

cedure used for rhizopterin.¹⁵ After evaporation of the reaction solution to dryness, the residue was taken up in water, and the pteridine in this solution purified by paper chromatography using dilute acetic acid as solvent. The material obtained in this way was rechromatographed in the solvents indicated in Table IV and compared with a sample of synthetic 2-amino-4-hydroxypteridine, deaminated and purified in the same way.

TABLE IV

Solvent	Fl 4B	De- amina- tion prod- uct	2,4- Dihy- droxy- pteri- dine
<i>n</i> -Propanol, 1% ammonia (2:1)	0.44	0.14	0.14
<i>n</i> -Butanol, acetic acid, water (4:1:5)	.37	.23	.23
3% Ammonia chloride	.55	.53	.53
5% Acetic acid	.66	.48	.48

The absorption spectrum of this deaminated material showed peaks at 255 and 360 $m\mu$ in 0.1 *N* sodium hydroxide and at 325 $m\mu$ in 0.1 *N* hydrochloric acid, again corresponding exactly to authentic 2,4-dihydroxypteridine.

Comparison of Fl 3 with Isoxanthopterin.—The absorption spectrum was identical with that of synthetic isoxanthopterin.⁹ The R_F values of the two are compared in Table V.

(15) D. E. Wolf, *et al.* THIS JOURNAL, **69**, 2753 (1947).

TABLE V

Solvent	Fl 3	Isoxan- thopterin
<i>n</i> -Propanol, 1% NH ₃ (2:1)	0.20	0.20
<i>n</i> -Butanol, acetic acid, water (4:1:5)	.37	.37
3% Ammonium chloride	.37	.37
5% Acetic acid	.42	.42

Identification of Uric Acid.—A small amount of the "ultraviolet absorbing material"³ (4 mg.) was isolated in the following way. In Part I of this series,² the purple compound, Fl 3, was described as being eluted from powdered cellulose columns, between the compounds described above and the yellow pigment. A concentrate of this band from a number of columns was made and the white solid so obtained was dissolved in dilute ammonia, treated with a large excess of charcoal, filtered, and the filtrate acidified. The resulting white solid was almost free of purple fluorescent material. Its absorption spectrum had a single maximum in both 0.1 *N* sodium hydroxide (at 295 $m\mu$) and 0.1 *N* hydrochloric acid (at 284 $m\mu$). These maxima are identical with those shown by uric acid. Paper chromatographic comparison with an authentic specimen (R_F in *n*-propanol, 1% ammonia, 0.35; in *n*-butanol, acetic acid, water, 0.26) and analysis confirmed this identity.

Anal. Calcd. for C₅H₄N₄O₃: N, 33.3. Found: N, 33.5.

PASADENA 4, CALIF.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

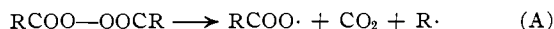
Reaction of Hydratropoyl Chloride with Sodium Peroxide

BY FREDERICK D. GREENE

RECEIVED MAY 4, 1955

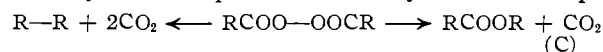
Hydratropoyl chloride (methylphenylacetyl chloride) has been treated with sodium peroxide under a variety of conditions. The products isolated, in the order of importance, were hydratropic acid, hydratropoyl hydratropoate (both racemates), styrene, α -phenylethanol, *meso*- and *dl*-2,3-diphenylbutane and acetophenone. With optically active starting material, the alcohol portion of the ester was of *retained* configuration (91% retention, 9% inversion); the α -phenylethanol and the 2,3-diphenylbutane were partially active and of *retained* configuration. The results are discussed in terms of the intermediate formation of the diacyl peroxide of hydratropic acid and decomposition within solvent "cages."

In spite of the wealth of data on the decomposition of diacyl and diaroyl peroxides, little is known of the primary decomposition processes. On the grounds of the usual products that have been isolated (acids, esters, hydrocarbons) two principal mechanisms^{1,2} have been advanced.



The decomposition of diaroyl peroxides has been interpreted in terms of mechanism B.^{3,4} The greatly accelerated rate of decomposition of phenylacetyl peroxide has been attributed to the operation of mechanism A, in which the formation of a relatively stable radical, the benzyl radical, in the rate-determining step might result in a lower activation energy than that required of mechanism B.⁵ The same authors suggested the possibility of cyclic decomposition processes, mechanism C, as another

means of accounting for the rapid decomposition of bis-phenylacetyl peroxide. By this mechanism, the ester and/or the dimeric hydrocarbon are formed directly from the peroxide in one synchronous step.



