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ORGANOMETALLIC REAGENTS IN ORGANIC SYNTHESIS—V[1,2]

AN ORGANOCUPRATE CONJUGATE ADDITION—ALDOL CONDENSATION SYNTHETIC PROCEDURE FOR SEQUENTIAL FORMATION OF TWO CARBON–CARBON BONDS

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Abstract—The enolates produced from the conjugate addition reaction of lithium dialkylcuprates with α,β-unsaturated ketones react with aldehydes in the presence of zinc chloride to give overall β-alkyl α-hydroxyalkyl addition to the original alkene. Reaction of these enolates with carbon dioxide and ethyl formate is also reported.

The utility of lithium organocuprate reagents in conjugate addition reactions is widely recognized as a powerful synthetic method in organic synthesis.[3] The mechanism for these reactions is still not fully resolved although there are strong indications that they proceed by an electron transfer process.[4] The intermediate formed prior to workup has anionic character as shown by the isolation of various enol derivatives following treatment with appropriate electrophilic reagents[5] and, although this intermediate has been thoroughly examined,[6] some difference in chemical reactivity from a lithium enolate has been noted.

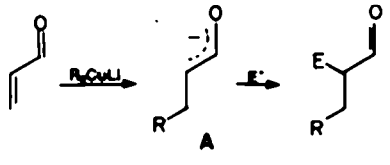
We were interested in the potential use of the anionic intermediates A (Scheme 1) resulting from conjugate addition reactions to α,β-unsaturated ketones for direct utilization in the formation of a carbon–carbon bond at the α-position of the original enone.

This sequence results in an overall β-followed by α-C–C bond formation process and has several attractive applications in organic synthesis. During the period of this investigation several reports have appeared of similar synthetic schemes using alkyl halides,[8] acyl halides,[9] chloroformate esters,[10] disulphides,[11] sulphinyl chlorides,[11] selenyl bromides,[12] modified methyl vinyl ketone derivatives[13,14] and Mannich bases.[15] Examples of intramolecular trapping of the anionic species with alkyl halides,[16] aldehydes,[17] and ketones[18] have also been reported. The use of copper(I)-catalysed Grignard reagent conjugate additions instead of lithium cuprates has allowed the utilization of saturated and unsaturated aldehydes.[19,20]

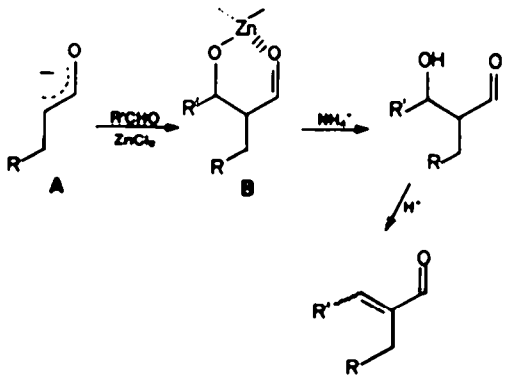
In concert with other reports[7] we found that A, produced from the reaction of enone substrate with lithium dialkylcuprates (R_2CuLi) in ether, was inert towards normally reactive alkylating reagents (e.g. MeI, CH_2=CH–CH_2I). Attempts to activate this intermediate towards alkylation by complexation with potential copper(I) ligands[21] or by operating in a more "activating" solvent (e.g. dimethoxyethane, tetrahydrofuran) gave unacceptable yields for the conjugate addition step and experiments involving a change of reaction solvent after the initial conjugate addition in ether lead to enolate isomerization, especially with sterically hindered substrates. We therefore resolved to retain the R_2CuLi/ether system and search for a suitable carbon electrophile which would react with the anionic species A without further activation.

Intermolecular reaction with aldehydes or ketones under various conditions of temperature and concentration gave little evidence for α-C–C bond formation, but modification of the reaction sequence according to House *et al.*[22] by the addition of $ZnCl_2$ to the reaction mixture prior to aldehyde addition gave acceptable yields of the β-alkylated, α-hydroxyalkylated ketones (Table 1) as outlined in Scheme 2.

Reaction of ketones or methyl iodide with A in the presence of $ZnCl_2$ gave only the simple conjugate addition product indicating a "zinc enolate"[23] is probably not involved in this reaction but the Zn^{2+} is acting as a stabilizing chelating metal centre (*viz.* B) for the β-ketoxide in accord with the original House proposal. Because of the labile nature of some of the β-ketols

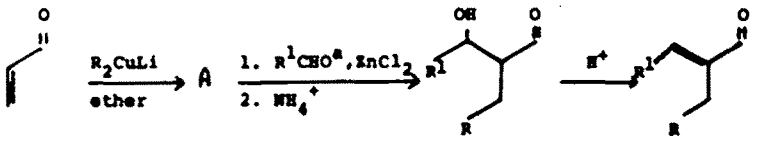


Scheme 1.



Scheme 2.

Table 1.



