B. Mono- and Dimethyltetrahydrochrysene (7, 8, and 9).—Reductive methylation of chrysene utilizing a procedure analogous to that employed for reduction to the tetrahydro stage afforded a complex product mixture. Major components **7** (48%), **8** (21%), and **9** (15%) were trapped off the glpc column and identified by nmr and mass spectrometry. The integrated proton nmr spectra were consistent with the assigned structures. In particular, the spectrum of **7** exhibited a methyl doublet at δ 1.33 (J = 7 Hz, 3 H) and a vinyl resonance at δ 6.30 (d, J = 4 Hz with fine splitting, 1 H); the spectrum of **8** had a methyl singlet at δ 0.95 (3 H) and vinyl protons as a pair of doublets (2 H) at δ 6.63 (J = 10 Hz) and 6.42 (J = 9 Hz), respectively; and the spectrum of **9** contained overlapping methyl doublets at δ 1.05 (J = 7 Hz, 3 H) and 1.18 (J = 7 Hz, 3 H). Alternative structures derived from **10**, *e.g.*, 5-methyl-4b,5,6,12-tetrahydrochrysene, were ruled out by the fact that analogous reductive methylation of **1** also provided the same three major products.

Equilibration of 3.—A solution of *trans*-**3** (200 mg) in 75 ml of THF was added to a solution of sodamide (from 980 mg of sodium and 40 mg of $FeCl_3$) in 120 ml of liquid ammonia and stirred at reflux for 3 hr. Conventional work-up provided recovered **3**. Repetition at various time intervals led to the following cis–trans ratios by glpc analysis.

Time, hr	% cis	% trans
3	20	80
8.5	50	50
15	75	25
21.5	85	15
25	86	14

Registry No.—**2**, 31570-60-2; *cis*-**3**, 31579-69-8; *trans*-**3**, 31579-70-1; **6**, 18930-97-7; chrysene, 218-01-9

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Stereochemistry of the Addition of Methylzinc and -cadmium Reagents to Acyclic Aldehydes[1a]

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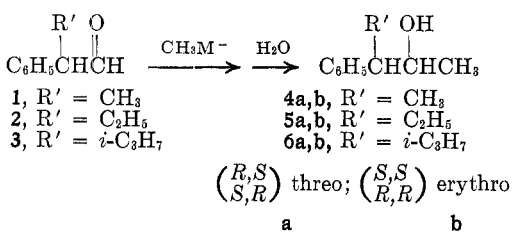
The reactivity and stereochemistry of addition of methyl Grignard and Cd and Zn reagents toward 2-phenylpropanal (**1**), 2-phenylbutanal (**2**), and 2-phenyl-3-methylbutanal (**3**) have been determined. The reactivity of *in situ* dimethylcadmium and -zinc reagents containing magnesium halide was comparable to that of the Grignards. The lower stereoselectivity observed with the cadmium and especially the zinc reagents toward **1** and **2** has been rationalized as resulting from a tight four-center transition state for such reactions. The anomalous results obtained for the addition of the methyl reagents to 2-phenyl-3-methylbutanal represent a violation of the postulates of Cram, Karabatsos, and Felkin.

In our continuing study of the addition reactions of *in situ* alkylzinc and -cadmium reagents, we have determined the stereochemistry of addition of various methyl reagents to a series of 2-phenylalkanals (**1**, **2**, and **3**). The stereochemistry of addition of isopropylmagnesium bromide to **3** has also been determined. The per cent stereoselectivity obtained with the various organometallic reagents was determined by glpc analysis with racemic reagents.



The absolute configurations of threo and erythro isomers of **4** and **5**, as well as those obtained from the reaction of isopropylmagnesium bromide with **3**, are known.[2] The identification of *threo*- and *erythro*-3-phenyl-4-methyl-2-pentanols (**6**) resulting from addition of methylmagnesium iodide to **3** is based on their order of elution on STAP and FFAP, their relative rates of dehydration, and their characteristic infrared spectra (see Experimental Section).

