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ASYMMETRIC SYNTHESIS AND CONFORMATION

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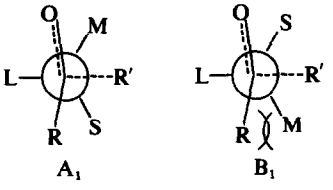
Abstract—The configuration of the 3-alkyl substituted 1,2,3-triphenyl-1-propanones is proved through use of pseudocontact shifts using $Eu(dpm)_3$. The conformation of all isomers, regardless of size of R, is similar (*trans* vicinal protons). The relative stability of the two isomers is also independent of R up to R = t-Bu. The conformation and configuration of the hydride reduction products, the alkyl substituted 1,2,3-triphenyl-1-propanols, are elucidated through use of NMR chemical shifts, coupling constants, pseudocontact shifts, and by IR spectra. The starting materials and reduction products (with one exception) have the same conformation at relevant centers, yet the mode of hydride attack is best explained by means of a different conformation in the transition state, in which the LAH approaches over a proton at either asymmetric center.

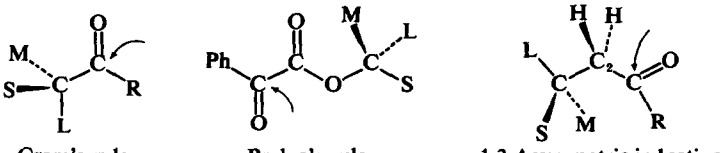
The stereoselectivity of hydride reductions or of Grignard additions to carbonyl compounds which contain an asymmetric center led to the formulation of Cram's Rule[1] and Prelog's Rule[2] (Scheme I). These rules emphasized the effective size of the groups substituted at asymmetric carbon as the determinative factor governing the approach of the reagent.[3] Cram *et al* also emphasized the fact that CO oxygen assumes a partial negative charge in the transition state, and this oxygen becomes rather highly space demanding because of co-ordination with metal ion and solvent. The CO then prefers an open conformation. Later work by Cornforth *et al* elucidated the effect of dipolar groups on the course of the reaction.[4] Cram and Kopecky studied the effects of co-ordinating substituents at the asymmetric center.[5] Recently Leitereg and Cram formulated a rule for 1,3 asymmetric induction (Scheme I) for Grignard additions to ketones.[6] In studies of 1,3-asymmetric induction in hydride reduction of certain ketones, Brienne *et al* found very small degrees of asymmetric induction where C_2 (Scheme I) unsubstituted, but substantial asymmetric induction where C_2 was doubly substituted by Me or Ph groups.[7].

Certain discrepancies prompted a re-examination of the basis for 1,2 asymmetric induction by Karabatsos,[8] and by Cherest *et al*.[9] Karabatsos suggested an improved model in which the lowest energy transition state has the reagent approaching over the smallest group. Unlike Cram's rule, this model utilizes a conformation that is consistent with the known conformational preferences of CO groups,[10] namely one in which the medium sized group (M) or the large group (L) is eclipsed with CO, most likely M. The lack of relevance of the ground state conformation, other than as a predictive device, has been pointed out by a number of workers on the basis of the Curtin-Hammett principle.[11] Karabatsos, however, considers the transition state conformation to be similar to that of the ground state. Cherest, *et al* agree that the transition state is essentially "reactant like" but consider bond making sufficiently advanced that torsional strains of the partially formed bond are important. These workers favor the models shown in Scheme II and consider the effect of the size of R especially important since the steric interference shown in B_1



A_1 B_1

SCHEME II



Cram's rule Prelog's rule 1,3 Asymmetric induction

SCHEME I

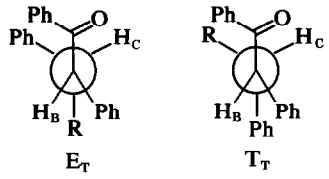
leads to a preference for A_1. The steric interaction of R′ and R is also considered important.

The most significant recent advance in asymmetric induction studies has been the linear free energy approach of Ugi and Ruch.[12] This work considers any group of three substituents at asymmetric carbon as a chiral unit, capable of inducing a certain degree of asymmetry at the reaction site. In this approach it is not necessary to consider any particular ground state conformation. Regretably, this approach has not been successfully applied to 1,2-asymmetric induction.

