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ASYMMETRIC INDUCTION—V

EFFECT OF R ON ASYMMETRIC INDUCTION IN ADDITIONS TO abcC-COR COMPOUNDS

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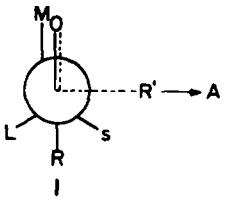
Abstract—The diastereomeric product ratios from reactions involving the addition of various reagents to the carbonyl of ϕCH_3HC–COR compounds varies over a wide range. This variation is interpreted as due partly to changes in the structure of the diastereomeric transition states with changes in the size of R. For example, when R is smaller than the ϕCH_3HC group the diastereomeric product ratios are close to those predicted on the assumption that 1 and 2 are the minimum energy diastereomeric transition states; and when R is larger than the ϕCH_3HC group, the diastereomeric product ratios are large and closer to those that one might expect if 5 and 6 were the minimum energy transition states.

In our model of asymmetric induction[1] structures 1 and 2 were chosen as the best representations of the two minimum energy transition states leading to diastereomers A and B. In both transition states the incoming group R′ is nearest the smallest group s. The diastereometric product ratio A/B was predicted from the relative magnitude of M ↔ O (1) vs L ↔ O (2) interactions.



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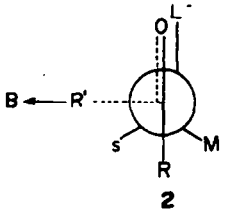

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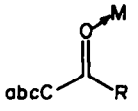
As pointed out[1] the model and the predicted A/B ratios may be meaningful only in those cases where the reagent coordinated to the oxygen has structure 3. If 4 were the structure, then the minimum energy transition states might very well be 5 and 6, i.e. those best represented by the conformations of *anti* isomers.[2] The model then would resemble that of Cram,[3] the diastereometric



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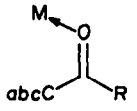

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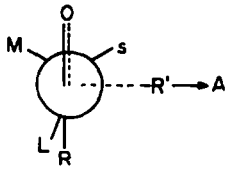
product ratio would be primarily controlled by the relative magnitudes of R ↔ s (5) vs R′ ↔ M (6) interactions, and would be expected to be substantially larger than that predicted by 1 vs 2.

The simplest way to test the validity of the above arguments is to compare results from compounds where 3 is more stable than 4 to those from compounds where 4



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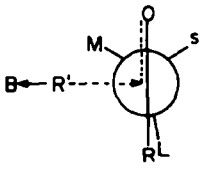

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is more stable than 3. Compounds falling in the latter category would be those in which the "effective" size of R is greater than that of abcC, such as where R is t-butyl.[2] In this paper we discuss the results obtained with compounds $C_6H_5(CH_3)CHCOR$, where R is neopentyl, isopropyl and t-butyl.

RESULTS AND DISCUSSION

In Table 1 are summarized the diastereomeric product ratios of the alcohols 10, 11, and 12 obtained from the reduction of ketones 7, 8, and 9 with LAH and the effect that temperature has on the ratio of these products.

$C_6H_5(CH_3)CHCOR$	$C_6H_5(CH_3)CH—CH(OH)R$
R, isopropyl 7	R, isopropyl 10
t-butyl 8	t-butyl 11
neopentyl 9	neopentyl 12

In all three cases the predominant diastereomer is the *threo* (RS and SR) alcohol. The following observations are pertinent to the discussion that will follow. In the reduction of 7 and 8 decrease of temperature favors slightly the formation of the predominant diastereomer; in contrast, in the reduction of 9 such decrease favors the minor diastereomer to the point that at −60° the value of the ratio of *threo*/*erythro* is less than one. The free energy differences between the two transition states leading to the products were calculated according to the Curtin–Hammett principle.[4] The experimental $\Delta\Delta G^{\neq}$

Table 1. Asymmetric reduction of $C_6H_5(CH_3)CHCOR$ with $LiAlH_4$ in ether. Effect of temperature

