(−)-diastereomers prepared by the addition of methyl lithium to pure (−)-phenyl-4-methyl-3-hexanone[2]) and 5.0 g. of phenyl isocyanate was allowed to react at from 180–220° for 30 minutes. After cooling, the reaction mixture was extracted four times with pure pentane, the extracts were washed with water, dried, and the solvent was evaporated. The residue was distilled at 13 mm. to yield first a forerun of phenyl isocyanate and then 5.0 g. of an impure oil. This material was dissolved in pure pentane and passed through a column of basic alumina. Removal of the solvent from the pentane eluate and distillation of the residue at 13 mm. gave 3.5 g. of olefinic material, $[\alpha]^{22}D$ +16.98° (homogeneous), $n^{25}D$ 1.5129. Ozonolysis of this material by the procedure outlined above gave ketone, $n^{25}D$ 1.5078 (Table IV, run 7). The control runs for the solvolyses in acetic acid were carried out as follows. The olefinic mixture prepared above (1.0 g.) was held at 75° for 48 hours in 50 ml. of dry pure acetic acid. The olefin was isolated by the same procedure recorded for the actual acetolysis, wt. 0.92 g., $n^{25}D$ 1.5127. Ozonolysis of this material to the ketone gave material whose index of refraction was $n^{25}D$ 1.5077 (see Table IV, run 5).

That the solvolysis (runs 1 and 2) produced no acetate was demonstrated in the following fashion. A sample of racemic-*threo*-II-*p*-bromobenzoate (0.97 g., m.p. 87–89°) was submitted to the above solvolytic conditions, and the product was extracted into pure pentane as indicated above. The resulting solution was evaporated through a short column (the pot temperature was never allowed to go above 30°) and the residual oil was treated with a solution of 0.5 g. of lithium aluminum hydride in 20 ml. of ether. After the resulting mixture had stood for one hour, water was added, and the mixture was extracted with ether. The ether layer was washed with water, dried, and the solvent was evaporated through a short column. The residue was flash distilled at 13 mm. to give olefin, 0.44 g., $n^{25}D$ 1.5135. When submitted to chromatographic absorption on a basic alumina column (20 g.) in a pentane solution (any alcohol would remain on the column under these conditions as shown by control experiments), the olefin readily was eluted with pentane, and 0.40 g. of material was recovered (flash distilled), $n^{25}D$ 1.5137.

The control runs for the formolyses were completely analogous to those carried out for the acetolyses. Thus 1.0 g. of the olefinic mixture (prepared above by the dehydration of II) was submitted to the action of dry pure formic acid for 72 hours (no color developed). The product isolated (0.92 g., $n^{25}D$ 1.5102) was submitted to ozonolysis to give ketone, $n^{25}D$ 1.5069, which was submitted to the action of silver oxide, $n^{25}D$ 1.5070 (see run 6, Tables III and IV).

LOS ANGELES, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

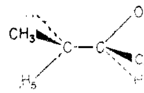
Studies in Stereochemistry. XIII. The 1,2-Diphenyl-1-propanol System

BY FATHY AHMED ABD ELHAFEZ[1] AND DONALD J. CRAM[2]

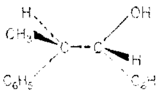
RECEIVED APRIL 25, 1952

Each racemate of 1,2-diphenyl-1-propanol has been shown to react with 3-nitrophthalic anhydride to give substantial amounts of both position isomers of the 3-nitrophthalic acid esters (the anhydride ring can open in either of two directions). The structures of these position isomers were elucidated through the use of spectral techniques. The differences in the balances of the two position isomers from the two racemates is interpreted in terms of the differences in steric requirements for ester formation. The two racemates of 1,2-diphenyl-1-propanol were completely resolved, and the configurations of all of the asymmetric carbon atoms of the system have been related by several unambiguous methods to the configuration of D-glyceraldehyde.

The relative configurations of the two asymmetric carbon atoms in each of the two racemate series of 1,2-diphenyl-1-propanol (I) have been previously determined[3] and were assigned the *erythro* and *threo* configurations. The present investigation reports: (1) the novel behavior of each of the racemates in their reaction with 3-nitrophthalic anhydride; (2) the complete resolution of each of these racemates; (3) a series of reactions that relates the configurations of both carbon atoms of all four isomers to D-glyceraldehyde.

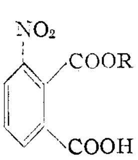


erythro-I

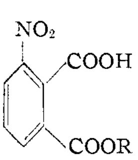


threo-I

The Reaction of the Diastereomeric Alcohols with 3-Nitrophthalic Anhydride.—The usefulness of 3-nitrophthalic anhydride as a reagent for attaching a handle to a secondary alcohol for purposes of resolution rests in part on the fact that ordinarily the anhydride ring opens predominantly one way.[4] Unlike any previous cases, each racemate of 1,2-diphenyl-1-propanol (I) gives substantial amounts of both the α- and β-position isomers. This observation is rationalized as follows.



α-ester



β-ester

That the α-ester is formed in the reaction of the anhydride with methanol has been demonstrated through a comparison of the conductivities of the α- and β-esters ($R = CH_3$). The β-isomer was formed through the Fischer esterification of the dicarboxylic acid.[4a] The structures of these two isomers were assigned on the basis of their conductivities, the β-ester being the better conductor of the two.[4a] It has been well established that *o*-nitrobenzoic acid is a stronger acid than *m*-nitrobenzoic acid,[5] and therefore this assignment is well founded.

