system (*threo*- and *erythro*-I) with a Perkin–Elmer recording spectrophotometer, model 21. The infrared spectra of pure *threo*- and *erythro*-I were examined from 4000–650 cm.$^{-1}$. The wave lengths most suitable for analysis and the optical densities of the pure alcohols were (resolution 940, suppression 0, speed 0, gain 5, response 1:1, cells NaCl, 0.10-mm. thickness, NaCl optics): at 1149.7 cm.$^{-1}$, *threo* 0.212, *erythro* 0.469; 1126.5 cm.$^{-1}$, *threo*, 0.631, *erythro*, 0.409; 1019.2 cm.$^{-1}$, *threo*, 0.287, *erythro*, 0.593; 987.1 cm.$^{-1}$, *threo*, 0.298, *erythro*, 0.726; 1129.2 cm.$^{-1}$, *threo*, 0.593, *erythro*, 0.392; 1197.0 cm.$^{-1}$, *threo*, 1.000, *erythro*, 0.629; 1081.6 cm.$^{-1}$, *threo*, 1022, *erythro*, 0.638; 1020.3 cm.$^{-1}$, *threo*, 0.286, *erythro*, 0.620. Known mixtures of about 25, 50 and 75% *threo*-I in *erythro*-I were prepared, and optical density *vs.* composition curves were prepared. The optical densities of the unknowns from runs 25 and 26 were then determined, and the composition thus became known. The results are listed in Table IV.

Preparation of 2,4-Dinitrobenzenesulfenyl Chloride Adducts from the Olefinic Mxitures Obtained from Runs 19 and 20.—The procedure is illustrated for the olefin obtained from run 19. A mixture of 0.217 g. of olefin, 4 ml. of glacial acetic acid and 0.378 g. of 2,4-dinitrobenzenesulfenyl chloride was heated to 80° for 20 minutes and then cooled. The yellow solid that separated was collected and extracted with boiling ethanol. The extract was filtered, and the filtrate was concentrated and cooled. The crude product that separated, 0.154 g. (26%), was recrystallized twice from ethanol, m.p. 147–148.5°.

Anal. Calcd. for $C_{16}H_{21}O_4N_2SCl$: C, 51.53; H, 5.63. Found: C, 51.70; H, 5.79.

The crude adduct obtained from olefin from run 20 was obtained in 25% yield. Two recrystallizations of the material from ethanol gave m.p. 147–149°. A mixed melting point of the two samples gave 146–149°.

Anal. Calcd. for $C_{16}H_{21}O_4N_2SCl$: C, 51.53; H, 5.63. Found: C, 51.27; H, 5.91.

When the above reactions were carried out at 25° for 24 hours, the adducts were isolated as long yellow needles in 38% yield in each case.

Los Angeles, Calif.

[Contribution from the Department of Chemistry of the University of California at Los Angeles]

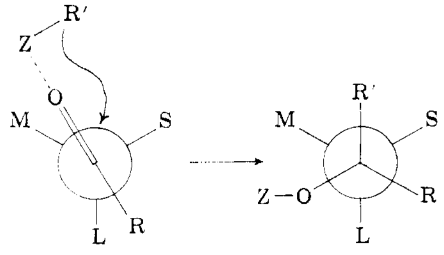
Studies in Stereochemistry. XXX. Models for Steric Control of Asymmetric Induction[1]

By Donald J. Cram and Karl R. Kopecky

Received October 28, 1958

The application of two different models to explain the steric course of asymmetric induction has been investigated in systems where each model predicts a different result. In syntheses of 2,3-diphenyl-2,3-butanediol and its monomethyl ether from various ketones, an asymmetric center is created in the presence of one already in the molecule. With systems of this type, rigid model II rather then open-chain model I predicts the configuration of the predominant product. Models are proposed which rationalize the formation of isotactic and syndiotactic polymers.

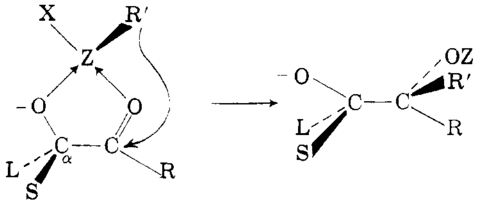
In previous papers of this series,[2] a model has been developed which correlates and rationalizes a large body of data pertaining to the steric direction of asymmetric induction. This model is represented by I, which depicts the reaction of an aldehyde or ketone with an organometallic reagent in which an asymmetric center is created on carbon adjacent to an asymmetric center already in the molecule. The symbols, L, M and S stand for large, medium and small groups attached to the old asymmetric center, and that conformation is selected which presents the least steric barrier to reaction.



transition state of lowest energy   predominant diastereomer

I (open-chain model)

A second model was also considered[2a] for systems in which the asymmetric center in the starting material carried a group such as OH or NH_2 which was capable of complexing with organometallic reagents. This model is represented by II, and it involves a relatively rigid, five-membered ring which fixes the conformation of the reacting species.



transition state of lowest energy   predominant diastereomer

II (rigid model)

In systems in which an amino or hydroxyl group on C_α is the medium sized group (*e.g.*, S is hydrogen and L is phenyl), the open-chain (I) and rigid models (II) predict the same result. All systems in which the configurations of the products have been clearly demonstrated belong to this class,[3] and none has been examined in which the two models unambiguously predict opposite results. To meet this condition, the complexing group on C_α(hydroxyl or amino) must be the small group.

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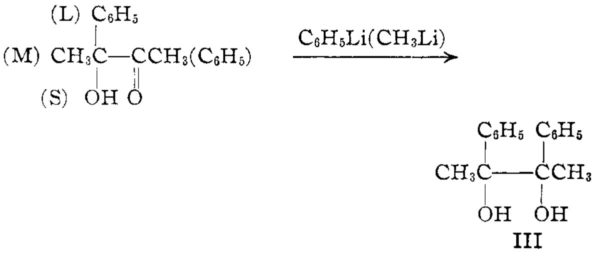
[1] This work was sponsored by the Office of Ordnance Research, U. S. Army.

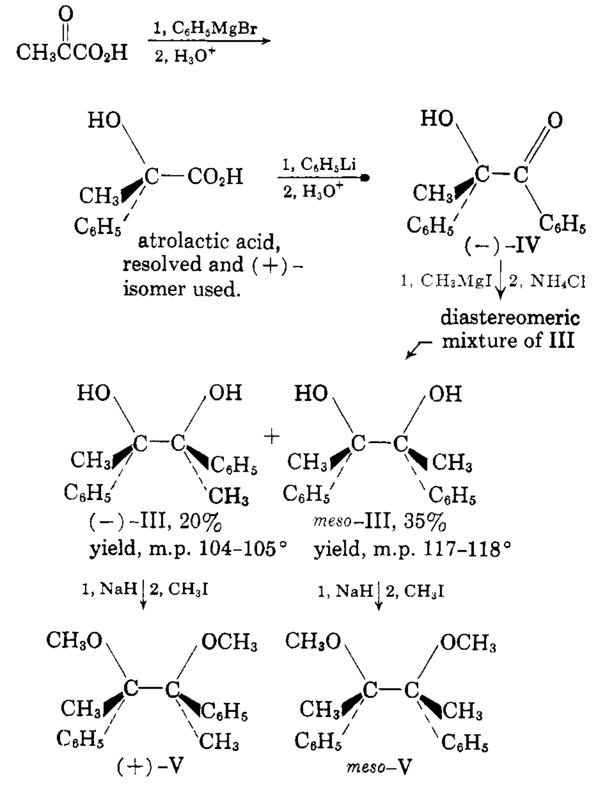
[2] (a) D. J. Cram and F. A. Abd Elhafez, This Journal, **74**, 5828 (1952); (b) D. J. Cram and J. D. Knight, *ibid.*, **74**, 5835, 5839 (1952); (c) D. J. Cram, F. A. Abd Elhafez and H. Weingarten, *ibid.*, **75**, 2293 (1953); (d) D. J. Cram and F. D. Greene, *ibid.*, **75**, 6005 (1953); D. J. Cram, F. A. Abd Elhafez, *ibid.*, **76**, 22 (1954); D. J. Cram and J. E. McCarty, *ibid.*, **76**, 5740 (1954).