Ketone R	Temp., °C	Products %[a] RS(SR)	RR(SS)	$-\Delta\Delta G^{\neq}$ cal/mole	$-\Delta\Delta H^{\neq}$ cal/mole	$-\Delta\Delta S^{\neq}$ e.u.
$(CH_3)_2CH$	36	81.7	18.3	915 ± 50	192 ± 44	2.33
	0	82.6	17.4	842 ± 38		
	-10	82.1	17.9	790 ± 47		
	-41	83.1	16.9	731 ± 40		
$(CH_3)_3C$	35	97.0	3.0	2117 ± 50	2666 ± 55	-2.1
	10	97.3	2.7	2005 ± 45		
	0	98.0	2.0	2100 ± 50		
	-15	98.7	1.3	2203 ± 50		
	-40	99	1.0	2115 ± 50		
$(CH_3)_3CCH_2$[b]	35	56.0	44.0	150 ± 10	-260	1.4
	0	55.5	44.7	110 ± 8		
	-12	54.0	46.0	86 ± 12		
	-20	53.4	46.6	66 ± 6		
	-40	52.7	47.3	52 ± 6		
	-60	49.5	50.5	-8 ± 5		

a. Average values of 3-5 experiments.
b. Reduction of 9 with alkaline solution of $NaBH_4$ in isopropyl alcohol at 80° gave RS/RR-alcohols 55/45%.

values from the reduction of 8 are much higher than 600 cal/mole predicted by the model.[1] Those from the reduction of 7 are closer to 600 cal/mole but still higher. In both cases differences in entropy contribute to the differences of the free energy of activation. The reduction of 7 not only is controlled by both enthalpy and entropy, but the values of $\Delta\Delta G^{\neq}$ and $\Delta\Delta H^{\neq}$ have opposite signs.

In Table 2 are summarized the results from the addition of alkyl lithium compounds and phenyl lithium to 2-phenylpropanal in ether. Notice now that the $\Delta\Delta G^{\neq}$ values for the corresponding diastereomeric product alcohols are not much different from 600 cal/mole predicted by the model. Proof that the major diastereomers are the *erythro* alcohols (RR and SS configuration) is given below. From Table 2 it can also be seen that when hydrocarbons are used as solvents for the addition reactions the stereospecificity of the reductions decreases.

Table 2. Addition of organolithium compounds to 2-phenylpropanal

Reagent	Solvent	Temp, °C	Products %[a] (SS)RR	RS(RS)	$-\Delta\Delta G^{\neq}$ cal/mole
$(CH_3)_2CHLi$	ether	-54	87	13	810 ± 50
$(CH_3)_2CHLi$	pentane	0	80	20	750 ± 60
$(CH_3)_3CLi$	ether	-50	86	14	850 ± 45
$(CH_3)_3CLi$	pentane	-50	75	25	485 ± 45
$(CH_3)_3CLi$	pentane	0	74	26	565 ± 40
$(CH_3)_3CLi$	pentane	25	74	26	616 ± 45
$(CH_3)_3C\text{-}CH_2Li$	ether	0	77	23	580 ± 30
C_6H_5Li	ether	35	75	25	670 ± 30
C_6H_5Li	ether	0	84	16	894 ± 30
C_6H_5Li	benzene	35	75	25	670 ± 30
CH_3Li	ether	0	76	24	580 ± 40
CH_3Li	ether	35	74	26	640 ± 40

a. Average values of 3-4 experiments.

This is in general agreement with results obtained by other investigators.[5,6] In Table 3 are summarized the results of several reactions involving the addition of organolithium compounds to ketones 7, 8 and 9 (entries 1–12) along with the results of several of their complementary reactions (entries 13–19). Again, the results are similar to those summarized in Table 1, i.e. the reactions involving ketone 8 gave $\Delta\Delta G^{\neq}$ values close to 2000 cal/mole, those involving ketone 7 somewhat smaller but still considerably higher than 600 cal/mole predicted by the model, and all others closer to the predicted value.

The data presented in Tables 1–3 are consonant with the ideas discussed in the introduction of this paper, namely that 1 and 2 are fair representations of the two diastereomeric transition states only in cases where 3 is much more stable than 4; and that structures 5 and 6 may be better representations in cases where 4 is more stable than 3. Thus, when R is hydrogen and 3 is more stable than 4, the model[1] is successful, as born out by the data presented in Table 2 where the $\Delta\Delta G^{\neq}$ values are close to the 600 cal/mole value predicted by the model. Also, when R is methyl the model again enjoys a fair amount of success as shown by the data of Table 3 (entries 13 and 14) and previous data.[1] When R is t-butyl and, therefore, 4 is expected to be more stable than 3, then $\Delta\Delta G^{\neq}$ is very large (*ca.* 2000 cal/mole, Tables 1 and 3) as one would have expected if 5 and 6 were the two diastereomeric transition states. When R is isopropyl, in which case 3 and 4 are comparable in stability, then $\Delta\Delta G^{\neq}$ values fluctuate considerably. They are larger than the predicted 600 cal/mole value, but smaller than those obtained for the t-butyl cases. Again, the case involving the reduction of ketone 9 with lithium aluminum hydride (Table 1), where $\Delta\Delta H^{\neq}$ favors the "wrong" diastereomer cogently illustrates the point made previously, namely, that models for asymmetric induction should be used primarily as starting points for further experimentation.