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[1] Predoctoral Fellow of the Egyptian Government. This paper is abstracted from the thesis of this author presented to the Department of Chemistry of the University of California at Los Angeles in partial fulfillment of the rquirements for the Ph.D. Degree.

[2] Requests for reprints should be addressed to this author.

[3] D. J. Cram and F. A. Abd Elhafez, THIS JOURNAL, **74**, 5828 (1952).

[4] (a) R. Wegscheider and A. Lipschitz, *Monatsh.*, **21**, 787 (1900); (b) A. Marckwald and A. McKenzie, *Ber.*, **34**, 485 (1901); (c) G. H. Dickinson, L. H. Crosson and J. E. Copenhaver, THIS JOURNAL, **59**, 1094 (1937).

[5] J. F. J. Dippy and R. H. Lewis, *J. Chem. Soc.*, 1426 (1927).

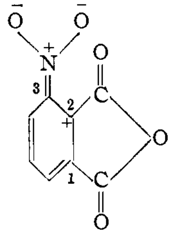
TABLE I

YIELDS, PHYSICAL PROPERTIES AND ANALYSES OF THE ISOMERS OF 1,2-DIPHENYL-1-PROPANOL AND THEIR DERIVATIVES

$C_6H_5\text{—}\overset{CH_3}{\overset{\vert}{C}}H\text{—}\underset{\vert}{C}H\text{—}C_6H_5$ Compound	M.p., °C.	Yield, %	$[\alpha]^{21-25}D^a$	Method prepn.	Molecular formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
			Alcohols						
L-*erythro*	71–72	95	+68.66	B	$C_{15}H_{16}O$	84.87	84.87	7.60	7.64
D-*erythro*	71–72	95	−68.81	B	$C_{15}H_{16}O$	84.87	84.65	7.60	7.85
L-*threo*	60–61	94	+47.12	B	$C_{15}H_{16}O$	84.87	84.60	7.60	7.62
D-*threo*	60–61	96	−47.17	B	$C_{15}H_{16}O$	84.87	84.66	7.60	7.71
			p-Nitrobenzoate						
L-*erythro*	132–133	92	+15.28	Ref. 3	$C_{22}H_{19}O_4N$	73.11	73.04	5.29	5.50
D-*erythro*	132–133	90	−15.42	Ref. 3	$C_{22}H_{19}O_4N$	73.11	72.84	5.29	5.38
L-*threo*	170–171	90	+87.94	Ref. 3	$C_{22}H_{19}O_4N$	73.11	73.00	5.29	5.40
D-*threo*	170–171	94	−88.62	Ref. 3	$C_{22}H_{19}O_4N$	73.11	73.01	5.29	5.34
			α-3-Nitrophthalic acid esters						
D,L-*erythro*	204–205	30–35	.....	A	$C_{23}H_{19}O_6N$	68.14	68.12	4.72	4.88
D,L-*threo*	199–200	50–60	.....	A	$C_{23}H_{19}O_6N$	68.14	67.93	4.72	4.56
L-*erythro*	174–175	40	+21.54	[b]	$C_{23}H_{19}O_6N$	68.14	67.88	4.72	4.59
D-*erythro*	174–175	15	−20.87	[b]	$C_{23}H_{19}O_6N$	68.14	68.20	4.72	4.78
L-*threo*	169–170	34	−38.42	[b]	$C_{23}H_{19}O_6N$	68.14	67.89	4.72	4.72
D-*threo*	169–170	27	+38.60	[b]	$C_{23}H_{19}O_6N$	68.14	68.24	4.72	4.72
			β-3-Nitrophthalic acid esters						
D,L-*erythro*	178–179	40–60	.....	A	$C_{23}H_{19}O_6N$	68.14	67.99	4.72	4.92
D,L-*threo*	172–173	20–30	.....	A	$C_{23}H_{19}O_6N$	68.14	67.94	4.72	4.98
			Phthalic acid esters						
D,L-*erythro*	151–152	80	.....	Ref. 3[c]	$C_{23}H_{20}O_4$	76.65	76.50	5.59	5.74
D,L-*threo*	128–129	70	.....	Ref. 3[c]	$C_{23}H_{20}O_4$	76.65	76.57	5.59	5.74
			l-Menthoxyacetates[d]						
L-*erythro*	81–82	90	−103.98	[d]	$C_{27}H_{36}O_3$	79.37	79.25	8.88	8.92
D-*erythro*	35–35.5	92	+4.32	[d]	$C_{27}H_{36}O_3$	79.37	79.16	8.88	8.95

[a] Taken in $CHCl_3$, *c* 4–5%. [b] See Experimental part for procedures. [c] Attempts to resolve each of these acid esters through the brucine, strychnine, cinchonine, cinchonidine and quinine salts failed. [d] These compounds were prepared by the usual method [A. W. Ingersoll, "Organic Reactions," Vol. II, John Wiley and Sons, New York, N. Y., 1944, p. 381] from the optically pure alcohols. Attempts to resolve the two racemates of 1,2-diphenyl-1-propanol through these esters were blocked by the formation of a series of solid solutions of diastereomerically related esters.

