Studies in Stereochemistry. XXXVIII. Open-Chain *vs.* Cyclic Models for 1,3-Asymmetric Induction in Addition Reactions[1]

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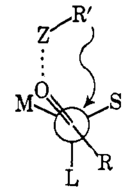
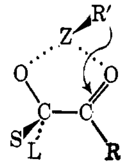
Abstract: In a study of 1,3-asymmetric induction in addition reactions, 4-hydroxy-4-phenyl-2-pentanone (III) and 4-methoxy-4-phenyl-2-pentanone (VI) were treated with phenylmetallics, and 1,3-diphenyl-3-hydroxy-1-butanone (IV) and 1,3-diphenyl-3-methoxy-1-butanone (VII) were treated with methylmetallics. The relative configurations of the diastereomeric products, α- and β-2,4-dihydroxy-2,4-diphenylpentanes (α- and β-V) and α- and β-2,4-diphenyl-2-hydroxy-4-methoxypentanes (α- and β-VIII), were determined through use of symmetry properties. Reduction of α-V with hydrogen on 10% palladium on charcoal gave predominantly (±)-2,4-diphenylpentane ((±)-IX), and β-V gave predominantly *meso*-IX. The fact that similar reductions in other systems go with predominant inversion of configuration coupled with the nmr spectra of α- and β-V demonstrate that α-V possesses the (±)- and β-V the *meso* configuration. The relative configurations of α- and β-VIII were determined from their optical properties. Optically pure α-(+)- and β-(+)-VIII were prepared from (+)-3-methoxy-3-phenylbutanoic acid (X) of maximum rotation and methylated to give (+)- and *meso*-2,4-dimethoxy-2,4-diphenylpentanes (XI), respectively. The diethers XI were identified by their optical and nmr spectral properties. Analyses of the diasteromeric mixtures of V and VIII by nmr techniques allowed the direction and degree of 1,3-asymmetric induction to be determined in the addition reactions to the four ketones. Temperature, the nature of the organometallic, and solvent were varied. In additions of phenylmetallics to hydroxy ketone III, α-V/β-V values varied between 2.1 and 7.4. In additions of methylmetallics to hydroxy ketone IV, α-V/β-V values varied from 0.64 to 1.3. In additions of phenylmetallics to methoxy ketone VI, α-VIII/β-VIII values varied from 1.2 to 3.5. In additions of methylmetallics to methoxy ketone VII, α-VIII/β-VIII values varied from 0.75 to 1.9. Cyclic, open-chain, and polar models for 1,3-asymmetric induction in these systems are discussed.

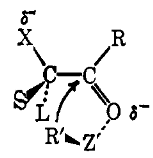
Three models were developed in earlier studies to explain and predict the results of 1,2-asymmetric induction when organometallics were added to carbonyl groups adjacent to asymmetric centers in acyclic systems. The "open-chain model" (A) was found to apply to transition states for additions to aldehydes and ketones that contained only nonpolar groups (L, M, and S standing for large, medium, and small, respectively) attached to the asymmetric center.[2] Later, a "cyclic model" (B) was found to be applicable to systems in which polar groups such as hydroxyl, methoxyl, and amino were attached to the asymmetric center adjacent to the carbonyl group.[3] A third model, "dipolar model" (C), was required to correlate the data of a study in which the asymmetric center carried a halogen atom.[4] When the small group on the asymmetric center is capable of complexing the organometallic, the open-chain and cyclic models predict products of different configurations, and only the cyclic model was found compatible with the results. Furthermore, the degree of stereospecificity was found to be higher when cyclic rather than open-chain models applied.[3a,c]



open-chain model
A

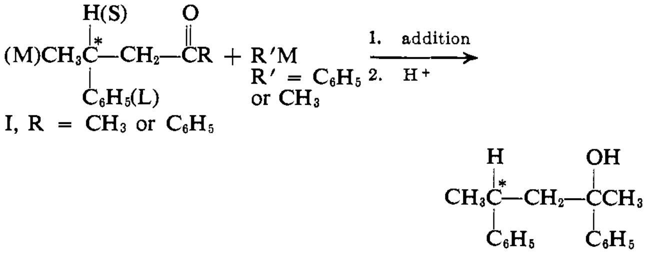


cyclic model
B
Z = metal



dipolar model
C

In the previous paper an open-chain model was developed to explain the predominant stereochemical direction of addition of organometallic reagents to ketones I to give alcohols II[5] and of the addition of 2-phenyl-1-propylmetallics to acetophenone to give alcohols II.[5] These models involved 1,3-asymmetric induction, and the stereospecificity observed was of the same order of magnitude as that found in addition polymerization leading to isotactic or syndiotactic polymers with asymmetric centers 1,3 to one another.



$$(M)CH_3\overset{H(S)}{\underset{C_6H_5(L)}{\overset{*}{C}}}-CH_2-\overset{O}{\overset{\|}{C}}R + R'M \xrightarrow[2.\ H^+]{1.\ addition}$$

R′ = C_6H_5 or CH_3

I, R = CH_3 or C_6H_5

$$CH_3\overset{H}{\underset{C_6H_5}{\overset{*}{C}}}-CH_2-\overset{OH}{\underset{C_6H_5}{C}}CH_3$$

II (diastereomers)

This investigation is concerned with 1,3-asymmetric induction in two systems in which the asymmetric

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[1] This research was supported by the Directorate of Chemical Sciences, Air Force Office of Scientific Research Grant No. AF-AFOSR-126-65.

[2] (a) D. J. Cram and F. A. Abd Elhafez, *J. Am. Chem. Soc.*, **74**, 5828 (1952); (b) D. J. Cram and J. D. Knight, *ibid.*, **74**, 5835 (1952); (c) F. A. Abd Elhafez and D. J. Cram, *ibid.*, **74**, 5846 (1952); (d) D. J. Cram, F. A. Abd Elhafez, and H. Weingarten, *ibid.*, **75**, 2293 (1953); (e) D. J. Cram and F. D. Greene, *ibid.*, **75**, 6005 (1953); (f) D. J. Cram, F. A. Abd Elhafez, and H. L. Nyquist, *ibid.*, **76**, 22 (1954); (g) D. J. Cram and J. Allinger, *ibid.*, **76**, 4516 (1954); (h) D. J. Cram and J. E. McCarty, *ibid.*, **76**, 5740 (1954); (i) Y. Gault and H. Felkin, *Bull. Soc. Chim. France*, 1342 (1960); (j) H. Felkin, *ibid.*, 1050 (1956); (k) I. Elphimoff-Felkin and H. Felkin, *ibid.*, 450 (1957); (l) G. J. Karabatsos, *J. Am. Chem. Soc.*, **89**, 1367 (1967).

[3] (a) D. J. Cram and K. R. Kopecky, *ibid.*, **81**, 2748 (1959); (b) J. H. Stocker, D. Sidisunthorn, B. M. Benjamin, and C. J. Collins, *ibid.*, **82**, 3913 (1960); (c) D. J. Cram and D. R. Wilson, *ibid.*, **85**, 1245 (1963).

