^4\delta_2$ (ii)	$10^4\delta_2$ (iv)	d_4^{25}	ψ_2	N_2	$10^4\delta_D^{25}$	$10^4\delta_2$ (ii)	$10^4\delta_2$ (iv)	d_4^{25}	ψ_2
0·0165	117·2	204·9	204·5	0·7965	157·9	0·0734	133·8	229·6	229·9	0·8317	156·9
0·0276	121·2	220·0	217·0	0·8039	156·6	0·0791	136·3	236·9	236·9	0·8348	157·5
0·0445	126·0	229·6	229·6	0·8415	157·4						
0·0580	129·7	228·5	228·5	0·8228	157·3		Mean	224·8	225·2		
						Standard error of mean		4·0	5·0		

Table 3 gives the various constants for the hydrochlorides of (−)- and ψ-ephedrine in water, and the last table summarises the results.

TABLE 3.

N_2	$10^4\delta_D^{25}$	$10^4\delta_2$ (ii)	$10^4\delta_2$ (iv)	d_4^{25}	ψ_2	N_2	$10^4\delta_D^{25}$	$10^4\delta_2$ (ii)	$10^4\delta_2$ (iv)	d_4^{25}	ψ_2
				(a) (−)-*Ephedrine hydrochloride in water.*							
0·0037	135·9	290·7	301·8	1·0035	161·3	0·0150	149·6	282·6	276·0	1·0216	169·1
0·0061	138·9	284·5	289·6	1·0096	164·2	0·0189	154·4	262·7	284·5	1·0264	170·1
0·0084	141·5	278·6	276·0	1·0129	165·8	0·0221	157·0	280·4	281·0	1·0308	169·6
0·0108	144·8	281·5	281·2	1·0149	169·7		Mean	283·4	285·6		
						Standard error of mean		2·0	3·0		
				(b) ψ-*Ephedrine hydrochloride in water.*							
0·0077	140·8	274·5	274·5	1·0096	171·0	0·0193	154·8	284·4	286·0	1·0266	170·0
0·0127	147·0	278·9	280·8	1·0171	171·5		Mean	279·3	280·4		
						Standard error of mean		2·0	3·0		

Summary of the Verdet constants ($\times 10^4$) *and the standard errors of the mean.*

	Volume fraction rule (ii)	Apparent volume fraction rule (iv)
Ephedrine	236·6 ± 3·7	236·6 ± 3·7
ψ-Ephedrine	224·8 ± 4·0	225·2 ± 5·0
Ephedrine hydrochloride	283·4 ± 2·0	285·6 ± 3·0
ψ-Ephedrine hydrochloride	279·3 ± 2·0	280·4 ± 2·0

Discussion.—The higher Verdet constant for (—)-ephedrine suggests that the bonding forces between the molecules of this isomer are less than those between the molecules of ψ-ephedrine. This is in agreement with the differences of melting point, solubility, and volatility of the isomers.

If restricted rotation between the carbon atoms of the propanol side-chain in the ephedrine molecule is accepted, these physical properties would appear to support the configurations suggested by Freudenberg, Schoeffel, and Braun (*J. Amer. Chem. Soc.*, 1932, **54**, 234).

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