59. *The Influence of Solvents and Other Factors on the Rotation of Optically Active Compounds. Part XXXVIII. Asymmetric Solvent Action (continued).*

By T. S. Patterson and Charles Buchanan.

Work described in Part XXXVI has been repeated and extended, from which it appears (1) that data formerly obtained with nitrobenzene as a solvent for *iso*butyl *d*- and *l*-tartrates were faulty; (2) that benzyl benzoate is more suitable as a solvent for this purpose than is nitrobenzene; (3) that the M.S.V. of *iso*butyl *d*-tartrate is definitely, although only slightly, *greater* than that of *iso*butyl *l*-tartrate in *l*-menthyl acetate, whereas they are equal within the limit of experimental error in benzyl benzoate; (4) the M.S.V. of ethyl diacetyl-*d*-tartrate is definitely *less* than that of ethyl diacetyl-*l*-tartrate in menthyl acetate, whereas they are equal within the limit of experimental error in benzyl benzoate. It is therefore claimed that asymmetry of solvent action has now been established. The fact that the volume-difference for the first pair of enantiomorphs is in the opposite sense from the volume-difference for the second pair helps considerably to justify this conclusion.

In Part XXXVI (J., 1937, 1453) one of us with Lamberton described experiments in which the solution-volumes of *iso*butyl *d*-tartrate and *iso*butyl *l*-tartrate in *l*-menthyl acetate were compared; and a definite, although small, difference was observed. Since, however, an almost similar difference was found in nitrobenzene—a symmetrical solvent—a positive decision as to the existence of a real difference did not seem justified. Further consideration suggested that the results obtained might be due to a constant difference in the purity of the *d*- and the *l*-tartaric ester, since the *d*-ester had been made direct from ordinary *d*-tartaric acid, whilst the *l*-ester was made from *l*-acid separated from racemic acid. The difference in the respective processes of purification might have been sufficient to cause the slight discrepancies observed. We have therefore repeated and extended the earlier experiments, adopting improved methods of procedure, as is described further on. The results for *iso*butyl tartrate in *l*-menthyl acetate are in Table I (a). They were obtained in the order in which they are numbered, and are not selected in any way; every experiment made in this and all the following series is reported. The M.S.V. of the *d*-ester, omitting V, is 242·783 ml., with a mean deviation of 0·015, whilst the *l*-ester gives 242·722, mean deviation, 0·009. The difference *d* — *l* is + 0·061 ml. This is thus very close to the values previously recorded for two entirely independent sets of experiments, namely, 0·054 ml. and 0·048 ml. The maximum difference between these three numbers (0·013 ml.) is thus of just the same order as the departure from the mean in Table I (a), whereas the numbers themselves are about four times this probable error. Our present results so far, therefore, fully confirm those previously obtained.

These two esters were then examined in nitrobenzene, a symmetrical solvent. The results are in Table I (b). Fortunately these experiments were made alternately with dextro- and lævo-ester, and when the series was completed it became apparent that the

TABLE I.

(a) iso*Butyl Tartrate in* l-*Menthyl Acetate* ($d_{4^\circ}^{20^\circ}$ = 0·925293).

No.	*p*, %.*	$d_{4^\circ}^{20^\circ}$.	M.S.V., ml.	No.	*p*, %.	$d_{4^\circ}^{20^\circ}$.	M.S.V., ml.
	d-Ester.				*l*-Ester.		
I	5·40036	0·932474	242·774	II	5·40061	0·932485	242·716
III	5·40644	0·932483	242·770	IV	5·40612	0·932489	242·735
V	5·39990	0·932463	(242·833)	VI	5·40025	0·932485	242·714
VII	5·39698	0·932464	242·806				
			Mean 242·783	Δ = 0·061 ml.			Mean 242·722

(b) iso*Butyl Tartrate in Nitrobenzene* ($d_{4^\circ}^{20^\circ}$ = 1·203012).

	d-Tartrate.				*l*-Tartrate.		
VIII	5·40098	1·195438	243·334	IX	5·38517	1·195464	243·320
X	5·40049	1·195437	243·340	XI	5·37152	1·195471	243·359
XIII	5·38750	1·195448	243·364	XII	5·40146	1·195423	243·382
				XIV	5·39930	1·195419	243·408

(c) iso*Butyl Tartrate in Benzyl Benzoate* ($d_{4^\circ}^{20^\circ}$ = 1·119204).

	d-Tartrate.				*l*-Tartrate.		
XV	5·39880	1·117319	241·410	XVI	5·40354	1·117308	241·447
XVII	5·39824	1·117317	241·420	XVIII	5·40054	1·117319	241·408
			Mean 241·415	Δ = 0·012 ml.			Mean 241·427