From an inspection of Table I it is evident that, for all threo–erythro pairs, the threo isomer possesses the shorter retention time (entries 3, 5, and 8). On this basis entry 10 is assigned the threo configuration. Thermal dehydration (see Experimental Section) of all threo–erythro pairs in the presence of zinc bromide indicated that the alcohol of longer retention time (erythro) in each instance underwent dehydration at the faster rate. A study of the rate of solvolysis of *threo*- and *erythro*-3-phenyl-2-butanols (**4**) by Cram[3] has revealed that the erythro isomer reacts at a faster rate than the threo isomer. All the threo and erythro isomers obtained by preparative glpc are consistent with the above assignments.

Results

From the results compiled in Table II, certain general observations can be made.

(1) On the basis of unchanged aldehyde, the reactivity of $(CH_3)_2M$ (M = Zn, Cd) toward the various aldehydes is greater than that toward 4-*tert*-butylcyclohexanone,[4] and is essentially equivalent to that of the Grignard reagents. The reactivity of organozinc reagents prepared from methyllithium is extremely low.

(2) The stereochemistry of addition of Grignard reagents to acyclic aldehydes is independent of concentration (association). CH_3MgBr is more stereoselective than CH_3MgI. By contrast, the stereochemistry of addition of zinc and cadmium reagents,

(1) (a) Taken in part from Ph.D. theses of E. J. G. and W. J. K., University of New Hampshire, 1969. (b) National Defense Education Act Fellow, 1966–1969. (c) Nationl Science Foundation Trainee, 1966–1969.

(2) G. J. Karabatsos, *J. Amer. Chem. Soc.*, **89**, 1367 (1967).

(3) D. J. Cram, H. L. Nyquist, and F. A. Abd Elhafez, *ibid.*, **79**, 2876 (1957).

(4) P. R. Jones, E. J. Goller, and W. J. Kauffman, *J. Org. Chem.*, **34**, 3566 (1969).

TABLE I

GLPC ANALAYSES OF ALDEHYDES AND THREO AND ERYTHRO ALCOHOLS

Entry	Compd	Registry no.	Liquid phase	Temp, °C	Flow rate, ml/min	Retention time, min
1	$PhC(CH_3)HCHO$		FFAP	150	67	9.5
2	*threo*-$PhC(CH_3)HC(CH_3)HOH$	1502-80-3	FFAP	150	67	17.2
			Carbowax 20M	150	67	20.4
3	*erythro*-$PhC(CH_3)HC(CH_3)HOH$	1502-79-0	FFAP	150	67	20.6
			Carbowax 20M	150	67	24.5
4	PhC(Et)HCHO		FFAP	150	67	9.6
5	*threo*-PhC(Et)HC(CH_3)HOH	6932-55-4	FFAP	150	67	16.1
6	*erythro*-PhC(Et)HC(CH_3)HOH	6932-54-3	FFAP	150	67	19.8
7	PhC(*i*-Pr)HCHO		FFAP	160	67	9.0
			STAP	160	70	9.8
8	*threo*-PhC(*i*-Pr)HC(*i*-Pr)HOH	6932-58-7	Carbowax 20M	150	70	42.6
9	*erythro*-PhC(*i*-Pr)HC(*i*-Pr)HOH	6932-57-6	Carbowax 20M	150	70	47.1
10	*threo*-PhC(*i*-Pr)HC(CH_3)HOH	31330-87-7	FFAP	160	67	13.4
			STAP	160	70	21.6
11	*erythro*-PhC(*i*-Pr)HC(CH_3)HOH	31330-88-8	FFAP	160	67	17.2
			STAP	160	70	27.6

TABLE II[a]