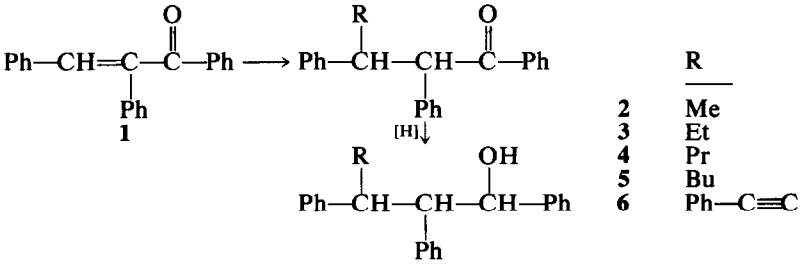
The purpose of this work was to study 1,2 *vs* 1,3 asymmetric induction in the reduction of the isomeric ketones **2–5**, as a function of the size of R (eq. 1 and Table 1).

Although the ketones **2–5** are in one sense quite complex, considerable data are easily obtained on the preferred conformations not only of starting materials, but also of products.

The NMR spectra of the ketones **2–6** were characterized by high J values (Table 1) indicative of a strong preference for a conformer having *trans* vicinal protons for both *erythro* and *threo* isomers.[13,14] The apparent conformational purity was not grossly sensitive to the size of R.[15] The preference for *trans* conformers (Scheme III) follows the

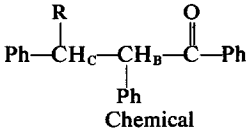


SCHEME III



(eq 1)

Table 1. 60 MHz NMR parameters and percentages of the isomers under equilibration conditions of ketones **2–6**



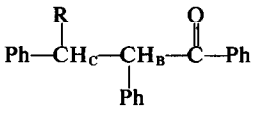
		R	mp	Chemical shift[a] (ppm) δC	δB	J_{BC}(Hz)	Percentage at equilibrium[d]
2	*threo*	Me	101°	3·63	4·58	10·6	33[g]
	erythro		186	3·63	4·68	10·5	67[g]
3	*threo*	Et	91	3·42	4·67	10·9	38
	erythro		170	3·38	4·76	10·9	62
4	*threo*	i—Pr	143	3·75	5·20	11·2	37
	erythro		189	3·67	5·30	11·2	63
5	*threo*[b]	t-Bu	217	4·01	5·15	10·4	61
	erythro[b]		170	3·55	5·31	11·6	39
6	*threo*[e]	Ph—C≡C—	154	4·86	4·86	10·5[h]	dec[c]
	erythro[e]		151	4·63	4·90	10·4	dec

[a] 15% w/v solutions in carbon tetrachloride unless otherwise noted.
[b] 10% w/v solution in deuterochloroform.
[c] Decomposed under basic conditions.
[d] Equilibration, in 40% methanol–60% DMSO, 0·4M. in $NaOCH_3$, was approached from both directions. These data are considered good to ± 5%. Temp was 28 ± 4° except for **5** (65°).
[e] Configuration uncertain.
[g] In fair agreement with Zimmerman and Chang[19] who gave an equilibrium ratio of 59% *erythro* and 41% *threo* **2**.
[h] Determined in the presence of pyridine.

now familiar pattern in molecules having Ph or CO groups in which two sets of *gauche* interactions exist, each set being separated by protons.[14] The similarity of the R=t-Bu compound **5** to **2–4** was rather unusual since many t-Bu compounds show very low coupling constants.[16–18]

The configuration of the isomers of ketone **2** (R=Me) was proved by Zimmerman and Chang.[19] Additional evidence was obtained by observation of the downfield nmr pseudocontact shifts.[20–21] Molecular models suggested that in conformer T_T (*threo* isomer, *trans* protons, as in Scheme III) the CO oxygen is quite close in space to the R group. Since the pseudo-contact shift depends upon the cube of the distance from the group in question to Europium,[20] which is complexed to oxygen, a much larger shift is expected for the *threo* isomer than for the *erythro* in which R is remote from oxygen.* For **2**, a much larger shift for the *threo* isomer (as indicated by Zimmerman) was indeed obtained ($\Delta\delta_R$, Table 2). For **4** and **5**, the isomer that gave the largest shift for R was also assigned the *threo* configuration. As Table 1 shows, the configuration assignments are consistent with chemical shift data; for the *threo* isomers H_C is found at lower field and H_B occurs at higher field than for *erythro* isomers. The anisotropy of the acetylene group renders the assignment for **6** uncertain. For compounds with relatively low steric hindrance, **2–4**, the rather common observation is upheld such that conformers with *trans* Ph groups (as in E_T) show complex Ph multiplets, whereas conformers with *gauche* Ph groups (as in T_T) many times show "singlet" phenyl resonances.[13] Molecular models indicate that the CO group in both E_T and T_T lies close in space to H_C. The data of Table 2 show that the pseudocontact shift for H_C is consistently larger than that for H_B, although the latter is separated from CO by fewer bonds. The term $\Delta\delta_C/\Delta\delta_B$ was calculated to minimize the effects of different degrees of complexing. This term (*ca* 1·7) is relatively insensitive to the size of R or to isomer.