[3] D. Y. Curtin, E. E. Harris and E. K. Meislich [*ibid.*, **74**, 2901 (1952)] developed a correlation between configuration of the predominant product and the order in which groups were introduced in the preparation of substituted, diastereomeric 1-hydroxyl-2-aminodibenzyl compounds.

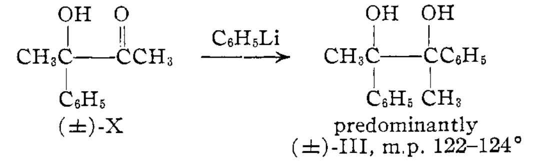
This paper reports the results of a study of the steric direction assumed by reactions leading to 2,3-diphenyl-2,3-butanediol (III) and its derivatives. In this system the two models can be differentiated, and the configurations of the products are easily established.



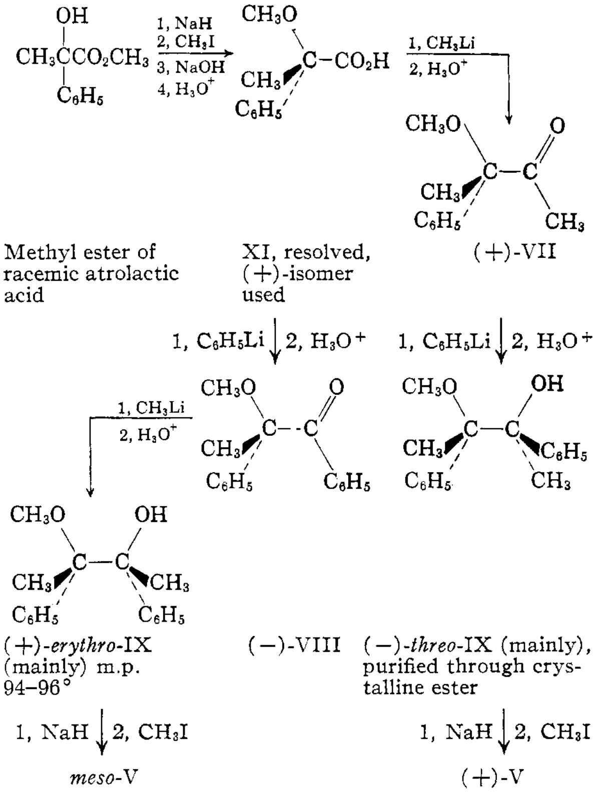
Configurations of Starting Materials and Products.—A large amount of atrolactic acid was synthesized,[4] resolved[5] and converted to optically pure (−)-methylbenzoin (IV) which with methyl Grignard reagent gave a mixture of *meso*-and (−)-III. These diastereomers were separated by fractional crystallization, and their configurations identified by the fact that only one was optically active. Both glycols were converted to their respective dimethyl ethers (V) whose configurations thus became established.[6]



Racemic 3-hydroxy-3-phenyl-2-butanone (X) was prepared[7] and converted with phenyllithium to predominantly (±)-III. This substance has been prepared a number of times before,[8] and has been assigned both the correct[8,9] and incorrect[2a] configuration in all cases on inconclusive grounds. The configuration of this racemate is demonstrated in the present investigation by the identification of the *meso*-isomer V prepared from (−)-IV as having m.p. 117–118°. This leaves only the (±)-configuration for the isomer, m.p. 122–124°.[10]



In a second series of reactions, the methyl ester of atrolactic acid was converted to its ether, which was hydrolyzed to the methyl ether of atrolactic acid (VI). This substance was resolved into its two optically pure antipodes, and the (+)-isomer was converted into methyl ketone VII and phenyl ketone VIII. These two substances were converted into diastereomeric mixtures of 2,3-diphenyl-3-methoxy-2-butanol (IX), one of whose components (*erythro*) was crystalline and the other



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(4) F. N. Peters, This Journal, **47**, 453 (1925).

(5) A. McKenzie and G. W. Clough, *J. Chem. Soc.*, **97**, 1018 (1910).

(6) The configuration of atrolactic acid has been determined by a variety of methods; for a summary of references, see J. H. Brewster, This Journal, **78**, 4061 (1956).

(7) J. Wegmann and H. Dahn, *Helv. Chim. Acta*, **29**, 101 (1946).

(8) (a) M. Tiffeneau and J. Levy, *Bull. soc. chim. France*, [4] **41**, 1351 (1931); (b) G. Ciamician and P. Silber, *Ber.*, **47**, 1806 (1914).

(9) (a) Ramart-Lucas and M. E. Salmon-Legagneur, *Bull. soc. chim. France*, [4] **45**, 718 (1929); (b) Ramart-Lucas and Biquard, *Compt. rend.*, **194**, 187 (1932).

(10) Incidental to this investigation, the identification of the configuration of this isomer demonstrates that the acid-catalyzed hydrolysis of *trans*-2,3-diphenyl-2-butene oxide does indeed[8a] represent an example of a *cis* opening of an ethylene oxide ring. J. H. Brewster (ref. 6) and D. Y. Curtin, A. Bradley and Y. G. Hendrickson [This Journal, **78**, 4064 (1956)] report examples of acid-catalyzed openings of ethylene oxide rings carrying aryl groups, and have invoked S_Ni reaction mechanisms that involve ion-pair intermediates [D. J. Cram, *ibid.*, **75**, 332 (1952)].

TABLE I

RESULTS OF REACTIONS THAT GIVE DIASTEREOMERIC 2,3-DIPHENYL-2,3-BUTANEDIOLS (III) OR DIASTEREOMERIC 2,3-DIPHENYL-3-METHOXY-2-BUTANOLS (IX)

Run[a]	Ketone	Reagent	% yld. III	Ratio diastereomers[b] meso-III	(±) or (−)-III	Isomer isolated[c] Config.	% yld.[d]	M.p., °C.	Model I predicts	Model II predicts
1	(±)-X	C_6H_5Li	92	1	6.7	(±)-III	44	122–124	*meso*	(±)
2	Biacetyl	C_6H_5Li	63	1	8	(±)-III	54	122–124	*meso*	(±)
3	(−)-IV	CH_3Li	74[e]	11.5	1	*meso*-III	20	115–117	(−)	*meso*
4	Benzil	CH_3Li	66	4.6	1	*meso*-III	26	116–118	(±)	*meso*
			% yld. IX	*erythro*-IX	*threo*-IX[f]					
5	(+)-VII	C_6H_5Li	78	1	9	(−)-*threo*-IX	..[g]	.....[g]	(+)-*erythro*	(−)-*threo*
6	(−)-VIII	CH_3Li	92	2	1	(+)-*erythro*-IX	38	94–96	(−)-*threo*	(+)-*erythro*

[a] Sample procedures are given in Experimental. [b] Measured by infrared analysis (see Experimental). [c] Data given for first crystallization. [d] Based on starting ketone. [e] The sample prepared for infrared analysis had $[\alpha]^{25}D$ −3.2° (ethanol, *c* 5.0). [f] Polarimetric analysis (see Experimental). [g] This diastereomer is an oil; it was purified through its crystalline *p*-bromobenzoate, over-all yield to crystalline material, 50%.