REACTION OF ORGANOMETALLIC REAGENTS WITH $C_6H_5C(R')HCHO$

Entry	R'	Reagent	Concn, *M*	% erythro[b,c]	% unchanged aldehyde[d]
1	CH_3	CH_3MgI	0.8	64.3	<1
2	CH_3	CH_3MgI	0.1	65.6	<1
3	CH_3	CH_3MgBr	0.8	69.5	<1
4	CH_3	$(CH_3)_2Cd$ (I, I)[e]	0.4	61.1	<1
5	CH_3	$(CH_3)_2Cd$ (Br, Br)[f]	0.4	59.8	<1
6	CH_3	$(CH_3)_2Cd$ (I, Cl)	0.4	60.4	<1
7	CH_3	$(CH_3)_2Cd$ (I, Cl)	0.4	62.1	<1
8	CH_3	CH_3CdX (I, Cl)[g]	0.8	56.8	<1
9	CH_3	CH_3CdBr (Br, Br)	0.8	62.2	<1
10	CH_3	CH_3CdI (I, I)	0.8	60.8	<1
11	CH_3	$(CH_3)_2Zn$ (I, I)	0.3	54.7	<1
12	CH_3	$(CH_3)_2Zn$ (Br, Br)	0.3	56.9	<1
13	CH_3	$(CH_3)_2Zn$ (I, Cl)	0.3	51.5	8
14	CH_3	CH_3ZnI (I, I)	0.3	54.3	<1
15	CH_3	CH_3ZnBr (Br, Br)	0.3	56.0	2
16	CH_3	CH_3ZnX (Br, I)	0.3	54.1	2
17	CH_3	CH_3ZnX (I, Cl)	0.3	59.7	40
18	CH_3	CH_3ZnX (CH_3Li, ZnI_2)	0.3	53.5	75
19	CH_3	CH_3ZnX (CH_3Li, $ZnBr_2$)	0.3		90
20	C_2H_5	CH_3MgI	0.8	65.2	<1
21	C_2H_5	CH_3MgBr	0.8	70.8	<1
22	C_2H_5	$(CH_3)_2Cd$ (Br, Br)	0.4	58.4	<1
23	C_2H_5	$(CH_3)_2Zn$ (I, I)	0.3	54.5	<1
24	*i*-C_3H_7	CH_3MgI	0.8	44.9	<1
25	*i*-C_3H_7	$(CH_3)_2Cd$ (I, I)	0.4	32.5	<1
26	*i*-C_3H_7	$(CH_3)_2Cd$ (I, Br)	0.4	29.3	<1
27	*i*-C_3H_7	$(CH_3)_2Zn$ (I, I)	0.3	36.3	<1
28	*i*-C_3H_7	*i*-PrMgBr	0.8	64.2	<1

[a] The ratio of organometallic to aldehyde was 1:1 unless otherwise noted. [b] Normalized %; % threo + % erythro = 100. [c] Results reproducible within ±1% in separate reaction runs. [d] % = $area_{aldehyde}/(area_{aldehyde} + area_{alcohols}) \times 100$. [e] Halogens in parentheses indicate, respectively, the methyl halide from which RMgX was prepared and the metal halide used for the exchange. [f] Zinc bromide solution was prepared from commercially available salt. [g] Ratio of organometallic to aldehyde was 2:1.

except those designated as (I, Cl), is independent of halide.

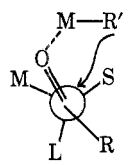
(3) Erythro alcohol is the major product of addition of the organometallics to 2-phenylpropanal and 2-phenylbutanal, the per cent erythro isomer being dependent on organometallic and independent of aldehyde. Threo alcohol is the major product of addition of methyl reagents (not *i*-PrMgBr) to 2-phenyl-3-methylbutanal.

(4) Except for the reactions with 2-phenyl-3-methylbutanal, the per cent erythro alcohol decreases according to the series $CH_3MgX > (CH_3)_2Cd$, $CH_3CdX > (CH_3)_2Zn$, CH_3ZnX. The dimethylzinc reagents are less stereoselective than are the cadmiums toward all aldehydes studied.

(5) Changing the magnesium reagent from methyl to isopropyl in reactions with 2-phenyl-3-methylbutanal causes an inversion in stereoselectivity (44.9% erythro *vs.* 64.2% erythro, respectively).

Classically, the stereochemistry of addition reactions of organometallic reagents to acyclic aldehydes containing an asymmetric carbon has been rationalized

by Cram's rule.[5] Although the diastereomeric product distribution for a large number of nucleophilic addition reactions has been correctly predicted qualitatively by the Cram model **7**, Karabatsos[2] has recently pointed out a number of shortcomings from a quantitative



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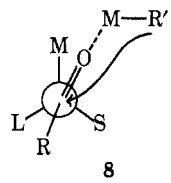

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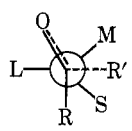
standpoint. The Karabatsos treatment, somewhat less empirical than that of Cram, is based on two assumptions which lead to the conclusion that the favored transition-state conformation may be represented by **8**. Unlike Cram, Karabatsos predicts the degree of stereoselectivity of the addition reactions to be independent of the steric bulk of the attacking reagent R′ but to decrease as the steric bulk of R increases.