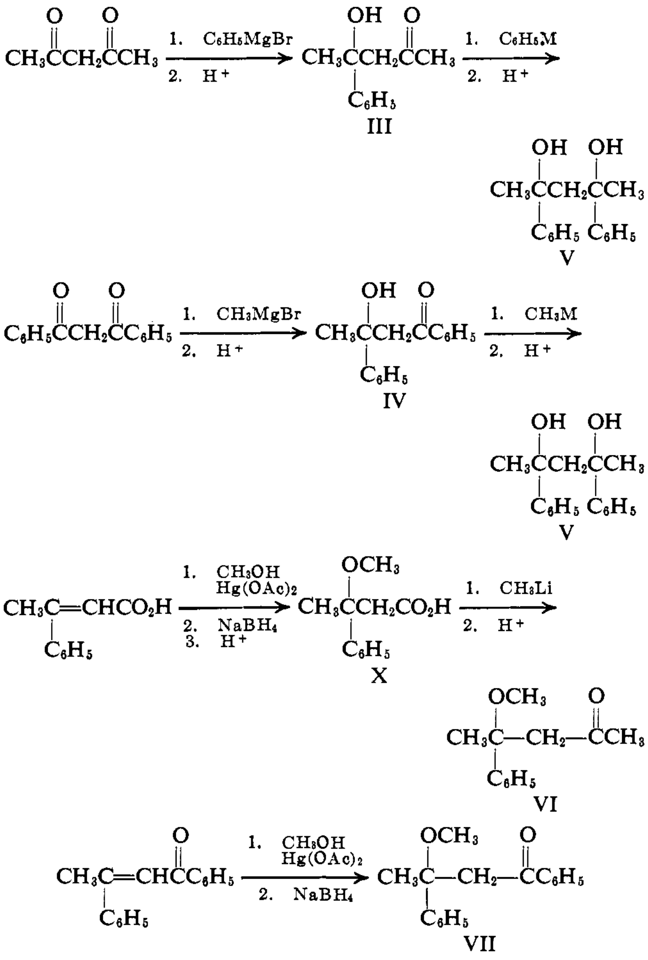
[4] J. W. Cornforth, R. H. Cornforth, and K. K. Mathews, *J. Chem. Soc.*, 112 (1959).

[5] T. J. Leitereg and D. J. Cram, *J. Am. Chem. Soc.*, **90**, 4011 (1968).

center carries a polar group such as hydroxyl or methoxyl. The additions of phenylmetallics to 4-hydroxy-4-phenyl-2-pentanone (III) and to 4-methoxy-4-phenyl-2-pentanone (VI) and of methylmetallics to 1,3-diphenyl-3-hydroxy-1-butanone (IV) and 1,3-diphenyl-3-methoxy-1-butanone (VII) lead to diastereomers of 2,4-dihydroxy-2,4-diphenylpentane (V) and of 2,4-diphenyl-2-hydroxy-4-methoxypentane (VIII). These systems were chosen for study for several reasons. (1) Some of the stereospecific polymerizations leading to chains with asymmetric centers 1,3,5, etc. to one another possess polar groups capable of serving as ligands of organometallic reagents (*e.g.*, methyl methacrylate polymerization).[6] Our addition reactions might serve as crude stereochemical models for these polymerization reactions. (2) The reaction products, diol V and methoxy alcohol VIII, are either like-ended or can be converted to like-ended compounds, and the relative configurations of the diastereomers can be readily determined by their symmetry properties. (3) Comparisons between the results in these systems as compared to those obtained in the reaction I → II might allow differentiation between open-chain, rigid, and polar models for 1,3-asymmetric induction.

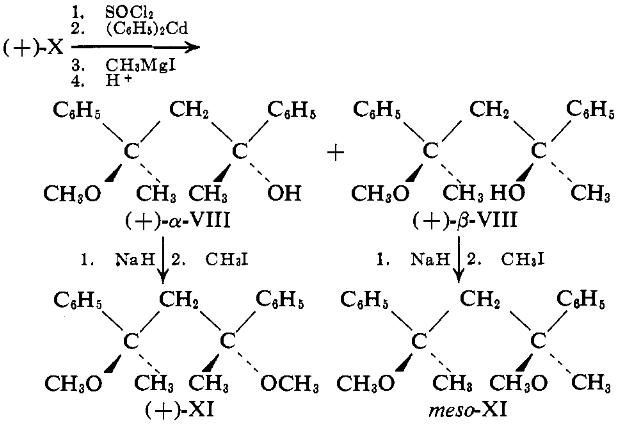
Results

Starting Materials and the Relative Configurations of Products. The syntheses of ketones III, IV, VI, and VII are formulated. When 1 equiv of Grignard reagent was added to either acetylacetone or dibenzoylmethane, ketones III and IV were formed, respectively. When III was treated with phenylmetallics and IV with methylmetallics, diastereomeric mixtures of α- and β-V were produced, which were separated by column chromatography, the α isomer eluting first. The configurations of these isomers were distinguished in two ways. The methylene protons of α-V occur as a singlet in nmr spectroscopy, whereas those of β-V provide an AB quartet. The two protons in the (±) isomer should have identical environments and therefore appear as a singlet as is observed for the α isomer. The two protons of the *meso* isomer should be in different environments, split one another, and appear as an AB quartet as is observed for the β isomer.



This configurational assignment was confirmed by reducing α-V to give predominantly (±)-2,4-diphenylpentane ((±)-IX) and β-V to give predominantly *meso*-IX with hydrogen and 10% palladium on charcoal. This kind of reaction has been demonstrated to occur with predominant inversion of configuration.[7] The hydrocarbons, (±)-IX and *meso*-IX, have been previously identified.[8]

Methoxy acid X was brought to maximum rotation as its cinchonidine salt, and the (+)-isomer was converted to VII which without purification was converted to (+)-α-VIII and (+)-β-VIII. These diastereomers were isolated by chromatography, the α isomer eluting first. Each isomer was then methylated: (+)-α-VIII gave (+)-XI which was identified by its optical activity, and (+)-β-VIII gave *meso*-XI which was identified by its lack of optical activity. As expected, the methylene hydrogens of (+)-XI exhibited a singlet in the nmr and those of *meso*-XI occurred as an AB quartet. These facts allow the relative configurations of (+)-α- and (+)-β-VIII to be assigned.[9] The relative configurations of racemic α- and β-VIII were assigned by nmr spectral comparisons between the racemates and the enantiomers and by their chromatographic behavior.



Stereochemical Course of the Addition Reactions. Methods were developed for analyzing the diastereo-

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

[7] (a) S. Mitsui, Y. Senda, and K. Konno, *Chem. Ind.* (London), **32**, 1354 (1963); (b) A. M. Khan, F. J. McQuillin, and S. Jardine, *Tetrahedron Letters*, 2649 (1966).

[8] (a) F. A. Bovey, F. P. Hood, III, E. W. Anderson, and L. C. Snyder, *J. Chem. Phys.*, **42**, 3900 (1965); (b) D. Lim, B. Obereigner, and D. Doskocilova, *J. Polymer Sci.*, **B3**, 893 (1965); (c) A. D. Williams, J. I. Brauman, N. J. Nelson, and P. J. Flory, *J. Am. Chem. Soc.*, **89**, 4807 (1967).

[9] The absolute configurations of these compounds have not been assigned. The three-dimensional structures written are arbitrary, and only one enantiomer is formulated in each case to economize space.