The configurations of the diastereomeric alcohols 10 and 11 (*erythro* or *threo*) obtained in the various reactions were established by their synthesis via hydroboration of the corresponding trisubstituted ethylenes. According to Brown *et al.*[7] the hydroboration of *cis*-2-phenyl-4-methyl-2-pentene (13) and *trans*-2-phenyl-4-methyl-2-pentene (14) should yield as the major product the *erythro* (RR and SS) and the *threo* (RS and SR) 2-phenyl-4-methyl-3-pentanols (10), respectively. Similarly hydroboration of *cis*- or *trans*-2-phenyl-4,4-dimethyl-2-pentene (15 and 16) should give *erythro* (RR and SS) and *threo* (RS and SR) 2-phenyl-4,4-dimethyl-3-pentanol (11), respectively. The results along with those obtained from the hydroboration of *cis*- and *trans*-2-phenyl-2-pentene (17 and 18) and of *trans*-2-*p*-methoxyphenyl-2-butene (19), are summarized in Table 4.

Olefins 13 and 14 were prepared by dehydration of 2-phenyl-4-methyl-2-pentanol with *p*-toluenesulfonic acid. Olefins 15 and 16 were prepared by the thermal decomposition of the cyanomethyl xanthates[8] of the diastereomeric alcohols 11 by a Chugaev reaction, since attempts to prepare them by dehydration of 2-phenyl-4,4-dimethyl-2-pentanol with *p*-toluenesulfonic acid or

Table 3. Addition reactions of organolithium compounds to $C_6H_5(CH_3)CHCOR$ where R = $(CH_3)_2CH$, $(CH_3)_3C$, $(CH_3)_3CCH_2$, CH_3, C_6H_5

No	Ketone	Reagent	Solvent	Temp., °C	Products %[a] SR(RS)	RR(SS)	$-\Delta\Delta G^{\neq}$ cal/mole
1	$(CH_3)_3C$	CH_3Li	ether	0	98.0	2.0	2100 ± 150
2		CH_3Li	pentane	35	96.0	4.0	1900 ± 120
3		CH_3MgBr	ether	0	97.0	3.0	
4		$(CH_3)_2CHLi$	ether	-50	100	-	
5		$(CH_3)_2CHLi$	pentane	0	100	-	
6		C_6H_5Li	ether	0	-	100	
7		$(CD)_3CLi$	ether	0		100	
8	$(CH_3)_2CH$	CH_3Li[b]	ether	0	95.5	5.0	1580 ± 90
8		CH_3Li[b]	ether	-12	95.5	4.5	1570 ± 90
8		CH_3Li[b]	ether	-20	96.0	4.0	1580 ± 90
9		$(CH_3)_3CLi$	ether	-46	1.5	98.5	1900 ± 100
10		C_6H_5Li	ether	0	7.5	92.5	1400 ± 80
11	$Ph(CH_3)DCCOCD(CH_3)_2$	$(CH_3)_2CHLi$	ether	-32	96.0	4.0	
12	$(CH_3)_3C\text{-}CH_2$	C_6H_5Li[c]	ether	35	21.0	79.0	820 ± 45
12		C_6H_5Li[c]	ether	0	19.0	81.0	790 ± 50
12		C_6H_5Li[c]	ether	-30	16.0	84.0	800 ± 50
13	CH_3	$(CH_3)_2CHLi$	ether	-52	15.5	84.5	750 ± 50
14		$(CH_3)_3CLi$	pentane	4	17.0	83.0	880 ± 50
15	C_6H_5	$(CH_3)_2CHLi$	ether	-36	90.0	10.0	1040 ± 90
16		$(CH_3)_2CHLi$	pentane	36	77.5	22.5	760 ± 40
17		$(CH_3)_3CLi$	ether	-30	79.0	21.0	590 ± 40
18		$(CH_3)_3CLi$	pentane	0	80.0	20.0	750 ± 50
18		$(CH_3)_3CLi$	pentane	25	74.0	26.0	620 ± 40
19		$(CH_3)CCH_2Li$	ether	-36	80.0	20.0	

a. Average values of 2-4 experiments
b. Calculated $\Delta\Delta H^{\neq}$ = -1280 ± 85 cal/mole; $\Delta\Delta S^{\neq}$ = +1.09 e.u.
c. Calculated $\Delta\Delta H^{\neq}$ = -635 ± 40 cal/mole; $\Delta\Delta S^{\neq}$ = +0.6 e.u.