(d) *Ethyl Diacetyltartrate in* l-*Menthyl Acetate* ($d_{4^\circ}^{20^\circ}$ = 0·925293).

	d-Diacetyltartrate.				*l*-Diacetyltartrate.		
XIX	5·39091	0·935056	252·711	XX	5·39105	0·935039	252·821
XXI	5·37568	0·935031	252·695	XXII	5·37535	0·935012	252·808
XXIII	5·39110	0·935056	252·715	XXIV	5·39105	0·935041	252·806
			Mean 252·707	Δ = 0·105 ml.			Mean 252·812

(e) *Ethyl Diacetyltartrate in Benzyl Benzoate* ($d_{4^\circ}^{20^\circ}$ = 1·119180).

	d-Diacetyltartrate.				*l*-Diacetyltartrate.		
XXV	5·40019	1·121345	249·855	XXVI	5·40234	1·121347	249·848
XXVII	5·40405	1·121348	249·848	XXVIII	5·40255	1·121344	249·863
			Mean 249·851	Δ = 0·004 ml.			Mean 249·855

(f) *Ethyl Diacetyltartrate in* l-*Menthyl Acetate* ($d_{4^\circ}^{20^\circ}$ = 0·925336).

	d-Diacetyltartrate.				*l*-Diacetyltartrate.		
XXIX	5·39640	0·935105	252·727	XXX	5·40039	0·935095	252·834
XXXI	5·40170	0·935118	252·706	XXXII	5·40010	0·935094	252·839
			Mean 252·716	Δ = 0·120 ml.			Mean 252·836

(g) *Ethyl Diacetyltartrate in Benzyl Benzoate* † ($d_{4^\circ}^{20^\circ}$ = 1·117310).

	d-Diacetyltartrate.				*l*-Diacetyltartrate.		
XXXIII	5·40101	1·119584	249·794	XXXIV	5·40114	1·119574	249·833
XXXV	5·40082	1·119577	249·820	XXXVI	5·40030	1·119577	249·819
XXXVII	5·40010	1·119573	249·837				
			Mean 249·817	Δ = 0·009 ml.			Mean 249·826

* Relative to tartrate.

† A fresh sample.

volume had been increasing almost steadily throughout. At the conclusion of the experiments the density of the nitrobenzene was found to have fallen to $d_{4^\circ}^{20^\circ} = 1{\cdot}202982$, *i.e.*, by 0·00003 unit, probably owing to the gradual absorption of moisture from the air. These results are therefore uncertain; but the means of the M.S.V.'s found for the first three measurements in each series give a difference $d - l$ of only $-$ 0·008 ml. The results seem, at least, to indicate the delicacy of the method of experiment used.

It is not clear how this peculiarity of nitrobenzene affected the results formerly found (*loc. cit.*, p. 1456), but it is evident that nitrobenzene was not suitable for our purpose. In its place, as a symmetrical solvent, we adopted benzyl benzoate, which was found by experiment to be adequate. Its specific gravity changed appreciably only after a month or two. Menthyl acetate, it may be mentioned, seems, happily, to be altogether unaffected; its density remained quite constant over long periods.

The difference between the mean M.S.V. values is 0·012 [Table I (c)], which is about the average experimental error, whence it may be concluded that there is no detectable difference between the volumes of these isomerides in benzyl benzoate.

We then extended the investigation to ethyl diacetyltartrate * as solute, which, being a well-crystallised compound, is easy to purify. The results obtained for the solutions in *l*-menthyl acetate are in Table I (d). The difference between the mean M.S.V. values for these enantiomorphs is 0·105 ml., which is not only nearly twice as great as for the *iso*butyl esters, but is also in the opposite sense; here the lævo-ester has the greater M.S.V. value, which makes the result considerably more convincing than if the difference of value had been in the same sense as before. The departures from the mean values are much the same as in the preceding series, the maximum divergence being 0·012 ml. The difference between the two volumes, 0·105 ml., is nine times as great as the maximum departure from the mean.

Data for these two diacetyl esters in benzyl benzoate are in Table I (e). Here the mean volumes for the *d*- and *l*-compounds are almost identical, differing only by 0·004 ml., whilst the departures from the means are of the same order. The benzyl benzoate had not altered in density at the conclusion of these experiments.

To confirm our results, the experiments epitomised in Table I (d) and (e) were then repeated *de novo*, with samples of ethyl diacetyltartrate freshly prepared from the original sodium ammonium tartrates, and with freshly distilled menthyl acetate. The results are in Table I (f) and (g), and are very closely similar to those previously obtained. In the asymmetric solvent the M.S.V. of the *l*-ester is greater by 0·120 ml., whereas in the symmetrical solvent the M.S.V.'s differ by only 0·009 ml.