On purely electronic grounds the opening of the anhydride ring by an alcohol to give the α-isomer seems reasonable. The 2-position of the benzene ring should be somewhat more positive than the 1-position because of the contribution that A makes to the resonance hybrid. Consequently the carbonyl group attached to the 2-position should be more positive (through the inductive effect) and thus more amenable to nucleophilic attack by alcohol or alcoholate anion. On the other hand steric effects should operate in the opposite direction and should favor β-ester. In all of the cases in which 3-nitrophthalic acid esters have been prepared in the past the alcohols were less bulky than the 1,2-diphenyl-1-propanol system, and it seems likely that the α-isomer was isolated (the yields were usually high). In the case of the isomers of 1,2-diphenyl-1-propanol steric effects become important enough to partially counterbalance the electronic effects, and mixtures of position isomers result.


A

The structure of each position isomer in each racemate series of I was determined through a comparison of its ultraviolet absorption spectrum with the spectra of the known α- and β-methyl-3-nitrophthalic acid esters.[4a] Figure 1 records these spectra in dilute basic solution.[6] Table I records the physical properties, yields and analyses of the derivatives of the isomers of I as well as references to the experimental part regarding their methods of preparation.

In the reaction of I with 3-nitrophthalic anhydride, the ratio of α- to β-isomer with *erythro* starting material was about one to two whereas with *threo* starting material the ratio was about two to one (see Table I). A plausible explanation for this phenomenon is the following. In models

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[6] Although the spectra in acid and neutral solution allow the α- and β-isomers to be differentiated, the differences are far smaller than those found in basic solution.

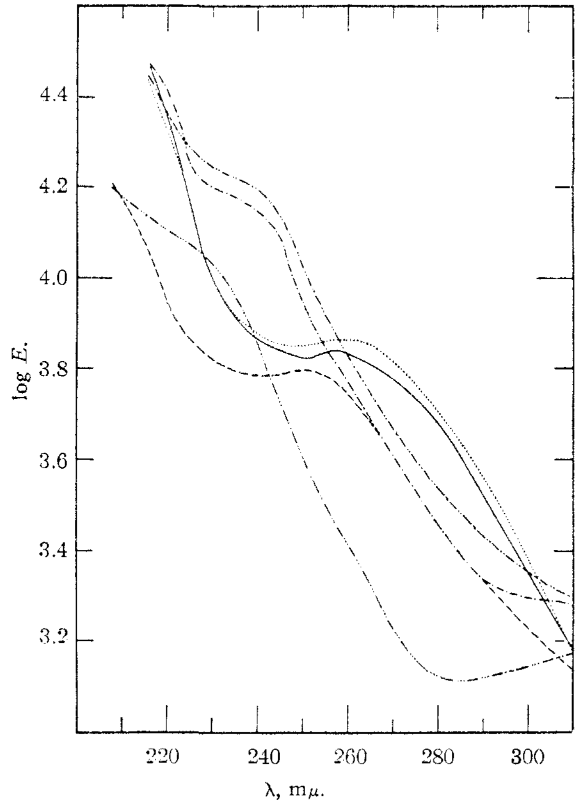
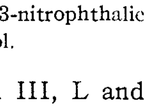
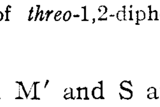


Fig. 1.—Ultraviolet absorption spectra (Cary spectrophotometer, model 11PMS) in 10^{-3} M potassium hydroxide in absolute ethanol: curve –···, β-3-nitrophthalic acid ester of methanol; curve ---, α-3-nitrophthalic acid ester of methanol; curve —, α-3-nitrophthalic acid ester of *erythro*-1,2-diphenyl-1-propanol; curve -·, β-3-nitrophthalic acid ester of *erythro*-1,2-diphenyl-1-propanol; curve. . . . , α-3-nitrophthalic acid ester of *threo*-1,2-diphenyl-1-propanol; curve –··, β-3-nitrophthalic acid ester of *threo*-1,2-diphenyl-1-propanol.

II and III, L and L′, M and M′ and S and S′ represent large, medium and small groups, respectively, attached to two asymmetric carbon atoms.

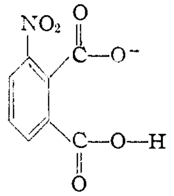


II



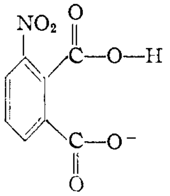
III

These models are assumed to represent *erythro*-I and *threo*-I, respectively, and of these models, II would appear to be the more thermodynamically stable.[7] On the other hand, when the two diastereomeric alcohols are converted to their α-3-nitrophthalic acid esters, the two models become inverted, *erythro*-I giving an ester corresponding to model III and *threo*-I an ester corresponding to model II. The reason for this inversion of models is that in the ester



$> C_6H_6 > H$

in bulk, and the phenyl group which was largest in the starting material becomes the medium group in the product. The same principles should apply to the transition states involved, and one can conclude that the activation energy for the formation of the *threo*-α-ester should be lower than for the *erythro*-α-ester. The formation of β-ester is in each case a competing reaction, and since the effective bulks of C_6H_5 and



are much closer together, the stabilities of the β-ester products as well as the transition states involved should be much closer together for the two diastereomers. Therefore, the product balances should favor the α-ester in the case of the *threo* and the β-ester in the case of the *erythro* starting material, as was indeed observed.[8]