Table 4. Hydroboration of *cis-trans*-trisubstituted ethylenes

Compounds		Method	Alcohols	(%)[b]
Ph, isopropyl / Me, H	cis-13	A	erythro-10	84
			threo-10	8
		A	Carbinol[c]	8
Ph, isopropyl / Me, H	cis-13	B	erythro-10	88
			threo-10	3
			Carbinol[c]	9
Ph, H / Me, isopropyl	trans-14	A	threo-10	85
			erythro-10	6
			Carbinol[c]	9
Ph, H / Me, isopropyl	trans-14	B	threo-10	87
			erythro-10	3
			Carbinol[c]	10
Ph, t-butyl / Me, H	cis-15	A	erythro-11	88
			threo-11	3
			Carbinol[d]	9
Ph, H / Me, t-butyl	trans-16	A	threo-11	70
			erythro-11	10
			Carbinol[d]	20
Ph, ethyl / Me, H	cis-17	A	erythro	85
			threo	4
			Carbinol[e]	11
Ph, ethyl / Me, H	cis-17	B	erythro	87
			threo	3
			Carbinol[e]	10
Ph, H / Me, ethyl	trans-18	A	threo	86
			erythro	6
			Carbinol[e]	8
Ph, H / Me, ethyl	trans-18	B	threo	88
			erythro	4
			Carbinol[e]	8
p-$CH_3OC_6H_4$, Me / Me, H	trans-19	A	erythro	96
			threo	4
p-$CH_3OC_6H_4$, Me / Me, H	trans-19	B	erythro	97
			threo	3

a. Method A: Diborane prepared in the generator and bubbled through the solution of olefin in THF. Method B: Diborane prepared in situ.
b. The values are averages from 2-4 runs.
c. 2-phenyl-4-methyl-2-pentanol.
d. 2-phenyl-4,4-dimethyl-2-pentanol.
e. 2-phenyl-2-pentanol.

oxalylchloride gave as the main product 2-phenyl-4,4-dimethyl-1-pentene and only small amounts of the *cis* and *trans*-2-pentenes. All the olefins were isolated by gas chromatography and characterized by their NMR and UV spectra. Similarly, all product alcohols (Table 4) were isolated and purified by gas chromatography and characterized by NMR. It is worth noting that in all cases except that of **19**, the regiospecificity of the reaction is less than 100%. In addition to the expected diastereomeric alcohol from the *cis*-addition of water small amounts (about 10%) of the regioisomers were detected by gas chromatography. Furthermore, the stereospecificity of the reaction is less than 100% as evidenced by the formation of 3–10% of the isomer resulting from *trans*-addition.

We found that the *threo*-alcohols have shorter retention times on Carbowax or Apiezon Columns, presumably because of intramolecular hydrogen bonding as previously observed by Gault and Felkin.[9] We also found that the proton chemical shifts of the isopropyl and the t-butyl groups of the *erythro*-diastereomers of **10** and **11** appear at higher fields than those of the *threo*-diastereomers. The chemical shift difference ($\Delta\tau$) between the *erythro* and *threo* diastereomers are 0.09 ppm for the t-butyl groups of **11** and 0.05 ppm for the isopropyl groups of **10**. These observations were used to establish the configuration of the diastereomeric alcohols **12**. The isomer which appeared first on the Carbowax column and whose proton chemical shift of the t-butyl group at $\tau = 9.05$ is lower than that of the other isomer ($\tau = 9.10$) was given the *threo* configuration. Consonant with this reasoning is the finding that the major diastereomer (77%) obtained from the addition of the neopentyl lithium to 2-phenylpropanal and predicted by the model to be the *erythro* isomer, appears second on the carbowax column and its t-butyl groups absorbs at $\tau =$ 9.10. The same reasoning, i.e. retention times on G.C. columns and chemical shift differences, were used to establish the configuration of the other carbinols listed in Table 3.