(*threo*) was an oil. The latter diastereomer was purified through its crystalline, *p*-bromobenzoate. The configurations of the compounds prepared in this sequence were identified by the conversion of (+)-*erythro*-IX into *meso*-V (diether); and (−)-*threo*-IX into (+)-V.

Results of Aymmetric Induction Study.—Mixtures of *meso*- and (±)-III were produced by reaction of biacetyl and of (±)-3-hydroxy-3-phenyl-2-butanone [(±)-X] with phenyllithium in ether, and by reaction of benzil with methyl lithium in ether. A mixture of *meso*-and (−)-III was produced by reaction of (−)-1,2-diphenyl-2-hydroxy-1-propanone [(−)-IV] with phenyllithium in ether. The relative amounts of the diastereomers produced in these reactions were measured by infrared analysis (see Experimental), and the results are summarized in Table I.

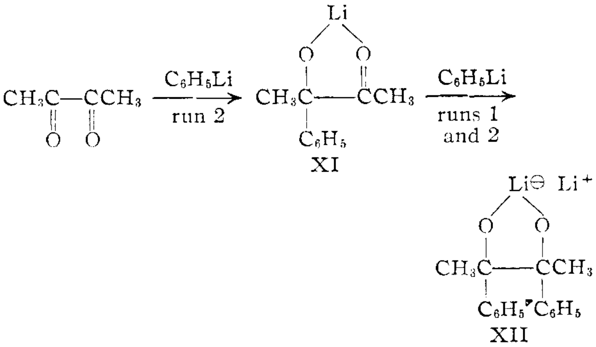
In similar reactions, (+)-3-methoxy-3-phenyl-2-butanone [(+)-VII] was treated with phenyllithium in ether, and (−)-1,2-diphenyl-2-methoxy-1-propanone [(−)-VIII] with methyllithium in ether to give mixtures of (+)-*erythro*-IX and (−)-*threo*-IX, respectively. The relative amounts of each diastereomer in each mixture was measured polarimetrically (see Experimental). Table I summarizes the results obtained.

Discussion

Models for Steric Control of Asymmetric Induction.—Consideration of the steric result compatible with model I depends on the classification of the groups attached to the asymmetric carbon atom as large, medium or small. Although $C_6H_5 > CH_3 > OH$, the OH group is undoubtedly involved with metal, either covalently bound, or as an ion-pair. In either case, methyl is still greater in *effective bulk*.[11] This selection is made clear by comparison of the "*A*-values" of Winstein,[12] which compare the relative tendency of various groups to occupy the less hindered equatorial position on a cyclohexane ring. The order of decreasing effective size of these groups is $CH_3 > OSO_2C_6H_4CH_3$-(*p*) > $OCOCH_3$ > OH. If methyl is effectively larger than *p*-toluenesulfonate, it should also exceed either O–Li or O–CH_3 in effective bulk. Thus model I predicts one steric result and model II the opposite.

The data of Table I clearly indicate that *the rigid model (II) applies to the systems studied in which either OH or OCH_3 occupies the asymmetric carbon of the starting material.* The same probably applies to any systems which carry groups on this carbon which are capable of reacting or complexing with organometallic reagents. Groups such as OH, OR, OAc, NH_2, NHR, $N(R)_2$, NHAc are all expected to fall in this category. The open-chain model(I) applies to systems which contain only groups attached to asymmetric carbon of the starting material which are incapable of complexing with organometallic reagents.[2]

Runs 2 and 4 (Table I) were made to see if the intermediates were the same as those in runs 1 and 3, respectively. If the same intermediates were involved, they should partition the same between the two diastereomers. In runs 1 and 2, the factors of predominance of (±)-III over *meso*-III are 6.7 and 8, respectively, which are the same within experimental error, and therefore XI or a similar species might be an intermediate. Compound XII is suggested as the final intermediate. An analogy for such a species is found in the work of Wittig,[13] who obtained evidence for the existence of $(C_6H_5)_2Li^-Na^+$. In runs 3 and 4, the factors of predominance of *meso*-III over (±)-III are 11.5 and 4.5, respectively. Unfortunately, the internal consistency of values obtained in the analysis of the product in run 4 (unlike the other runs) is low (see Table III), and these factors are equal within experimental error.



XI

XII

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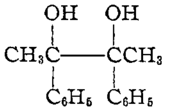
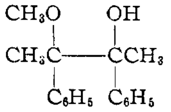
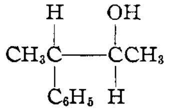
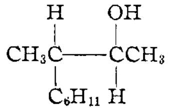
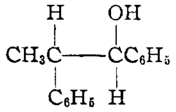
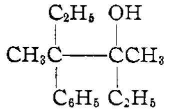
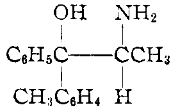
[11] This measures the blocking ability of the group with respect to approaches to the carbonyl group.

[12] S. Winstein and N. J. Holness, THIS JOURNAL, **77**, 5562 (1955).

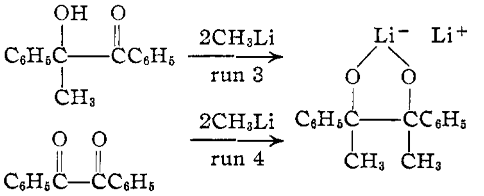
[13] G. Wittig, R. Ludwig and R. Polster, *Ber.*, **88**, 294 (1955).