The Resolution of the 1,2-Diphenyl-1-propanol System.—Attempts to resolve the racemates of I through alkaloid salts of the phthalic acid esters and the α-3-nitrophthalic acid esters (and in the case of the *erythro* racemate through the *l*-menthoxyacetate) were made. In only the case of the nitroesters were these attempts successful. The α-3-nitrophthalic acid ester of *erythro*-1,2-diphenyl-1-propanol was resolved through its brucine salt to give the (+)-*erythro*-α-ester. The enantiomeric (−)-*erythro*-α-ester was obtained by fractional crystallization of the ester obtained by freeing the original filtrates of brucine. The α-3-nitrophthalic acid ester of *threo*-1,2-diphenyl-1-propanol was resolved through its cinchonidine salt to give the (+)-*threo*-α-ester, and the (−)-*threo*-α-ester was recovered from the filtrates and subjected to fractional crystallization to give material of similar melting point. The fact that in each case the rotations of enantiomerically related materials are about equal in magnitude and opposite in sign (see Table I) is taken as evidence that optical purity was reached. Substantiation of this point is found in the similar relationships that exist between the rotations of the isomeric alcohols produced by hydrolysis of the 3-nitrophthalic acid esters, and between the rotations of the *p*-nitrobenzoates prepared from these alcohols (see Table I).

The Configurations of the Stereoisomers of 1,2-Diphenyl-1-propanol.—Several methods were employed to relate the configurations of the asym-

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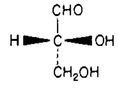
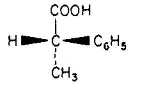
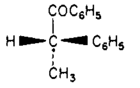
[7] Of the three staggered conformations for each of II and III, the most stable is indicated. In II, the steric repulsions are 1 L>–<M′, 1 L′>–< M, 1 L>–<S′, 1 L′>–<S, 1 M′>–<S and 1 S′>–<M′; in III they are 1 L>–<M′, 1 L′>–<M, 1 L>–<S′, 1 L′>–<S, 1 M>–<M′ and 1 S>–<S′. The difference between the diastereomers is that II has 1 M′>–<S and 1 M>–<S′ and III has 1 M>–<M′ and 1 S>–<S′ repulsions.

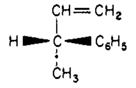
[8] Similar concepts are applied in paper XIV of this series [D. J. Cram and F. A. Abd Elhafez, This Journal, **74**, 5851 (1952)] to explain other differences in reactivites of diastereomerically related materials.

metric carbon atoms in the stereoisomers of 1,2-diphenyl-1-propanol to D-(+)-glyceraldehyde (IV). Two of these methods involved the previously established relationship between IV, D-(+)-2-phenylpropionic acid (V) and D-(+)-methyldesoxybenzoin (VI).[9] In the first method, (+)-*threo*-1,2-diphenyl-1-propanol was oxidized with chromic acid to give optically pure L-(−)-methyldesoxybenzoin. In the second method, D-(+)-2-phenylpropionic acid (V) was prepared in an optically pure state[10] and converted *via* the acid chloride to D-(+)-methyldesoxybenzoin (VI) through the use of diphenylcadmium reagent. This ketone (optically pure) was reduced with lithium aluminum hydride to give a mixture of diasteromers in which (−)-*erythro* material predominated.[3] From the mixture was isolated optically pure (−)-*erythro*-I, and from the filtrates was isolated a diastereomeric mixture of alcohols which was converted to a mixture of *p*-nitrobenzoates from which was isolated the optically pure *p*-nitrobenzoate of (−)-*threo*-I.