Felkin and coworkers[6] have attempted to show that the interpretation of the steric outcome of the nucleophilic addition reactions can encompass both open-chain carbonyls and cyclohexanones. According to Felkin, the importance of torsional strain in the transition states for acyclic systems requires that staggered (**9**, **10**, and **11**) rather than eclipsed (**7** and **8**) conformations be considered. Given certain basic assumptions,[6] **9** is considered to represent the lowest energy transition state. Contrary to the prediction of Karabatsos, one would expect, on the basis of **9**, **10**, and **11**, an increase in the stereoselectivity of the reaction as the steric bulk of M, L, or R increases.



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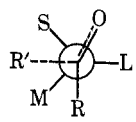

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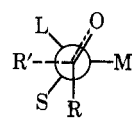

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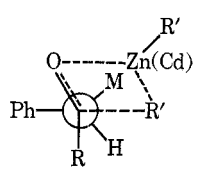
In view of the recent success of the Felkin approach to explain the stereochemistry of addition reactions in cyclic and acyclic systems, the results outlined above will be discussed primarily in terms of transition state conformers **9**, **10**, and **11**. Our earlier hypothesis[4] that the zinc and cadmium additions can be visualized as involving a bridged, four-center transition state leads more specifically to contrasting structures **12** and **13** for the transition states for zinc or cadmium and



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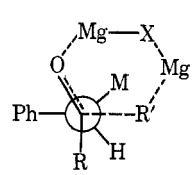

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magnesium, respectively. The observed trend in stereoselectivity with a change in metal, absence of halide dependence on the stereochemistry for zinc and cadmium reactions, and the inertness of Me_2Zn and Me_2Cd reagents prepared from MeLi are all characteristics consistent[4] with the four-center transition state.

(5) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 69.

(6) M. Cherest, H. Felkin, and N. Prudent, *Tetrahedron Lett.*, 2199 (1968).

With a given organometallic series, the stereochemistry of addition was essentially insensitive to the change of the medium group from methyl to ethyl (**1** and **2**) in the aldehyde substrate. The reaction of **3** with *i*-PrMgBr proceeds to give the erythro alcohol in 64.2% isomeric purity. However, an inversion in stereoselectivity was observed for the addition of methyl reagents to **3**, threo alcohol being the major product. This result represents a violation of the postulates of Cram, Karabatsos, and Felkin.

According to Felkin, the important steric interactions involve R′ and R (H). The interaction between complexed carbonyl oxygen and the substituents attached to the α carbon is believed to be insignificant.

Inspection of **12** and **13** reveals that, while interactions between a magnesium-coordinated carbonyl and M may be small, this need not be the case for zinc- or cadmium-coordinated species. If the four-center transition state is tighter, as previously postulated,[4] then cadmium and especially zinc reactions may be more sensitive to the steric bulk of M, destabilizing **9** relative to **10** (leading to more threo alcohol). Thus, modification of the Felkin model to include the M–O interactions would account for the greater proportion of threo alcohol obtained for Zn and Cd reactions and explain the observed stereoselectivity series Mg > Cd > Zn for reactions involving **1** and **2**. Both Cram and Karabatsos models would predict the opposite for a tighter four-center transition state. Additional support for this argument can be seen from consideration of entries 20 and 24 *vs.* 22 and 25 of Table II. The change in stereochemistry with increasing M is greater for the cadmium than for the magnesium reagents.

The fact that no change in stereoselectivity was observed as M varies from methyl to ethyl among the various organometallic reagents implies that either the M–H steric interactions (**10**) do not increase significantly or that the increase which does occur is counterbalanced by a similar increase in the magnitude of the M–O steric interactions (**9**).

Although it is tempting to extend the above arguments to explain the per cent threo alcohol (>50%) obtained through the interaction of the methyl reagents and 2-phenyl-3-methylbutanal, such rationalization appears untenable on the basis of existing data.[2] While the results agree qualitatively with the modified Felkin analysis described above, quantitatively they are less appealing. The experimentally determined free-energy difference of 0.31 kcal calculated from the threo/erythro ratio of 1.8 for **6** appears to be larger than expected.