TABLE II

Entry no.	Structure of reaction product	Reagents involved	Model which predicts result	Index of stereo-specificity	Reference
1	 $\mathrm{CH_3}\overset{\mathrm{OH}}{\underset{\mathrm{C_6H_5}}{\mathrm{C}}}-\overset{\mathrm{OH}}{\underset{\mathrm{C_6H_5}}{\mathrm{C}}}\mathrm{CH_3}$	C_6H_5Li and CH_3Li in pentane	Rigid model	77	Runs 1 and 3, Table I, this paper
2	 $\mathrm{CH_3}\overset{\mathrm{CH_3O}}{\underset{\mathrm{C_6H_5}}{\mathrm{C}}}-\overset{\mathrm{OH}}{\underset{\mathrm{C_6H_5}}{\mathrm{C}}}\mathrm{CH_3}$	C_6H_5Li and CH_3Li in pentane	Rigid model	18	Runs 5 and 6, Table I, this paper
3	 $\mathrm{CH_3}\overset{\mathrm{H}}{\underset{\mathrm{C_6H_5}}{\mathrm{C}}}-\overset{\mathrm{OH}}{\underset{\mathrm{H}}{\mathrm{C}}}\mathrm{CH_3}$	CH_3MgI and $LiAlH_4$ in ether	Open-chain model	5	Runs 1 and 2, Table I, ref. 2a
4	 $\mathrm{CH_3}\overset{\mathrm{H}}{\underset{\mathrm{C_6H_{11}}}{\mathrm{C}}}-\overset{\mathrm{OH}}{\underset{\mathrm{H}}{\mathrm{C}}}\mathrm{CH_3}$	CH_3MgI and $LiAlH_4$ in ether	Open-chain model	2.7	Runs 1 and 4, Chart I, ref. 2d
5	 $\mathrm{CH_3}\overset{\mathrm{H}}{\underset{\mathrm{C_6H_5}}{\mathrm{C}}}-\overset{\mathrm{OH}}{\underset{\mathrm{H}}{\mathrm{C}}}\mathrm{C_6H_5}$	C_6H_5MgBr and $LiAlH_4$ in ether	Open-chain model	>16	Runs 7 and 8, Table I, ref. 2a
6	 $\mathrm{CH_3}\overset{\mathrm{C_2H_5}}{\underset{\mathrm{C_6H_5}}{\mathrm{C}}}-\overset{\mathrm{OH}}{\underset{\mathrm{C_2H_5}}{\mathrm{C}}}\mathrm{CH_3}$	C_2H_5Li in pentane CH_3Li in ether	Open-chain model	9	Runs 1 and 3, Table II, ref. 2b
7	 $\mathrm{C_6H_5}\overset{\mathrm{OH}}{\underset{\mathrm{CH_3C_6H_4}}{\mathrm{C}}}-\overset{\mathrm{NH_2}}{\underset{\mathrm{H}}{\mathrm{C}}}\mathrm{CH_3}$	$CH_3C_6H_4MgBr$ in ether	Both rigid and open-chain models	>2500[a]	....[a]

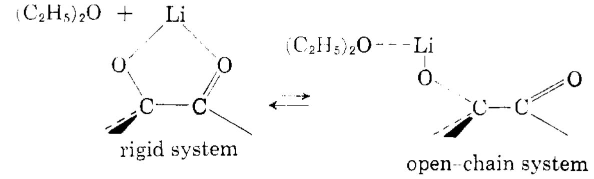
[a] This number was derived as follows: B. M. Benjamin, H. J. Schaeffer and C. J. Collins [THIS JOURNAL, **79**, 6160 (1957)] found that in the addition of $CH_3C_6H_4MgBr$ to $C_6H_5COCHNH_2CH_3$, one diastereomer predominated over the other by a factor of at least 50. Since p-tolyl and phenyl are the same in effective bulk, had C_6H_5MgBr been added to p-CH_3-$C_6H_5COCHNH_2CH_3$ the other diastereomer would have predominated by the same factor; thus 50 × 50 = 2500.

Comparisons of the stereospecificity found in reactions of various systems reveal interesting trends. Stereospecificity can be measured in a general sense by multiplying the factor by which one diastereomer predominates in one synthesis by the factor obtained when the synthesis is carried out by inverting the order of introduction of groups. With this "index of stereospecificity" a number of systems are compared in Table II.

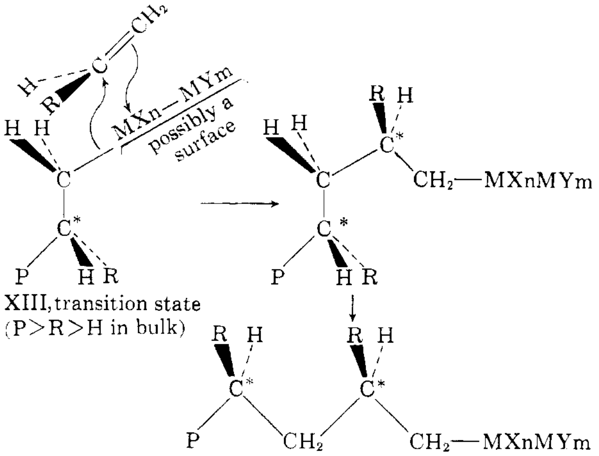

$$\mathrm{C_6H_5}\overset{\mathrm{OH}}{\underset{\mathrm{CH_3}}{\mathrm{C}}}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{C_6H_5}\xrightarrow[\text{run 3}]{2\mathrm{CH_3Li}}\qquad \mathrm{C_6H_5}\overset{\mathrm{O}}{\overset{|}{\mathrm{C}}}\overset{}{-}\overset{\mathrm{O}}{\overset{|}{\mathrm{C}}}\mathrm{C_6H_5}\ (\mathrm{Li^-}\ \mathrm{Li^+})\ \xleftarrow[\text{run 4}]{2\mathrm{CH_3Li}}\ \mathrm{C_6H_5}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{C_6H_5}$$

Systems roughly fall into three classes: (1) those to which the open-chain model only can apply (entries 3–6); (2) those in which only the rigid model predicts the correct result (entries 1 and 2); (3) those in which both models predict the same result (entry 7). It appears that when both models predict the same result (class 3) the indexes of stereospecificity are an order of magnitude higher than those obtained when the two models predict different results (class 2). Furthermore, systems to which only the rigid model can apply (class 2) give indexes of stereospecificity which are definitely higher than those of systems to which only the open-chain model can apply (class 1). These data suggest that in classes 2 and 3 the molecules react by two mechanisms which involve stages simulated by both of the two models. When both mechanisms lead to the same steric result (class 3), very high stereospecificity is observed. When both mechanisms lead to different results, the rigid model prevails, but the steric result is less one sided (class 2). In systems to which the open-chain model only can apply (class 1), the lowest stereospecificity is observed since conformation adapts itself to mechanism rather than mechanism to conformation.

Although quantitative data were not obtained, it is quite clear that the reaction of methylmagnesium bromide in ether with ketone (−)-IV went with lower stereospecificity than the reaction of methyllithium in pentane with the same ketone (run 3). For the former reaction, *meso*-III/(−)-III < 5, whereas for the latter, *meso*-III/(−)-III = 11.5. A plausible explanation for this difference is: The predominance of the rigid model depends on the ability of the metal to maintain a five-membered ring. Not only does the character of the metal play a role, but the solvent might be even more important. In solvents such as ether, an open-chain model might be more favored than in pentane, since the former solvent is capable of competing with oxygen of the five-membered ring for the metal.



A number of examples were reported[2a] in which aluminum alkoxides were employed as a reducing agent for α-hydroxy-or α-amino-ketones, and to which either model I or model II would predict the result observed. Later it was found[2d] that 3-cyclohexyl-2-butanone with the same reagent gave results (kinetically controlled) incompatible with model I. Sicher and co-workers also have observed that model I cannot be applied to reactions that involve this reagent, but that rigid models can be used to predict the correct steric result.[14] Unfortunately, these workers did not determine whether their reductions were kinetically or thermodynamically controlled (the Meerwein–Ponndorf reduction is reversible), did not determine the amount of the diastereomer produced which was not isolated, and did not invert the order of addition of substituents to the carbonyl group to see if rigid models held for both modes of addition. However, their interpretations are eminently reasonable and useful.