Enone	R	R^1	Product	Yield of β-Ketol[c](%)	Yield of Enone[c](%) (method[g])	Structure
methyl vinyl ketone	Bu	Me	(1)	92[d]	15(I)	(19)
	Bu	Et[b]	(2)	65[d]	17(I)	(20)
mesityl oxide	Me	Me	(3)	96,77[b]		
	Me	Et[b]	(4)	50[e]		
	Me	Ph[b]	(5)	72[e]		
	Me	p(OMe)Ph[b]	(6)	46[e]		
	Bu	Et[b]	(7)	93[d,e]		
	Bu	Ph[b]	(8)	85[e,f]		
3-penten-2-one	Me	Ph[b]	(9)	75[e,f]		
benzalacetone	Me	Me	(10)	83		
1-phenyl-3-penten-2-one	Me	Me	(11)	91[e]	67(II), 56(I)	(21)
cyclohexenone	Me	Me	(12)	97	30(I), 23(II)	(22)
3-methyl-cyclohexenone	Me	Me	(13)	98	98(II)	(23)
3,5,5-trimethyl-cyclohexenone	Me	Me	(14)	82[d]	93(I)[d], 36(II)	(24)
10-methyl-$\Delta^{1(9)}$-octal-2-one	Me	Me	(15)	76[d]	60(I), 25(II)	(25)

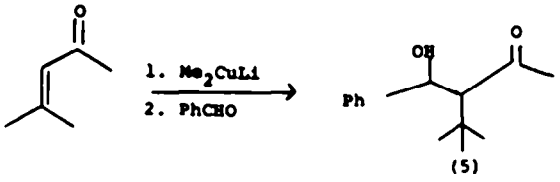
[a] 10 Equivalents of R^1CHO were used unless stated otherwise, at 0°C.
[b] Reaction with 1 equivalent of R^1CHO.
[c] Isolated yield of purified product unless stated otherwise.
[d] Determined by ^1H NMR analysis of the crude reaction mixture.
[e] Diastereoisomeric mixture of β-ketols (see Table 3).
[f] Reaction carried out at −78°.
[g] Method I: $CHCl_3$/HCl; method II: p-toluene sulphonic acid/benzene.

produced in this study they were dehydrated to the corresponding enones using *p*-toluene sulphonic acid/benzene or HCl/chloroform[24] before purification was attempted. The more stable β-ketols were characterized as such and it was noted that β-ketols of the general structure 16 did not readily dehydrate. The yields were generally acceptable with lower yield noted when the stability of the complex B (Scheme 2) was destabilized by large steric interactions.

The structures for the products followed routinely from spectroscopic analysis, especially using ^1H NMR and specific homonuclear decoupling (see Experimental). The results indicate high regioselectivity for the aldol condensation and enolate equilibration was not observed including a situation, i.e. 17 where enolate isomerization could be expected to be provoked by enabling conjugation to the phenyl ring.[25]

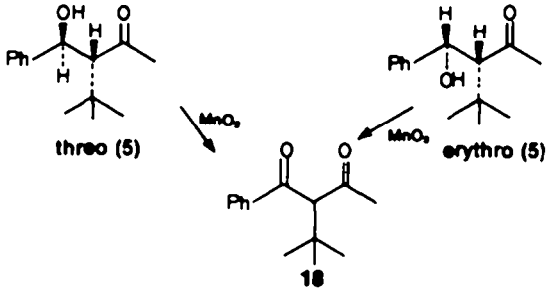
When the reaction was performed with acetaldehyde an excess (10 equivs) of aldehyde was generally used. In the formation of 3, use of one equivalent of acetaldehyde lowered the yield from 96% to 77%. For the less volatile aldehydes one equivalent of aldehyde was used simply to facilitate workup. A brief study of the effect of the change in reaction conditions on the yield of 5 (Table 2) showed that temperature and reaction time are very important parameters in determining conditions for

Table 2. Effect of temperature and reaction time on yield of (5)



PhCHO (/equivalents)	Reaction Time (/min)	Temp. (/°C)	Yield (%)	
			(5)	PhCHO
1	5	0	73	19
1	5	-78	66	39
10	5	0	23	52
10	30	0	a	74

[a] Only unidentified hydrocarbon products.

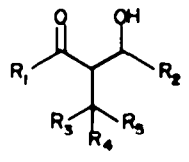


Scheme 3.

optimum yield which is in agreement with the original report.[22]

Aldol condensations with aldehydes produce two adjacent chiral centres, hence the possibility of diastereoisomers exists and this was noted in some cases. The *erythro* and *threo* diastereoisomers could be separated by chromatography, and the relationship between the diastereoisomers was established by symmetrizing the chiral carbinol centre by oxidation of the individual diastereoisomers to a common β-diketone (e.g. 18 Scheme 3).

The stereochemical assignments were made by examination of the vicinal coupling constants in the ^{1}H NMR (Table 3) using the rule $J_{AB}(threo) > J_{AB}$ (*erythro*) for diastereoisomerically related compounds.[22] This method for stereochemical analysis seems generally accepted although application in the case of 5 gives stereochemical assignments contrary to other reports.[26] The assignment of *erythro* and *threo* configurations based on vicinal coupling constants may be tenuous in some situations and, although the β-ketols showed strong hydrogen bonding hydroxyl IR absorption, examination of dilute solutions did not clarify the situation as may have reasonably been expected from studies with diastereoisomeric olefinic alcohols.[27]