Table I. Diastereomer Ratios of 2,4-Dihydroxy-2,4-diphenylpentane (V) Produced by Addition of Organometallics to 4-Hydroxy-4-phenyl-2-pentanone (III) and 1,3-Diphenyl-3-hydroxy-1-butanone (IV)

Run	Ketone	Organometallic	Solvent	Temp, °C	Time, hr	% yield[a]	% α-V	% β-V	α-V/β-V
1	III	C_6H_5Li	Ether	0	1.3	100	68	32	2.1
2	III	C_6H_5MgBr	Ether	0	1.4	100	85	15	5.7
3	III	C_6H_5MgBr	Ether	−78	9	59	88	12	7.4
4	III	C_6H_5MgBr	Heptane	0	2.1	45	78	22	3.6
5	III	C_6H_5MgBr[b]	Ether	0	1.1	91	78	22	3.6
6	III	C_6H_5MgBr[c]	Ether	0	1.1	90	78	22	3.6
7	IV	CH_3Li	Ether	0	1.1	3[d]	50	50	1[e]
8	IV	CH_3MgBr	Ether	35	0.7	82	41	59	0.69
9	IV	CH_3MgBr	Ether	0	1.1	75	39	61	0.64
10	IV	CH_3MgBr	Ether	−78	12	28[d]	54	44	1.3
11	IV	CH_3MgI	Ether	0	1.1	56	48	52	0.92

[a] Based on weight of V after chromatography. Unless otherwise specified, starting material was recovered in those reactions where alcohol yield was less than 100%. [b] Grignard reagent was added to ketone. In all other cases, ketone was added to the organometallic. [c] Cupric sulfate was mixed with the ketone before the reagent was added. [d] Acetophenone was isolated. [e] ±5% due to low yield of V.

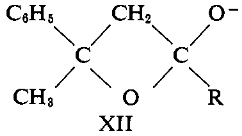
Table II. Diastereomer Ratios of 2,4-Diphenyl-2-hydroxy-4-methoxylpentane (VIII) Produced by Addition of Organometallics to 4-Methoxy-4-phenyl-2-pentanone (VI) and 1,3-Diphenyl-3-methoxy-1-butanone (VII)

Run	Ketone	Organometallic	Solvent	Temp, °C	Time, hr	Yield, %		% α-VIII	% β-VIII	α-VIII/β-VIII
						XIV[a]	VIII[a,b]			
12	VI	C_6H_5Li	Ether	35	0.8	13	87	43	57	0.75
13	VI	C_6H_5Li	Ether	0	1.1	5	89	49	51	0.96
14	VI	C_6H_5Li	Ether	−78	21	0	100	58	42	1.4
15	VI	C_6H_5MgBr	Ether	35	0.7	15	85	44	56	0.79
16	VI	C_6H_5MgBr	Ether	0	1.1	7	87	65	35	1.9
17	VI	C_6H_5MgBr	Ether	−78	20	0	67	51	49	1.0
18	VII	CH_3Li	Ether	0	0.7	10	82	70	30	2.4
19	VII	CH_3Li	DME[c]	0	1.1	20	75	55	45	1.2
20	VII	CH_3MgBr	Ether	35	0.7	7	56	77	33	3.4
21	VII	CH_3MgBr	Ether	0	1.1	8	89	78	22	3.5
22	VII	CH_3MgBr	Ether	−78	1.7	0	59	74	26	2.9
23	VII	CH_3MgCl	Ether	0	1.1	14	84	71	29	2.5
24	VII	CH_3MgI	Ether	0	1.1	11	80	57	43	1.3
25	VII	CH_3MgBr	DME[c]	0	1.1	23	61	68	32	2.1
26	VII	CH_3MgBr	Benzene	28	1.1	7	89	71	29	2.5
27	VII	CH_3MgBr	Ether–HMPA,[d] 1:1	35	1.1	7	31	56	44	1.3
28	VII	CH_3MgBr[e]	Ether	0	1.1	23	77	69	31	2.2

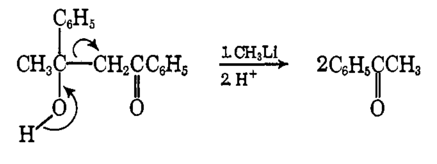
[a] Yield based on weight after chromatography. [b] In cases where yields of XIV and VII combined were less than 100%, starting material was recovered. [c] 1,2-Dimethoxyethane. [d] Hexamethylphosphoramide. [e] Cupric sulfate was first mixed with the ketone followed by the addition of the organometallic reagent.

meric products of addition to ketones III, IV, VI, and VII. In all of the addition reactions, an excess of organometallic reagent was employed. The crude reaction mixtures were chromatographed, and the alcohol fractions were separated from other materials. Approximately 30% solutions of the alcohols in dimethyl-d_6 sulfoxide were analyzed by integration of their nmr spectra with dimethyl sulfoxide as an internal standard with a chemical shift of τ 7.48. Alcohols α- and β-V have different chemical shifts for their hydroxyl and methyl proton singlets, and these bands were used for analysis. The hydroxyl and C-methyl protons of α- and β-VIII also have different chemical shifts, and these bands were employed for analysis. Synthetic mixtures of diastereomers of V and VIII were prepared and analyzed, and the known and calculated per cent compositions agreed within 1%. The yields of alcohol were in most cases determined gravimetrically but in a few cases by an nmr integration method using the internal standard.

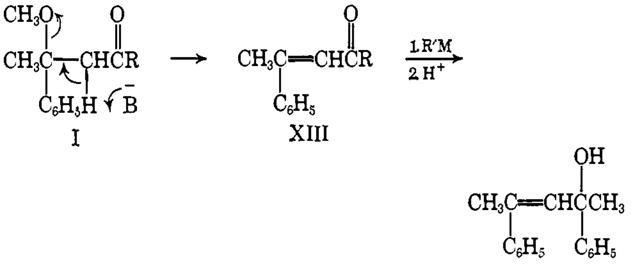
Table I records the results of the addition reactions of hydroxy ketones III and IV. In many runs considerable starting material was recovered. Either insoluble precipitates of metal alkoxides were formed or, more likely, the carbonyl group was partially involved in a ketal anion such as XII and rendered inactive.


XII

When methyllithium was added to IV, V was formed in low yield, and much of the ketone cleaved to give acetophenone.



The results of the addition reactions of methoxy ketones VI and VII are found in Table II. A side reaction of addition was β elimination to give XIII which in turn underwent addition to provide XIV, whose structure was identified by its nmr spectrum.



I

XIII

XIV

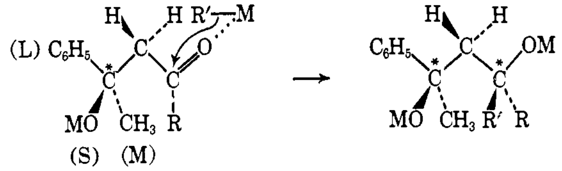
Discussion

Asymmetric Induction in Reactions of the Hydroxy Ketones. Addition of phenylmetallics to hydroxy ketone III gave ratios of α-V/β-V that ranged from 2.1 to 7.4 (runs 1–6). The low temperature of −78°, ether as solvent and phenylmagnesium bromide as reagent, provided the highest specificity (run 3), whereas the lowest involved a temperature of 0°, ether as solvent and phenyllithium as reagent (run 1). The effect of lower temperatures increasing the stereospecificity parallels a similar effect when phenylmetallics were added to 4-phenyl-2-pentanone.[5] Addition of methylmetallics to hydroxy ketone IV gave α-V/β-V ratios that ranged from 0.64 to 1.3 (runs 7–11). Temperature appeared to be the most important experimental variable since the extremes were reached with methylmagnesium bromide at −78 and 0° (runs 10 and 9). Only one value exceeded unity, that of run 10 carried out at −78°. Thus, the generalization emerges that under most conditions, the predominant diastereomer produced depends on the order in which the substituents are introduced at the second asymmetric center. This generalization resembles that observed in 1,2- and 1,4-asymmetric induction.[2,3,10]