In order to get information on the relative importance of these processes we have attempted to prepare an optically active peroxide.^{6,7}

Results

The original intent was to prepare the diacyl peroxide of optically active hydratropic acid. All attempts to isolate this material failed; and, indeed, it was shown that even at -20° the rate of decomposition exceeded the rate of formation. Because of this limitation, the investigation involved the close scrutiny of the products derived from reaction of hydratropoyl chloride with sodium peroxide by four procedures.

- (1) D. H. Hey and W. A. Waters, *Chem. Revs.*, **21**, 169 (1937).
- (2) A. V. Tobolsky and R. B. Mesrobian, "Organic Peroxides," Interscience Publishers, Inc., New York, N. Y., 1954.
- (3) G. S. Hammond, THIS JOURNAL, **72**, 3737 (1950); G. S. Hammond and L. M. Soffer, *ibid.*, **72**, 4711 (1950).
- (4) C. G. Swain, W. H. Stockmayer and J. T. Clarke, *ibid.*, **72**, 5426 (1950).
- (5) P. D. Bartlett and J. E. Leffler, *ibid.*, **72**, 3030 (1950). In addition to radical decomposition processes, phenylacetyl peroxide may decompose also by a general acid-catalyzed process.

(6) M. S. Kharasch, J. Kuderna and W. Nudenberg, *J. Org. Chem.*, **19**, 1283 (1954), recently have reported the decomposition of the optically active peroxide of α -methylbutyric acid in benzotrichloride solution at $75-80^\circ$. The ester, *sec*-butyl α -methylbutyrate, was isolated in 30-40% yield. Hydrolysis of the ester afforded optically active *sec*-butyl alcohol of 78% retention, 22% racemization.

(7) C. S. Marvel, R. L. Frank and E. Prill, THIS JOURNAL, **65**, 1647 (1943), reported the preparation of optically active *p*-*sec*-butylbenzoyl peroxide.

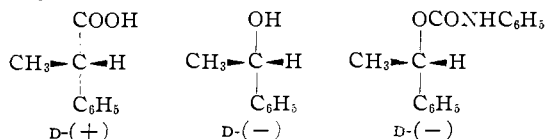
TABLE I
 PRODUCTS OF REACTION OF HYDRATROPYL CHLORIDE AND SODIUM PEROXIDE

Run	Pro- cedure	Hydratropyl chloride	Hydra- tropic acid, %	Styrene, %	Aceto- phenone, %	α -Phenyl- ethanol, %	2,3- Diphenyl- butane, %	Hydratropyl hydra- tropoate %	Total, %
4	A	Racemic	23	12	8	9	6	19 ^a	77
10	A	Racemic	23	15	8	11	8	18	83
5	A	L ^b	20	12	6	10	7.5	21	76.5
6	A	D ^c	13	6	5	4.5	6.5	37	72
8	B	Racemic	26	4.5	5.5	4.5	8	17.5	66
7	C	Racemic	<i>d</i>	<i>d</i>	<i>d</i>	<i>d</i>	5	23.5	
9	C	D ^e	18	<i>d</i>	<i>d</i>	<i>d</i>	6	27	
11	D	Racemic	23	15	4	15	8	19	84

^a D,D-L-ester, m.p. 74–75°, isolated in 39% yield of total ester. ^b From hydratropic acid, $[\alpha]^{26D} - 54.35^\circ$, 55% optically active. ^c From acid, $[\alpha]^{26D} + 98.72^\circ$, optically pure. ^d Not isolated. ^e 92.8% optically active.

Reaction of an ethereal solution of hydratropyl chloride with sodium peroxide and a small amount of water at 0° for 48 hours (procedure A) produced the following products: hydratropyl hydratropoate (both racemates, the D,D-L-racemate is a solid, m.p. 74–75°; the D,L-L,D-racemate failed to crystallize), hydratropic acid, styrene, acetophenone, α -phenylethanol and *meso*- and *dl*-2,3-diphenylbutane. Procedure B involved the very slow addition of an ethereal solution of the acid chloride to a mixture of sodium peroxide and ether at 0° containing a small amount of water. Procedure C was a modification of the procedure used by Vanino and Thiele⁸ to prepare bis-phenylacetyl peroxide, in which an aqueous alkaline solution of sodium peroxide at –15° was shaken vigorously with the acid chloride for ten minutes. Procedure D was a variant of procedure A, in which a mixture of the acid chloride, anhydrous sodium carbonate and ether containing hydrogen peroxide was stirred at 0° for 48 hours. The data of the experiments utilizing these procedures are summarized in Tables I and II.