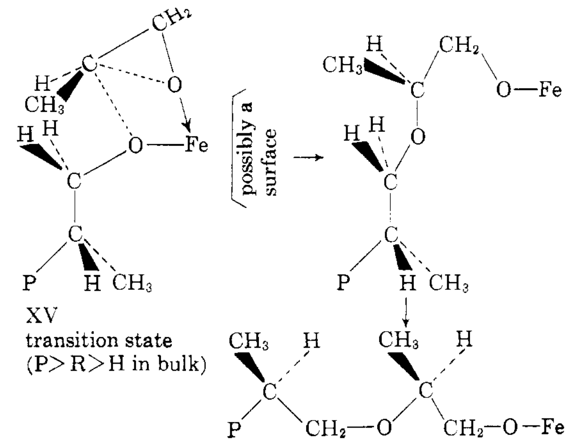


XIII, transition state (P>R>H in bulk)

XIV, isotactic polymer

Stereospecific Polymerization.—Some of the ideas developed in this and other papers[2] might be employed to explain the stereospecificity observed in certain types of polymerization. The anionic polymerization of monosubstituted ethylenes (*e.g.*, propene) to give isotactic polymers usually involves a bimetallic complex[15] (which may or may not be soluble) as catalyst. Formula XIII in which P > R > H in size is a possible model for the transition state in which a new asymmetric center is created. In this model, the growing polymer chain is in that conformation which leaves the carbon–metal bond the most exposed to electrophilic attack by the more substituted end of the polarized, olefinic monomer molecule. If monomer is oriented as in XIII, the steric repulsions between substituents on the old and the incipient asymmetric carbon atoms are R>–<H and H>–<R. This orientation is more sterically feasible than that in which the repulsions are R>–<R and H>–<H. As a result, the asymmetric centers along the chain in the resulting polymer have the configuration shown in XIV. This model might apply to either a homogeneous reaction, or to one that occurs at an interface with the polymer chain extending out into solution.

The formation of isotactic polymer XVI from (±)-propylene oxide which has been described by Price[16] might involve a configuration in the critical chain-lengthening step which resembles XV. In this model (XV), the *cis* opening of the oxide ring suggested by Price[16] is in harmony with the observations of others.[10] Model XV could also apply to either heterogeneous or hemogeneous catalysis, but greater stereospecificity would be expected for the former, in which the transition state would be more compressed.



XV transition state (P> R>H in bulk)

XVI, isotactic polymer

Anionic or radical polymerization of methyl methacrylate in dissociating solvents gives a syndiotactic polymer (XVIII).[17] Structure XVII provides a model for the chain-lengthening step. In this structure, the growing polymer chain is pictured in a conformation which most exposes the carbanion or radical to attack, and which at the same time provides for the least internal steric compression within the chain. It is assumed that P > CO_2CH_3 > CH_3 in effective bulk. The syndiotactic polymer formed by anionic polymerization of butadiene[18] might be explained with a similar model.

Anionic polymerization of methyl methacrylate in non-dissociating solvents gives isotactic polymer XX.[17] A cyclic and semirigid model for the anionic process is formulated (XIX) in which a six-membered ring is repeatedly made and destroyed at the end of the growing chain. In this cycle, the polymer chain and methoxyl groups occupy equa-

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(15) (a) G. Natta, P. Pino, P. Corradini, F. Danusso, E. Mantica, G. Mayzanti and G. Moraglio, This Journal, **76**, 1709 (1955); (b) G. Natta, P. Pino, G. Massanti and U. Giannini, *ibid.*, **79**, 2975 (1957); (c) G. Natta, P. Corradini and I. W. Bassi, *ibid.*, **80**, 755 (1958); (d) J. K. Stille, *Chem. Revs.*, **58**, 541 (1958).

(16) C. C. Price and M. Osgan, This Journal, **78**, 4787 (1956).

(17) (a) T. G. Fox, B. S. Garrett, W. E. Goode, S. Gratch, J. F. Kincaid, A. Apell and J. D. Stroupe, *ibid.*, **80**, 1769 (1958); (b) J. D. Stroupe and R. E. Hughes, *ibid.*, **80**, 2341 (1958).

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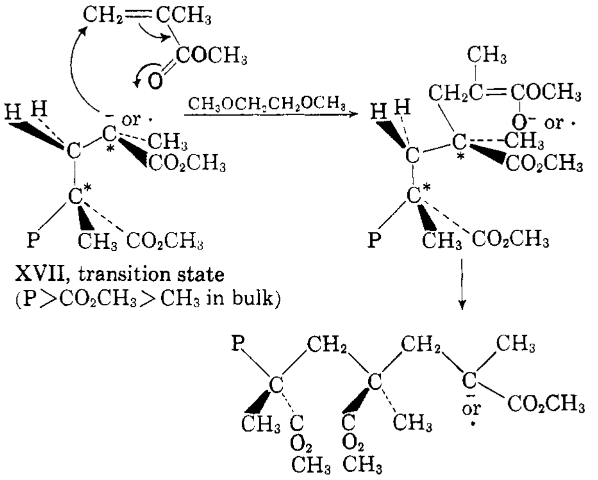
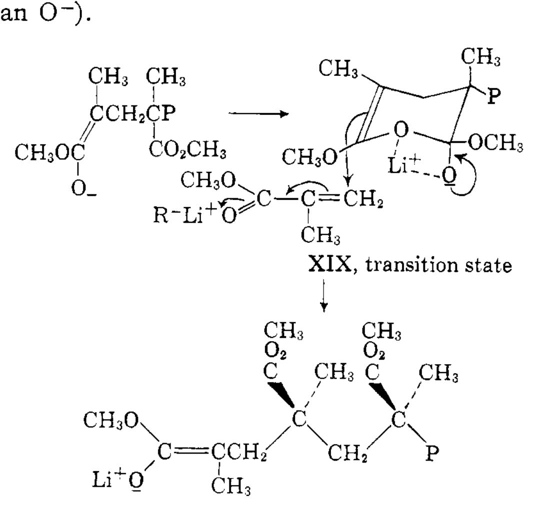


XVII, transition state
($P > CO_2CH_3 > CH_3$ in bulk)

XVIII, syndiotactic polymer

torial positions, and the ring is opened by axial attack from the least hindered side (CH_3 is larger than O^-).

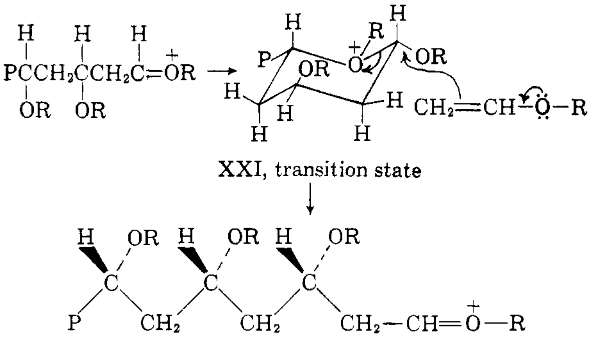


XIX, transition state

XX, isotactic polymer

A somewhat similar model might apply to the boron trifluoride-catalyzed polymerization of isobutyl vinyl ether which leads to isotactic polymer XXII.[15a,19,20] In this model for cationic polymerization, a six-membered oxonium ring is formulated at the end of the growing chain. In XXI, since P > OR in size, P occupies an equatorial position, as does RO attached to the growing end of the chain. This carbon is inverted in the ring-opening step, and XXII is formed, which forms a new ring, etc.