Thus there have now been obtained five entirely independent sets of observations, in which differences have been found in all cases between the M.S.V. of the dextro- and the lævo-forms, several times greater than the probable experimental error. For the *iso*butyl tartrates the *d*-isomeride has the greater volume by 0·054 ml. on the average; for the ethyl diacetyltartrates, the *l*-isomeride has the greater volume by 0·112 ml., whereas in the symmetrical solvent benzyl benzoate, any difference in the volumes of the isomerides was within or very near the probable error. We therefore think we may now claim to have established, quite definitely, the existence of asymmetric solvent effect. The effect is indeed small, and, to realise its order, it is of some interest to contrast it with the comparatively gross difference in volume of one of each pair of the isomerides we have used, in *l*-menthyl acetate on the one hand and in benzyl benzoate on the other. This is shown in the table below.

	M.S.V., ml.		
	In *l*-menthyl acetate.	In benzyl benzoate.	Δ, ml.
*iso*Butyl *d*-tartrate	242·783	241·415	1·368
Ethyl diacetyl-*d*-tartrate	252·707	247·851	4·856

The differences in these two instances are some thirty times greater than those which we have found in the M.S.V. of enantiomorphs in an asymmetric solvent.

* *iso*Butyl diacetyltartrate, which we had thought of using, is liquid, and therefore much more difficult to purify.

EXPERIMENTAL.

Density Determinations.—A delicate transparent quartz pyknometer of *ca.* 29 c.c. capacity was used, and special care was taken in determining the temperatures at which the densities were observed. A fairly large thermostat (20 l.) was brought to a temperature in the neighbourhood of 20° by means of a good ordinary thermometer graduated in $\frac{1}{20}$ degrees. A Beckmann thermometer was also placed in the thermostat, and the mercury thread adjusted to some suitable graduation, that mark being taken, once for all, as representing the temperature then indicated by the other thermometer. For each solution density determinations were made at five or six temperatures ranging from 19·75 to 20·25° according to the Beckmann thermometer. These readings taken as actual temperatures have, each, only the accuracy of the ordinary thermometer, but they have amongst themselves, as relative temperatures, the accuracy of the Beckmann thermometer. The density at 20° was calculated by the centre of gravity method (Bond, " Probability and Random Errors," E. Arnold, 1935, p. 89). Large-scale graphs showed that practically all determinations lay within 5×10^{-6} unit of the mean line representing the change of density with temperature, and none without 1×10^{-5} unit. The probable error for a relative density value at 20° we consider to be less than 5×10^{-6} unit.

Preparation of the Esters.—For this purpose a considerable quantity (8 lb.) of racemic acid was resolved by simultaneous separation, by slow cooling, of fairly large (about 10 g.) dextro- and lævo-crystals, from a solution of sodium ammonium tartrate. These were then recrystallised the same number of times until complete constancy and equality of rotation were reached.

From the samples of sodium ammonium *d*- and *l*-tartrates thus obtained, *iso*butyl *d*-tartrate and *iso*butyl *l*-tartrate were prepared in the usual way, and after being recrystallised three times from benzene, were vacuum-distilled. *iso*Butyl *d*-tartrate had s.p. 72·9° ± 0·05°; $[\alpha]_{5461}^{20^\circ}$ + 68·3° in pyridine ($c = 6{\cdot}880$). *iso*Butyl *l*-tartrate had s.p. 72·9° ± 0·05°; $[\alpha]_{5461}^{20^\circ}$ − 68·3° in pyridine ($c = 6{\cdot}876$). The slight difference in the value for [α] from that (67·65°) recorded in J., 1937, 1458 is due to difference in the pyridine, which was not specially purified in either case.

Ethyl diacetyl-*d*-tartrate and ethyl diacetyl-*l*-tartrate were prepared from sodium ammonium tartrate resolved as above. Two samples of each ester were prepared independently, recrystallised three times from aqueous alcohol, and vacuum-distilled. In all cases the s.p. was 66·9°. For the *d*-compound: 1st sample, $[\alpha]_{5461}^{20\cdot5^\circ}$ − 17·0°; 2nd sample, $[\alpha]_{5461}^{20^\circ}$ − 17·3; for the *l*-compound: 1st sample, $[\alpha]_{5461}^{20\cdot5^\circ}$ + 17·0°; 2nd sample, $[\alpha]_{5461}^{20^\circ}$ + 17·3°, all in benzene solution ($c = 5$).

l-Menthyl acetate. The first sample used had $d_{4^\circ}^{20^\circ} = 0{\cdot}925293$ (this identical value was found after keeping for several months) and $\alpha_{5461}^{20^\circ}$ (100 mm.) − 86·97°. The second sample had $d_{4^\circ}^{20^\circ}$ 0·925336; $\alpha_{5461}^{20^\circ}$ (100 mm.) − 86·94°.

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