Configurations.—The interrelationship in configuration of hydratropic acid and α -phenylethanol has been established: (+)-hydratropic acid has been related to (–)- α -phenylethyl chloride^{9a} which in turn has been related to (–)- α -phenylethanol.^{9b} These enantiomers have been related to D-(+)-glyceraldehyde.^{9c} (+)- α -Phenylethanol affords a phenylurethan of positive rotation.¹⁰



Two runs in which optically active acid chloride was treated according to procedure A yielded the same products as obtained with racemic material, but differing slightly in the relative amounts. The run with partially active L-material (run 5) and the one with pure D-material (6) afforded partially active α -phenylethanol, partially active ester and a mixture of *meso* and *dl*-2,3-diphenylbutane possessing a small specific rotation.

(8) L. Vanino and E. Thiele, *Chem. Ber.*, **29**, 1727 (1896).

(9) (a) See H. Hart and H. S. Eleuterio, *THIS JOURNAL*, **76**, 516 (1954), and earlier references cited therein; (b) J. Kenyon, H. Phillips and F. M. H. Taylor, *J. Chem. Soc.*, 173 (1933); (c) F. A. Abd El-hafez and D. J. Cram, *THIS JOURNAL*, **74**, 5849 (1952), footnote 9.

(10) A. McKenzie and G. W. Glough, *J. Chem. Soc.*, **103**, 687 (1913).

 TABLE II
 CONFIGURATION OF ALCOHOL PORTION OF HYDRATROPYL
 HYDRATROPOATE

Run	Retention, %	Inversion, %
5	74	26
6	84	16
9	91	9

The alcohol was converted to the phenylurethan and the degree of optical activity was determined by optical analysis of the urethan.¹¹ In both runs the alcohol was partially racemized but of *retained* configuration. The run with optically pure acid chloride afforded alcohol of 51% retention, 49% racemization of configuration.

Recrystallization of the ester mixture from run 6 gave optically pure D,D-hydratropyl hydratropoate, identified by hydrolysis and conversion of the alcohol fraction to the phenylurethan. The optical activity of the alcohol part of the non-crystallizable ester residue, a mixture of the two diastereomers of hydratropyl hydratropoate, was determined in the same manner. The alcohol group in the total ester fraction thereby was calculated to be 84% retention, 16% inversion of configuration (or 68% retention, 32% racemization).

A sample of pure L,L-hydratropyl hydratropoate was obtained from the reaction utilizing partially active L-acid chloride (run 5). In this experiment, the alcohol group of the total ester fraction was shown to have 74% retention, 26% inversion of configuration. (These differences may be attributed, in part, to the complication that two diastereomeric peroxides are possible when the starting material is racemic or partially active. Only when the starting material is optically pure may a single diacyl peroxide be formed.)

From optically active hydratropyl chloride subjected to procedure C (run 9) was isolated hydratropyl hydratropoate in which the alcohol group had 91% retention, 9% inversion of configuration.

The mixture of *meso*- and *dl*-2,3-diphenylbutane comprised 4–8% of the product. Samples of pure *meso* (m.p. 126°)¹² and *dl* (m.p. 12–13°)¹³ material were prepared as standards. The mixture, isolated from the decompositions by distillation and

(11) This procedure was required because of the small amounts of alcohol involved. Upon recrystallization of the partially active urethan from hexane racemic material precipitates preferentially. The values recorded are based on rotations of all crops of crystals.

(12) J. B. Conant and A. H. Blatt, *THIS JOURNAL*, **50**, 555 (1928).

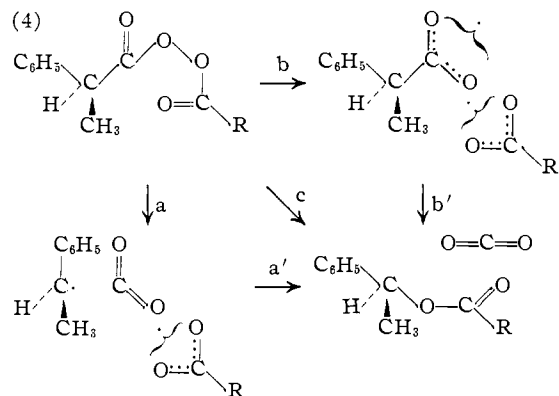
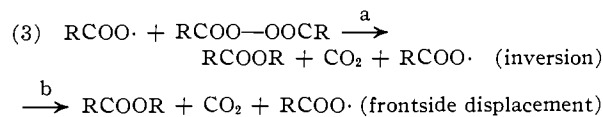
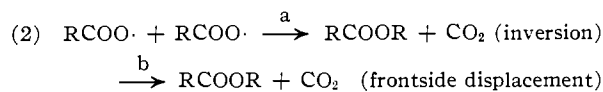
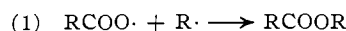
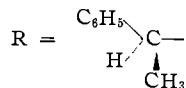
(13) F. V. Wessely and H. Welleba, *Chem. Ber.*, **74**, 777 (1941).

chromatography on alumina, was analyzed by spectrophotometric means and shown to consist of about equal amounts of the two hydrocarbons. A sample, which was rich in the *dl*-isomer after removal of the bulk of the *meso*-compound by recrystallization, had a slight rotation, $[\alpha]^{25D} + 2^\circ$ (from L-acid, run 5) and $[\alpha]^{25D} - 2^\circ$ (from D-acid, run 6). The total hydrocarbon mixture from run 9 had a considerably higher rotation, $[\alpha]^{25D} - 17^\circ$ (from D-acid).