EXPERIMENTAL

Diastereomeric alcohols and olefins were separated with a thermal conductivity Varian aerograph Model 90-A and their percentages were calculated by comparison with standard compounds. The NMR spectra were taken with a Varian A-60 spectrometer. The UV spectra were recorded with a Cary-15 spectrophotometer and refractive indices were measured with a Baush and Lomb, Abbe-3L Refractometer. High resolution mass spectra of new compounds were taken with an RMU-6 spectrometer.

Organolithium reagents

The organolithium compounds were prepared by addition of alkyl and aryl halide into Li shot[11] under vigorous stirring and in an Argon atmosphere. Methyl iodide, ethyl bromide, isopropyl chloride, t-butyl chloride, neopentyl chloride and bromobenzene were purified by distillation prior of use. The addition was done at −30° for the branched alkyl halides and at 0° for methyl iodide and bromobenzene. The molarity of the organolithium solutions was determined by titration.[12]

Preparation of diastereomeric alcohols **10, 11, 12**

To a suspension of the appropriate organolithium reagent (isopropyllithium for **10**, t-butyllithium for **11** and neopenthyllithium for **12**) in ether or pentane was added a solution of 2-phenylpropanal in ether or pentane at constant temperature controlled by an ultra Kryostat K-75 DW Lauda. Temperatures were measured with calibrated iron-constantan thermocouples and low temp. thermometers immersed in the reaction mixture. Temperatures were controlled to within ±2–3°. The ratio of reagents used was 1.2–1.3 organolithium compound to 2-phenylpropanal. After completion of the reaction, the mixture was hydrolysed by dropwise addition of 10% ammonium chloride soln at 0° and the organic material was extracted with ether. The etherial soln was washed with water, dried over $MgSO_4$, and the solvent was removed by evaporation. The ratios of diastereomeric alcohols were determined by gas chromatography before and after distillation of the residue. No differences in the diastereomeric product ratios were found. The yields of the reactions were 70–95%. The columns used for the separation of the diastereomers of these as well as of those of other alcohols and olefins used in this study were: Carbowax 20M, 20% on Chromosorb W (column A); Apiezon-L, 6% on Chromosorb W or P (column B); FFAP 20% on Chromosorb W (column C). In all cases He was the carrier gas.

Properties of alcohols **10, 11, 12**

(a) *2-Phenyl-4-methyl-3-pentanols*, **10**.[13] The ratio of retention time of *erythro/threo* isomers was found to be 1.23 on column A at 150° and 1.1 on column B at 110°; $n_{25} = 1.5073$ for *erythro*-**10**; $n_{25} = 1.5085$ for *threo*-**10**. The pertinent NMR absorptions are: *erythro*-**10** in benzene: $\tau = 9.15$ with $J = 6$ Hz (i-Pr quartet); $\tau = 8.73$ with $J = 7$ Hz (Me doublet); *threo*-**10** in benzene: $\tau = 9.04$ (i-Pr quartet), $\tau = 8.85$ (Me doublet).

(b) *2-Phenyl-4,4-dimethyl-3-pentanols*, **11**.[13] The ratio of retention time of *erythro/threo* isomer was found to be 1.33 on column A at 180° and 1.22 on column B at 145°. *Erythro*-**11**, $n_{26} = 1.5201$; *threo*-**11**, $n_{26} = 1.5210$. The pertinent proton absorptions in CCl_4 are: *erythro*-**11**: $\tau = 9.20$ (t-Bu group); $\tau = 8.66$ with $J = 7$ Hz (methyl doublet); $\tau = 7.06$ (multiplet of C_4–H) and $\tau = 6.87$ with $J = 3.75$ Hz (doublet of C_3–H). *Threo*-**11**: $\tau = 9.12$ (t-Bu group); $\tau = 8.78$ with $J = 7$ Hz (Me doublet); $\tau = 7.15$ (multiplet of C_4–H); $\tau = 6.75$ with $J = 3.9$ Hz (doublet C_3–H).

(c) *2-Phenyl-5,5-dimethyl-3-hexanols*, **12**. The ratio of retention time of *erythro/threo* isomer was found to be 1.1 on column C at 125°. The pertinent proton absorptions in CCl_4 are: $\tau = 9.10$ and $\tau = 9.05$ for the t-butyl groups for the *erythro*-**12** and *threo*-**12**, respectively; and $\tau = 8.73$ and $\tau = 8.85$ for the methyl doublets respectively.

