36. *Studies in the Phenylsuccinic Acid Series. Part XI. Interaction of the Optically Active and Inactive Diphenylsuccinic Anhydrides with Butyl Alcohol and Aniline.*

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The action of water and ethyl alcohol on the optically active diphenylsuccinic anhydrides has already been examined (Wren and Still, J., 1915, **107**, 1451; Wren and Williams, J., 1918, **113**, 832; Wren and Wright, J., 1929, 139).

For the further investigation of the problem *n*-butyl alcohol was selected, since it is more readily kept anhydrous than ethyl alcohol. The alcohol reacts somewhat sluggishly with *r*-diphenylsuccinic anhydride in various media, giving analytically homogeneous butyl hydrogen diphenylsuccinates in which the proportion of *r*- and *meso*-compound has been determined by comparison of their m. p.'s with those of synthetic mixtures of the substances. The amount of *meso*-derivative in the product varies from 0% to 16·5% and is greatly affected by the nature of the solvent and by the material of the vessel, the extent of isomerisation being greater in glass than in silica. With the *d*-anhydride, the percentage of inactive material has been determined polarimetrically and the question of its existence as *r*- or *meso*-form has not been examined. The influence of the two factors is very pronounced, racemisation in non-basic solvents appearing to be due almost entirely to the glass. The very marked effect in hot benzene is almost entirely due to racemisation of the *d*-anhydride before it enters into reaction, since control experiments performed in the absence of butyl alcohol show that it is optically unstable under these conditions, which have little effect on the optical activity of butyl hydrogen *d*-diphenylsuccinate. An adequate explanation of the effect appears difficult, since it is doubtful if solubility of the alkali of the glass in benzene can be assumed or if an alkali could exist as such in the presence of an acid anhydride. In the interaction of the *d*-anhydride with aniline in various solvents the influence of the material of the vessel is largely eliminated, since the reaction occurs so rapidly and under such mild conditions that the anhydride is transformed into the hydrogen ester before racemisation is appreciable. If, however, the solvent is sufficiently basic, racemisation is very pronounced. The customary assumption that an *r*-compound behaves in dilute solution as a mixture of the *d*- and the *l*-form does not appear universally valid; *e.g.*, in ethyl benzoate in silica vessels the *r*-anhydride becomes isomerised to the extent of 12·6%, whereas the percentage racemisation of the *d*-anhydride is only 1·9.

Experimental.

Resolution of r-*Diphenylsuccinic Acid into its Optical Antipodes.*—The resolution by brucine in aqueous solution (Wren and Still, J., 1915, **107**, 444) involves the use of very large volumes of solvent. The substitution of 50% aqueous alcohol for water gives better yields of the active acids and is much more economical of time and labour. The following experiment is typical. *r*-Diphenylsuccinic acid (50 g.) and brucine (162 g.) were dissolved in a warm mixture of water (530 c.c.) and rectified spirit (530 c.c.). The solution was filtered, seeded with brucine *d*-

diphenylsuccinate, and kept at rest at room temperature for 24 hours. Prolongation of the time of contact of crystals and solution leads to separation of brucine *l*-diphenylsuccinate. The crystalline crop (110 g.), recrystallised from 50% alcohol (5 c.c. of solvent per g. of salt), gave 90 g. of salt which, when decomposed with acid and extracted with ether, yielded 20 g. of *d*-diphenylsuccinic acid having $[\alpha]_{5461}$ + 390° in acetone. One crystallisation from water (160 c.c. per g.) yielded 13 g. of homogeneous *d*-acid. In acetone ($l = 2, c = 0{\cdot}7490$), $\alpha_{5461}^{21^\circ}$ + 7·09°, $[\alpha]_{5461}^{21^\circ}$ + 473·3°; $\alpha_{5780}^{20^\circ}$ + 6·21°, $[\alpha]_{5780}^{20^\circ}$ + 414·7°.