Table 2. Pseudocontact shifts in **2**, **4**, and **5** at 100 MHz[a] using $Eu(dpm)_3$



Substrate		R	$\Delta\delta_C^a$ (Hz)	$\Delta\delta_B$	$\Delta\delta_R$	$\frac{\Delta\delta_C}{\Delta\delta_B}$	$\frac{\Delta\delta_R}{\Delta\delta_B}$
2	*threo*	Me	63	46	30	1·4	0·64
	erythro		66	40	15	1·7	0·36
4	*threo*	i-Rr	99	62	76[b]22[c]8[c]	1·6	1·2[b]
	erythro		59	36	18[b]11[c]6[c]	1·6	0·50[b]
5	*threo*	t-Bu	54	33	12	1·6	0·37
	erythro		23	15	1	1·8	0·05

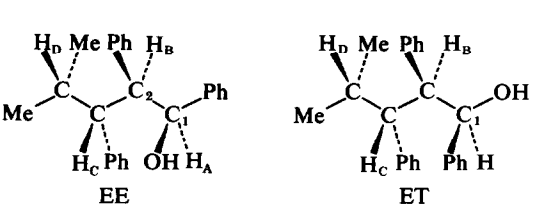
[a]$\Delta\delta_C$ signifies the difference in chemical shift of the proton in question in the presence and in the absence of $Eu(dpm)_3$. For **2** and **4** the $CDCl_3$ solutions were 0·076M in substrate. For **5**, the solutions were 0·038M. All solutions were 0·0286M in $Eu(dpm)_3$ where this was used.

[b]Isopropyl methine shift.

[c]Shift of the methyls, assuming no crossover of resonances.

[d]Using an XL-100 instrument at 500 Hz width with frequency counter calibration of resonances.

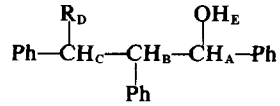
The ketones **2–4** were reduced to alcohols under various conditions. An attempt was made to characterize those products from reaction of ketones **4** and **2**. The NMR parameters and configurational assignments are listed in Table 3. The reduction products of *erythro* **4** (**11** and **12**) differ in their configuration with respect to C_1—C_2. Both have a large J_{BC} and a small J_{AB}. This suggests *trans* and *gauche* sets of protons respectively, as shown in the conformers of Scheme IV in which 1,3 interactions are minimized.[23]



SCHEME IV

*An angular dependence of the pseudocontact shift is also important.[22] However, it was difficult to ascertain from molecular models of **2–5** and **15–18** which of several orientations of Europium complexed to oxygen would be the more important. The pseudocontact shifts are probably the average overa variety of Eu—O—C angles. We also did not notice any major change in the coupling constants of complexed compounds compared to uncomplexed species.

Table 3. NMR parameters[a] of the isomeric alkyl substituted 1,2,3-triphenylpropanols at 60 MHz.



Starting ketone	Compound, R	Configuration	mp	Chemical shift (ppm) δA	δB	δC	J_{AB}	J_{BC}	J_{CD}	Other
erythro **2**	**7**, Me	EE	108°	4·50	2·77	3·41	3·0	10·9		
	8, Me[b,e]	ET	oil	4·83	*ca* 3·3	*ca* 3·3	*ca* 6·8[d]	*ca* 8·4[d]		
threo **2**	**9**, Me	TE	95°	5·10	2·92	3·31	4·8	9·2		
	10[c], Me[b,c]	TT	oil	4·70	*ca* 3·8	*ca* 3·5	10·0[d]	4·8[d]		
erythro **4**	**11**, i-Pr	EE	160°	4·63	3·17	3·47	2·4	12·3	3·6	J_{AE} = 5·8[d]
	12, i-Pr	ET	123	4·72	3·66	2·79	4·2	11·9	3·8	
threo **4**	**13**, i-Pr	TE	78°	5·03	3·44	2·97	5·5	8·2	6·3	
	14, i-Pr	TT	oil	4·62	3·57	3·30	9·9	4·2	10·0	

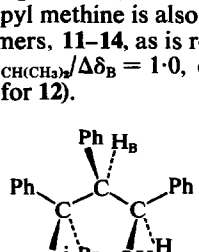
[a]All solutions *ca* 10% w/v in CCl_4.
[b]Nearly superposed resonances prevented obtainment of accurate values.
[c]Separation from **13** was impossible. These nmr data were taken from a mixture of **13** and **14**.
[d]Obtained using a 100 MHz instrument.
[e]A considerable change in these parameters did not alter the appearance of the simulated spectrum. These values should be regarded as approximate.