In the formation of XXII, the relative configurations of the first two asymmetric centers formed in each polymer chain determine the overall configuration of that chain. If the configurations are similar, the polymer chain becomes isotactic, if different, syndiotactic. Molecular models suggest that XXI provides a better configuration for formation of the next ring than does a structure with *both* OR's equatorial. Thus isotactic polymer might propagate faster than syndiotactic.



XXI, transition state

XXII, Isotactic polymer

In these polymerizations, questions arise as to the degree of configurational homogeneity which these chains of asymmetric carbon atoms actually possess, and whether the models suggested here could provide the required stereospecificity. Neither question can be answered without far more results, but some impression of how high steric selectivity could be associated with the models suggested can be gained through consideration of the factors by which one diastereomer predominates in simple reactions of organometallic reagents with ketones. When rigid models such as II clearly apply, factors ranging from 4 to 50 have been observed. Models XIX and XXI contain highly substituted six-membered rings, and therefore possess some rigid character. When open-chain models such as I are involved, factors that vary from 2 to 10 have been found. Models XIII, XV and XVII might give higher factors for either of two reasons. If the growing end of the chain is attached to a surface, the transition state for making the carbon–carbon bond becomes more restricted, and stereospecificity should increase. Since P is probably coiled, it is in effect a very large group.[21] Both of these features could drastically increase the stereospecificity of the polymerization over that observed for the simpler organometallic reactions.

Experimental

(−)-Methylbenzoin (IV).—A solution of phenyllithium prepared from 62.4 g. (0.4 mole) of bromobenzene and 5.6 g. (0.8 mole) of lithium in 400 ml. of anhydrous ether was slowly added to a vigorously stirred solution of 20 g. (0.12 mole) of (+)-atrolactic acid,[5] $[\alpha]^{28}\text{D}$ +37.3° (ethanol, *c* 3.4), in 200 ml. of anhydrous ether (nitrogen atmosphere). The resulting white suspension was refluxed for 8 hours, cooled, and was mixed with water. The ether layer was washed with water, dried, and concentrated to an oil (12 g.). This material was chromatographed on 400 ml. of neutral, activated alumina. Pentane eluted benzene and bromobenzene, whereas 50% ether–pentane eluted in nine 500-ml. fractions a total of 8 g. (74%) of IV, which was isolated as an undistilled oil, $[\alpha]^{24}\text{D}$ −171° (ethanol, *c* 5.4), literature[22] $[\alpha]^{20}_{5461}$ −177° (ethanol, *c* 5.4). This oil crystallized at −15° from either chloroform or methanol, but the crystals dissolved at 0°.

***meso*- and (−)-2,3-Diphenyl-2,3-butanediol (III).**—A solution of 8 g. of (−)-methylbenzoin in 50 ml. of ether was slowly added to a well-stirred solution of methylmagnesium iodide prepared from 14 g. (0.1 mole) of methyl iodide and 2.4 g. (0.1 mole) of magnesium in 200 ml. of ether. The reaction was carried out at 0°, and the resulting suspension

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(19) C. E. Schildknecht, S. T. Cross, H. R. Davidson, I. M. Lambert and A. O. Zoss, *Ind. Eng. Chem.*, **40**, 2104 (1948).

(20) C. E. Schildknecht, *ibid.*, **50**, 107 (1958).

(21) It is clear from the results of V. Prelog, E. Philbin, E. Watanabe and M. Wilhelm, *Helv. Chim. Acta*, **39**, 1086 (1956), that as the large group on the asymmetric center is increased in size, the stereospecificity increases.

(22) A. McKenzie and A. Ritchie, *Ber.*, **70**, 33 (1937).

TABLE III

INFRARED ANALYSIS OF DIASTEREOMERIC MIXTURES OF 2,3-DIPHENYL-2,3-BUTANEDIOL(III)

Run	1143		1356		1335		1127		1111		Av.	
	meso	±	*meso*	±	*meso*	±	*meso*	±	*meso*	±	*meso*	±
1	15	85	10	90	3	97	16	84	9	91	13	87
2	14	86	12	88	8	92	12	88	9	91	11	89
3[a]	92	8	92	8	92	8	93	7	93	7	92	8
4	96	4	100	0	62	38	72	28	79	21	82	18

[a] Run gave a mixture of (−)-and *meso*-III.

was stirred at 0° for another 5 hours. The mixture was treated with aqueous ammonium chloride, the resulting ether layer washed with water, with sodium carbonate solution and again with water. The solution was dried and evaporated under reduced pressure. The residual oil was crystallized from pentane to give 7 g. (85%) of a mixture of cubes and needles, m.p. 80–117°, $[\alpha]^{28}\mathrm{D}$ −18.4° (ethanol, *c* 3.2). Careful, repeated crystallization of this mixture from ethanol gave 3.1 g. of *meso*-III,[9] m.p. 116.2–117.8°, $[\alpha]^{28}\mathrm{D}$ 0.00° (ethanol, *c* 3.2), and 2.0 g. of (−)-III, m.p. 104.5–105°, $[\alpha]^{25}\mathrm{D}$ −34.4° (ethanol, *c* 2.7).

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.34; H, 7.44. Found: C, 79.17; H, 7.48.

***meso*-2,3-Diphenyl-2,3-dimethoxybutane (V).**—To a solution of 0.5 g. of *meso*-diol III in 20 ml. of 1,2-dimethoxyethane was added 0.1 g. of sodium hydride, and the resulting mixture was stirred at room temperature for 24 hours. After adding 5 ml. of iodomethane, the mixture was stirred for an additional 6 hours and was filtered. The filtrate was shaken with a mixture of ether and pentane, the ether layer was washed with water, dried and evaporated under reduced pressure. The residue was absorbed on a column of 20 g. of neutral activated alumina, and the product was eluted with 500 ml. of pentane. When concentrated to a small volume, the eluant gave 0.14 g. (28%) of dense white cubes (*meso*-V), m.p. 171–173°.

Anal. Calcd. for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 80.02; H, 8.35.

(+)-2,3-Diphenyl-2,3-dimethoxybutane (V).—The above procedure when applied to 0.25 g. of (−)-2,3-diphenyl-2,3-butanediol ($[\alpha]^{25}\mathrm{D}$ −34.4°, ethanol, *c* 3.2) gave 0.1 g. (40%) of (+)-2,3-diphenyl-2,3-dimethoxybutane (V) as fine white needles, m.p. 93–94°, $[\alpha]^{24}\mathrm{D}$ +71.6° (chloroform, *c* 3.1).

Anal. Calcd. for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 79.74; H, 8.22.