Discussion

The experimental conditions and the products isolated are suggestive of the transient occurrence of hydratropoyl peroxide. The isolation of hydratropoyl hydratropoate in 23% yield from run 7 and 27% from run 9 (reaction time ten minutes) and in approximately 20% yield from runs 4, 10 and 5 requires the diacyl peroxide as the only reasonable intermediate which can account for ester formation. A control experiment in which hydratropoyl chloride and α -phenylethanol were treated under similar conditions (with replacement of sodium carbonate for sodium peroxide) failed to yield any of the ester.

There are numerous processes by which ester may be formed. Step 1 involves the recombination



of radicals after they have achieved statistical distribution throughout the solution. The isolation of ester with optical activity in the ester group does not rigorously exclude this step inasmuch as ester formation by this process would be, in effect, an asymmetric synthesis. Since step 1 involves the recombination of two radicals and since the old asymmetric center is not directly adjacent to the reacting atoms we consider it unlikely that asymmetric induction in the alcohol group is effected in this way.

Steps 2a and 3a cannot constitute a major route for ester formation since they would yield ester of

inverted configuration in the alcohol group. Apart from the unlikelihood of a frontside displacement, steps 2b and 3b (as well as 1, 2a and 3a) are rendered improbable by the independence of product composition on concentration (see below).

The observed products may be accounted for by the occurrence of 4a-a', 4b-b' and 4c. Steps 4a and 4b constitute two modes of primary fission. Step 4c involves the direct conversion of the peroxide to the ester by a cyclic decomposition. The great reactivity of the peroxide is suggestive of greater importance for 4a than for 4b.⁵ In steps 4a' and 4b', the radicals are considered to recombine before achieving statistical distribution in the reaction mixture (the "cage" effect of Franck and Rabinowitsch).^{14a,b} If this recombination occurs within the solvent cages *before the α -phenylethyl radicals have even achieved statistical orientation with respect to the hydratropoyl radicals*, then the ester produced would be of partially retained configuration in the alcohol group. In any event, the fact that considerable racemization, 18-32%, has occurred at least requires ester formation by a process other than 4c alone. From the standpoint of simplicity of mechanism, 4a-a' is favored as the principal process for ester formation, though 4b-b' and 4c may be operative.

The formation of the same product composition under circumstances involving large changes in concentration (10, 4, 5 vs. 8) lends further support to product formation within the cage. This also may be the case with the decomposition of apocamphoyl peroxide in benzene at 80° in which the product composition was observed to be independent of peroxide concentration over a 64-fold variation in concentration.¹⁵ The cage effect appears to be important in the decomposition of acetyl peroxide in benzene.¹⁶ In this case, the ratio of ethane to carbon dioxide was independent of the peroxide concentration, and decomposition in the presence of quinone did not alter the yield of ethane while producing a large decrease in the yield of methane. Neither Szwarc's data nor that presented here permit an estimate of the temperature dependence of a cage effect although it is reasonable to expect the cage effect to be of greater importance at low temperatures. Procedure C (-15°) afforded products of greater optical purity than procedure A (compare 5 with 9) but the reaction media are too dissimilar to warrant interpretation in terms of the temperature difference.¹⁷

The products acetophenone, styrene, α -phenylethanol and 2,3-diphenylbutane all may be derived from the α -phenylethyl radical. The isolation of α -phenylethanol of retained configuration warrants special consideration. Control experiments have shown that it is not formed by hydrolysis of optically active ester in the reaction mixture or during any of the procedures used in product isolations. Formation *via* asymmetric α -phenylethyl radicals

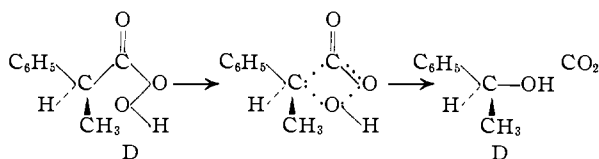
(14) (a) J. Franck and E. Rabinowitsch, *Trans. Faraday Soc.*, **30**, 120 (1934); (b) M. S. Matheson, *J. Chem. Phys.*, **13**, 584 (1945).

(15) W. F. Sager, Ph.D. Thesis, Harvard University, 1948.