1: R_1, R_2 = Me; R_3 = Bu; R_4, R_5 = H
2: R_1 = Me; R_2 = Et; R_3 = Bu; R_4, R_5 = H
3: R_1, R_2, R_3, R_4, R_5 = Me
4: R_1, R_3, R_4, R_5 = Me; R_2 = Et
5: R_1, R_3, R_4, R_5 = Me; R_2 = Ph
6: R_1, R_3, R_4, R_5 = Me; R_2 = p(OMe)Ph
7: R_1, R_3, R_4 = Me; R_2 = Et, R_5 = Bu
8: R_1, R_3, R_4 = Me; R_2 = Ph, R_5 = Bu
9: R_1, R_3, R_4 = Me; R_2 = Ph, R_5 = H
10: R_1, R_3, R_2 = Me; R_4 = Ph; R_5 = H
11: R_1 = CH_2Ph; R_2, R_3, R_4 = Me; R_5 = H
16: R_1, R_3, R_4 = Me; R_2 = Me, Et or Ph; R_5 = Me or Bu

Examination of the ^{1}H NMR of the *erythro* and *threo* isomers of 8 in very dilute solution showed that the coupling constants were unchanged, an effect also noted with the aforementioned diastereoisomeric olefinic alcohols.[28] The problem of the definitive determination of stereochemistry of β-ketols is at present under investigation. In the reaction giving 10 three chiral centres are introduced in the reaction sequence and three of the four possible diastereoisomers were detected. One of the isolated diastereoisomers of 10 was subjected to ^{1}H NMR homonuclear and ^{13}C[^{1}H] specific heteronuclear decoupling which enabled full analysis of the nonaromatic portion of the ^{1}H and ^{13}C NMR spectra[29] (see Experimental).

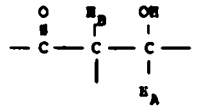
As mentioned previously, difficulties in handling some of the β-ketol products were recognised early in this work and, in order to produce stable compounds for structural analysis, several β-ketols were dehydrated to the less labile α,β-unsaturated ketones. In particular, the stereochemistry of 1 and 2 could not be readily ascertained and these materials were subjected to immediate dehydration after workup (see Table 1). Using the additivity rules for olefinic protons,[31] the olefinic stereochemistry of the dehydrated products could be assigned (Table 3).

Considerable retro-aldol reaction occurred on acid treatment in some cases which generally accounts for the variable yields of isolated materials. The stereochemical relationship between the β-ketol and the dehydrated products for the cyclic enone cases studied could be satisfactorily explained using a *trans* elimination mechanism whence the *threo* β-ketol gives the Z-alkene and the *erythro* β-ketol gives the E-alkene (Scheme 4).

The E configuration of 22 was confirmed by ^{1}H NMR study using Eu(fod)$_3$ (Fig. 1) which shows, for successive addition of the shift reagent, the olefinic proton and the methylene adjacent to the CO having the largest chemical shift change. If 22 had the Z configuration the expectation would be that the olefinic Me and C-6 methylene should be the most affected.

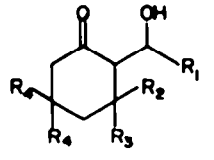
^{1}H NMR homonuclear decoupling on the Eu(fod)$_3$ shifted spectrum also showed that the C-3 methine multiplet was not coupled to the methylene adjacent to the CO hence confirming the structure as E-22 and not

Table 3. Stereochemistry of β-ketols and dehydrated products

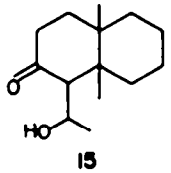


	β-Ketol			Dehydrated Product	
	H_A	J_{AB} (/Hz)	Stereochemistry		Stereochemistry
(3)	4.13	7	threo[a]		
(4)	3.77	<1	erythro		
	3.83	9	threo		
(5)	4.9	10	threo		
	5.07	3.5	erythro		
(6)	4.88	10	threo		
	4.98	4.5	erythro		
(7)	3.73	1.5	erythro		
	3.87	8	threo		
(8)	4.93	10	threo		
	5.07	3	erythro		
(9)	4.85	8.3	threo		
	4.95	5	erythro		
(12)	4.00	<1	erythro[a]	(22)	Σ
(13)	4.13	6	threo[a]	(23)	Σ
(14)	4.18	6	threo[a]	(24)	Σ
(15)	4.00	6	threo[a]	(25)	Σ

[a] = only one stereoisomer observed.



12: R_1, R_2 = Me; R_3, R_4 = H
13: R_1, R_3, R_4 = Me; R_2 = H
14: R_1, R_2, R_3, R_4 = Me



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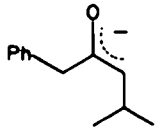

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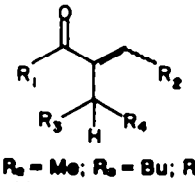
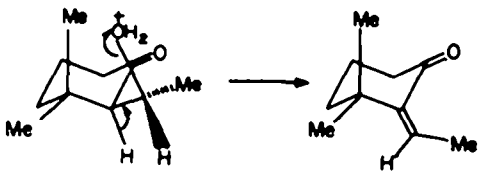
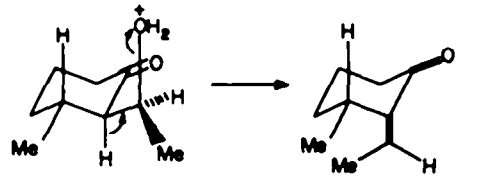


19: R_1, R_2 = Me; R_3 = Bu; R_4 = H
20: R_1 = Me; R_2 = Et; R_3 = Bu; R_4 = H
21: R_1 = CH_2Ph; R_2, R_3, R_4 = Me

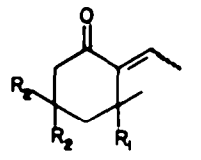
the isomeric 26. The effect of lanthanide shift reagents on coupling constants in acyclic diastereoisomeric diols has been noted[30] and Nitz[29] used $Eu(fod)_3$ to rigorously prove the structure of 13. Application of this technique to 15 was thwarted by the ready dehydration on addition of $Eu(fod)_3$. The reactions involving cyclic enone substrates generally gave only one diastereoisomer whose β-ketol stereochemistries have been tentatively assigned from J_{AB} values (Table 3). The relative amounts of *erythro* and *threo* isomers were found to vary with reaction temperature (Table 4) using the same reaction period although generally the *threo* isomer was formed preferentially.