In isomer ET, H_C lies over the face of the C_1 Ph group and should be shielded by the aromatic ring current by *ca* 0·5 ppm.[24] This expectation is met for **12** (δ_C = 2·8 ppm) and not for **11** (δ_C = 3·45 ppm). Thus **11** is assigned the EE (*erythro-erythro*) configuration and **12** the ET configuration. To verify this assignment, the ratio of the pseudocontact shifts was determined for protons B and C. In EE, H_C is near in space to the hydroxyl and H_B is comparatively remote. For ET the opposite is the case. For **11** a very large ratio, $\Delta\delta_C/\Delta\delta_B$ = 2·0 was observed, whereas for **12** a small ratio was found, $\Delta\delta_C/\Delta\delta_B$ = 0·38, consistent with the previous assignment.

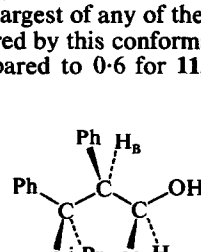
The configurations of the alcohols derived from *threo* **4** are more difficult to assign since the conformations of the two isomers are grossly different. For **13** predominantly *gauche* protons A and B, and *trans* protons B and C are evident which suggests one of the structures in Scheme V. The relatively high pseudocontact shift for H_C and the low shift for H_B ($\Delta\delta_C/\Delta\delta_B$ = 1·7) suggest that **13** has the TE configuration (conformer 1). The shift for the isopropyl methine is also the largest of any of the four isomers, **11–14**, as is required by this conformation ($\Delta\delta_{CH(CH_3)_2}/\Delta\delta_B$ = 1·0, compared to 0·6 for **11**, and 0·2 for **12**).

For **14**, the large J_{AB} and the small J_{BC} suggest a preference for conformer 2 of the TT configuration. If **14** were conformer 2 of the TE configuration, H_C would have been shielded by the C_1 Ph group; the data of Table 3 indicate the opposite. The configurations of the reduction products of **2** and **3** are assigned by analogy to **11–14**. The similarity in chemical shift of corresponding products is evident upon inspection of the data of Table 3.

The IR data are also consistent with the above assignments of configuration.[25–28] In most cases two major peaks were observed in the OH region: for **11**, 3612 cm^{-1} (s) and 3565 (w); for **12**, 3610 (s) and 3580 (m); and for **13**, 3614 (s) and 3580 (m). The high frequency peak is due to an OH group weakly interacting with a pi system.[26] The less intense, lower frequency peak (*ca* 3580) results from a stronger OH-pi interaction.[26] The similarity of the spectra of **12** and **13** suggest that the 3580 cm^{-1} peak results from a OH-C_2 phenyl interaction and not a OH-C_3 phenyl interaction. The C_3 Ph is distant from OH in **12**, but not in **13**. However, for **14**, only a single, rather broad OH absorption is noted at 3602 cm^{-1}. An important feature of the spectrum of **14** was the lack of 3580 cm^{-1} peak. In the major conformer of **14**, the OH is *trans* to the C_2 phenyl, and in the minor conformer (TT, con-

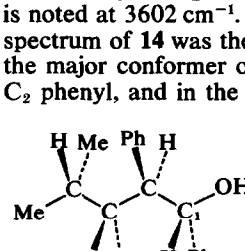


TE (conformer 1)

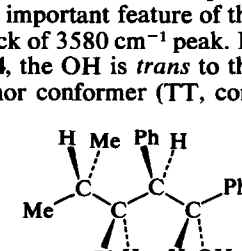


TT (conformer 1)

SCHEME V



TE (conformer 2)



TT (conformer 2)

SCHEME VI

former 1), the OH—pi interaction is possible, but a higher frequency probably results due to steric hindrance between OH and the ortho hydrogen of the C_1 phenyl. All OH absorptions noted above were concentration independent.

Stereochemistry of reduction. Table 4 lists the relative yields of the reduction products. Reduction of *threo* **2–4** consistently gives more of the TE isomer using either hydride. The steric course of reduction is consistent with either the Cram 1,3 or the Cram *et al* rules for 1,2 asymmetric induction. Reduction of *erythro* **2** or **3** with either hydride gives more of the EE isomer. This is consistent with the 1,2 rules but not with the Cram 1,3 rule. In the case of *erythro* **4**, the ET isomer predominates using LAH, which is consistent only with the Cram 1,3 rule. These rules were applied using the literature precedent[1,3] that phenyl > alkyl or aralkyl > hydrogen in effective size. The reason for this empirical order of size remains unknown, and it is certainly not the order necessarily found in conformation work.