An alternate suggestion might be that, when M = isopropyl, the phenyl group at the α carbon may be so orientated that steric and electronic interactions are reduced considerably toward the attacking methyl reagent. Thus isopropyl may act as the largest group in **9**, **10**, and **11**. Although such a model would predict threo alcohol as the major product from all organometallic reagents studied, one would expect the order of stereoselectivity of reagents to remain Mg > Cd > Zn and not the observed Cd > Zn > Mg.

It is clear that the results reported here fail to fit consistently any of the hypotheses proposed for the stereochemistry of addition reactions. Further exploration into the configurational composition of prod-

ucts from a wider variety of organometallics and acyclic carbonyl compounds is warranted.

Experimental Section

Several of the following experimental procedures are modeled closely after those described in previous papers.[4,7]

Preparation of 2-Phenylbutanoyl Chloride.—Thionyl chloride (224 g, 1.9 mol) was added slowly with stirring to 50 g (0.31 mol) of 2-phenylbutanoic acid. The mixture was refluxed for 1.5 hr and stirred for an additional 0.5 hr at room temperature. After removal of excess thionyl chloride at reduced pressure, 54 g (97%) of 2-phenylbutanoyl chloride was collected at 84–87° (3.7 mm) [lit.[8] bp 97–98° (14 mm)].

Preparation of the Imidazolide of 2-Phenylbutanoic Acid.[9]—To a solution of imidazole (40.4 g, 0.59 mol) in 300 ml of anhydrous THF was added, over a period of 30 min at room temperature, a solution of 54 g (0.29 mol) of 2-phenylbutanoyl chloride in 200 ml of THF. The contents were refluxed for 1 hr and stirred at room temperature for an additional 4 hr. Then the solution was cooled to 0° and the imidazole hydrochloride removed by filtration. After removal of the solvent *in vacuo*, the solid residue was washed with cold benzene and 45 g of white imidazolide collected by suction filtration. The benzene washings were extracted with dilute hydrochloric acid and saturated sodium bicarbonate and dried, and the benzene was removed *in vacuo* on a rotary evaporator. The solid residue was washed with an ice-cold petroleum ether (bp 30–60°)–benzene (3:1, v/v) solution and 10 g of white imidazolide was obtained. The combined product, mp 86.5–89° (lit.[10] mp 87–89°), weighed 55 g (87%). The ir spectrum of the imidazolide is characterized by a carbonyl band at 1730 cm^{-1}.

Preparation of 2-Phenylbutanal.—A procedure similar to that described by Staab[9] was employed. A solution of 55 g (0.26 mol) of the imidazolide of 2-phenylbutanoic acid in 250 ml of ether was cooled to −20° in an ethanol–snow bath. Then 2.7 g (0.07 mol) of lithium aluminum hydride in 200 ml of ether was added, with stirring, at such a rate that the temperature did not exceed −15°. After completion of the addition the reaction mixture was stirred at −20° for 0.5 hr and then allowed to reach ambient temperature. The reaction was carried out under an atmosphere of dry nitrogen. Hydrolysis was accomplished with 100 ml of dilute hydrochloric acid. The aqueous layer was extracted twice with ether, the ether layers were combined and dried, and the solvent was removed on a rotary evaporator. Distillation of the crude product gave 20.0 g {0.13 mol, 50% of 2-phenylbutanal, bp 50.5–59° (0.7 mm) [lit.[11] bp 97–99° (15 mm)]}.

Preparation of 2-Phenyl-3-methylbutanonitrile.—2-Phenyl-3-methylbutanonitrile [bp 110° (7 mm)] was prepared in 59% yield from phenylacetonitrile and isopropyl bromide in 50% aqueous sodium hydroxide according to the method of Makosza and Serafin.[12] The final product contained approximately 22% unchanged phenylacetonitrile.

Preparation of 2-Phenyl-3-methylbutanamide.—The reaction was carried out as previously described[13] with a solution of 106 g (0.67 mol) of nitrile, 270 ml of hydrogen peroxide (30%), 250 ml of ethanol, and 27 ml of 6 *N* sodium hydroxide. The crude, air-dried product weighed 93.7 g (79%), mp 93–103° (lit.[14] 111°). The ir spectrum was consistent with the assigned structure.