In a further study of the reaction of A (Scheme 1) with various electrophiles it was found that Simmons Smith reagent[32] (CH_2I_2/Zn) and diazomethane did not produce the desired C–C bond formation. A report of the reversible insertion of CO_2 into the copper-metal bond of 27[33] prompted the investigation of CO_2 as a potential electrophile. Reaction of benzalacetone with $LiCuMe_2$ followed by addition of CO_2 was found to give highest yields of 28 in the absence of any external ligands. The base-soluble 28 was sensitive towards decarboxylation and hence was subsequently immediately treated with

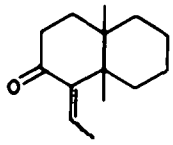




Scheme 4.



22: R_1, R_2 = H
23: R_1 = Me; R_2 = H
24: R_1, R_2 = Me



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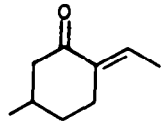

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Table 4. Variation of relative amounts of β-ketol diastereoisomers

(reaction time = 5 min.)

β-Ketol	Threo/Erythro ratio	
	0°	-78°
(4)	7.4	2.8
(5)	1.0	2.0
(6)	0.2	1.8
(7)	2.5	5.5
(8)	-	0.8
(9)	-	1.5

diazomethane to give the ester 29 as a mixture of the keto and enol tautomers (Scheme 5).

Reactions of vinyl copper intermediates with CO_2 under specific conditions have also been reported.[34]

Reactions of A (Scheme 1) with ethyl formate also proceeded readily (Scheme 6) in the absence of added ligands, e.g. cyclohexenone (see Experimental).

Conclusive structural determination of the products from these reactions have, to date, been hindered by a facile decarbonylation process. Attempts to transform the reaction products into stable compounds by acylation, thallation,[35] hydride reduction at low pH[36] or reductive amination[37] were unrewarding. In a model study, reaction of 30[30] with BF_3·MeOH[38] was found to occur rapidly at room temperature to give the complex

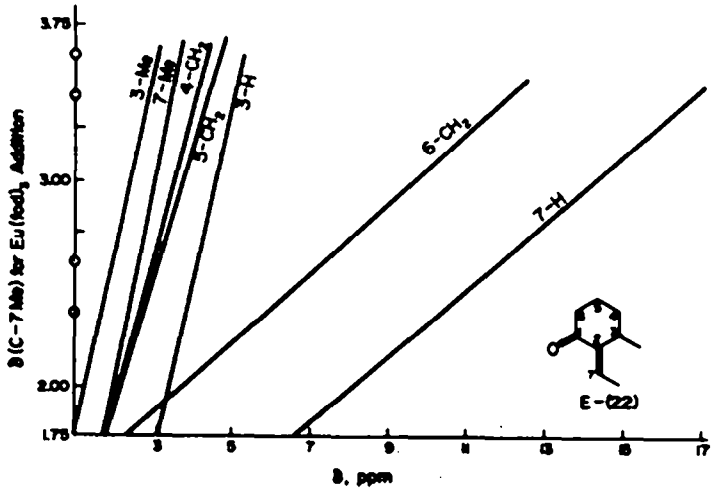
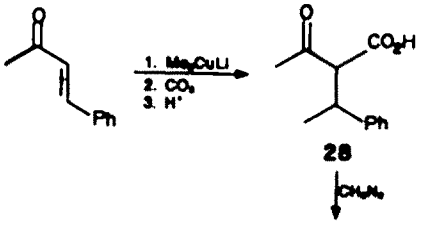
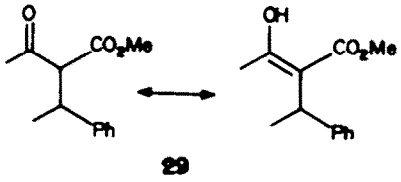


Fig. 1. ^{1}H NMR chemical shifts changes for successive addition of Eu(fod)$_3$ to E-(22).





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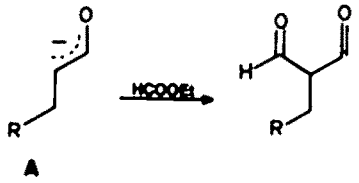
Scheme 5.



A

Scheme 6.