The starting materials, *erythro* **2** and **3** and *threo* **2–4**, and their respective predominant reduction products have essentially the same orientation in space of major groups including oxygen. The similarity in conformation of starting material and product is the result of minimized non-bonded repulsions in either case. Since the sensitivity to non-bonded repulsions is also present and magnified in the transition state, the possibility exists that similar conformations may exist in the transition state as well.

In the reduction of *threo* **2–4**, approach of hydride as shown in structure **15** would lead over the transition state to products with little change in the orientation of major groups. However, since the R group offers interference to the approach of hydride, it is difficult to explain why an increase in the size of R has so little effect on product ratio (Table 4). An alternate conformation, **16**, may be important for the approach to the transition state, since hydride may enter over hydrogens at C_2 and at C_3. The size of R then would have no major effect on the approach of hydride.

In the reduction of the *erythro* ketones, the size of R has a large effect on the EE/ET ratio. If the transition state conformation were similar to the ground state conformation (e.g. **17**), R should have little effect on the approach of hydride since R is remote from the reaction zone. The predominance of the EE product from *erythro* **2** and **3** could be explained by an alternate conformation such as **18** in which hydride again approaches over hydrogens at C_2 and at C_3. In the approach to the transition

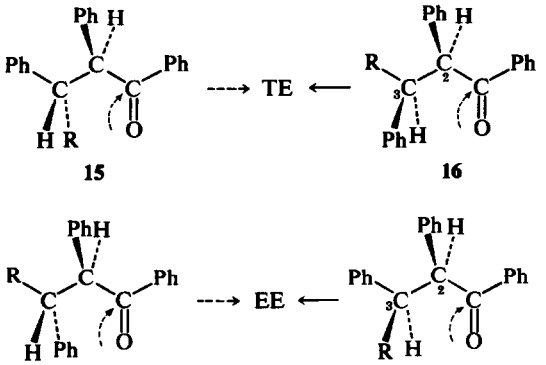


Table 4. Relative product yields[a,g] from reduction of the diastereomeric ketones **2–4**

Reducing agent =		LAH[b]	$LiAlH(O\text{-}t\text{-}Bu)_3^b$
Substrate	R	Yield (configuration)	Yield (configuration)
threo **2**	Me	78% (TE); 22% (TT)	70% (TE); 30% (TT)
threo **3**	Et	80% (TE); 20% (TT)[d]	64% (TE); 36% (TT)
threo **4**	i-Pr	72% (TE); 28% (TT)	61% (TE); 39% (TT)
erythro **2**	Me	79% (EE); 21% (ET)[e]	83% (EE); 17% (ET)
erythro **3**	Et	72% (EE); 28% (ET)[e]	70% (EE); 30% (ET)
erythro **4**	i-Pr	25% (EE); 75% (ET)[e,f]	45% (EE); 55% (ET)

[a]Average of 2–3 runs except for **3**. The variation from run to run was 0–5%.

[b]The solvent was ether. These runs were done at room temperature.

[c]THF rather than ether as solvent gave very similar results.

[d]At −78°C, the product yields were 91% (TE), 9% (TT).

[e]At −78°C, the product yields were 90% (EE), 10% (ET).

[f]The reaction was also run at −78°C, but insolubility of erythro **4** hindered reaction. About 5% conversion to product was noted; the product was mostly ET.

[g]Reduction of *threo* **5** gave 74% of a material tentatively identified as the TE isomer. Reduction of *erythro* **5** gave *ca* 90% of a material whose configuration remains unproven.

state, R becomes eclipsed with oxygen. An increase in the size of R would result in a higher energy transition state. For *erythro* **4**, this isopropyl-oxide interaction would be very severe, and steric problems may force the utilization of another transition state, leading to the ET product. Although the above rationalization adequately explains the results, we basically prefer an approach such as that of Ugi and Ruch,[12] which does not require the discussion of conformations (which have comparatively small energy differences) of the energy rich transition state.

EXPERIMENTAL

Preparation of 1,2,3-triphenyl-2-propen-1-one(**1**). This material was prepared by essentially the method of Kohler (55% yield), mp 100–101° (lit.[29] mp 101°).