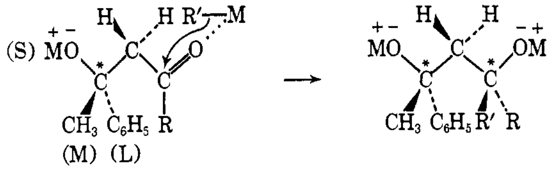
The direction of the asymmetric induction in the reactions of hydroxy ketones III and IV is compatible with either an *open-chain model* designed to minimize steric interactions in the transition state or a *polar model* which compromises steric, pole–pole, and dipole–dipole interactions in the transition state. In the polar model, the two negative oxygens are placed as far from one another as possible in the transition state, which distributes the bonds being made and broken in the least hindered position. The incoming R′ group enters the molecule from the least hindered side (side of M). A half-chair cyclic *model* predicts the wrong result. In the open-chain and polar models, assumptions are made that $C_6H_5 > CH_3 > OM$ in effective bulk, and that the conformation of lowest energy has the carbonyl and the adding group distributed between the two hydrogens on the adjacent center. Group R′ then approaches the carbonyl from the least hindered face to give the predominant diastereomer. The open-chain model resembles that suggested to correlate the results of addition of phenylmetallics to 4-phenyl-2-pentanone and methylmetallics to 1,3-diphenyl-1-butanone.[5]

These models are drawn in such a way that the incoming group, R′, is attached to the metal atom coordinating the carbonyl group. Even if they were drawn with R′ attached to a different metal atom, no change would occur in the prediction.

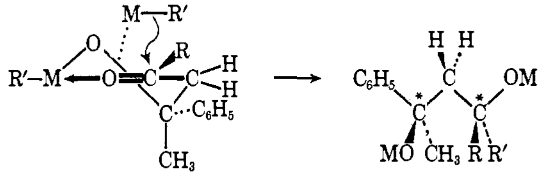
Open-chain model



Polar model



Cyclic model



Just as in the case of systems designed to study 1,2-asymmetric induction[3] the open-chain and polar models on the one hand and the cyclic models on the other predict the opposite results. However, in the case of 1,2-asymmetric induction, the cyclic model correlated the results and the other two models did not when they were in conflict. Possibly, the five-membered chelated ring is more stable than the six. The fact that a "crossover" in result was observed in run 10 at low temperature suggests that the models might compete with one another particularly in the case of the phenyl ketone.

Asymmetric Induction in Reactions of the Methoxy Ketones. The predominant diastereomer produced from additions to the methoxy ketones depended less on the order of introduction of groups at the second asymmetric center than was the case with the hydroxy ketones. Thus, addition of phenylmetallics to ketone VI gave α-VIII/β-VIII ratios that ranged from 0.75 to 1.9 (runs 12–17), the values being distributed about equally on either side of unity. Addition of methylmetallics to ketone VII gave α-VIII/β-VIII ratios that ranged from 1.2 to 3.5 (runs 18–28). Solvent, temperature, and the character of the organometallic were of about equal importance in determining the stereospecificity.

The three models drawn for the transition state of the addition reactions to the hydroxy ketones can also be visualized for the methoxy ketones. Of these the polar model seems the least likely because of the absence of a formal negative charge in the methoxy system. Although not clear-cut, the results are best correlated in terms of a competition between the open-chain and cyclic models, which predict opposite results. In application of the open-chain model, it is assumed that $C_6H_5 > CH_3 > OCH_3$ in effective bulk. Its formulation resembles that drawn for the hydroxy ketones and is not reproduced here. It predicts that α-VIII should predominate in the diastereomers produced from methyl ketone VI and that phenyl ketone VII should give mainly β-VIII. The results indicate that VI in runs 14 and 16 gave results predicted by this model and

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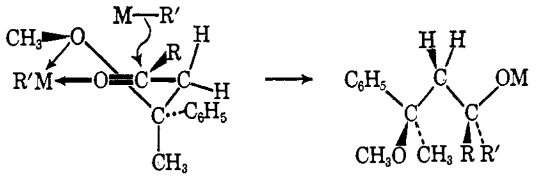
[10] (a) V. Prelog, *Helv. Chim. Acta*, **36**, 308 (1953); (b) V. Prelog and G. Tsatsas, *ibid.*, **36**, 1178 (1953).

that VII never gave results predicted by this model. The cyclic (half-chair) model should also resemble that drawn for the hydroxy ketone. It predicts that VI should give predominantly β-VIII and VII predominantly α-VIII. This model correlates all of the results (13 runs) of Table II except those of runs 14, 16, and 17. Thus, the results over-all are more compatible with the cyclic than with the open-chain model. The stereospecificities of the reactions are decidedly less than those observed with either the hydroxy ketones or the ketones without the extra oxygen function.[5] The fact that a change in temperature alone changed the predominant isomer in addition reactions of VI (compare runs 12 and 14, or runs 15 and 16) suggests that the open-chain and cyclic models have different temperature coefficients, which is expected. In general, the data suggest that the cyclic model transition state might have a less positive entropy of activation than the open chain.

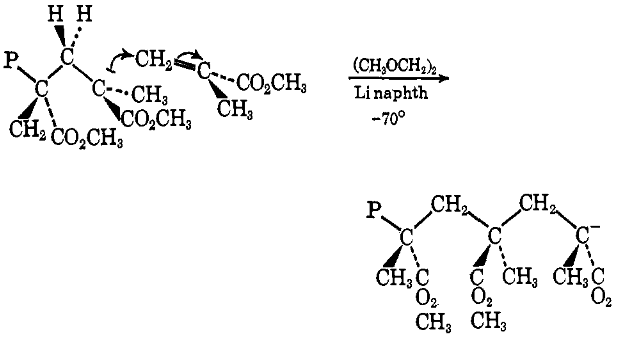
Cyclic model



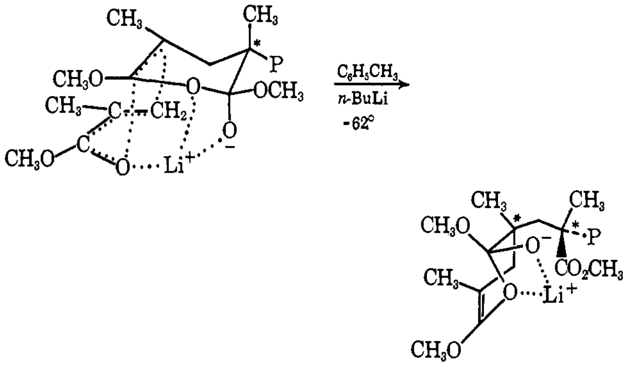
The "turnover" in stereochemical direction in going from the reactions of the hydroxy ketones to those of the methoxy ketones supports the thesis that the polar model is largely responsible for the relatively high stereospecificity observed in the additions to the hydroxy ketones. The absence of a formal negative charge in the transition state for the methoxy ketone addition reactions makes the polar model less important.

1,3-Asymmetric Induction in Stereospecific Addition Polymerization. In methyl methacrylate anionic addition polymerization, either isotactic or syndiotactic polymer can be made to predominate depending on solvent, the metal, and the temperature. Both cyclic and open-chain models controlled by the interplay of steric and dipole–dipole effects have been suggested to explain the results.[11] The degree of configurational homogeneity in the polymers has been estimated[12] to range from 68% isotactic to 90% syndiotactic. The experimental variables, the blend of steric, pole–pole, and dipole–dipole effects, the stereochemical directions of their reactions, and their stereospecificities all combine to provide a pattern of similarity between the polymerization and our model reactions. The stereochemical outcome of our reactions clearly results from 1,3-asymmetric induction, and the similarities outlined above provide strong evidence that the same is true in the polymerization reactions.