(±)-3-Hydroxy-3-phenyl-2-butanone (X) was prepared from biacetyl in 60% yields by a method previously reported.[7]

Asymmetric Induction Studies which Lead to Diastereomeric 2,3-Diphenyl-2,3-butanediols.—All runs (1–4) were carried out in the same manner. A solution of the carbonyl compound in dry ether (50 ml. per 10 g.) was added dropwise to a well-stirred excess (2.5 moles in runs 1 and 3, and 4 moles in runs 2 and 4) of organolithium reagent in 500 ml. of dry ether. The reaction mixture was kept at 0° during the addition, and was stirred at 0° for two additional hours. The reaction mixture was poured onto ice and 0.1 *N* sulfuric acid. The organic layer was washed with cold aqueous bisulfite (only runs 3 and 4), with dilute sodium bicarbonate solution and again with water. The solution was dried, and evaporated to an oil under reduced pressure. This oil was weighed, and a 2-g. aliquot was taken. This aliquot was absorbed on a column of neutral, activity II alumina, 40 cm. by 2 cm. Benzene, bromobenzene, biphenyl (in some cases unreacted carbonyl compound) were eluted with 50% ether–pentane. The glycols were eluted with ethyl acetate. The eluate was concentrated to an oil under reduced pressure, the oil was again dissolved in ether, and the solution was again evaporated to an oil under reduced pressure. This process was repeated a total of 4 times to completely get rid of the ethyl acetate. This material gave no carbonyl absorption in the infrared. It solidified, was weighed, and the yield of glycol was calculated on the basis of this weight. The samples were analyzed for the relative amounts of *meso*- and (±)-glycol as described below. The original samples of the reaction products from which the aliquots were taken were dissolved in ethanol, and the resulting solution was cooled to crystallize the glycol present in the greater amount. Yield data are summarized in Table I.

Infrared Analysis of Mixtures of Diastereomers of III.—The infrared spectrum of *meso*-2,3-diphenyl-2,3-butanediol contained absorption bands at 1335, 1129 and 1111 cm.$^{-1}$ which were absent in the infrared spectrum of (±)-III. The spectrum of (±)-III gave bands at 1356 and 1143 cm.$^{-1}$ which were absent in the spectrum of *meso*-III. These five bands were employed for analyses of the mixtures.

To remove the last traces of solvent, the samples prepared in the previous section were placed in 100-ml. round-bottom flasks, and were heated as films at 120° at 2 mm. pressure for 2 hours. Carbon tetrachloride solutions were prepared which contained 0.399 g. of sample in 3.0 ml. of solution. Hot pipets were used for transfer to keep the oils from solidifying. Standard solutions of pure *meso*-III and (±)-III (1.332 g. per 10.0 ml. of carbon tetrachloride) were prepared, and known synthetic mixtures of these glycols were prepared from these solutions. The method of absolute density was used. Optical densities of known mixtures at a standard concentration at the five different wave lengths were plotted against percentage composition. The compositions of the unknowns were then read from the plots. A Perkin-Elmer model 21 recording spectrophotometer, NaCl prism, cell thickness 0.107 (1.332 g. of solute per 10 ml. of solution) was used for all measurements. The optical densities of the pure isomers are: at 1356 cm.$^{-1}$, (±)-III, 0.530, *meso*-III, 0.330; at 1335 cm.$^{-1}$, (±)-III, 0.332, *meso*-III, 0.470; at 1143 cm.$^{-1}$, (±)-III, 0.845, *meso*-III, 0.325; at 1127 cm.$^{-1}$, (±)-III, 0.350, *meso*-III, 0.470; at 1111 cm.$^{-1}$, (±)-III, 0.242, *meso*-III, 0.417. The results of the measurements are recorded in Table III.

(±)-Methyl 2-Methoxy-2-phenylpropionate.—From 988 g. of racemic atrolactic acid was prepared 798 g. (75%) of methyl atrolactate,[23] b.p. 110° (6 mm.), $n^{25}\mathrm{D}$ 1.5120. To a well-stirred mixture of 88 g. (3.76 moles) of sodium hydride and 3 liters of dry dioxane was added dropwise 547 g. (3.0 moles) of (±)-methyl atrolactate over an 8-hour period. Gas evolution ceased 20 hours after addition was complete. Iodomethane (900 g. or 6.3 moles) was then added over a period of 9 hours. The reaction mixture was cooled in an ice-bath to keep the temperature below 40°. The mixture was stirred for an additional 18 hours, after which 100 ml. of methanol was added dropwise to the reaction mixture to decompose the excess sodium hydride. The reaction mixture was shaken with 2 liters of pentane and 8 liters of water. The aqueous layer was washed with 2 liters of pentane, and the combined pentane layers were washed with water, dried and concentrated. The residue was distilled to give 470 g. (82%) of methyl 2-methoxy-2-phenylpropionate, b.p. 112° (6 mm.), $n^{25}\mathrm{D}$ 1.5015. The infrared spectrum of this compound gave no hydroxyl band.

Resolution of 2-Methoxy-2-phenylpropionic Acid.—The above methyl 2-methoxy-2-phenylpropionate was stirred with excess 1 *N* sodium hydroxide solution until the mixture became clear. The basic solution was then washed with ether three times, acidified, and extracted with ether. The latter ether extract was dried and evaporated to an oil which was used directly in the resolution as follows. Quinine, 1152 g. or 4 moles, was dissolved in 2100 ml. of boiling ethanol, and 546 g. (3.3 moles) of the above oil was added followed by 1300 ml. of water. The resulting solution was cooled to 0°, and after 2 weeks the supernatant solution was decanted from the crystalline cake that separated. The crystals were washed twice with cold 50% aqueous ethanol, and were recrystallized twice from ethanol–water to give 260 g. of salt. After each crystallization 1.0 g. of salt was converted to the acid, and in ether was converted to the methyl ester with diazomethane. Rotations were taken

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[23] K. Freudenberg, J. Todd and R. Seidler, *Ann.*, **501**, 199 (1933).

on the methyl ester (neat, l = 1 dm.) as follows: 1st, $\alpha^{30}\text{D}$ −50.2°; 2nd, $\alpha^{28}\text{D}$ −52.4°; 3rd, $\alpha^{24}\text{D}$ −52.2°. A rotation for this compound has been reported, $\alpha^{20}{}_{578}$ −56.4° (neat, l = 1 dm.).

The entire crop of salt from the second recrystallization was shaken with a mixture of cold dilute sulfuric acid (excess) and ether. The water layer was washed with ether, and the combined ether extracts were washed with water, dried and evaporated. The residual oil amounted to 94 g. (35%), and was not further purified, $\alpha^{26}\text{D}$ +24° (l = 1 dm., neat).

The mother liquors from the original crystallization of the salt of the (+)-acid was diluted with 300 ml. of water. After standing for one week at 0°, 180 g. of salt was precipitated. Conversion of a sample of this material to the ester of the acid gave material, $\alpha^{25}\text{D}$ +50° (neat, l = 1 dm.).