Preparation of 1,2,3-*triphenyl*-1-*butanones* (**2**). In a round bottom 3-neck 500 ml flask, fitted with stirrer, reflux condenser and addition funnel, was placed 1·0 g (0·04 mol) of Mg turnings. Enough ether was added to cover the Mg and 1 ml of MeI was added. When the reaction started, 3 ml MeI in 15 ml ether was added dropwise. The resulting mixture was refluxed for 1 hr, and then cooled in an ice-bath. To this vigorously stirred mixture was added 10 g (0·038 mol) of **1**. Stirring was continued for 30 min at room temp, and for 1 hr at reflux. To the cooled mixture 50 ml dil HCl was added. The layers were separated and the combined ether layers were extracted with water, and dried ($MgSO_4$). Evaporated of the solvent yielded *ca* 10 g of an oil which was taken up in CCl_4 and to this 0·5 ml trifluoroacetic acid was added. The resulting mixture slowly crystallized. The maximum amount of *erythro* **2** was collected (*ca* 1·8 g) and this was recrystallized from EtOH-$CHCl_3$ mp 184–185° (5·7 g). The low melting isomer was obtained from the remaining material by repeated recrystallization from ether-pentane rejecting any initially formed high melting crystals. A total of 5·7 g of *threo* **2** was obtained, mp 100–101°. Chromatography on silica gel (Baker) using a progression of eluants (hexane, benzene-hexane) was used in other runs. The combined yields of the diastereomers represent a 68% yield.

erythro **2**, NMR (CCl_4): δ1·07 (d, 3, J = 7 Hz, CH—C<u>H</u>$_3$), 3·63 (m, 1, C<u>H</u>—CH_3), 4·68 (d, 1, J = 10·4 Hz, C<u>H</u>—COPh), and 6·8–7·7 (m, 15, aryl); IR (KBr on a Perkin Elmer Infracord): 1690, 1505, 1455, 1290, 1220, 772, 698 cm^{-1}. Found, C, 87·83; H, 6·85. Calcd for $C_{22}H_{20}O$: C, 87·96; H, 6·71; *threo* **2**, NMR (CCl_4): δ1·36 (d, 3, J = 6·8 Hz, CH—C<u>H</u>$_3$), 3·64 (m, 1, C<u>H</u>—CH_3), 4·60 (d, 1, J = 10·6 Hz, C<u>H</u>—COPh), 7·0 (s, 10, aryl), 7·2–7·4 (m, 3, aryl), and 7·8–8·1 (m, 2, aryl); IR (KBr): 1670, 1590, 1575, 1485, 1448, 1290, 1270, 1205, 1170, 985, 768, 740, 695. Found, C, 88·02; H, 6·79. Calcd for $C_{22}H_{20}O$: C, 87·96; H, 6·71.

Preparation of 1,2,3-*triphenyl*-1-*pentanones* (**3**). These were prepared by the method of Kohler and Thompson;[29] *erythro* **3**, mp 169–170° (lit.[29] mp 170); *threo* **3**, mp 91–92° (lit.[29] mp 92°).

Preparation of 1,2,3-*triphenyl*-4-*methyl*-1-*pentanones* (**4**). These materials were prepared similarly to **2**. The enol was quite stable for this compound and it was desirable to protect it from oxygen. Treatment with TFA, as above, gave the ketone. The NMR spectra of the crude product showed a *ca* 4:1 predominance of the *erythro* isomer. The maximum amount of high melting isomer (*erythro* **4**) was crystallized out and this was recrystallized from EtOH-$CHCl_3$ mp 189–190°, usually about a 20% yield. The minor isomer (*threo* **4**) was obtained by chromatography of the remaining oil on silica gel (Baker) using 95% hexane-5% benzene as eluent, mp 144–145°, usually 2–4% yield in most runs.

erythro **4**, NMR ($CDCl_3$): δ0·70 and 0·81 (d, 3 each, CH(C<u>H</u>$_3$)$_2$), 1·4–1·9 (m, 1, C<u>H</u>—$(CH_3)_2$), 3·67 (d of d, 1, J = 3·1, 11·2 Hz, CH—R), 5·28 (d, 1, J = 11·2, C<u>H</u>—COPh), and 7·0–7·9 (m, 15, aryl); IR (KBr): 1667, 1587, 1545, 1485, 1445, 1270, 1210, 1070, 982, 715, and 695 cm^{-1}. Found, C, 87·67; H, 7·32. Calcd for $C_{24}H_{24}O$: C, 87·76; H, 7·37.

threo **4**, NMR ($CDCl_3$): δ0·83 (d, 6, J = 6 5 Hz, CH (C<u>H</u>$_3$)$_2$), 3·76 (d of d, 1, J = 5·0, 11·2 Hz, C<u>H</u>—R), 5·20 (d, 1, J = 11·2, C<u>H</u>—COPh), 7·05 (s, 10, aryl), 7·1–7·5 (m, 3, aryl), and 8·0–8·2 (m, 2, aryl); IR (KBr) 1667, 1582, 1575, 1482, 1441, 1272, 1202, 1070, 1026, 981, 760, and 690. Found, C, 87·92; H, 7·30. Calcd for $C_{24}H_{24}O$: C, 87·76; H, 7·37.