PhC≡C—Cu(PBu$_3$)$_n$

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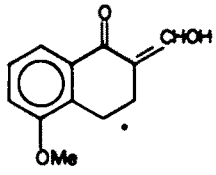

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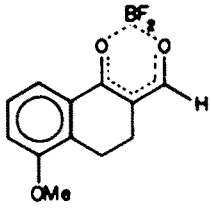

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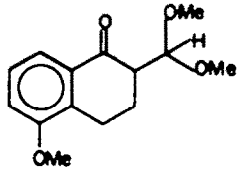

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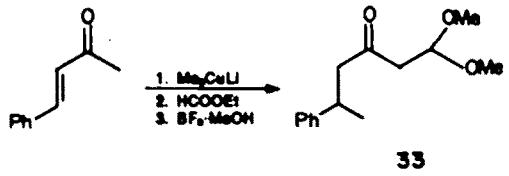
31[39] which on further treatment gave 32 in good yield. Repetition of this procedure using benzalacetone gave a product whose ^{1}H NMR is consistent with 33 (Scheme 7). This result implies either lack of regioselectivity of A or, alternatively, a rearrangement process during the



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Scheme 7.

ketalization reaction. The propensity for decarbonylation of these β-keto aldehydes appears to be related to the extent of substitution at the α-position and useful realization of this reaction sequence (Scheme 6) must await the development of suitable methods for stabilizing β-keto aldehydes having bulky substituents at the α-position.

EXPERIMENTAL

M.Ps were determined on a Reichert apparatus. They are expressed in degrees Celsius and are corrected. IR spectra were obtained on Perkin Elmer model 357 and 137 spectrophotometers. Solid samples were examined in Nujol and liquid samples as liquid films unless stated otherwise.

^{1}H NMR spectra were recorded at 59.8 MHz in FT mode with a JBOL FX-60 spectrometer, 60 MHz with a Varian T-60 spectrometer and 100 MHz with a Varian HA-100 spectrometer. Samples were normally examined with the Varian T-60 spectrometer in $CDCl_3$ soln using TMS as an internal standard. The chemical shifts (δ) are quoted in ppm downfield from TMS. Spectra are reported according to the convention: chemical shift (number of protons, multiplicity, observed coupling constant (Hz), assignment). Multiplicities are reported as: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet.

^{13}C NMR spectra were examined with a JEOL FX-60 FT/NMR spectrometer operating at 15.04 MHz in the FT mode. Samples were examined in $CDCl_3$ solns and the spectrometer was field/frequency locked to the deuterium resonance of the solvent. Chemical shifts (δ) are given in ppm downfield from TMS. The letter in brackets following each chemical shift indicates the peak appearance with single frequency off-resonance decoupling (S.F.O.R.D.). Mass spectra were recorded using a Varian MAT CH-7 mass spectrometer with an ionizing voltage of 70 eV.

Chromatography (a) Analytical tlc were obtained using Merck tlc aluminium roll silica gel $^{60}F_{254}$ strips with a layer thickness of 0.20 mm. (b) Preparative layer chromatograms (plc) were obtained on glass plates (20 cm × 20 cm or 20 cm × 50 cm) coated with Merck silica gel $PF_{254+366}$ with a layer thickness of 1.25 mm. E = ether, H = hexane.

Microanalyses were carried out by Prof. A. D. Campbell and associates at this department. All organic products were subjected to combustion analysis, however several of the compounds synthesized proved to be extremely unstable and gave unsatisfactory, inconsistent results which are not reported.

Reactions involving organometallic reagents were performed under an atmosphere of dry, oxygen-free N_2 in 3-necked round-bottom flasks, dried by heating at 110° and cooling under N_2 or alternatively by heating with a flame under a stream of N_2, and equipped with septum stoppers.

Na-dried diethyl ether was refluxed with LAH under N_2 for 1–2 hr and distilled directly into the reaction flask. Tetrahydrofuran was refluxed with Na under N_2 in the presence of small quantities of benzophenone until a blue colour appeared, then the solvent distilled directly into the reaction flask.

Copper(I) iodide was obtained from E. Merck and purified according to the literature.[40] MeLi was obtained as an ether soln and n-BuLi as a hexane soln from Alpha Inorganics Inc. and were analysed directly before use by the Gilman double titration method.[41] All organic reactants were commercial samples or prepared using standard procedures and were redistilled or recrystallized before use.

Synthesis of 1-phenyl-3-penten-2-one. Redistilled crotonaldehyde (14 g, 0.2 mole) in ether (30 ml) was added dropwise at 0° to a stirred benzyl Grignard soln (0.3 mole). When the addition of the aldehyde was complete, the mixture was allowed to stand at room temp. for 0.5 hr, then saturated NH_4Cl soln (50 ml) was added cautiously to the stirred soln at 0° and allowed to stand for a further 1 hr. The organic layer was separated, then evaporated and distillation of the residue gave crude 1-phenyl-3-penten-2-ol (15 g, 46%). CrO_3 (4.901 g, 49 mmoles) was added at 0° to a stirred soln of pyridine (7.751 g, 98 mmoles) in CH_2Cl_2 (113 ml). The flask was stoppered with a drying tube and the dark burgundy soln was stirred at room temp. for 15 min then the crude alcohol (1.22 g, 7.54 mmoles) in CH_2Cl_2 (2 ml) was added in one portion. After stirring for 1 hr at room temp. the soln was decanted and the residue washed with ether (150 ml). The combined organic solns were washed and evaporation of the solvent at reduced pressure afforded crude 1-phenyl-3-penten-2-one (998 mg, 82%).