The mother-liquor from the first crop of brucine salt yielded 18 g. of *l*-acid with $[\alpha]_{5461}$ − 310° in acetone; two crystallisations from water yielded 9 g. of the homogeneous *l*-acid. In acetone ($l = 2, c = 0{\cdot}6160$), $\alpha_{5461}^{20^\circ}$ − 5·80°, $[\alpha]_{5461}^{20^\circ}$ − 471·5°; $\alpha_{5780}^{20^\circ}$ − 5·08°, $[\alpha]_{5780}^{20^\circ}$ − 412·2°.

Less satisfactory results were obtained with solvents composed of alcohol and water in the volume ratios 1 : 3 and 3 : 1.

*Di-*n-*butyl and* n-*Butyl Hydrogen Diphenylsuccinates.*—These were obtained by esterification of the requisite diphenylsuccinic acid with *n*-butyl alcohol containing 3% of hydrogen chloride at 100°. The excess of alcohol was removed under diminished pressure and the residue was dissolved in ether and shaken with a slight excess of dilute potassium carbonate solution. The hydrogen esters were obtained by extracting the acidified aqueous solution with chloroform.

n-*Butyl* r-*diphenylsuccinate* separates from rectified spirit in rectangular platelets, m. p. 46—47°, readily soluble in acetone, ether, benzene, chloroform, and light petroleum (b. p. 60—80°) (Found : C, 75·3; H, 7·8. $C_{24}H_{30}O_4$ requires C, 75·4; H, 7·9%).

n-*Butyl hydrogen* r-*diphenylsuccinate* crystallises from light petroleum, containing 10% of benzene, in cubic crystals, m. p. 129—130°, readily soluble in hot benzene, sparingly in hot or cold light petroleum (b. p. 60—80°), and freely in alcohol, acetone, ether, or chloroform (Found : C, 73·5; H, 6·6. $C_{20}H_{22}O_4$ requires C, 73·6; H, 6·8%).

n-*Butyl* meso*diphenylsuccinate* crystallises from rectified spirit, in which it dissolves freely when hot, sparingly when cold, in well-defined needles, m. p. 100—101°, readily soluble in acetone, ether, chloroform, benzene, and light petroleum (b. p. 60—80°) (Found : C, 75·7; H, 7·8%).

n-*Butyl hydrogen* meso*diphenylsuccinate* separates from benzene in ill-defined, hair-like crystals, m. p. 159·5—160·5°, insoluble in hot or cold light petroleum (Found : C, 73·5; H, 6·8%).

n-*Butyl* d-*diphenylsuccinate*, m. p. 64—64·5°, forms rectangular platelets from rectified spirit (Found : C, 75·4; H, 7·8%). In acetone : ($l = 2, c = 1{\cdot}4675$) $\alpha_{D}^{19\cdot5^\circ}$ + 6·678°, $[\alpha]_{D}^{19\cdot5^\circ}$ + 227·5; ($l = 2, c = 1{\cdot}0350$) $\alpha_{5780}^{20^\circ}$ + 5·09°, $[\alpha]_{5780}^{20^\circ}$ + 246·1°; $\alpha_{5461}^{20^\circ}$ + 5·77°, $[\alpha]_{5461}^{20^\circ}$ + 279·5°. In chloroform ($l = 2, c = 1{\cdot}5235$) : $\alpha_{5780}^{20^\circ}$ + 8·15, $[\alpha]_{5780}^{20^\circ}$ + 267·6°; $\alpha_{5461}^{20^\circ}$ + 9·18°, $[\alpha]_{5461}^{20^\circ}$ + 301·2°.