Preparation of 1,2,3-*triphenyl*-4,4-*dimethyl*-1-*pentanones*, (**5**). These compounds were prepared using excess t-butyl Grignard with **1** (0·03 mol) by the general procedure described for **2**, with the following modification; after addition of **1** to the Grignard reagent, the ether solvent was replaced by benzene. Work-up as usual afforded 0·25 g (3% yield) of *threo* **5**, mp 216–217°, and 0·50 g (7% yield) of *erythro* **5**, mp 168–170°. The purification of the latter was again difficult, requiring repeated recrystallizations (EtOH-CH_2Cl_2), then chromatography.

erythro **5**, NMR (CCl_4): δ0·69 (s, 9, C_4H_9), 3·53 (d, 1, J = 11·6 Hz, CH—R), 5·30 (d, 1, J = 11·6 Hz, CH—COPh), and *ca* 7·0–8·0 (m, 15, aryl). Found, C, 87·72; H, 7 76). Calcd for $C_{25}H_{20}O$: C, 87·67; H, 7·65.

threo **5**, NMR (CCl_4): δ0·90 (s, 9, C_4<u>H</u>$_9$), 4·02 (d, 1, J = 10·4 Hz, C<u>H</u>—R), 5·16 (d, 1, J = 10·4 Hz, C<u>H</u>—COPh), and 6·9–8·2 (m, 15, aryl); IR(KBr): 1670, 1592, 1575, 1450, 1440, 1268, 1198, 1075, 1030, 980, 771, 752, and 695. Found, C, 87·39; H, 7·74. Calcd. for $C_{25}H_{20}O$: C, 87·67; H, 7·65.

Preparation of 1,2,3,5-*tetraphenyl*,4-*pentyn*-1-*ones* (**6**). Isopropyl Grignard was prepared in the usual manner using Mg turnings (0·07 ml) and 6·7 ml (0·071 mol) 2-bromopropane. To the Grignard, 10 ml (0·071 mol) phenylacetylene was added. The mixture was stirred at reflux for 1 hr, then cooled in an ice bath. To this solon 20 g (0·07 mol) of **1** was added as a solid and the mixture was refluxed for 2 hr, then cooled, and 60 ml dil HCl added slowly. The ether layer was separated, washed with water, dried ($MgSO_4$), and evaporated yielding an oily residue which was taken up in CCl_4 to which 0·5 g TFA had been added. Crystallization was induced and the two isomers were recrystallized apart using ether-light petroleum solvents yielding 2·0 g "*erythro*" **6**, mp 150–151° and 4·5 g "*threo*" **6**, mp 152–154°. The combined yields are 24% of theoretical.

"*erythro*" **6**, NMR (CCl_4): δ4·63 (d, 1, J = 10·4 Hz), 4·90 (d, 1, J = 10·4 Hz), and 7·0–8·2 (m, 20, aryl); IR (KBr): 1670, 1596, 1482, 1445, 1283, 1260, 1195, 1070, 1025, 960, 915, 760 and 695. Found, C, 89·89; H, 5·81. Calcd for $C_{29}H_{22}O$: C, 90·12; H, 5·74.

"*threo*" **6**, NMR (CCl_4): δ4·86 (s, 2, superposed C<u>H</u>), and 7·1–7·9 (m, 20, aryl), addition of pyridine permitted observation of the coupling constant J = 10·5 Hz; IR (KBr): 1670, 1590, 1485, 1440, 1282, 1262, 1195, 1073, 1025, 960, 755, and 695; calcd. molecular weight, 386; observed MW = 386 (mass spec).

Equilibration of ketones 2-6-. Approximately 200 mg of the substrate was mixed with 10 ml MeOH and 15 ml DMSO, and 500 mg solid NaOMe was added. The mixture was stirred at room temp (28 ± 3°) for 18 hr and then poured into dil HNO_3 and extracted with ether. The ether extract was washed with dil $NaHCO_3$ aq, and then with water, dried ($MgSO_4$), and evaporated. The residue was analyzed by NMR integration over the characteristic resonances and is considered accurate to ± 5%. With **5** the equilibration mixture was refluxed for *ca* 20 hr because of solubility difficulties. Compound **6** decomposed upon treatment with base.