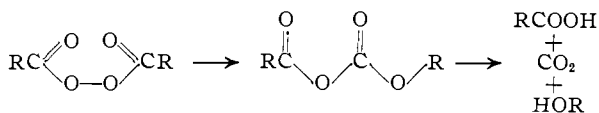
(16) M. Szwarc, *THIS JOURNAL*, **76**, 5975, 5978, 5981 (1954).

(17) For examples of radicals trapped in "rigid" cages at very low temperatures (86°K.) see I. Norman and G. Porter, *Nature*, **174**, 508 (1954).

is considered highly unlikely. Cyclic decomposition of an intermediate peracid might be expected to yield alcohol of retained configuration.¹⁸



A second possible source of optically active alcohol involves the rearrangement of the diacyl peroxide to the mixed anhydride-ester with retention of configuration; hydrolysis in the process of isolation would yield the optically active alcohol.¹⁹



meso- and *dl*-2,3-diphenylbutane were isolated in approximately equal amounts. The very small rotation ($\pm 2^\circ$) observed in runs 5 and 6 is in contrast with the rotation, $[\alpha]^{25}_D -17^\circ$ (*l* 1 dm., 4.1% CS_2), for a mixture of 53% *dl*-, 47% *meso*-hydrocarbon observed in run 9 in which *D*-acid chloride was used. From the data of Ott,²⁰ who prepared dextrorotatory 2,3-diphenylbutane of unknown optical purity but probably of *L,L*-configuration by the Wurtz reaction on *D*- α -phenylethyl chloride, one may calculate a minimum rotation of $+50.8^\circ$ for optically pure *d*-2,3-diphenylbutane.²¹ The negative rotation of the hydrocarbon mixture from run 9 indicates the presence of a considerable amount of *D,D*-2,3-diphenylbutane, corresponding to *retention* of configuration. Formation by a cyclic decomposition of the peroxide (similar to 4c) or by recombination of α -phenylethyl radicals in the "cages" before the radicals had achieved statistical orientation with respect to each other are both compatible with retention of configuration.

Experimental

1,2-Diphenyl-1,2-propanediol was prepared by the action of methylmagnesium iodide on benzoin according to the procedure of Tiffeneau and Dorlencourt.²² Recrystallization from methanol gave material of m.p. 102–104°.

2,2-Diphenylpropionaldehyde.—The method of Lévy²³ was used to rearrange the diol to the aldehyde (50% aqueous oxalic acid at reflux temperature). The aldehyde had b.p. 111–113° (1 mm.), n^{25}_D 1.5800.

***trans*-2,3-Diphenylbutene.**—Reaction of 2,2-diphenylpropionaldehyde with methylmagnesium iodide according

(18) Only a few cases have been reported in which the decomposition of a peracid yields an alcohol. See D. Swern, *Chem. Revs.*, **45**, 1 (1949). F. Fichter and E. Kruppenacher, *Helv. Chim. Acta*, **1**, 146 (1918), isolated some ethanol from the decomposition of perpropionic acid in a steel autoclave. All attempts to prepare the peracid of hydratropic acid to investigate this point further were unsuccessful.

(19) Such processes have been shown to be operative in the decomposition of *p*-nitro-*p*'-methoxybenzoyl peroxide under ionizing conditions by J. E. Leffler, *This Journal*, **72**, 67 (1950). That they may be of more widespread occurrence is suggested by the work of P. D. Bartlett and F. D. Greene, *ibid.*, **76**, 1088 (1954).

(20) E. Ott, *Chem. Ber.*, **61**, 2137 (1928).

(21) From *D*-chloride, $[\alpha]^{25}_D -50.27^\circ$, was isolated a mixture of *meso*- and *dl*-2,3-diphenylbutane. The *dl*-material had a positive rotation ($[\alpha]_D +20.24^\circ$). R. L. Burwell, Jr., A. D. Shields and H. Hart, *This Journal*, **76**, 908 (1954), have calculated 126° for the rotation of optically pure α -phenylethyl chloride.

(22) M. Tiffeneau and Dorlencourt, *Ann. chim. (Paris)*, [8] **16**, 252 (1909).

(23) J. Lévy, *Bull. soc. chim. France*, [4] **29**, 872 (1921).

to the method of Lévy²³ gave 2,2-diphenyl-3-butanol. Distillation of the alcohol in the presence of a small amount of sulfuric acid gave a mixture of *cis*- and *trans*-2,3-diphenylbutene, consisting predominantly of the latter compound. Five recrystallizations from hexane afforded pure *trans*-olefin, m.p. 104–105°.