Preparation of ketones **7, 8, 9**

Ketones **7**, **8** and **9** were prepared by oxidation of the corresponding diastereomeric alcohols **10**, **11** or **12** (0.05 mole) with a soln containing sodium dichromate (0.04 mole) and sulfuric acid (0.1 mole) at 55° for 5–4 hr.[14] The ketones were purified by fractional distillation and gas chromatography and identified by NMR. Their pertinent absorptions were: 2-phenyl-4-methyl-3-pentanone, **7**: $\tau = 9.14$ and 8.98 (i-Pr doublets); $\tau = 8.65$ (Me doublet). 2-Phenyl-4,4-dimethyl-3-pentanone, **8**: $\tau = 8.98$ (t-Bu group); $\tau = 8.72$ (Me doublet); and $\tau = 5.76$ (methine proton). 2-Phenyl-5,5-dimethyl-3-hexanone **9**: $\tau = 9.06$ (t-Bu group); $\tau = 8.67$ (Me doublet); $\tau = 7.75$ (methylene singlet, broad); and $\tau = 6.29$ (methine quartet).

Reduction of ketones **7, 8, 9** *with LAH in ether*

A soln of ketone (10 mmoles in 50 ml of ether was added dropwise to a soln of LAH (5 mmoles) in 200 ml of ether at constant temp. and under an atmosphere of He and vigorous stirring. The mixture was hydrolysed by addition of water followed by addition of NaOH aq at 0°. The mixture of alcohols was purified by distillation, gas chromatography and characterized by NMR.

Carbinols prepared from the addition of organolithium compounds to ketones **7, 8, 9**, *3-phenyl-2-butanone, and 2-phenylpropiophenone*

(a) *2-Phenyl-3,4-dimethyl-3-pentanol.* The *threo* isomer was obtained as the major isomer from the addition of MeLi to **7**. The *erythro* isomer was obtained as the major isomer from the addition of i-PrLi to 3-phenyl-2-butanone. The ratio of retention time of *erythro/threo* was found to be 1.14 on column A at 190°. *Threo*-isomer: $\tau = 9.17$ and 9.14 (i-Pr doublets); $\tau = 8.78$ (C-1 Me doublet); and $\tau = 9.04$ (C-3 Me). *Erythro*-isomer: $\tau = 9.11$ and $\tau = 9.04$ (i-Pr doublets); $\tau = 8.75$ (C-1 Me doublet); and $\tau = 9.22$ (C-3 Me).

(b) *2-Phenyl-3-t-butyl-4-methyl-3-pentanol.* The *erythro*-isomer was obtained as the major isomer by the addition of t-BuLi to **7**; and the *threo* by the addition of i-PrLi to **8**. NMR spectra in pyridine: *Erythro*-isomer: $\tau = 8.74$ (t-Bu); $\tau = 9.11$ and $\tau = 8.89$ (i-Pr doublets); and $\tau = 8.46$ (Me doublet). *Threo*-isomer: $\tau = 9.0$ (t-Bu); $\tau = 8.78$ and $\tau = 8.71$ (i-Pr doublets); and $\tau = 8.56$ (Me doublets).

(c) *2,3-Diphenyl-4-methyl-3-pentanol.* The *erythro* isomer was obtained as the major isomer by addition of phenyllithium to **7**; and the *threo* by addition of i-PrLi to 2-phenylpropiophenone. The ratio of retention time *erythro/threo* isomers was found to be 1.11 on column B at 150°. NMR spectra in CCl_4: *Erythro* isomer: $\tau = 9.20$ (i-Pr); and $\tau = 8.89$ (Me). *Threo*: $\tau = 9.12$ (i-Pr); and $\tau = 8.67$ (Me).

(d) *2-Phenyl-4-methyl-2,4-dideutereo-3-pentanol.* This alcohol was prepared by addition of i-PrLi to 2-phenyl-4-methyl-2,4-dieutereo-3-pentanone. This ketone was prepared by exchange of the protons of **7** in D_2O under mild alkaline conditions. The NMR spectrum showed protons at $\tau = 9.13$ (s) and 8.98 (s) for the i-Pr groups and $\tau = 8.65$ (s) for the Me group. The NMR spectrum of the carbinol in CCl_4 showed proton absorptions at $\tau = 8.7$ (s) for the Me; $\tau = 9.19$ and 9.07 (singlets for the Me_2CD); and $\tau = 8.97$ and 8.95 (doublets for the Me_2CH group).