n-*Butyl hydrogen* d-*diphenylsuccinate* crystallises from light petroleum in rectangular prisms, m. p. 93·5—94° (Found : C, 73·7; H, 6·7%). In acetone : ($l = 2, c = 1{\cdot}6085$) $\alpha_{D}^{18^\circ}$ + 9·00°, $[\alpha]_{D}^{18^\circ}$ + 280·0°; ($l = 2, c = 0{\cdot}9800$) $\alpha_{5780}^{17^\circ}$ + 6·16°, $[\alpha]_{5780}^{17^\circ}$ + 314·2°; $\alpha_{5461}^{17^\circ}$ + 6·95°, $[\alpha]_{5461}^{17^\circ}$ + 349·6°. In benzene ($l = 2, c = 0{\cdot}7030$) : $\alpha_{5780}^{17^\circ}$ + 4·93°, $[\alpha]_{5780}^{17^\circ}$ + 350·8°; $\alpha_{5461}^{17^\circ}$ + 5·58°, $[\alpha]_{5461}^{17^\circ}$ + 397·0°.

n-*Butyl* l-*diphenylsuccinate*, m. p. 64—64·5°, resembles its antipode (Found : C, 75·4; H, 7·9%). In acetone ($l = 2, c = 1{\cdot}274^\circ$) : $\alpha_{D}^{19\cdot5^\circ}$ − 5·79°, $[\alpha]_{D}^{19\cdot5^\circ}$ − 227·3°.

n-*Butyl hydrogen* l-*diphenylsuccinate*, m. p. 93·5—94°, is similar to its optical antipode in preparation and properties (Found : C, 73·7; H, 6·8%). In acetone ($l = 2, c = 1{\cdot}4740$) : $\alpha_{D}^{15\cdot4^\circ}$ − 8·22°, $[\alpha]_{D}^{15\cdot4^\circ}$ − 278·8°.

Preparation of n-*Butyl Hydrogen Diphenylsuccinates by Semihydrolysis of the Normal Esters.*—As expected from the behaviour of the optically inactive ethyl diphenylsuccinates under analogous conditions (Wren and Still, J., 1917, **111**, 1019), the butyl esters undergo isomerisation in presence of alkali and the change becomes almost quantitative under suitable experimental conditions : a solution of butyl *r*-diphenylsuccinate (3 g.) in butyl alcohol (10 c.c.) containing a little sodium butoxide became cloudy after 3 hours at room temperature and had solidified throughout after 20 hours; the dried product (2·5 g.), after crystallisation from rectified spirit, yielded butyl *meso*diphenylsuccinate, m. p. 100·5°. Similar isomerisation occurs to a less extent under the influence of aqueous-alcoholic potassium hydroxide : a solution of *n*-butyl *r*-diphenylsuccinate (17 g.) in a hot mixture of rectified spirit (255 c.c.) and water (76 c.c.) was boiled, until it was neutral, with the quantity of aqueous-alcoholic potassium hydroxide required for semi-hydrolysis. After removal of alcohol, the mixture of normal esters was extracted with ether. The aqueous solution was acidified and extracted with chloroform and the extract was shaken with concentrated sodium carbonate solution until further addition did not cause further precipitation. The precipitate consisted essentially of sodium *n*-butyl *r*-diphenylsuccinate, from which the hydrogen ester, m. p. 128°, was obtained by acidification and crystallisation from benzene–light petroleum. The filtrate from the sodium salt yielded *n*-butyl hydrogen *meso*diphenylsuccinate. A precisely similar result was obtained with *n*-butyl *meso*-diphenylsuccinate as initial material.

Freezing Points of Mixtures of the Normal and the Hydrogen Esters.—These were determined by the method of the B.P. 1932. The temperature of the external bath required careful adjustment to enable consistent values to be obtained. The mixtures generally crystallised more definitely than the homogeneous materials.