Preparation of 3-Methyl-2-phenylbutanoic Acid.—A solution of 20 g (0.11 mol) of the above amide, 60 ml of glacial acetic acid, 60 ml of concentrated HCl, and 20 ml of water was cooled to 0° by means of an ice–salt bath. A solution of 16 g of $NaNO_2$ (0.23 mol) in 30 ml of water was added dropwise over a period of 1.5 hr with stirring. After the addition was complete, the bath was removed and the mixture was stirred for 12 hr. It was then diluted with water and extracted twice with 100-ml portions of ether. The ether extracts were combined and extracted six times with 50 ml of saturated NaCl solution. The ether solution was dried and then concentrated on a rotary evaporator. Distillation yielded 13.1 g (65%) of acid product, bp 109–114° (0.7 mm).

Preparation of 2-Phenyl-3-methylbutanoyl Chloride.—The procedure described by Cram[3] was employed. 2-Phenyl-3-methylbutanoic acid (24.1 g, 0.135 mol) and 19.2 g (0.16 mol) of thionyl chloride were stirred overnight at room temperature. The excess thionyl chloride was removed at room temperature (20 mm). The desired acid chloride (23.7 g, 89%) was collected at 75–79° (1.4 mm) [lit.[3] bp 125° (13 mm)].

Preparation of 2-Phenyl-3-methylbutanal.—The procedure described by Brown[15] for the reduction of acid chlorides to aldehydes was employed. To a solution of 15.2 g (0.077 mol) of 2-phenyl-3-methylbutanoyl chloride in 50 ml of diglyme, cooled to −78°, was added 20.3 g (0.08 mol) of lithium aluminum tri-*tert*-butoxyhydride in 100 ml of diglyme over a period of 1 hr in a nitrogen atmosphere. The Dry Ice–acetone bath was removed and the mixture allowed to warm to room temperature (*ca.* 1 hr). Hydrolysis was accomplished by pouring the contents onto crushed ice, and the resultant mixture was extracted several times with ether. Extraction of the combined ether layers with aqueous sodium bisulfite failed to remove any of the aldehyde. The combined ether layers were then dried over $MgSO_4$, the solvent was removed on a rotary evaporator, and the residue distilled at 70–73° (1.6 mm) [lit.[16] bp 72–73° (1.0 mm)], to yield 5.0 g (33%) of 2-phenyl-3-methylbutanal.

Reaction of Methylmagnesium Bromide with 2-Phenylpropanal.—The following procedure will serve to illustrate the reaction of the various Grignard reagents with 2-phenylpropanal, 2-phenylbutanal, and 2-phenyl-3-methyl-butanal.

An ethereal solution of 14.5 ml of 2.07 *M* methylmagnesium bromide (0.03 mol) was added by means of a 20-ml syringe to 39 ml of anhydrous ether with stirring. The reagent was then cooled with an ice–salt bath and stirred until the internal temperature reached 0°. A solution of 2.0 g (0.015 mol) of 2-phenylpropanal in 15 ml of ether was added at such a rate that the temperature did not exceed 5°. The ether layer was separated and the aqueous layer extracted twice with ether. The combined ether layers were dried ($MgSO_4$) and the solvent was removed at room temperature on a rotary evaporator to give 2.0 g of crude product.

Glpc analysis was conducted on a 10 ft × 0.25 in. column packed with 10% FFAP on Chromosorb W at a temperature of 170° and a flow rate of 67 ml/min. The two major components of the reaction of methylmagnesium iodide and 2-phenylpropanal were collected by preparative glpc. The nmr spectra of the diastereomeric alcohols are in accord with published values:[17] nmr (CCl_4) (threo) δ 1.10, 1.22 (overlapping d, 6, $J \cong 7$ Hz, $(CH_3)_2CH$), 1.48 (s, 1, OH), 2.61 (m, 1, $CH_3(Ph)CH$), 3.70 (m, 1, $CH_3(OH)CH$), 7.15 (s, 5, Ph); (erythro) 0.92 (d, 3, $J \cong 8$ Hz, CH_3CHCH_3), 1.22 (d, 3, $J \cong 7$ Hz, CH_3CHCH_3), 2.58 (m, 1, $CH_3(Ph)CH$), 2.79 (s, 1, OH), 3.74 (m, 1, $CH_3(OH)CH$), and 7.14 ppm (s, 5, Ph). The chromatograms indicated in all cases a nearly quantitative conversion of aldehyde to a mixture of threo and erythro alcohols. The results obtained with the Grignard reagents (Table II) were reproducible within ±1% in separate reaction runs.