(e) *2-Phenyl-3,4,4-trimethyl-3-pentanol.* This alcohol was prepared by the addition of MeLi to **8** in ether or pentane. The ratio of retention time of the *erythro/threo* isomer was found to be 1.27 on column A at 165°. The major isomer (98%) was the *threo*, whose NMR spectrum showed: $\tau = 9.0$ (t-Bu); $\tau = 8.94$ and 8.71 (Me's). The *erythro* isomer, prepared by addition of t-BuLi to 3-phenyl-2-butanone, showed absorptions at $\tau = 9.15$ (t-Bu); $\tau = 8.97$ and 8.68 (Me's).

(f) *2,3-Diphenyl-4,4-dimethyl-3-pentanol.* This alcohol was prepared by the addition of PhLi to **8**. The *erythro* isomer was purified by distillation and showed absorptions at $\tau = 9.33$ (t-Bu); and $\tau = 9.04$ (methyl-1). The *threo*-isomer was obtained by addition of t-BuLi to 2-phenylpropiophenone and purified by gas chromatography. The ratio of retention time was 1.27 on column A at 210°. The NMR spectra showed $\tau = 8.96$ (t-Bu); and $\tau = 8.47$ (Me-C-1).

(g) *2-Phenyl-4,4-dimethyl-3-t-butyl-3-pentanol.* This alcohol was prepared by the addition of t-BuLi to **8** and purified by distillation and gas chromatography on column A. The NMR showed two singlets at $\tau = 8.92$ and 8.74 for the t-Bu and a

doublet at $\tau = 8.34$ for the methyl-1. The carbinol with t-Bu-d_9 was prepared by addition of t-butyl-d_9-lithium to 8, and purified by gas chromatography. It showed only the singlet at $\tau = 8.74$ and the Me-1 doublet at $\tau = 8.34$.

(h) *2,3-Diphenyl-5,5-dimethyl-3-hexanol.* This alcohol, in *erythro/threo* ratio of 4/1, was prepared by the addition of PhLi to 9. The NMR spectrum showed $\tau = 9.40$ (s) and $\tau = 9.27$ (s) for the t-Bu groups of the *erythro* and *threo* respectively; $\tau = 9.04$ (doublet) for the Me-1 of both isomers (no resolution for the two diastereomers in pyridine, CCl_4 and other solvents); and $\tau = 8.32$ for the slightly separated quarters of the methylene protons of the two isomers. The *threo* isomer was obtained as the major isomer (80%) from the addition of neopentyllithium to 2-phenyl-propiophenone.

Preparation of 2-phenyl-4-methyl-2-pentenes[15]

Dehydration of 2-phenyl-4-methyl-2-pentanol, which was prepared by the addition of isobutyllithium to acetophenone with p-toluenesulfonic acid in benzene (reflux) gave a mixture of olefins which were isolated on a preparative Column Carbowax 20M, 25% on chromosorb W, 10 feet and 3/8". Yield: 22% *cis*-2-pentene (13), 70% *trans*-2-olefin (14) and 8% 1-olefin. The retention times at 175° and 28 psi He were: 6, 9.6 and 11.6 min for 13, 1-olefin and 14, respectively; $n_{27} = 1.5013$ for 13, $n_{25} = 1.5186$ for 14, and $n_{25} = 1.5901$ for 1-olefin; ϵ_{max} at 245 mμ = 13.500 for *trans*-2-olefin and ϵ_{max} at 232 mμ = 6600 for *cis*-2-olefin.[16] The pertinent NMR absorptions of 13 and 14, respectively, were: i-Pr (doublet) at $\tau = 9.09$ and 8.96; Me (doublet) at $\tau = 8.04$ and 8.00 ($J_{H-CH_3} = 1.4$ and 1.3 Hz); and vinylic protons at $\tau = 4.77$ and 4.63 ($J_{H-H} = 10.25$ and 9.25 Hz). The NMR spectrum of 1-pentene showed: i-Pr (doublet) at $\tau = 9.13$; methylene (doublet) at $\tau = 7.64$; and vinylic protons at $\tau = 4.8$ and 5.03.[17]