Open-chain model for 1,3-asymmetric induction leading to syndiotactic methyl methacrylate polymer



Cyclic model for 1,3-asymmetric induction leading to isotactic methyl methacrylate polymer



Experimental Section

General. Nuclear magnetic resonance (nmr) spectra were recorded on a Varian A-60 instrument. For all analytical spectra, hexadeuterated (97–98%) dimethyl sulfoxide was used as solvent. Unless otherwise specified spectral grade carbon tetrachloride with 2–5% added tetramethylsilane was used as solvent for all other nmr spectra. Infrared (ir) spectra were taken on a Perkin-Elmer Model 421 machine with concentrations approximately 10% in carbon tetrachloride. Rotations were taken on a Perkin-Elmer Model 141 polarimeter. All melting points are corrected and all boiling points are uncorrected. Thin-layer chromatographs (tlc) were made on silica gel G plates and developed with 10% phosphomolybdic acid in ethanol unless otherwise indicated. Reagent grade magnesium metal was used throughout.

4-Hydroxy-4-phenyl-2-pentanone (III). In a dry, pure nitrogen environment was placed 4.88 g of magnesium turnings and 50 ml of dry ether. To this with stirring was added 31.4 g of bromobenzene, and 10 ml of ether was used to complete the addition. After 30 min of stirring, this Grignard solution was added dropwise with stirring to 10 g of acetylacetone in 90 ml of dry ether at 0° in a dry, pure nitrogen environment (10 ml of ether was used to complete the addition). The resulting mixture was stirred at 25° for 1 hr and held at reflux for 20 min. The mixture was then cooled and quenched with 100 ml of water, and the aqueous layer was extracted with two 50-ml portions of ether. The ether layers were combined, washed with 50 ml of water, dried, and evaporated. The crude material (10.2 g) was chromatographed on 50 g of silica gel. Three fractions were eluted and characterized by tlc (30% ether–pentane). The nmr spectra of fractions 1 and 2 contained vinyl protons and these compounds were not further investigated. Fraction 3 (2.88 g) gave an nmr spectrum consistent with the desired ketone. This material was chromatographed on 50 g of silica gel with 0, 1, 2, 4, 5, and 10% ether in pentane. By tlc criterion, all but the first three 100-ml fractions of the eluate contained pure ketone III and were combined. The solvent was evaporated and the residue distilled at 68° (0.16 mm) to give 1.87 g (11%) of ketone III. *Anal.* Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.23; H, 7.99.

The nmr spectrum of III exhibited an aromatic multiplet at τ 2.48–2.99 (6 H) assigned to the phenyl protons and the hydroxyl proton, an AB quartet centered at τ 7.18 (2 H with J = 16.5 cps) assigned to the methylene protons, a singlet at τ 8.10 (3 H) assigned to the methyl protons adjacent to the carbonyl group, and a singlet at τ 8.58 (3 H) assigned to the methine methyl protons. The infrared spectrum showed a broad absorption at 3480 cm^{-1} for the hydroxyl group and a strong band at 1694 cm^{-1} for the carbonyl group with a shoulder at 1674 cm^{-1}.

1,3-Diphenyl-3-hydroxy-1-butanone (IV). As in the preparation of III, methylmagnesium iodide was prepared from 2.18 g of mag-

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(11) (a) D. J. Cram, *J. Chem. Educ.*, **37**, 317 (1960); (b) D. J. Cram and D. R. Wilson, *J. Am. Chem. Soc.*, **85**, 1249 (1963).

(12) (a) F. A. Bovey and G. V. D. Tiers, *J. Polymer Sci.*, **44**, 173 (1960); (b) Y. Kato and A. Nishioka, *Bull. Chem. Soc. Japan*, **37**, 1614, 1762 (1964); (c) Y. Kato, H. Watanabe, and A. Nishioka, *ibid.*, **37**, 1762 (1964).

nesium and 12.8 g of methyl iodide in 60 ml of ether. The Grignard solution was added dropwise to 9.7 g of 1,3-diphenyl-1,3-propanedione in 80 ml of ether at 25°. As the first mole of Grignard was added, a gelatinous precipitate formed which redissolved to give a deep green solution upon addition of the second mole. After 3 hr at 25°, 50 ml of water was added to quench the reaction. The aqueous layer was extracted with ether, and the combined ether layers were washed with a saturated solution of sodium thiosulfate and with water, dried, and evaporated. The residue was dissolved in 20 ml of absolute ethanol and then was cooled to $-15°$. After 1 hr, 3.0 g of starting material precipitated and was collected. The remaining 7 g was chromatographed on 50 g of silica gel, and products were eluted with 10, 20, 50, and 100% ether–pentane. The materials came off the column in the order of 2.13 g of starting material, 1.42 g of two unidentified compounds which were not identified, 2.71 g of crude IV (nmr spectrum), and 0.54 g of presumed 1,3-diphenyl-1,3-dihydroxypentane (V). The desired ketone IV solidified and was recrystallized from hexane to give 1.57 g (15%) of pure ketone IV, mp 49.3–50.3° (lit.[13] mp 63°). *Anal.* Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 80.11; H, 6.86.

The nmr spectrum of IV in deuterated chloroform exhibited an aromatic multiplet at τ 1.93–2.90 (10 H), a broad singlet at τ 5.32 (1 H) assigned to the hydroxyl proton, an AB quartet centered at τ 6.48 (2 H, J = 17.5 cps) assigned to the methylene protons, and a singlet at τ 8.40 (3 H) assigned to the methine methyl protons. The infrared spectrum of this ketone showed a broad absorption at 3482 cm^{-1} for the hydroxyl group and a strong peak at 1662 cm^{-1} for the carbonyl group with slight shoulders at 1678, 1644, and 1638 cm^{-1}.

2,4-Diphenyl-2,4-pentanediols (V). Mixtures of diols produced from several of the runs of Table I were combined to give 0.286 g of a mixture of diastereomers, which was chromatographed on 80 g of silica gel with 5, 10, and 15% ether–pentane as the eluent. Isomer α-V eluted from the column first (0.183 g) and was crystallized and recrystallized from hexane, mp 105.9–107.2°. *Anal.* Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.77; H, 7.89. The nmr spectrum of this isomer exhibited an aromatic multiplet at τ 2.43–2.98 (10 H), a singlet at τ 5.23 (2 H) assigned to the hydroxyl protons, a singlet at τ 7.72 (2 H) assigned to the methylene protons, and a singlet at τ 8.85 (6 H) assigned to the methyl protons.

Isomer β-V eluted from the chromatography column after α-V with empty fractions in between, weight 0.055 g, mp 115.7–116.9°. Recrystallization from hexane gave material, mp 117.1–118.2°. *Anal.* Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.82; H, 7.85. The nmr spectrum of β-V gave an aromatic multiplet centered at τ 3.07 (10 H), a singlet at τ 5.83 (2 H), an AB quartet centered at τ 7.56 (2 H, J = 25 cps) assigned to the methylene protons, and a singlet at τ 8.50 (6 H).