***dl*-2,3-Diphenylbutane.**—To 4.8 g. of *trans*-2,3-diphenylbutene in 40 ml. of ethyl acetate was added 3 g. of palladium catalyst (10% palladium-on-carbon).²⁴ The mixture was hydrogenated at a pressure of 40 lb. per sq. in.; the theoretical amount of hydrogen was taken up in 30 minutes. Filtration and removal of the ethyl acetate from the filtrate afforded 4.44 g. of oil. This material was purified by chromatography on a 160-g. column of neutral activated alumina (Brockman Activity I), eluting with petroleum ether, b.p. 30–60°. A middle fraction of 1.3 g. was flash distilled twice at 12 mm. pressure giving material of m.p. 12–13°, n^{25}_D 1.5530; reported m.p. 12.5° .^{13,25}

***meso*-2,3-Diphenylbutane.**—This compound was prepared by the method of Conant and Blatt¹² and purified by two recrystallizations from methanol, two recrystallizations from hexane, giving material of m.p. 125–126°.

Hydratropic Acid.—The acid was prepared by the oxidation of hydratropaldehyde,²⁶ b.p. 93–94° (12 mm.). Resolution was effected through the strychnine salts²⁷ giving material of the following physical constants: b.p. 121–123° (0.5 mm.), n^{25}_D 1.5211, $[\alpha]^{25}_D +98.72^\circ$ (*l* 1 dm., neat). After several months at 0° the optically pure material solidified.

Hydratropoyl Chloride.—A solution of the acid $[\alpha]^{25}_D -55.43^\circ$, and thionyl chloride was left at 25° for two days. The excess thionyl chloride was removed under reduced pressure and the residual acid chloride was flash distilled twice, b.p. 93–96° (11 mm.), n^{25}_D 1.5216. Hydrolysis of a portion of the product with dilute sodium hydroxide afforded hydratropic acid, $[\alpha]^{25}_D -55.4^\circ$, indicating that no racemization occurred in the preparation and distillation of the acid chloride.

Reaction of Hydratropoyl Chloride with Sodium Peroxide. Procedure A.—To a sample of 6.0 g. (0.0356 mole) of hydratropoyl chloride in 60 ml. of reagent ether at 0° was added 1.67 g. (0.0195 mole) of 91% sodium peroxide and 0.23 g. (0.013 mole) of water (run 10). The resulting mixture was stirred vigorously at 0° for 48 hours. The mixture was filtered, giving a residue of 3.00 g. from which 0.60 g. of hydratropic acid was isolated by dissolution in water, acidification, ether extraction and solvent removal. The ethereal filtrate was extracted with dilute sodium carbonate solution from which was isolated an additional 0.65 g. of acid: total acid, 1.25 g. (0.00835 mole). The ether layer was passed through a column of 30 g. of neutral alumina, Brockman Activity I–II (to remove any hydratropic anhydride or hydratropoyl chloride), and an additional 100 ml. of ether was used as eluent. By further elution of the column with methanol–ether, 0.46 g. (0.0038 mole) of α -phenylethanol was isolated and identified by its infrared absorption spectrum and by conversion to the corresponding phenylurethan, m.p. 93–94° after recrystallization from hexane, reported m.p. 94°.¹⁰

The bulk of the ether was removed from the eluate, which contained the remaining neutral products, by distillation through a Vigreux column. The residue was heated at 70° under water aspirator pressure and the distillate was collected in a Dry Ice-cooled flask. The addition of bromine in ether to the distillate afforded 1.30 g. (0.0051 mole) of styrene dibromide, m.p. 73–74° after one recrystallization from ethanol–water.

The residue was chromatographed on a 50-g. column of neutral alumina (Brockman Activity I–II) in petroleum ether, b.p. 30–60°, giving 0.30 g. (0.0014 mole) of a mixture of *meso*- and *dl*-2,3-diphenylbutane (see below), 0.84 g. (0.0033 mole) of a mixture of diastereomeric esters of hydratropoyl hydratropoate,²⁸ and 0.19 g. of acetophenone.

(24) R. Mozingo, *Org. Synth.*, **26**, 77 (1946).

(25) A. L. Lepin has reported a m.p. of 8°, n^{25}_D 1.55516, for this compound (*J. Russ. Phys. Chem. Soc.*, **44**, 1190 (1912)).

(26) H. D. Kay and H. S. Raper, *Biochem. J.*, **16**, 469 (1922).

(27) C. L. Arcus and J. Kenyon, *J. Chem. Soc.*, 916 (1939); A. Campbell and J. Kenyon, *ibid.*, 25 (1946).

(28) No ethyl hydratropoate was present, based on the infrared spectrum of the ester mixture and that of ethyl hydratropoate, a sample of which was prepared by the action of ethanol–pyridine on the acid chloride, n^{25}_D 1.4908.

identified by conversion to the phenylhydrazone, m.p. 104–105°, and the 2,4-dinitrophenylhydrazone, m.p. 249–250°.