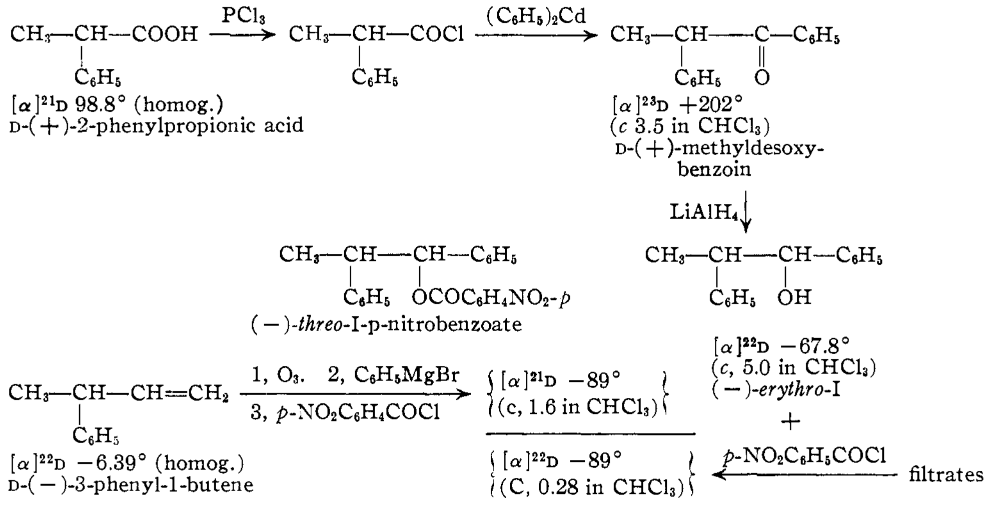

D-(+)-glyceraldehyde
IV


D-(+)-2-phenylpropionic acid
V

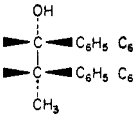

D-(+)-methyldesoxybenzoin
VI

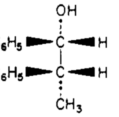

D-(−)-3-phenyl-1-butene
VII

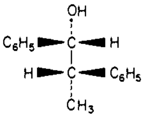
In a third series of interconversions optically pure D-(−)-3-phenyl-1-butene[11] (VII) was submitted to ozonolysis, and the 2-phenylpropionaldehyde produced was converted with phenylmagnesium bromide to a mixture of diastereomers of I in which the (−)-*threo* material predominated.[3] This carbinol was converted to a diastereomeric mixture of *p*-nitrobenzoates from which the optically pure ester of (−)-*threo*-I was isolated. The formulations trace these interconversions. The correspondence of the rotations of the compounds involved in these reactions with those rotations reported in the literature or Table I attest to the fact that not only was optical purity obtained in each resolution but also the reactions themselves did not involve any racemizing stage.

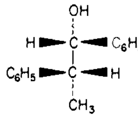


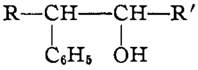
It is now possible to make assignments of configuration to the four stereoisomers of 1,2-diphenyl-1-propanol (I). The projection formulas set forth the relationships of structure with physical properties of the isomers. The conventions previously adopted[11c] have been preserved here. The correlations between configurations and rotations which were noted in the 3-phenyl-2-butanols, the 2-phenyl-3-pentanols and the 3-phenyl-2-pentanols[12,11c] appear also to apply to the 1,2-diphenyl-1-propanols. The correlation can be stated as follows: in formula VIII when R and R′, H and H and C_6H_5 and OH are in each case treated as analogous groups and the diastereomers are named accordingly, the L-*threo* isomer always has a more positive rotation than the L-*erythro* isomer.[13]


D-(−)-
erythro-I
[α]²⁴D
−68.8°
(*c* 5.1
in $CHCl_3$)


L-(+)-
erythro-I
[α]²³D
+68.7°
(*c* 4.9
in $CHCl_3$)


D-(−)-
threo-I
[α]²⁴D
−47.2°
(*c* 5.1
in $CHCl_3$)


L-(+)-
threo-I
[α]²⁴D
+47.1°
(*c* 5.1
in $CHCl_3$)



$$\underset{\displaystyle C_6H_5}{R{-}CH}{-}\underset{\displaystyle OH}{CH}{-}R'$$

VIII

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[9] M. L. Wolfrom, R. U. Lemieux and S. M. Olin [THIS JOURNAL, **71**, 2870 (1949)] related L-(−)-glyceraldehyde to L-(+)-alanine. H. I. Bernstein and F. C. Whitmore, *ibid.*, **71**, 1324 (1939) related the configuration of L-(+)-alanine to that of D-(+)-2-phenylpropionic acid (V), and J. B. Conant and G. H. Carlson [*ibid.*, **54**, 4055 (1932)] converted D-(+)-2-phenylpropionic acid (V) to D-(+)-methyldesoxybenzoin (VI).

[10] A. Campbell and J. Kenyon, *J. Chem. Soc.*, 25 (1946).

[11] The synthesis of this compound has been previously reported [(a) D. J. Cram, THIS JOURNAL, **74**, 2137 (1952)] and its configuration has been related to D-glyceraldehyde [(b) D. J. Cram, *ibid.*, **71**, 3883 (1949); (c) **74**, 2149 (1952)].

[12] D. J. Cram and R. Davis, *ibid.*, **71**, 3872 (1949).

[13] The names given to the isomers of the 1,2-diphenyl-1-propanol system to make them fit into the correlation differ from the names used previously through the discussion. Thus the L-*threo*-isomer in one system of nomenclature becomes the L-*erythro*-isomer in the other, and *vice versa*. Aside from the correlation, the names adopted in the discussion (see ref. 3) are the most reasonable from a general standpoint.

Experimental Part

Reaction of *threo*-1,2-Diphenyl-1-propanol with 3-Nitrophthalic Anhydride (Procedure A).—A solution 158 g. of *threo*-1,2-diphenyl-1-propanol[3] in 250 ml. of dry pyridine was mixed with 148 g. of pure 3-nitrophthalic anhydride. The resulting solution was heated on the steam-bath for one hour, allowed to stand at room temperature for 12 hours, and poured onto ice and 6 *N* sulfuric acid. The mixture was extracted with ether, the organic layer was washed with water, dried, and the solvent was evaporated. The solid that separated during evaporation of the solvent was collected, and the filtrates were concentrated to give 160 g. of a thick oil. The solid was recrystallized twice from an ethyl acetate–pentane mixture to give 157 g. (52% yield) of α-ester, m.p. 199–200°.

The thick oil was dissolved in ether, the solution was extracted twice with dilute alkali (0°), and the combined basic extracts were washed with ether. The ether solutions were combined, dried and evaporated to give 2.8 g. of starting alcohol, identified as its *p*-nitrobenzoate (5.5 g.), m.p. 142–143° (undepressed by admixture with an authentic sample).[3] The basic solution was acidified with dilute sulfuric acid (0°) and extracted with ether. The ether layer was washed with water, dried and evaporated to an oil. This oil was dissolved in two volumes of ethyl acetate and pentane was added until the solution became slightly turbid. After standing for several days at 0° a solid separated which was recrystallized four times from an ethyl acetate–pentane mixture to give β-ester, m.p. 172–173° (with α-ester, m.m.p. 151–187°). This reaction was carried out a number of times, and the yield of α-ester varied between 50 and 60%, and of β-ester between 20 and 30% (see Table I for yields of each ester of *erythro* configuration).