Separation and Identification of Diastereomers.—Identification of the threo and erythro alcohols obtained from addition of methyl Grignard reagents to 2-phenylpropanal and 2-phenylbutanal, as well as of threo and erythro alcohols obtained from addition of isopropylmagnesium bromide to 2-phenyl-3-methylbutanal, is based on previous literature reports[2] indicating that the major product is the erythro isomer. In addition, *threo*-3-phenyl-2-butanol (**4a**) was isolated *via* its monoacid phthalate,[18] while *erythro*-3-phenyl-2-butanol (**4b**) was obtained by column chromatography on neutral alumina (activity I) with pentane–ether as eluent. The identification of *threo*- and *erythro*-3-phenyl-4-methyl-2-pentanols (Table I, entries 10 and 11), resulting from

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addition of methylmagnesium iodide to 2-phenyl-3-methylbutanal, follows from their order of elution on STAP and FFAP (Table I) and on their relative rates of dehydration (see below). The nmr spectra of the two diasteromeric alcohols were inconclusive for configurational assignment, but their infrared spectra[19] were characteristically distinct and bear close analogies with the other threo-erythro pairs. The alcohols **4–6** contain a weak OH stretching band at 3550–3570 cm^{-1}, assignable to nonbonded or π-bonded[19b] hydroxyl, which is better resolved and relatively stronger in the threo isomers **4a–6a**. The range for the polymeric OH in the threo isomers is 3420–3430 cm^{-1}, whereas that in the erythro isomers is 3300–3380 cm^{-1}. A larger frequency shift between the two OH bands is observed with the erythro alcohols: $\Delta\nu_{(OH)}$ **4a**, 140; **5a**, 140; **6a**, 140; **4b**, 180; **5b**, 180; **6b**, 250 cm^{-1}. The greater strength of the polymeric hydrogen bond in the erythro isomers[19a] is attributed to conformational differences and less sterically crowded OH functions in these alcohols.[17]

Pure samples (>99%) of *threo*- and *erythro*-3-phenyl-2-butanol and 3-phenyl-4-methyl-2-pentanol were obtained by preparative glpc on FFAP (10%, Chromosorb W, 10 ft). The purity was determined by reinjection for analysis on FFAP and Carbowax 20M–TPA. The response ratios determined on Carbowax 20M–TPA are as follows: **4a/4b** = 1.01 ± 0.01; **6a/6b** = 1.01 ± 0.01.

Dehydration of Threo and Erythro Alcohols.—From an inspection of Table I it is clear that for all threo–erythro pairs, the threo isomer possesses the shorter retention time. The relative rates of dehydration of the various diastereomeric pairs of addition products were monitored by glpc analysis on STAP. The injector port of the chromatograph (265°) was coated with salt by injection of ether solutions of zinc bromide. Subsequent injection and analysis of the various diastereomeric product pairs (Table I) showed the appearance of several new peaks (presumably olefins) with retention times slightly longer than that of the ether solvent and an accompanying decrease in the amount of threo and erythro alcohols.

Comparison of the isomeric composition of the alcohol addition products before and after dehydration revealed that the alcohol of longer retention time (erythro) in each instance underwent dehydration faster than the isomer of shorter retention time (threo). Similar results were observed for solvolysis of the 3-phenyl-2-butanols[3] and give additional support to the assignment made for *threo*- and *erythro*-3-phenyl-4-methyl-2-pentanols (**6a**, **6b**).

Reaction of *in Situ* Dimethylcadmium (I, Cl) with 2-Phenylpropanal.—The following procedure will serve to illustrate the reaction of the various *in situ* cadmium reagents (Table II) with 2-phenylpropanal, 2-phenylbutanal, and 2-phenyl-3-methylbutanal.