Purification of a sample (100 mg) by plc (30E:70H) gave pure ketone (65 mg, 65%); ν_{max} (film) 1695, 1665, 730, 690 (phenyl) cm^{-1}; NMR δ 1.83 (3H, d of d, J_{BX} = 7 Hz, J_{AX} = 1.5 Hz, C-5 Me), 3.77 (2H, s, C-1 benzylic protons), 6.10 (1H, d of q, J_{AB} = 15 Hz, J_{AX} = 1.5 Hz, C-3 methine), 6.75 (1H, d of q, J_{AB} = 15 Hz, J_{BX} = 7 Hz, C-4 methine), 7.21 (5H, s, phenyl). Identical NMR (CCl_4) and IR with reported values.[42]

Aldol condensation reactions of enolates with aldehydes in the presence of zinc chloride

Typical procedure. The enone (1 mmole) in ether (1 ml) was added to a soln of lithium dimethylcuprate (Me_2CuLi; 2 mmoles) in ether (20 ml) at 0° under N_2. A yellow ppt developed immediately. After stirring 30 min at 0°, a saturated ethereal soln of freshly fused $ZnCl_2$ (3 ml (0.69 M), 2 mmoles) was added followed by the aldehyde (10 mmoles). After stirring for 5 min at 0° (or −78°), the reaction was poured into 10% NH_4Cl (100 ml), which gave a blue aqueous phase and the mixture was then extracted with ether.

Lithium di-n-butylcuprate (Bu_2CuLi) reactions were carried out in the same manner at −78°.

Dehydration of β-ketols

Typical procedures. Method I.[34] The aldol product (1 mmole) was added to $CHCl_3$ (15 ml) previously saturated with gaseous HCl for 5 min and the soln stirred at room temp. until tlc indicated completion of reaction. The mixture was then washed with sat $NaHCO_3$ (3×), sat NaCl (2×), dried (Na_2SO_4) and evaporated.

Method II. The aldol product in benzene (10 ml/mmole) containing *p*-toluenesulphonic acid (10 mg) was stirred at room temp. for 24 hr then washed with water and the solvents evaporated.

Oxidation of β-ketols

Typical procedure.[43] MnO_2[44] (5 g) in benzene (30 ml) was stirred and refluxed for 1–2 hr, using a Dean-Stark apparatus until no further water was evolved. The resulting activated MnO_2 was brownish-black in colour. The β-ketol (200 mg) in benzene (1 ml) was added and the MnO_2 suspension stirred under N_2 at room temp. until tlc indicated completion of reaction. The black ppt was filtered off, washed with benzene (3×), and the combined filtrates evaporated under reduced pressure to give the oxidation product.

(E)-3-Ethylideneoctan-2-one (19). Methyl vinyl ketone with Bu_2CuLi at −78° followed by acetaldehyde at 0° gave a crude 1 (159 mg, 92%); ν_{max} (film) 3350 (OH), 1700 (C=O) cm^{-1}; NMR δ 0.95(m), 1.28(m), 2.21(m), 3.63(m), which was immediately dehydrated (Method I) to afford a crude mixture (3 spots tlc). Purification by p.l.c. (20E:80H) gave pure (*E*)-3-*ethylideneoctan*-2-*one* (19) (23 mg, 15%); ν_{max}(film) 1675(C=O), 1640(C=C) cm^{-1}; NMR δ 0.92 (3H, t, J = 6 Hz, C-8 methyl), 1.27 (8H, m, C-4, C-5, C-6, C-7 methylenes), 1.85 (3H, d, J = 7 Hz, =CHCH_3), 2.24 (3H, s, −COCH_3), 6.65 (1H, q, J = 7 Hz, =CHCH$_3$); *m/e* 154 (M^+), 139, 125.46 (m*, 154–139), 83, 69, 55, 43 (base peak), 41, 29.

2,4-Dinitrophenylhydrazone had m.p. 83° (Found: C, 57.49; H, 6.80; N, 16.51; $C_{16}H_{22}N_4O_4$ requires: C, 57.47; H, 6.63; N, 16.76%).

(E)-3-Propylideneoctan-2-one (20). Methyl vinyl ketone and Bu_2CuLi at −78° followed by propionaldehyde at 0° gave crude 2 (120 mg, 65%); ν_{max} (film) 3460(OH), 1715(C=O) cm^{-1}; NMR δ 0.88–1.28(m), 2.20–2.93(m), 3.63(m), which was immediately dehydrated (method I) to give a crude mixture which, after plc (20E:80H), gave (*E*)-3-*propylideneoctan*-2-*one* 20 (28 mg, 17%); ν_{max}(film) 1670(C=O), 1640(C=C) cm^{-1}; NMR δ 0.88, 0.95, 0.98, 1.08 (6H, m, C-8 Me and =CH–CH$_2$–CH_3), 1.28 (6H, m, C-5, C-6, C-7 methylenes), 2.15–2.40 (4H, m, C-4 methylene and =CH–CH_2–CH$_3$), 2.28 (3H, s, −COCH_3), 6.54 (1H, t, J = 7 Hz, =CH–CH$_2$–CH$_3$); *m/e* 168 (M^+), 139, 115.01 (m*, 168–139), 111, 83, 69, 55, 43 (base peak), 41, 36.45 (m*, 83–55), 29.

2,4-Dinitrophenylhydrazone had m.p. 97° (Found: C, 58.61; H, 7.03; N, 15.86. $C_{17}H_{24}N_4O_4$ requires: C, 58.60; H, 6.94; N, 16.09%).