The filtrates from the various crystallizations gave oils which upon hydrolysis gave back starting alcohol (identified as the *p*-nitrobenzoate).

Preparation of the α- and β-3-Nitrophthalic Acid Ester of Methanol.—These α- and β-esters were prepared by the methods of Wegscheider, *et al.*[4a]: α-ester, m.p. 152.5–153.5° (lit. 152.9–153.4°),[4c] yield 76%; β-ester, m.p. 166–167° (lit. 157–158°).[4a] The two esters showed the same solubility characteristics as previously reported,[4a] and in each case the melting points are about ten degrees higher than those reported by Wegscheider.[4a] Since the β-isomer had not been made since the original work, the substance was analyzed.

Anal. Calcd. for $C_9H_7O_6N$: C, 48.01; H, 3.13. Found: C, 48.05; H, 3.20.

Resolution of α-3-Nitrophthalic Acid Ester of *threo*-1,2-Diphenyl-1-propanol.—A mixture of 271 g. (0.67 mole) of the *threo*-α-ester and 160 g. (0.64 mole) of cinchonidine was dissolved in about an equal volume of chloroform, and warm methanol was added (5–6 ml. per ml. of chloroform). The resulting solution was allowed to stand overnight at room temperature. The solid that separated was recrystallized from the same solvents eight times to give 170 g. of salt (white needles). This material was shaken with a mixture of ether and 6 *N* sulfuric acid, the ether solution was washed with water, dried and evaporated to solid, wt. 93 g., m.p. 170–171° (varies with rate of heating). A sample of this material was converted back to the cinchonidine salt which was subjected to three more crystallizations. Recovered ester was unchanged in rotation. Three different preparations of ester gave the following rotations, $[\alpha]^{23}_{\mathrm{D}}$ +38.7°, $[\alpha]^{23}_{\mathrm{D}}$ +38.5° and $[\alpha]^{23}_{\mathrm{D}}$ +38.7° (*c* 5 in $CHCl_3$).

The combined filtrates of the cinchonidine salt crystallizations were concentrated and the salt was converted to the free acid ester. Attempts to purify the (−)-α-ester through the brucine, strychnine, cinchonine and quinine salts failed. However, the free ester was fractionally recrystallized from an ethyl acetate–pentane mixture (six cycles) to give a total of 50.4 g. of pure (−)-*threo*-α-ester, m.p. 170–171°, $[\alpha]^{23}_{\mathrm{D}}$ −38.42° (*c* 5% in $CHCl_3$).

The combined filtrates from this fractional crystallization were concentrated and the resulting oil was hydrolyzed to free alcohol by procedure B. This alcohol when submitted to fractional crystallization from pentane gave (five cycles) 10.6 g. of L-(+)-*threo*-1,2-diphenyl-1-propanol, wt. 10.6 g., m.p. 60.5–61.5°, $[\alpha]^{21}_{\mathrm{D}}$ +47.2° (*c* 5 in $CHCl_3$).

Resolution of α-3-Nitrophthalic Acid Ester of *erythro*-1,2-Diphenyl-1-propanol.—A mixture of 102 g. (0.25 mole) of the *erythro*-α-ester, 98.5 g. (0.25 mole) of anhydrous brucine and two volumes of chloroform was brought to the boiling point, and methanol was added (6–8 ml. per ml. of chloroform). The mixture upon cooling produced needles which after recrystallization (twice) from the same solvent gave 85 g. of salt which was converted by the usual method to the free ester, wt. 40.5 g., m.p. 175–176°, $[\alpha]^{23}_{\mathrm{D}}$ +21.5° (*c* 5 in $CHCl_3$).

The filtrates from the brucine salt were converted to the free ester by the usual method. Attempts to purify the (−)-ester through the strychnine, cinchonidine, cinchonine and quinine salts failed. The impure (−)-ester was recrystallized nine times from ethyl acetate–pentane to give 4.5 g. of pure (−)-*erythro*-α-ester, m.p. 175–176°, $[\alpha]^{23}_{\mathrm{D}}$ −20.9° (*c* 5 in $CHCl_3$).

The filtrates from the above crystallizations were concentrated and the oil produced was hydrolyzed by procedure B. The free carbinol was subjected to fractional crystallization from pentane (12 cycles) to give 5.0 g. of pure D-(−)-*erythro*-1,2-diphenyl-1-propanol, m.p. 71.5–72.5, $[\alpha]^{21}_{\mathrm{D}}$ −68.8° (*c* 3.0 in $CHCl_3$).

Hydrolyses of the 3-Nitrophthalic Acid Esters of the Various Isomers of 1,2-Diphenyl-1-propanol (Procedure B).—A mixture of 0.1 mole of acid ester, 0.15 mole of potassium hydroxide, 0.15 mole of sodium hydroxide, 100 ml. of methanol and 100 ml. of water was heated at reflux for 12 hours. The mixture was cooled, poured onto 500 g. of ice, and the solid that separated was collected. The filtrates were extracted twice with pentane, the solid was dissolved in these extracts; the resulting solution was washed with water and dried. When solvent was evaporated, product separated and was collected. This material was recrystallized from pentane.