Preparation of the diastereometic alkyl substituted 1,2,3-*triphenylpropanols* (**7–14**). A typical procedure follows. A mixture of 100 ml ether and 0·1 g (2·6 mmol) of LAH was prepared in a 500 ml 3-necked flask, equipped with stirrer. To this, 1·0 g (3·3 mmol) of *erythro* **2** was added as a solid (soluble substrates were added as ether solutions). The resulting mixture was refluxed for 1 hr, then cooled, and hydrolyzed by cautious addition of cold dil HCl. The ether layer was separated, washed with water, dried ($MgSO_4$) and evaporated yielding 1·1 g of a mixture of **7** and **8**. Ratios of isomers were determined by NMR integration. The high melting isomer was usually separated by crystallization (light petroleum) yielding 0·8 g, mp 107–108° (80% yield) in this case. The low melting isomer was cleanly separated by chromatography on silica gel (Baker), using 10% ether in light petroleum as eluant yielding *ca* 0·10 g. (10% yield) The non-crystalline alcohols were analyzed by mass spectrometry; these consistently showed the highest mass peak at (M^+-18) due to facile loss of water from the molecular ion which was extremely weak.

EE 1,2,3-*Triphenyl*-1-*butanol* (**7**), mp 107–108°, IR (CCl_4): 3610(s), 3565(w), 1486, 1448, 1063, 1025, and 900 cm^{-1}. Found, C, 86·94; H, 7·18. Calcd for $C_{22}H_{22}O$: C, 87·37; H, 7·33.

ET 1,2,3-*Triphenyl*-1-*butanol* (**8**), oil; IR (CCl_4): 3610(s), 3578(w), 1486, 1448, 1025, and 900 cm^{-1}; mass spectrum: highest mass peak $(M^+-18) = 284$.

TE 1,2,3-*Triphenyl*-1-*butanol* (**9**), mp 94–95°; IR (CCl_4): 3616(s), 3583(m), 1484, 1447, 1041, 1023, 901 and 688. Found, C, 87·55; H, 7·38. Calcd for $C_{22}H_{22}O$: C, 87·37; H, 7·33.

The fourth isomer (**10**) could not be separated from **9** either by crystallization or chromatography.

EE-1,2,3-*Triphenyl*-4-*methyl*-1-*pentanol* (**11**), mp 159–160°, IR(CCl_4): 3612(s), 3565(w), 1594, 1498, 1450, 1380, 1365, 1070, 1052, 1027, and 708 cm^{-1}. Found, C, 86·73; H, 7·77. Calcd for $C_{24}H_{26}O \cdot 1/2\ H_2O$· C, 86·44; H, 7·55.

ET-1,2,3-*Triphenyl*-4-*methyl*-1-*pentanol* (**12**), mp 122–123°; IR(CCl_4) 3609(s), 3580(m), 1487, 1448, 1380, 1364, 1068, 1032, and 1028 cm^{-1}. Found, C, 87·24; H, 8·20. Calcd for $C_{24}H_{26}O$: C, 87·23; H, 7·93.

TE-1,2,3-*Triphenyl*-4-*methyl*-1-*pentanol* (**13**), mp 76–78°; IR 3614(s), 3582(m), 1483, 1450, 1383, 1366, 1072, 1051, 1028, and 692 cm^{-1}. Found, C, 86·64; H, 7·58. Calcd. for $C_{24}H_{26}O \cdot 1/2\ H_2O$: C, 86·44; H, 7·58.

TT-1,2,3-*Triphenyl*-4-*methyl*-1-*pentanol* (**14**), oil; IR (CCl_4): 3602(s), 1520, 1480, 1405, 1390, 1095, 1060, 970, 938, and 726 cm^{-1}; mass spectrum $(M^+-18) = 312$, corresponds to a molecular weight of 330.

NMR spectra were taken on a Varian A60-D or XL-100 instruments at normal probe temp. Coupling constants were taken from the average of several traces using a 100 Hz expansion of the region in question. The ir spectra were run on a Perkin-Elmer 231 or Perkin-Elmer 621 except as noted. The solvent, CCl_4, was dried by distillation from phosphorous pentoxide prior to use. Mass spectra were determined on a Hitachi RMU-6D. The nmr spectral parameters were determined by computer simulation. These parameters were varied until the computer generated plot was superimposable on the observed spectrum.

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