Threo - 3 - (1' - Hydroxyethyl) - 4,4 - dimethylpentan - 2 - one (3). Mesityl oxide with Me_2CuLi followed by acetaldehyde as described gave tlc pure *threo - 3 - (1' - hydroxyethyl) - 4,4 - dimethylpentan - 2 - one* 3 (152 mg, 96%); ν_{max}(film) 3410(OH), 1695(C=O) cm^{-1}; NMR δ 1.07 (9H, s, t-Bu), 1.18 (3H, d, J = 7 Hz, −CH(OH)CH_3), 2.18 (3H, s, −COCH_3), 2.58 (1H, d, J = 7 Hz, C-3 methine), 4.13 (1H, m, J = 7 Hz, −CH(OH)CH$_3$); ^{13}C NMR δ 23.4(q), 29.1(3q), 33.6(s), 35.4(q), 67.9(2d), 212.5(s); *m/e* 102 (M^+−C_4H_8), 101 (M^+−C_4H_9), 99 (base peak).

Repetition of the reaction using acetaldehyde (0.056 ml, 1 mmole) gave tlc pure 3 (121 mg, 77%), as indicated by tlc and NMR.

Oxidation of 3 (158 mg, 1 mmole) gave *3-t-butyl-2,4-pentanedione* (98 mg, 63%); ν_{max}(film) 1740, 1700 (β-diketone) cm^{-1}; NMR δ 1.18 (9H, s, t-Bu), 2.15 (6H, s, −COCH_3), 3.95 (1H, s, C-3 methine).

Diastereoisomeric 3 - (1' - hydroxypropyl) - 4,4 - dimethylpentan - 2 - one (4). Mesityl oxide with Me_2CuLi followed by propionaldehyde as described at −78°, gave diastereoisomeric 3 - (1' - *hydroxypropyl*) - 4,4 - *dimethylpentan* - 2 - *one* 4 (126 mg, 73%). Purification by plc (50E:50H) gave, in order of decreasing R_f; erythro 3 - (1' - *hydroxypropyl*) - 4,4 - *dimethylpentan* - 2 - *one* (21 mg, 12%); ν_{max}(film) 3395(OH), 1695(C=O) cm^{-1}; NMR δ 1.02 (3H, t, J = 4 Hz, −CH(OH) CH$_2$CH_3), 1.07 (9H, s, t-Bu), 1.28 (2H, m, −CH(OH) CH_2CH$_3$), 2.23 (3H, s, −COCH_3), 2.57 (1H, s broad, C-3 methine), 3.13 (1H, s broad, OH), 3.77 (1H, t broad, −CH(OH)Et). The doublet at δ 2.57 collapsed to a singlet when the adjacent −CH(OH)Et peak at δ 3.77 was irradiated. ^{13}C NMR δ 10.8(q), 29.1(3q), 31.3(t), 34.1(s), 36.2(q), 63.4(d), 72.6(d), 216.4(s); and threo 3 - (1' - *Hydroxypropyl*) - 4,4 - *dimethylpentan* - 2 - *one* (58 mg, 34%); ν_{max}(film) 3360(OH), 1700(C=O) cm^{-1}; NMR δ 1.03 (3H, t, J = 5 Hz, −CH(OH) CH$_2$CH_3), 1.07 (9H, s, t-Bu), 1.33 (2H, m, −CH(OH) CH_2CH$_3$), 1.90 (1H, s broad, OH), 2.17 (3H, s, −COCH_3), 2.59 (1H, d, J = 9 Hz, C-3 methine), 3.83 (1H, d of t, J = 9 Hz, 3 Hz, −CH(OH)Et). The doublet at δ 2.59 collapsed to a singlet when the adjacent −CH(OH)Et peak at δ 3.83 was irradiated. When the C-3 methine at δ 2.59 was irradiated, the multiplet at δ 3.83 collapsed to 4 lines of equal intensity at 227, 231, 234, 237 Hz. ^{13}C NMR δ 10.2(q), 29.1(3q + t), 33.6(s), 35.1(q), 66.7(d), 73.2(d), 212.7(s).

Repetition of the reaction at 0° gave diastereoisomeric 4 (126 mg, 73%). Purification by plc gave *erythro* (10 mg, 6%) and *threo* (74 mg, 44%) isomers.

Diastereoisomeric 3 - (1' - hydroxybenzyl) - 4,4 - dimethylpentan - 2 - one (5). Mesityl oxide with Me_2CuLi followed by benzaldehyde at −78° gave a mixture (204 mg) of benzaldehyde (41 mg) and diastereoisomeric 5 (163 mg). Purification by plc (40E:60H) gave in order of decreasing R_f: threo 3 - (1' - *hydroxybenzyl*) - 4,4 - *dimethylpentan* - 2 - *one* (97 mg, 44%); m.p. 72°; ν_{max} (nujol) 3480(OH), 1710(C=O), 3040, 760, 710 (phenyl) cm^{-1}; NMR δ 1.13 (9H, s, t-Bu), 1.56 (3H, s, −COCH_3), 2.90 (1H, d, J = 10 Hz, C-3 methine), 3.80 (1H, s, broad, OH), 4.90 (1H, d, J = 10 Hz, −CH(OH)Ph), 7.23 (5H, s, phenyl). The C-3 methine at δ 2.90 collapsed to a singlet when the adjacent −CH(OH)Ph peak at δ 4.90 was irradiated and *vice versa*. ^{13}C NMR δ 29.2(3q), 34.2(s), 34.6(q), 67.7(d), 75.0(d), 127.3(2d), 127.9(d), 128.4(2d), 143.7(s), 211.8(s); *m/e* 220 (M^+), 163, 144, 107, 105, 99 (base peak), 85.97 (m*, 114–99), 79, 77, 56.47 (m*, 105–77), 52.04 (m*, 220–107), 43. (Found: C, 76.54; H, 9.00; $C_{14}H_{20}O_2$