Preparation of 2-phenyl-4,4-dimethyl-2-pentenes

A 1/3 mixture of *erythro/threo* alcohol was converted to the cyanomethyl xanthates.[8] Thermal decomposition of the xanthates at 140° yielded after distillation 80% of olefins. These were separated on a Carbowax column and gave 50% *cis*-2-olefin, 22% *trans*-2-olefin and 27% 1-olefin. The retention times at 175° and 30 psi were 6.25, 9.2 and 15.5 min for 15, 1-olefin and 16 respectively. $n_{27} = 1.4960$ for 15, $n_{27} = 1.5152$ for 16 and $n_{25} = 1.5054$ for 1-olefin: ϵ_{max} at 238 mμ = 11.900 for *trans* and ϵ_{max} at 222 mμ = 4.200 for the *cis*. The pertinent NMR absorptions of 15 and 16 in chloroform-d were: $\tau = 9.13$ and 8.8 (t-Bu singlets); $\tau = 8.08$ and 7.92 (Me doublets with $J_{H-CH_3} = 1.5$ and 1.36 Hz); and $\tau = 4.58$ and 4.33 (vinyl quartets). The NMR of the 1-olefin showed absorptions at $\tau = 9.19$ (t-Bu); $\tau = 7.55$ (methylene, broad); and $\tau = 4.80$ and 5.03 (vinyl doublets).

Preparation of 2-phenyl-2-pentenes (cis-17 *and* trans-18)[17]

These olefins were prepared by dehydration of 2-phenyl-2-pentanol with p-toluenesulfonic acid. The yield was 72% *trans*-18, 23% *cis*-17 and 5% 2-phenyl-1-pentene. They were separated on a FFAP 20% on Chromosorb W column and characterized by their NMR spectra. *cis*-17: $\tau = 8.0$ (Me-C-1 doublet with $J_{CH_3-H} = 1.44$ Hz); $\tau = 9.07$ (Me-C-5 triplet with $J_{CH_3-CH} = 7$ Hz); and $\tau = 4.6$ (vinyl proton, multiplet). *trans*-18: $\tau = 8.0$ (Me C-1 doublet with $J_{CH_3-H} = 1.36$ Hz); $\tau = 8.97$ (Me C-5 triplet with $J_{CH_3-CH_2} = 7$ Hz); $\tau = 7.84$ (methylene quartet, C-4); and $\tau = 4.3$ (vinyl proton, multiplet). 2-Phenyl-pentene-1: $\tau = 9.03$ (triplet, Me-5); $\tau = 8.59$ methylene C-4, multiplet); $\tau = 7.52$ (methylene C-3, multiplet); and $\tau = 4.8$ and 5.03 for vinylic gem-protons.

Preparation of trans-*2-p-methoxyphenyl-2-butene*

This olefin was prepared according to Winstein *et al.*[19] It had the following NMR in $CDCl_3$: $\tau = 8.42$ and 8.36 (Me C-4 doublet with $J = 7$ Hz); $\tau = 8.00$ (Me C-1 doublet with $J = 1.5$ Hz); $\tau = 5.6$ (vinyl quartet with J's 1.5 and 7 Hz); $\tau = 6.2$ (*p*-OMe group); and $\tau = 3.0$ (aromatic proton quartet).

Hydroboration of olefins

The olefins were hydroborated according to the methods described by Brown.[7] Diglyme and THF were purified and were free from peroxides. Two different methods were used for the hydroboration. In method A a 2- to 4-fold excess of gas diborane (prepared from the reaction of solns of $NaBH_4$ and BF_3 etherate in diglyme) was introduced into the soln of olefins in THF at 0°. In method B, the diborane was generated *in situ*. The excess diborane was hydrolysed with ice and 3M NaOH and the organoborate was oxidized by alkaline sodium peroxide. The yield of alcohols was 65–80% by method A and 95% by method B. The products were characterized by gas chromatography and NMR. In all cases the expected major diastereomer from *cis*-addition was contaminated with small amounts of the other diastereomers and the regioisomer as shown in Table 4. Alcohols 10 and 11 and their corresponding regioisomers were separated on 6% Apiezon-L columns 6 ft 1/8 in. The retention times at 110° and 45 psi He for the 2-phenyl-4-methyl-2-pentanol, *erythro*-10 and *threo*-10 were 33.6, 41.0 and 45.0 min, respectively. The retention times at 145° and 45 psi He for 2-phenyl-4,4-dimethyl-2-pentanol, *threo*-11 and *erythro*-11 were 12.6, 14.8 and 18.0 min. Authentic 2-phenyl-4,4-dimethyl-2-pentanol, was prepared by addition of neopenthyllithium to acetophenone. The percentages of *threo* and *erythro*-2-phenyl-3-pentanol obtained from the hydroboration of *trans* and *cis*-2-phenyl-2-pentenes and the 2-phenyl-2-pentanol were estimated by using a combination of columns: Apiezon L, and butanediol siccinate on Chromosorb W. The 3-*p*-methoxyphenyl-2-butanols obtained from the hydroboration of *trans*-19 were separated on a Carbowax Column and characterized by NMR.

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