Oxidation of (+)-*threo*-1,2-Diphenyl-1-propanol to (−)-Methyldesoxybenzoin.—A solution of 2.12 g. of (+)-*threo*-I was oxidized by the usual procedure[3] to give 1.1 g. (52% yield) of (−)-methyldesoxybenzoin, m.p. 34–35°, $[\alpha]^{25}_{\mathrm{D}}$ −206° (*c* 4.2 in $CHCl_3$).

Synthesis of (+)-Methyldesoxybenzoin from (+)-2-Phenylpropionic Acid.—The (+)-2-phenylpropionic acid used in this synthesis was prepared and resolved by the method of Kenyon[10] (through the strychnine salt), to give material, b.p. 123–124° (2.5–3.5 mm.), n^{20}_{D} 1.5210, $[\alpha]^{21}_{\mathrm{D}}$ +98.8° (homog.), $[\alpha]^{21}_{\mathrm{D}}$ +95.5° (*c* 3.5 in C_6H_6).[14]

A mixture of 4.45 g. of the above acid and 2 g. of phosphorus trichloride was heated on the steam-bath for an hour, cooled to room temperature and the upper mobile layer of acid chloride was decanted. This material was flash-distilled under reduced pressure and used directly in the next step.

To an ice-cold solution of 0.035 mole of phenylmagnesium bromide (5.49 g. of bromobenzene and 0.88 g. of magnesium) in 200 ml. of ether was added in portions 2.75 g. (0.015 mole) of dry powdered cadmium chloride. After the addition was complete, the ice-bath was removed and the mixture was allowed to stand at room temperature for three hours. A solution of the acid chloride in 10 ml. of dry ether was added dropwise to the solution and the mixture was stirred for three hours, cooled and decomposed with 1 *N* sulfuric acid (0°). The ether layer was washed twice with water, with dilute sodium bicarbonate solution, was dried and evaporated to an oil. Upon distillation under reduced pressure two fractions were obtained: first, wt. 2.1 g., b.p. 100–117° (3–5 mm.); second, wt. 2.3 g., b.p. 114–116° (1 mm.). The low-boiling fraction was demonstrated to be acid chloride through its conversion to the starting acid. The second fraction was redistilled to give (+)-methyldesoxybenzoin which solidified at 0°, m.p. 34–35°, $[\alpha]^{23}_{\mathrm{D}}$ +202° (*c* 3.5 in $CHCl_3$).[15]

An attempt to prepare this ketone by the action of phenylmagnesium bromide on optically pure 2-phenylpropionamide gave a very low yield of largely racemized ketone.

Conversion of (+)-Methyldesoxybenzoin to Diastereomers of 1,2-Diphenyl-1-propanol.—The methyldesoxybenzoin prepared above (2.19 g.) was reduced in the usual way[3] with lithium aluminum hydride. Decomposition of the re-

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[14] A rotation of α^{21}_{D} +102° (*l* 1 dm., homog.) was calculated for this acid making use of Kenyons data (ref. 10) and the Drude equation. In the present work the observed value was α^{21}_{D} +101° (*l* 1 dm., homog.).

[15] A. McKenzie, R. Roger and G. O. Wills [*J. Chem. Soc.*, **129**, 779 (1926)] reported m.p. 34–35°, $[\alpha]^{17}_{\mathrm{D}}$ +207° (*c* 1.07 in $CHCl_3$) for this compound prepared by a different method.

action mixture produced carbinol which was crystallized four times from pentane, wt. 1.5 g., $[\alpha]^{22}D$ −67.8° (*c* 0.28 in $CHCl_3$), m.p. 71.5–72.5°, m.m.p. with (−)-*erythro*-1,2-diphenyl-1-propanol, 71.5–72.5°. The filtrates from the above crystallizations were combined, the solvent was evaporated and the resulting oily carbinol was converted to the *p*-nitrobenzoate. This solid was submitted to fractional crystallization (nine times) from an ether–pentane mixture to give 2.8 mg. of *p*-nitrobenzoate, $[\alpha]^{22}D$ −89° (*c* 0.28 in $CHCl_3$), m.p. 168.5–170.5°, m.m.p. with *p*-nitrobenzoate of (−)-*threo*-1,2-diphenyl-1-propanol, 169.5–170.5°.

Conversion of (−)-3-Phenyl-1-butene to (−)-*threo*-1,2-Diphenyl-1-propanol.—Ozone was passed through a solution of 1.4 g. of (−)-3-phenyl-1-butene ($[\alpha]^{22}D$ −6.39°, homog.)[11] in 10 ml. of freshly distilled methylene chloride until no more ozone was absorbed (25 minutes). The solution of the ozonide was added dropwise to a stirred boiling mixture of 20 ml. of water, 0.7 g. of zinc dust and a small crystal of silver nitrate. The reaction mixture was cooled, filtered and extracted with ether. The ether layer was washed with water, dried and evaporated to an oil. This oil was flash-distilled at 20 mm. to give 0.80 g. of 2-phenylpropionaldehyde.