Reduction of the Diastereomers of 2,4-Diphenyl-2,4-pentanediol (**α-V and β-V**). In an atmosphere of hydrogen, 0.070 g of α-V, 20 ml of absolute ethanol, and 0.100 g of 10% palladium on charcoal were stirred at 25° for 24 hr. The mixture was then filtered through a Celite pad, and the solvent was evaporated. On tlc (pentane) the residue showed only one spot. This material (0.057 g or 97%) gave an nmr spectrum identical with that of (±)-2,4-diphenylpentane[5,14] contaminated with a few per cent of *meso*-2,4-diphenylpentane.

In a similar reaction, 0.043 of β-V was reduced to hydrocarbon (0.037 g or 100%) which also gave only one spot on tlc (pentane). This material gave an nmr spectrum identical with that of *meso*-2,4-diphenylpentane[5,14] contaminated with a few per cent of (±)-2,4-diphenylpentane.

3-Methoxy-3-phenylbutanoic Acid (X).[15] Mercuric acetate, 92.5 g, was added to 900 ml of anhydrous methanol. The mixture was swirled, heated, and filtered (5.8 g was collected). To the stirred filtrate was added 10 ml of 0.24 *M* aqueous perchloric acid and then 25 g of β-methylcinnamic acid dissolved in 100 ml of methanol. A 50-ml portion of methanol was used to complete the latter transfer. A white precipitate formed within 2 to 3 min after addition of the organic acid. The mixture was stirred at 25° for 3 days. The mixture was cooled in an ice bath, and to the stirred solution was added 24 g of sodium hydroxide in 80 ml of cold water, followed by a solution of 8.31 g of sodium borohydride in 70 ml of 0.1 *M* aqueous sodium hydroxide. After the mixture had stirred at 0° for 30 min, 3 *M* sulfuric acid solution was added slowly until gas evolution stopped and the mixture reached a pH of *ca.* 2. The mixture was filtered, and the gray residue washed with two 50-ml portions of methanol. The combined filtrates were concentrated under vacuum, and saturated sodium bicarbonate solution was added periodically to prevent the solution from becoming too acidic. After removal of about 200 ml of methanol, the remaining solution was shaken with 1 l. of ether and 1.5 l. of water (aqueous phase had a pH of 2). The aqueous phase was acidified to a pH of <1 and washed with 1 l. of ether. The combined organic phases were washed with two 750-ml portions of water and one 750-ml solution of brine, dried, and evaporated. The crystalline residue (27.7 g) was dissolved in hot hexane, the solution was filtered, and crystallization affected from 200 ml of hot hexane. The resulting small white plates were collected and dried, weight 22.6 g (75%), mp 76.5–77.5°. The absence of starting material was demonstrated by tlc (3:1 chloroform:chloroform saturated with 90% formic acid and iodine spotting). The unsaturated acid showed a retardation factor of 0.5–0.6, whereas X gave a retardation factor of 0.3–0.4. *Anal.* Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.12; H, 7.40.

The nmr spectrum of the acid exhibited an aromatic multiplet at τ 2.48–2.89 (5 H), a singlet at τ -1.30 (1 H) assigned to the acid proton, a singlet at τ 6.99 (3 H) assigned to the methoxy protons, a singlet at τ 7.24 (2 H) assigned to the methylene protons, and a singlet at τ 8.28 (3 H) assigned to the methyl protons.

(+)-3-Methoxy-3-phenylbutanoic Acid. A hot solution of 93.0 g of the acid and 131.0 g of cinchonidine in 3 l. of acetone was filtered and allowed to stand 10 days. The precipitate (95.0 g) was filtered; the filtrate was concentrated and allowed to stand 5 days. The salt which crystallized was added to the previous crop and redissolved (163.0 g) in 3.8 l. of hot acetone. After filtration, concentration of the filtrate, and filtration, 132.0 g of salt was obtained and dissolved in 2.1 l. of acetone. This crop (86.0 g) was filtered after 3 days and then was dissolved in 1.5 l. of acetone. After 1 day, 64 g of salt was recovered and dissolved in 1.3 l. of acetone. After 2 days, 36 g of precipitate was filtered and shaken with 250 ml of ether and 500 ml of 2 *N* hydrochloric acid. After hydrolysis and three recrystallizations from hexane to a constant melting point and rotation, 11.5 g of (+)-X, mp 59.2–60.1°, $[\alpha]$ +35.2° (*c* 0.9, ethanol), was obtained. *Anal.* Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.13; H, 7.23.

4-Methoxy-4-phenyl-2-pentanone (VI). To 10 g of 3-methoxy-3-phenylbutanoic acid in a dry flask under a pure nitrogen atmosphere was added through a serum cap with a syringe 250 ml of dry ether. The solution was cooled to 0° and to the solution (stirred) was added dropwise 77 ml of a 1.7 *M* solution of methyllithium in ether over a period of 45 min. After stirring for 1 hr at 0° the reaction was quenched with 125 ml of water added dropwise. The layers were separated, and the aqueous layer was extracted with 100-ml and 75-ml portions of ether. The combined ether layers were extracted with 100 ml of 0.5 *M* sodium hydroxide and 100 ml of water. The ether layer was dried and evaporated to give 5.7 g of crude product. The aqueous and basic aqueous layers were combined, acidified, and extracted to give 4.3 g of recovered acid X. The crude ketonic fraction was submitted to chromatography on 800 g of silica gel with pentane to 10% ether–pentane as developer. In this way 1.5 g of 4-phenyl-3-penten-2-one and 3.2 g of desired ketone VI (impure) were obtained. Separation of these two compounds by vpc failed. The chromatographed ketone VI was found by nmr to contain about 15% of the unsaturated ketone, which was removed as follows. A mixture of 1.5 g of impure ketone and 50 ml of ether was stirred with 100 ml of 2% aqueous potassium permanganate. After 1.25 hr aqueous oxalic acid was added until the solution was colorless. The layers were separated, and the aqueous layer was extracted with 50 ml of ether. The ether extracts were combined, dried, and evaporated to give 1.3 g of crude ketone which was chromatographed and distilled to give 1.0 g of pure VI as an oil. *Anal.* Calcd for $C_{12}H_{16}O_2$: C, 74.96; H, 8.39. Found: C, 75.11; H, 8.20.

The nmr spectrum of VI exhibited a tightly grouped aromatic multiplet at τ 2.54–2.91 (5 H), a singlet at τ 6.95 (3 H) assigned to the methoxy protons, an AB quartet centered at τ 7.33 (2 H with J = 13.5 cps) assigned to the methylene protons, a singlet at τ 8.11 (3 H) assigned to the carbonyl methyl protons, and a singlet at τ 8.38 (3 H) assigned to the methine methyl protons.

The nmr spectrum of 4-phenyl-3-penten-2-one showed a tightly grouped aromatic multiplet at τ 2.44–2.87 (5 H), a doublet at τ 3.58–3.60 (1 H with J = 2 cps) assigned to the vinyl proton, a doublet at τ 7.52–7.54 (3 H with J = 2 cps) assigned to the vinyl

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(13) J. Colonge, *Compt. Rend.*, **196**, 1414 (1933).

(14) D. Doskocilova and B. Schneider, *J. Polymer Sci.*, **B3**, 213 (1965).

(15) The authors thank Dr. S. W. Ela for the initial preparation.

methyl protons, and a singlet at τ 7.82 (3 H) assigned to the carbonyl methyl protons.