A solution of 15 ml of 2.0 *M* MeMgI (30 mmol) was added *via* a 20-ml syringe to a stirred, cold mixture of 2.74 g of $CdCl_2$ (14.9 mmol) and 22 ml of anhydrous ether. This addition was carried out such that no ebullition occurred. The solution was then stirred at room temperature for 20–30 min before the Gilman test was performed. In all cases the test was negative before the reaction was allowed to proceed to the next step.

The dimethylcadmium reagent was cooled in an ice–salt bath to an internal temperature of 0°; 2 g of 2-phenylpropanal (14.9 mmol) dissolved in 10 ml of anhydrous ether was added at such a rate that the internal temperature did not exceed 5°. The solution was stirred for 15 min after the addition was complete at the ice–salt bath temperature. The bath was subsequently removed and the solution stirred at ambient temperature for an additional 105 min.

The solution was then cooled in an ice–salt bath and hydrolyzed with 30 ml of saturated $NaHCO_3$ solution at such a rate that the internal temperature did not exceed 10°. The layers were separated, the aqueous layer being extracted twice with ether. The ether layers were combined, dried over $MgSO_4$, and concentrated on a rotary evaporator at 25° or below, yielding 2.1 g of crude product. Glpc analysis of the crude product was carried out on FFAP as above.

Reaction of *in Situ* Dimethylzinc (Br, Br) with 2-Phenylpropanal.—The procedure followed was essentially that described for the reactions of *in situ* cadmium reagents. Glpc analysis of the crude reaction mixtures indicated that, in some instances a considerable amount of zinc salt was carried through the work-up procedure, as evidenced by the presence of variable amounts of olefin in addition to the expected threo and erythro alcohols. The per cent olefin increased unless the injector port of the chromatograph was cleaned regularly. The nmr spectrum gave no evidence of olefin in the samples prior to injection.

In cases where the presence of zinc salt was suspected, the crude product was taken up in benzene and a small amount of petroleum ether added until the solution became cloudy. The flask was cooled to 0° and allowed to stand for several minutes. Generally, a quantity of zinc salt settled out, and additional amounts of petroleum ether were added until no more solid separated. The salts were removed by filtration, the solution concentrated on a rotary evaporator, and the residue analyzed by glpc as outlined above. Values denoting the relative amounts of threo and erythro alcohols (Table II) were reproducible within ±1% and those of unchanged aldehyde within ±5% in separate reaction runs.

Control Experiment.—The individual *threo*- and *erythro*-3-phenyl-2-butanols were mixed with 1 molar equiv of 2-phenylpropanal and 2 molar equiv of dimethylzinc or dimethylcadmium under conditions similar to those described for the reaction of the *in situ* reagents. After hydrolysis and work-up, percentages obtained by glpc indicated no equilibration of diastereomers.

Preparation of 2-Phenyl-1-propanol.—Lithium aluminum hydride reduction of 2-phenylpropanal afforded 2-phenyl-1-propanol, which had a longer retention time on FFAP than either of the diastereomeric addition alcohols (**4a** and **4b**).

Preparation of 3-Phenyl-2-butanone.—Preparation of 3-phenyl-2-butanone was accomplished by CrO_3 oxidation in acetone solution of a crude mixture of the butanols obtained by the reaction of 2-phenyl-propanal with MeMgI. The ketone was not isolated from the reaction mixture, but the reaction was followed by nmr and glpc. The latter indicated that the ketone had a retention time on FFAP slightly longer than that of 2-phenylpropanal. For all experiments with dimethylcadmium and 2-phenylpropanal, 3-phenyl-2-butanone and 2-phenylbutanol (reduction product) constituted no more than 3% of the total product.

Registry No.—**1**, 93-53-8; **2**, 2439-43-2; **3**, 2439-44-3; 3-methyl-2-phenylbutanoic acid, 3508-94-9; methylmagnesium iodide, 917-64-6; methylmagnesium bromide, 75-16-1; dimethylcadmium, 506-82-1; methylcadmium bromide, 25837-91-6; methylcadmium iodide, 25837-90-5; dimethylzinc, 544-97-8; methylzinc iodide, 18815-73-1; methylzinc bromide, 18815-74-2.

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