Successive recrystallizations of the ester mixture from carbon tetrachloride and from hexane afforded 0.33 g. of the D,D-L,L-racemate as short fat needles, m.p. 74–75°.

Anal. Calcd. for $\text{C}_{17}\text{H}_{18}\text{O}_2$: C, 80.28; H, 7.13. Found: C, 79.95; H, 6.85.

The residual ester fractions of several runs, after removal of the solid racemate, were distilled yielding an oil of b.p. 95–96° (0.05 mm.), n_D^{25} 1.5390, presumed to be largely the D,L-L,D-racemate.

Anal. Calcd. for $\text{C}_{17}\text{H}_{18}\text{O}_2$: C, 80.28; H, 7.13. Found: C, 80.63; H, 7.11.

Treatment of 10.8 g. of hydratropoyl chloride, prepared from 55% optically active L-acid of $[\alpha]_D^{26}$ -54.35° (l 1 dm., neat), under the same conditions afforded the products indicated in Table I, run 5. Recrystallization of the ester fraction, 1.73 g., from petroleum ether afforded 0.545 g. of L,L-hydratropoyl hydratropoate, m.p. 94–95°, $[\alpha]_D^{25}$ $+24.6^\circ$ (l 1 dm., 3.05% in benzene).

Anal. Calcd. for $\text{C}_{17}\text{H}_{18}\text{O}_2$: C, 80.28; H, 7.13. Found: C, 80.67, 80.66; H, 7.47, 7.46.

A 0.5-g. sample of solid ester was heated under reflux with 600 mg. of sodium hydroxide, 8 ml. of methanol and 4 ml. of water for 16 hours. The hydratropic acid from hydrolysis was levorotatory; the α -phenylethanol was isolated and converted to the phenylurethan, $[\alpha]_D^{25}$ $+99^\circ$ (l 1 dm., 5.1% in benzene), reported for the rotation of the phenylurethan of optically pure L-(+)- α -phenylethanol, $[\alpha]_D^{18}$ $+101.5^\circ$ (l 1 dm., 4.86% in benzene),¹⁰ thereby establishing the L,L-configuration for the solid ester. In the same manner the alcohol part of the remaining ester mixture was shown to be 6.5% optically active and of retained (L) configuration. These data indicate that the alcohol part of the total ester fraction was 27% optically active and of retained configuration, corresponding to 49% retention of the activity of the starting chloride (49% retention, 51% racemization; or 74% retention, 26% inversion).

The α -phenylethanol, 0.66 g., isolated from this run (5) was converted to the phenylurethan and shown to be 46% optically active and of retained configuration. A 0.5-g. sample of a mixture of *meso*- and *dl*-2,3-diphenylbutane was isolated and the bulk of the *meso*-isomer was removed by recrystallization from cyclohexane. The residue had a slight rotation, $[\alpha]_D^{25}$ $+2^\circ$ (l 1 dm., 12% in benzene).

Treatment of hydratropoyl chloride, prepared from optically pure D-(+)-acid under the same conditions afforded the products shown in Table I, run 6. The ester fraction, 3.02 g., was recrystallized from petroleum ether, giving 2.16 g. of D,D-ester, m.p. 93.5–94.5°, $[\alpha]_D^{27}$ -23.4° (l 1 dm., 5.1% in benzene).

Anal. Calcd. for $\text{C}_{17}\text{H}_{18}\text{O}_2$: C, 80.28; H, 7.13. Found: C, 80.38; H, 7.15.

The mixed melting point (50–50 mixture) with the L,L-ester was 73–75°, identical with the melting point of the D,D-L,L-ester. The 0.86 g. of residual ester mixture from above was hydrolyzed and the alcohol was converted to the phenylurethan, 0.47 g. of $[\alpha]_D^{27}$ $+3.75^\circ$ (l 1 dm., 5.0% in benzene) and 0.16 g. of $[\alpha]_D^{27}$ $+46.5^\circ$ (l 1 dm., 4.9% in benzene), *i.e.* the ester residue was 57% DL and 43% DD, and the total ester fraction of 3.02 g. was 84% DD and 16% DL.

From the reaction mixture was isolated a 0.24-g. sample of α -phenylethanol, which was converted to the urethan, $[\alpha]_D^{27}$ -53.2° (l 1 dm., 4.8% in benzene), corresponding to 51% over-all retention of configuration, 49% racemization. The mixture of *meso*- and *dl*-2,3-diphenylbutane amounted to 0.44 g., $[\alpha]_D^{27}$ -2° (l 1 dm., 18.5% in carbon disulfide).