An ether solution of 0.40 g. of the above aldehyde was added dropwise to an ether solution of phenylmagnesium bromide (large excess). The reaction mixture was worked up in the usual way[3] to give an oil which was flash-distilled at 20 mm. This material was dissolved in 2 ml. of pentane and chromatographed on a 1.5 × 5 cm. column of alumina. The column was thoroughly washed with pentane, and the carbinol was eluted with methanol. The methanol eluate was concentrated using a Vigreux column to give about 30 mg. of an oil which was converted to the *p*-nitrobenzoate by the usual method.[3] This material was crystallized six times from an ether–pentane mixture to give 17 mg. of pure ester, $[\alpha]^{21}D$ −89° (*c* 1.6 in $CHCl_3$), m.p. 167–168.5°, m.m.p. with the *p*-nitrobenzoate of (−)-*threo*-1,2-diphenyl-1-propanol, 168.5–170°.

LOS ANGELES, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Studies in Stereochemistry. XIV. Differences in the Reactivity of Diastereomerically Related Alkyl Halides and Sulfonates in the SN2 and E_2 Reactions

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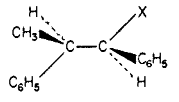
RECEIVED APRIL 25, 1952

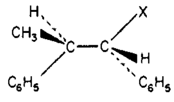
The *p*-bromobenzenesulfonates of D-, L- and racemic *erythro*- and *threo*-1,2-diphenyl-1-propanol were prepared. When treated with lithium chloride, bromide or iodide in acetone, these esters gave the corresponding D-, L- and racemic *threo*- and *erythro*-1,2-diphenyl-1-propyl halides, respectively. In each case, simple Walden inversion occurred at the carbon carrying the *p*-bromobenzenesulfonate group. The differences found in reactivity between diastereomerically related starting materials is correlated with the differences in steric strains in the two types of starting material. The E_2 reactions of these alkyl halides and *p*-bromobenzenesulfonates were studied. Substantial differences in reactivity were observed between the two classes of compounds as well as between diastereomerically related alkyl halides. These differences are interpreted in terms of the effects of the bulks of the departing and remaining groups on the respective starting and transition states of the E_2 reaction. The results of these reactions serve to establish the configurations of all the 1,2-diphenyl-1-propyl halides relative to D-glyceraldehyde. An attempt to carry out an asymmetric degradation as applied to the E_2 reaction of these alkyl halides failed. A novel, lithium–amine catalyzed substitution of chloride by iodide in *threo*-1,2-diphenyl-1-propyl chloride that occurs in benzene and with retention of configuration is reported.

Differences in reactivity between diastereomerically related starting materials in acyclic systems have been noted in the cases of Wagner–Meerwein[2] and pinacol-like rearrangements,[3] the E_1,[4] E_2[5] and pyrolytic elimination reactions,[6] reactions involving neighboring group participation,[7] and reactions involving O- to N-acyl migration.[8]

The present investigation is concerned with the differences in reactivities in the E_2 and SN2 reactions between the *erythro*- and *threo*-isomers of the *p*-bromobenzenesulfonates (brosylates), chlorides, bromides and iodides of the 1,2-diphenyl-1-propyl system.



L-*erythro*-isomer of 1,2-diphenyl-1-propyl-X ($X = p\text{-}BrC_6H_4SO_3$, Cl, Br, I)



L-*threo*-isomer of 1,2-diphenyl-1-propyl-X ($X = p\text{-}BrC_6H_4SO_3$, Cl, Br, I)

SN2 Reactions of Halide Ions with Brosylates of 1,2-Diphenyl-1-propanol.—The brosylates of the stereoisomeric 1,2-diphenyl-1-propanols[9] were prepared by the method usually employed for the sulfonation of benzylhydroxyl groups.[10] In the case of both the active and racemic forms the *erythro*-esters were stable and could be stored without deterioration whereas the *threo*-esters were unstable and had to be used as soon as prepared. The *p*-toluenesulfonates (tosylates) of racemic and L-*erythro*-1,2-diphenyl-1-propanol were also prepared and found to be equally stable. Although the tosylates of the *threo*-alcohol could be prepared, their extreme instability made them impractical as starting materials. Table I reports the physical properties, the configurations[9] and analyses of these substances.

The displacement reactions of the brosylate

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[1] Predoctoral Fellow of the Egyptian Government. This paper is abstracted from the thesis of this author presented to the University of California at Los Angeles in partial fulfillment of the requirements for the Ph.D. degree.

[2] (a) D. J. Cram, THIS JOURNAL, **74**, 2149 (1952); (b) **74**, 2152 (1952).

[3] (a) D. Y. Curtin and P. I. Pollak, *ibid.*, **72**, 961 (1950); (b) **73**, 992 (1951).

[4] D. J. Cram, *ibid.*, **74**, 2137 (1952).

[5] P. T. Dillon, W. G. Young and H. J. Lucas, *ibid.*, **52**, 1953 (1930); W. G. Young, D. Pressman and C. D. Coryell, *ibid.*, **61**, 1640 (1939).

[6] (a) D. J. Cram, *ibid.*, **70**, 3883 (1948); (b) D. J. Cram and F. A. Abd Elhafez, *ibid.*, **74**, 5828 (1952).

[7] S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber and J. Corse, *ibid.*, **74**, 1118 (1952). Other pertinent references are listed here.

[8] G. Fodor, V. Bruckner, J. Kiss and G. Ohegyi, *J. Org. Chem.*, **14**, 337 (1949).

[9] F. A. Abd Elhafez and D. J. Cram, THIS JOURNAL, **74**, 5846 (1952).

[10] S. Winstein and B. K. Morse, *ibid.*, **74**, 1133 (1952).