1,3-Diphenyl-3-methoxy-1-butanone (VII). To a solution of 168 g of mercuric acetate in 1200 ml of reagent grade methanol was added 10 ml of 0.25 *M* aqueous perchloric acid solution to give a white precipitate. To this mixture was added 59.2 g of 1,3-diphenyl-2-buten-1-one[16] in 100 ml of methanol. After 3 min the initial precipitate disappeared, and after 2 hr another white precipitate formed. After stirring 3 days at room temperature, the mixture was cooled to 0°, and 10 g of sodium borohydride in 300 ml of methanol was added dropwise with stirring. The mixture was then stirred for 30 min at 0°, and a saturated solution of sodium bicarbonate was added until effervescence ceased. The gray solid that separated was filtered, and the filtrate was evaporated under vacuum. The residue was dissolved in 100 ml of ether, and the solution was washed twice with 50-ml portions of water. The organic layer was dried and evaporated to yield 9.26 g of a mixture of starting material and product as shown by tlc (10% ether–pentane). The gray solid was extracted with two 300-ml portions of warm 95% ethanol from which 11.1 g of solid product was obtained on evaporation. Two recrystallizations of this material from ethanol and one from hexane gave 7 g of ketone VII, mp 56.0–57.0°. *Anal.* Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.17; H, 7.02.

The nmr of ketone VII exhibited an aromatic multiplet at τ 2.08–3.02 (10 H), an AB quartet centered at τ 6.77 (2 H with J = 14.5 cps) assigned to the methylene group, a singlet at τ 7.04 (3 H) assigned to the methoxy protons, and a singlet at τ 8.27 (3 H) assigned to the methine methyl protons.

2,4-Diphenyl-4-methoxy-2-pentanols (VIII). A mixture of α-VIII and β-VIII obtained by combining the products of several of the runs of Table II (1.2 g) was chromatographed on 200 g of silica gel with 0, 1, 2, and 5% ether–pentane mixtures as eluent. Isomer α-VIII was eluted first, 0.554 g as a viscous oil which was distilled at low pressure. *Anal.* Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 80.02; H, 8.11. On tlc (20% ether–pentane, 10% phosphomolybdic acid in ethanol spray or iodine), α-VIII had a retardation factor of 0.61.

Isomer β-VIII (tlc retardation factor of 0.44) could not be separated chromatographically from olefin XIV which from nmr analysis was present in the original mixture to the extent of 8%. The nmr spectrum of XIV in deuterated dimethyl sulfoxide exhibited an aromatic multiplet, a doublet at τ 3.65 (1 H with J = 1.5 cps) assigned to the vinyl proton, a singlet for the hydroxyl protons at τ 4.60 (1 H), a doublet at τ 7.98 (3 H with J = 1.5 cps) assigned to the vinyl methyl protons, and a singlet at τ 8.23 (3 H) assigned to the methine methyl protons.

(+)-2,4-Diphenyl-4-methoxy-2-pentanols ((+)-α-VIII and (+)-β-VIII). The acid chloride of (+)-X of maximum rotation was prepared from 5.0 g of the acid, 3.0 g of thionyl chloride, and 0.1 ml of dimethylformamide. This mixture was stirred for 4 hr at 25°.

Phenylmagnesium bromide was prepared in the usual way from 2.4 g of magnesium, 15.7 g of bromobenzene, and 65 ml of ether. To a stirred mixture of this Grignard reagent under dry nitrogen held at 0° was added 13.8 g of dry cadmium chloride, and the mixture was stirred for 5 min and then refluxed for 2 hr. The ether was then evaporated under reduced pressure, and 30 ml of dry benzene was added. The volume was reduced to 20 ml and an additional 30 ml of benzene was introduced. The mixture was held at reflux for 15 min, the flask was cooled to 0°, and the acid chloride (dissolved in 30 ml of dry benzene) was added. After 1 min at 0°, the mixture was held at reflux for 15 min. The mixture was then cooled quickly and ice was added. After an aqueous layer separated, 100 ml of 3 *M* sulfuric acid solution was added, and the mixture was shaken. The aqueous layer was separated and extracted with 50 ml of ether. The organic layers were combined, washed with 50 ml of water, 50 ml of saturated sodium bicarbonate solution, 50 ml of 10% sodium hydroxide, and 50 ml of water, dried, and evaporated. The crude material was chromatographed to remove decomposition products of phenylmagnesium bromide. Although mainly the desired phenyl ketone, the product mixture (4.4 g) was contaminated with three impurities which moved faster on tlc (20% ether–pentane).

Methylmagnesium iodide was prepared under dry nitrogen from 2.54 g of magnesium, 14.9 g of methyl iodide, and 110 ml of dry ether. The Grignard solution was cooled to −78° and 4.4 g of the above ketone in 60 ml of dry ether was added dropwise with stirring under nitrogen. After 10 hr at this temperature 50 ml of methanol was added, and the mixture was shaken at 25° with 100 ml of water. The aqueous layer was extracted with 50 ml of ether, and the combined ether layers were washed with water, dried, and evaporated. The residue was chromatographed on 900 g of silica gel with 0, 1, 2, 3, and 5% ether–pentane mixtures. In this way 0.49 g of (+)-α-VIII and 0.29 g of (+)-β-VIII were obtained, and each was rechromatographed on 100 g of silica gel and purified by molecular distillation at <0.1 mm pressure. Isomer (+)-α-VIII gave $[\alpha]^{25}_{546}$ +75.3° (*c* 1.6, carbon tetrachloride). *Anal.* Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 80.25; H, 8.03. The nmr spectra of racemic and (+)-α-VIII in dimethyl-d_6 sulfoxide were identical: an aromatic multiplet at τ 2.35–2.90 rising to a singlet at τ 2.59 (10 H), a singlet at τ 4.75 (1 H) assigned to the hydroxyl proton, a singlet at τ 7.02 (3 H) assigned to the methoxyl protons, a singlet at τ 7.68 (2 H) assigned to the methylene protons, a singlet at τ 8.55 (3 H) assigned to the methyl protons adjacent to the hydroxyl group, and a singlet at τ 8.68 (3 H) assigned to the methyl protons adjacent to the methoxyl group.

Isomer (+)-β-VIII had a rotation $[\alpha]^{25}_{546}$ +44.6° (*c* 1.1, carbon tetrachloride). *Anal.* Calcd for $C_{18}H_{22}O_4$: C, 79.96; H, 8.20. Found: C, 80.24; H, 7.93. The nmr spectra of racemic and optically active β-VIII were identical: an aromatic multiplet centered at τ 2.72 (10 H), a singlet at τ 5.06 (1 H) assigned to the hydroxyl proton, a singlet at τ 7.03 (3 H) assigned to the methoxyl protons, a singlet at τ 7.62 (2 H) assigned to the methylene protons, a singlet at τ 8.25 (3 H) assigned to the methyl protons adjacent to the hydroxyl group, and a singlet at τ 8.56 (3 H) assigned to the methyl protons adjacent to the methoxyl group.

(±)-2,4-Dimethoxy-2,4-diphenylpentane ((±)-XI). A mixture of 0.100 g of sodium hydride (55% in mineral oil suspension) and 0.132 g of α-VIII in 20 ml of dry, pure 1,2-dimethoxyethane was stirred under a positive pressure of dry nitrogen for 15 hr at 25°. Methyl iodide (5 ml) was added, and the mixture was stirred an additional 3 hr. The reaction was quenched with 20 ml of water, and the aqueous layer was extracted with pentane. The organic layers were combined, washed with 30 ml of water and 30 ml of a saturated sodium thiosulfate solution, dried, and evaporated. Two components were present in the residue by tlc (10% ether–pentane), the more intense and slower moving spot corresponding to starting α-VIII. The crude material was chromatographed on 20 g of silica gel with 0, 2, and 3% ether–pentane mixtures. Thus, 0.060 g (44%) of (±)-XI was obtained and crystallized from hexane, mp 67.9–69.0°. *Anal.* Calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.19; H, 8.59. The nmr spectrum of (±)-XI exhibited an aromatic multiplet at τ 2.52–3.05 (10 H), a singlet at τ 7.02 (6 H) assigned to the methoxyl protons, a singlet at τ 7.97 (2 H) assigned to the methylene protons, and a singlet at τ 8.38 (6 H) assigned to the methyl protons.