(−)-1,2-Diphenyl-2-methoxy-1-propanone (VIII).—A solution of 70 g. (0.39 mole) of optically pure (+)-2-methoxy-2-phenylpropionic acid was added slowly with stirring to 300 ml. of a methanolic solution of lithium methoxide made from 2.72 g. (0.39 gram atom) of lithium. The methanol was evaporated, and the white solid that remained was pulverized and dried at 60° at 1 mm. pressure for 4 hours. This solid was suspended in 1.5 liters of vigorously stirred ether under a dry nitrogen atmosphere. To this refluxing mixture was added 500 ml. of an ethereal solution of phenyllithium prepared from 79 g. (0.51 mole) of bromobenzene and 7.1 g. (1.02 gram atom) of lithium. The suspension was refluxed for 8 hours, cooled, and mixed with cold, dilute sulfuric acid. The aqueous layer was washed with ether, and the combined ether layers were washed with two volumes of 100 ml. of 2 N sodium hydroxide solution. Acidification of these basic extracts gave 5 g. of starting material. The ether layer was dried, concentrated, and the residual oil was fractionally distilled through a 45-cm. Podbielniak column at 5 mm. pressure. The fraction boiling at 138–140° weighed 34 g. (37%), $n^{25}\text{D}$ 1.5683, $[\alpha]^{25}\text{D}$ −256° (ethanol, c 4.7).

Anal. Calcd. for $C_{16}H_{16}O_2$: C, 80.00; H, 6.67. Found: C, 80.24; H, 6.53.

The forerun weighed 32 g., b.p. 128–138°, $[\alpha]^{25}\text{D}$ −152° (ethanol, c 4.4).

(+)-3-Methoxy-3-phenyl-2-butanone (VII).—This synthesis was carried out by the same procedure as was employed for the preparation of VIII (see above). From 13 g. of optically pure 2-methoxy-2-phenylpropionic acid and 2.5 moles of methyllithium (ketone equals one mole) was prepared 9.0 g. (69%) of (+)-3-methoxy-3-phenyl-2-butanone, b.p. 77° (0.5 mm.), $\alpha^{25}\text{D}$ +107.8° (neat, l = 1 dm.).

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.31; H, 7.92. Found: C, 74.16; H, 8.14.

Reaction of Methyllithium with (−)-1,2-Diphenyl-2-methoxy-1-propanone (VIII); Run 6.—A solution of 10 g. (0.04 mole) of optically pure (−)-1,2-diphenyl-2-methoxy-1-propanone (VIII) in 50 ml. of ether was added dropwise to a well-stirred solution of 0.12 mole of methyllithium in 300 ml. of ether. The addition was carried out at 0°, and the reaction mixture was stirred at 0° for one hour after the addition was complete. The mixture was then poured into a mixture of ice and 0.1 N sulfuric acid. The ether layer was washed with dilute aqueous sodium bicarbonate, sodium bisulfite and water. The solution was dried, and concentrated to an oil under reduced pressure to give 9.5 g. (92%) of 2,3-diphenyl-3-methoxy-2-butanol, whose infrared spectrum showed no carbonyl absorption in the 1680 cm.$^{-1}$ region. A thin film of alcohol was heated at 80° at 1 mm. pressure for 2 hours, $[\alpha]^{24}\text{D}$ +4.7° (chloroform, c 5.1). The main portion of the product was dissolved in 50 ml. of pentane, and the resulting solution was kept at −10° for 10 hours. The crystals that separated were recrystallized from pentane to give 4.0 g. (38%) of (+)-*erythro*-2,3-diphenyl-3-methoxy-2-butanol (IX) as dense white cubes, m.p. 94–96°, $[\alpha]^{25}\text{D}$ +11.9° (chloroform, c 4.8).

Anal. Calcd. for $C_{17}H_{20}O_2$: C, 79.69; H, 7.81. Found: C, 79.72; H, 7.72.

Reaction of Phenyllithium with (+)-3-Methoxy-3-phenyl-2-butanone (VII); Run 5.—The reaction was carried out in the same manner as described for the reaction of methyllithium with VIII. The crude product was absorbed on 400 g. of neutral activated alumina. Unreacted ketone, benzene and bromobenzene and biphenyl were eluted from the column with two liters of 10% ether–pentane. The alcohol portion of the reaction mixture was eluted with pure ether. Evaporation of solvent gave 10.0 g. (78%) of an oil whose infrared spectrum gave no carbonyl absorption. The oil could not be induced to crystallize. A thin film of this oil was heated at 80° and one mm. pressure for 2 hours, $[\alpha]^{24}\text{D}$ −9.07° (chloroform, c 5.4).

***p*-Bromobenzoate of (−)-*threo*-2,3-Diphenyl-3-methoxy-2-butanol.**—In a completely dry flask and under an atmosphere of pure, dry nitrogen, a solution of 8 g. of the above alcohol in 100 ml. of dry benzene was placed. Sodium–potassium alloy (one mole) was added, and the mixture was stirred for 10 hours at 50°. The mixture was cooled and filtered under dry nitrogen through a plug of dry glass wool into a clean, dry flask. To the solution was added 11.0 g. of *p*-bromobenzoic anhydride, and the mixture was stirred at room temperature for 4 hours. The solution was then filtered from precipitated material, and the precipitate was washed with ether (several times). The organic filtrates were washed with water, dried, and evaporated to a viscous oil. This material was dissolved in 50 ml. of pentane, and the solution was cooled at −20° for 24 hours. The crystals that separated, 9.7 g. (64%), were washed with pentane, m.p. 95.6–97.0°, $[\alpha]^{24}\text{D}$ −11.8° (chloroform, c 3.8). Recrystallization of this material did not alter its melting point.

Anal. Calcd. for $C_{24}H_{23}BrO_3$: C, 65.61; H, 5.28. Found: C, 66.01; H, 5.36.

(−)-*threo*-2,3-Diphenyl-3-methoxy-2-butanol (IX).—The free alcohol (−)-*threo*-IX was prepared by lithium aluminum hydride reduction of the *p*-bromobenzoate according to the procedure of Cram and Knight.[2b] From 5.0 g. of ester was obtained 1.7 g. of (−)-*threo*-IX. A portion was heated as a thin film at 80° and 2 mm. pressure for 2 hours, $n^{25}\text{D}$ 1.5630, $[\alpha]^{24}\text{D}$ −11.4° (chloroform, c 5.0).

Anal. Calcd. for $C_{17}H_{20}O_2$: C, 79.69; H, 7.81. Found: C, 79.56; H, 7.61.

Polarimetric Analysis of Products in Preparations (Runs 5 and 6) of 2,3-Diphenyl-3-methoxy-2-butanol (IX).—Synthetic mixtures of optically pure (−)-*threo*-IX and (+)-*erythro*-IX were prepared and their rotations taken in chloroform solution at concentrations near those used for the diastereometic mixtures of alcohols obtained in runs 5 and 6. The rotations of the known mixtures were plotted against percentage composition, and the percentage of each isomer produced in runs 5 and 6 were determined from their rotations. The results are recorded in Table II.

Methylation of (+)-*erythro* and (−)-*threo*-2,3-Diphenyl-3-methoxy-2-butanol (IX).—The procedure employed is that used for the conversion of *meso*-2,3-diphenyl-2,3-butanediol into *meso*-2,3-dimethoxy-2,3-diphenylbutane (V). From 0.5 g. of (+)-*erythro*-IX was obtained 0.45 g. of *meso*-V, m.p. 171.5–173°, undepressed by admixture with authentic material. From 0.25 g. of (−)-*threo*-IX was obtained (+)-V, $[\alpha]^{25}\text{D}$ +75° (chloroform, c 2.0), m.p. 93.2–93.8°, undepressed by admixture with the product from the methylation of (−)-2,3-diphenyl-2,3-butanediol.

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