Mixtures of *n*-butyl hydrogen *r*- and *meso*-diphenylsuccinate :

% *meso*-Ester	100	85·7	75·3	67·8	61·6	56·5	52·0	48·0
F. p.	158°	147·2°	141·3°	136·7°	130·3°	125·3°	120·2°	113·7°
% *meso*-Ester	45·2	42·6	39·3	32·4	24·4	13·8	6·0	0
F. p.	109·7°	107·2°	100·5°	97·5°	100·7°	110·8°	120°	127·5°

Mixtures of *n*-butyl *r*- and *meso*-diphenylsuccinates :

% *meso*-Ester	100	85·2	74·4	66·2	59·2	52·5	48·4
F. p.	101·05°	85·7°	80·9°	77·5°	74·5°	70·4°	68·35°
% *meso*-Ester	44·9	37·0	28·0	24·4	14·4	7·0	0
F. p.	66·1°	55·6°	28·3°	27·4°	28·0°	35·0°	46·3°

Action of n-*Butyl Alcohol on* r-*Diphenylsuccinic Anhydride in Various Solvents in Glass and in Silica Vessels.*—In each case 3 g. of the anhydride were heated with 5 c.c. of *n*-butyl alcohol (20 c.c. in the case in which no solvent was used) and 20 c.c. of solvent. The analytical purity of the mixture of *n*-butyl hydrogen diphenylsuccinates was controlled by titration with standard alkali and the composition was deduced from f. p.

The product obtained by the use of ethyl benzoate in a glass vessel was separated by treatment with aqueous sodium carbonate and ether into *n*-butyl hydrogen *meso*diphenylsuccinate, m. p. 157—160°, and *n*-butyl hydrogen *r*-diphenylsuccinate, m. p. 129—130°.

	In glass vessels.				In silica vessels.			
Solvent.	Temp.	Hours of heating.	F. p. of product.	% of hydrogen *meso*-ester in product.	Temp.	Hours of heating.	F. p. of product.	% of hydrogen *meso*-ester in product.
Butyl alcohol	100°	6	117°	8	100°	9·5	127·6	0
Benzene	100	14	127	0	80—85	12	128·0	0
Carbon tetrachloride	75	25	119	6·7	80—85	9·5	127·0	0
Dimethylaniline ...	100	12·5	117·5	7·7	100	13	125·5	2
Acetophenone	100	13·5	118·5	7·0	100	14	123·5	3·5
Chloroform	100	13·5	118·8	7·0	70	10	121	5
Ethyl benzoate	100	21	107·5	16·5	100	8	112	12·6
Acetonitrile	—	—	—	—	80—90	18	122·3	4

Action of n-*Butyl Alcohol on* d-*Diphenylsuccinic Anhydride in Various Solvents in Glass and in Silica Vessels.*—The anhydride (0·4 g.) was heated with 1 c.c. of *n*-butyl alcohol (5 c.c. in the case in which a solvent was not employed) and 5 c.c. of solvent as shown below. The analytical purity of the product was checked by titration with standard alkali hydroxide, and $[\alpha]_{5461}$ determined in acetone.

	In glass vessels.				In silica vessels.			
Solvent.	Temp.	Hours of heating.	$[\alpha]_{5461}$ of product.	Inact. material, %, in product.	Temp.	Hours of heating.	$[\alpha]_{5461}$ of product.	Inact. material, %, in product.
n-Butyl alcohol ...	100°	8	+297·1°	15·0	100°	11	+339·3°	2·9
Chloroform	100	10	+345·7	1·1	70	13	+348·7	0·5
Carbon tetrachloride	100	10	+336·0	3·9	80—85	9·5	+344·8	1·4
Acetophenone	100	10	+327·9	6·2	100	11	+342·0	2·2
Ethyl benzoate ...	100	17	0·0	100·0	100	8·5	+342·9	1·9
Acetonitrile	—	—	—	—	80—90	10	+344·9	1·4
Dimethylaniline ...	—	—	—	—	100	10·5	0·0	100
Benzene	100	14	+ 57·8	84·12	80—85	10	+346·3	1·0
„	100	13·5	+ 74·6	77·5	—	—	—	—
„	100	10	+ 45·7	86·9	—	—	—	—
„	80—85	10	+108·4	69·0	—	—	—	—

Homogeneous *d*-diphenylsuccinic anhydride in acetone ($l = 2$, $c = 1{\cdot}0360$) has $\alpha^{20°}_{5780} + 6{\cdot}25°$, $[\alpha]^{20°}_{5780} + 301{\cdot}7°$; $\alpha^{20°}_{5461} + 7{\cdot}098°$, $[\alpha]^{20°}_{5461} + 342{\cdot}6°$.