(+)-2,4-Dimethoxy-2,4-diphenylpentane ((+)-XI). The procedure of the following section was applied to (+)-α-VIII. From 0.109 g of material with $[\alpha]^{25}_{546}$ +75.3° (*c* 1.6, carbon tetrachloride) was obtained 0.052 g (45%) of (+)-XI recrystallized from hexane, mp 75.7–76.7°, $[\alpha]^{25}_{546}$ +51.2 (*c* 0.5, carbon tetrachloride). *Anal.* Calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.27; H, 8.36. The nmr spectrum of this compound was superimposable on that of (±)-XI.

***meso*-2,4-Dimethoxy-2,4-diphenylpentane.** By the same procedure, 0.196 g of (+)-β-VIII, $[\alpha]^{25}_{546}$ +44.6° (*c* 1.1, carbon tetrachloride), was converted to 0.089 g (44%) of *meso*-XI, $[\alpha]^{25}_{546}$ +0.05° (*c* 1.9, carbon tetrachloride), which was an oil. *Anal.* Calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 79.99; H, 8.42. The nmr spectrum of *meso*-XI exhibited an aromatic multiplet at τ 2.52–2.93 (10 H), a singlet at τ 2.52–2.93 (10 H), a singlet at τ 7.19 (6 H) assigned to the methoxy protons, an AB quartet centered at τ 7.77 (2 H with J = 25 cps) assigned to the methylene protons, and a singlet at τ 8.70 (6 H) assigned to the methyl protons.

Analysis of Mixtures of the Diastereomeric 2,4-Diphenyl-2,4-pentanediols (α-V and β-V) and the Mixtures of the Diastereomeric 2,4-Diphenyl-4-methoxy-2-pentanols (α-VIII and β-VIII). The crude reaction products were purified by column chromatography. A ratio of about 150 parts of silica gel to one part of substrate was employed. The column was eluted with mixtures of 5–30% ether–pentane for α-V and β-V and 0–10% ether–pentane for α-VIII and β-VIII. Solvent was removed from all fractions under reduced pressure. Per cent yields were determined by weight or by integration of the nmr spectrum. Approximately 30 mol % solutions of the product in dimethyl-d_6 sulfoxide were prepared and analyzed by integration of the nmr spectra. In this solvent the diastereo-

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[16] W. Wayne and H. Adkins, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p 367.

meric alcohols have slightly different chemical shifts, and the dimethyl sulfoxide was used as an internal standard with a chemical shift of τ 7.48.[17] To determine the relative amounts of α-V and β-V, the singlets for the hydroxyl and methyl protons were integrated. For α- and β-VIII, the singlets for the hydroxyl and for the methyl protons were integrated. When known amounts of the diastereomers were mixed together in different proportions in dimethyl-d_6 sulfoxide, experimental and calculated ratios agreed to within ±1%.

General Procedure for Addition of Ketones to Organometallics. The Grignard reagents were prepared by the usual method in ether. In runs where a different solvent for the reaction was required, the ether was evaporated in the presence of the new solvent in several evaporations. Methyllithium in ether (Foote Mineral Co.) was either used directly, or the ether was displaced with the desired solvent. Phenyllithium in ether (Columbia Organic Chemical Co.) was used directly. In all reactions unless otherwise specified in the footnotes of Tables I and II, the ketones were added to the organometallic solutions while being stirred under dry nitrogen at the desired temperatures. A large excess of organometallic over ketone was employed in all cases. With the hydroxy ketones the excess on a molar basis ranged from 3.1 to 3.0. With the methoxyketones the excess on a molar basis ranged from 4.0 to 0.6. Those reactions conducted at 0 to 35° were carried out for about 70 min and then quenched with water. Reactions carried out at −78° were stirred for about 20 hr before quenching with methanol. In runs 6 and 28 dry cupric sulfate (1 mol/mol of organometallic) was added to the organometallic prior to addition of the ketone. In all runs involving ether, heptane, or benzene as solvent, the reaction mixtures were shaken with water, and the water phase was extracted with ether. The combined organic phases were washed with water, dried, and evaporated. In those runs carried out in 1,2-dimethoxyethane, the reaction mixture was shaken with a mixture of water and methylene chloride, and the organic layer was treated in the usual way. The crude product was subjected to the above chromatographic and analytical procedures.

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[17] N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "NMR Spectral Catalogue," Varian Associates, Palo Alto, Calif., 1962.

Structural Studies of Pentacoordinate Silicon. I. Phenyl-(2,2′,2″-nitrilotriethoxy)silane

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Abstract: The crystal structure of $(C_6H_5)Si(OCH_2CH_2)_3N$ has been determined by three-dimensional X-ray diffraction methods and confirms the predicted pentacoordination of silicon in this compound. The distorted trigonal bipyramid coordination geometry of the silicon has the three equatorial oxygens bent away from the phenyl group toward the nitrogen as shown by the average C–Si–O angle of 97.1° and the average O–Si–O angle of 118.5°. Bond distances to the silicon are Si–O(1) 1.638 Å, Si–O(2) 1.664 Å, Si–O(3) 1.665 Å, Si–C 1.882 Å, and Si–N 2.193 Å. The space group is Pbca with a = 13.220 Å, b = 18.524 Å, c = 10.050 Å and eight molecules per unit cell. The structure was solved by iterative application of Sayre's method in three dimensions using a visual data set. Refinement was by full matrix least squares to a final reliability index of 10.8%.

The existence of pentacoordinate silicon has been postulated for some time. Compounds of such extracoordinate silicon have been proposed as intermediates in the theory of organosilicon reactions,[1] and there has been evidence for pentacoordinate silicon in some stable organic[2-6] and inorganic[7] ions. Stable, easily isolated nitrilotriethoxysilanes, $XSi(OCH_2CH_2)_3N$, have been synthesized,[8-10] and subsequent dipole moment, infrared, neutralization, and solute association studies[10,11] have strongly indicated pentacoordinate silicon in these compounds. A recently published investigation of the crystal structure of dimethylsilylamine pentamer[12] has provided evidence for pentacoordinated Si in that compound. However, the inherent difficulty of locating hydrogen atoms with X-ray diffraction data prevented this study from providing the complete geometry for the coordination.

The determination of the crystal structure of phenyl-(2,2′,2″-nitrilotriethoxy)silane was undertaken to provide direct evidence for or against the existence of a transannular dative bond between nitrogen and silicon such as would be required by the postulated bonding, and to allow a thorough analysis of the geometry of the Si atom coordination in this compound. It is also interesting to note that, of 13 nitrilotriethoxysilanes tested for biological activity, only the phenyl derivative gave significant results[11] showing high activity with respect to the central nervous system in several species.

Experimental Section

Data Collection. Crystals of phenyl-(2,2′,2″-nitrilotriethoxy)silane are colorless with a lath-like habit and a melting point of 207–

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