Procedure B.—To a mixture of 80 ml. of anhydrous ether, 16 g. of 93% sodium peroxide and 3.1 g. of water, stirred at 0°, was added a solution of 6.0 g. of racemic hydratropoyl chloride in 80 ml. of dry ether by means of a high dilution

funnel at approximately 0.07 ml. per minute (run 8). The mixture was stirred for 24 hours after completion of addition. The mixture afforded 1.42 g. of the acid, 0.17 g. of styrene (a minimum value), 0.24 g. of acetophenone, 0.20 g. of α -phenylethanol, 0.30 g. of a mixture of *meso*- and *dl*-2,3-diphenylbutane, and 0.82 g. of hydratropoyl hydratropoate.

Procedure C.⁸—To 5.64 g. of racemic hydratropoyl chloride was added 7.5 ml. of 30% hydrogen peroxide solution and 50 ml. of 3.5 *N* sodium hydroxide solution cooled to -15° (run 7). The mixture was swirled alternately in a bath at -50° and vigorously shaken by hand. After 10 minutes, the mixture was transferred to a cold separatory funnel and extracted with three 10-ml. portions of ether (cooled to -50°). The ether extracts were cooled to -80° . Titration of an aliquot of the ether solution for peroxide content (by liberation of iodine in acetic acid and titration with thiosulfate solution) indicated a total peroxide content of 0.1 g. From the ether was isolated 0.18 g. of *meso*- and *dl*-2,3-diphenylbutane and 1.00 g. of hydratropoyl hydratropoate.

Treatment of 5.64 g. of hydratropoyl chloride, prepared from D-(+)-acid of 92.8% optical purity, under the same conditions afforded 0.23 g. of a mixture of *meso*- and *dl*-2,3-diphenylbutane, $[\alpha]_D^{25}$ -17.1° (l 1 dm., 4.1% in carbon disulfide) and 1.14 g. of hydratropoyl hydratropoate. Analysis of the hydrocarbon mixture by infrared (see below) showed that it consisted of $47 \pm 5\%$ *meso*- and $53 \pm 5\%$ *dl*-2,3-diphenylbutane (rich in the *l*-isomer). The alcohol portion of the ester fraction was converted to the urethan and analyzed polarimetrically as before: 91% retention, 9% inversion of configuration.

Procedure D.—A 6.0-g. sample of racemic hydratropoyl chloride was added to a mixture of 4.0 g. of anhydrous sodium carbonate and 60 ml. of anhydrous ether containing 0.0195 mole of hydrogen peroxide (run 11). The mixture was stirred at 0° for 48 hours and the products were isolated as described previously.

Isolation and Determination of *meso*- and *dl*-2,3-Diphenylbutane.—The petroleum ether eluates from run 4 contained a mixture of 0.70 g. of *dl*- and *meso*-hydrocarbons. Recrystallization from cyclohexane afforded 218 mg. of *meso*-compound, m.p. 124–125°, mixed m.p. with authentic material, 123–124°. The material in the filtrate was purified by distillation, 0.48 g. Spectroscopic analysis, making use of the difference in intensity of the bands in the infrared absorption spectra at 9.5μ for the *dl*-compound and at 9.6μ for the *meso*-compound indicated $30 \pm 5\%$ *meso*, 0.14 g., and $70 \pm 5\%$ *dl*-compound, 0.34 g., corresponding to a total yield of 0.36 ± 0.02 g. of *meso*- and 0.34 ± 0.02 g. of *dl*-compound.

Control Experiments. (a) **Hydratropoyl Hydratropoate and Ethereal Sodium Peroxide.**—A mixture of 1.06 g. of D,D-L,L-ester, 60 ml. of ether, 1.6 g. of sodium peroxide and 0.3 g. of water was stirred at 0° for 48 hours. Workup afforded 1.04 g. of ester. The same result was obtained with D,L-L,D-ester.

(b) **Hydratropoyl Hydratropoate and Alumina.**—A 1.04-g. sample of D,D-L,L-ester was chromatographed on 30 g. of neutral alumina (Brockman Activity I–II) in petroleum ether, b.p. 30–60°. Elution was carried out slowly so that the ester remained on the alumina for three times the contact time in product isolations. The ester, 1.02 g., was recovered unchanged. The same result was obtained with the D,L-L,D-ester.

(c) **Hydratropoyl Chloride and α -Phenylethanol.**—A mixture of 1.83 g. of α -phenylethanol, 2.5 g. of hydratropoyl chloride, 1.0 g. of sodium carbonate and 50 ml. of ether was stirred at 0° for 24 hours. The mixture was filtered onto a column of 60 g. of alumina and eluted with ether. (The acid chloride is hydrolyzed on alumina to the acid which is not eluted by ether.) Distillation of the eluates yielded 1.38 g. of α -phenylethanol, $n_D^{22.5}$ 1.5248, a 75% recovery.

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