Behaviour of d-*Diphenylsuccinic Anhydride and* n-*Butyl Hydrogen* l-*Diphenylsuccinate when heated in Benzene in Glass Flasks.*—The anhydride (0·4 g.) was heated in benzene (5 c.c.) during 13·5 hours at 100°. After removal of the solvent the residue, m. p. 115—116°, was optically inactive, consisting of the *r*-anhydride. When *n*-butyl hydrogen *l*-diphenylsuccinate (0·4 g.) was similarly treated, the optical activity ($[\alpha]_{5461}$) was only slightly reduced, from $- 320{\cdot}1°$ to $- 313{\cdot}2°$. The *d*-anhydride (0·4 g.), when heated in benzene (5 c.c.) during 10 hours at 100° in a silica flask, remained practically unchanged in optical activity, the product having $[\alpha]_{5461} + 340{\cdot}9°$ in acetone.

Treatment of *r*-diphenylsuccinic anhydride with benzonitrile at 100° during 10 hours, followed by removal of the solvent under diminished pressure, yielded an additive *product*, $C_{23}H_{17}O_3N$, which, after being crystallised from benzene–light petroleum, melted at 218—222° after shrinking at 160—170°; the re-solidified product melted at 228—230° without previous softening (Found : C, 77·9; H, 4·9; N, 3·9. $C_{23}H_{17}O_3N$ requires C, 77·8; H, 4·8; N, 3·9%).

Interaction of d-*Diphenylsuccinic Anhydride and Aniline in Various Solvents in Glass and in Silica Vessels.*—In each case 0·276 g. of the anhydride was mixed with 0·1 c.c. of aniline and 5 c.c. of solvent at room temperature. The diphenylsuccinanilic acid produced was isolated either by removal of the solvent in a vacuum or by extraction with dilute sodium carbonate solution, followed by acidification and extraction with ether. The analytical purity was controlled by titration with standard alkali. The specific rotations were determined in acetone.

	In glass.		In silica.	
Solvent.	$[\alpha]_{5461}$.	Inactive material, %.	$[\alpha]_{5461}$.	Inactive material, %.
Acetophenone	394·6°	0·08	394·8°	0·03
Chloroform	393·5	0·3	393·8	0·3
Benzene	393·2	0·4	393·4	0·4
Carbon tetrachloride	390·4	1·2	391·3	0·9
Ethyl benzoate	388·8	1·5	387·6	1·6
Anisole	386·9	2·1	386·9	2·1
Dimethylaniline	251·1	36·4	245·5	37·8
,,	251·3	36·4	—	—

Behaviour of d-*Diphenylsuccinanil when heated in Benzene and in Ethyl Alcohol.*—*d*-Diphenylsuccinanil in chloroform ($l = 2$, $c = 1{\cdot}1525$) has : $\alpha_{5780} + 2{\cdot}77°$, $[\alpha]_{5780} + 120{\cdot}2°$; $\alpha_{5461} + 3{\cdot}11°$ $[\alpha]_{5461} + 134{\cdot}9°$.

The specific rotation of 0·1 g. of the anil, heated at 80·85° during 6 hours in benzene (5 c.c.) in silica and in glass, diminished only to + 133·4° and + 131·8° respectively. The products, when heated in ethyl alcohol (20 c.c.) at 75° during 10 hours, suffered slight further diminution of optical activity to + 126·3° and + 125·2° respectively.

One of us (G. L. M.) thanks the Ministry of Education (N.I.) for a grant.

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[*Received, November 17th, 1934.*]