requires: C, 76.32; H, 9.15%); erythro 3 - (1' - *hydroxybenzyl*) - 4,4 - *dimethylpentan* - 2 - *one* (48 mg, 22%) ν_{max}(film) 3460(OH), 1700 (broad, C=O), 1197, 1155 (aryl ketone), 3060, 3025, 760, 700 (phenyl) cm^{-1}; NMR δ 1.09 (9H, s, t-Bu), 1.84 (3H, s, $-COCH_3$), 2.86 (1H, d, J = 3.5 Hz, C-3 methine), 3.94 (1H, s broad, OH), 5.07 (1H, s broad, $-CH$(OH)Ph), 7.23 (5H, s, phenyl). The doublet of C-3 methine at δ 2.86 collapsed to a singlet when the adjacent $-CH$(OH)Ph peak at δ 5.07 was irradiated and *vice versa*. NMR (C_6D_6) δ 0.93 (9H, s, t-Bu), 1.55 (3H, s, $-COCH_3$), 2.58 (1H, d, J = 3.5 Hz, C-3 methine), 3.75 (1H, s broad, OH), 4.95 (1H, d, J = 3.5 Hz, $-CH$(OH)Ph), 7.13 (5H, s, phenyl). ^{13}C NMR δ 28.9(3q), 34.1(s), 35.7(q), 66.5(d), 72.7(d), 125.3(2d), 127.1(d), 128.2(2d), 144.1(s), 215.6(s); *m/e* 220(M^+), 114, 107, 99 (base peak), 85.97 (m*, 114–99), 79, 77, 43, 18.68 (m*, 99–43). (Found: C, 76.48; H, 9.08. $C_{14}H_{20}O_2$ requires: C, 76.32; H, 9.15%).

Repetition of the reaction at 0° gave a mixture (200 mg) of benzaldehyde (20 mg) and diastereoisomeric 5 (180 mg) from NMR. Purification by plc gave *threo* (79 mg, 36%) and *erythro* (79 mg, 36%) isomers.

Repetition of the reaction at 0° with 10 mmole of benzaldehyde gave diastereoisomeric 5 (52 mg, 23%) which was a 44:56 ratio of the *threo* and *erythro* isomers (^1H NMR).

1 - *Phenyl* - 2 - *t-butyl* - 1,3 - *butanedione* (18). Oxidation of *threo* 5 (185 mg, 0.84 mmole) gave tlc pure 1 - *phenyl* - 2 - *t* - *butyl* - 1,3 - *butanedione* 18 (108 mg, 59%); m.p. 62°; ν_{max} (Nujol) 1700, 1650 (β-diketone), 1220, 1180 (aryl ketone), 758, 688 (phenyl) cm^{-1}; NMR [100 MHz] δ 1.13 (9H, s, t-Bu), 2.19 (3H, s, $-COCH_3$), 4.53 (1H, s, C-2 methine), 7.45–7.52, 7.91–8.02 (5H, m, phenyl); ^{13}C NMR δ 28.6(3q), 30.8(q), 35.9(s), 69.8(d), 128.2(2d), 128.7(2d), 133.3(d), 138.5(s), 197.0(s), 203.4(s); *m/e* 218 (M^+), 162 ($M^+-C_4H_8$), 161 ($M^+-C_4H_9$) (base peak), 105, 77, 68.48 (m*, 161–105), 56.47 (m*, 105–77). (Found: C, 77.26; H, 8.19. $C_{14}H_{18}O_2$ requires: C, 77.03; H, 8.31%).

Repetition of the oxidation using *erythro* 5 (185 mg, 0.84 mmole) also gave tlc pure 18 (69 mg, 38%).

Diastereoisomeric 3 - (1' - *hydroxy* - 1' - p - *methoxyphenyl*-*methyl*) - 4,4 - *dimethylpentan* - 2 - *one* (6). Mesityl oxide (2 mmole) with Me_2CuLi (4 mmoles) followed by *p*-methoxybenzaldehyde (2 mmoles) at −78° gave a crude mixture (4 spots tlc) which was purified by plc (60E:40H) to give in order of decreasing R_f: threo 3 - (1' - *Hydroxy* - 1' - p - *methoxyphenyl*-*methyl*) - 4,4 - *dimethylpentan* - 2 - *one* (6) (108 mg, 22%); ν_{max}(film) 3400(OH), 1715(C=O), 1260(=C–O–C), 865 (*p*-substituted aryl) cm^{-1}; NMR [100 MHz] δ 1.15 (9H, s, t-Bu), 1.61 (3H, s, $-COCH_3$), 2.93 (1H, d, J = 10 Hz, C-3 methine), 3.76 (3H, s, $-OCH_3$), 4.88 (1H, d, J = 10 Hz, $-CH$(OH)Ar), 6.81, 7.22 (4H, AB system, J_{AB} = 9 Hz, aromatic protons); *m/e* 250 (M^+), 193, 137 (base peak), 135, 99, 45, 44, 43, 31; *p-methoxybenzaldehyde* (91 mg); erythro 3 - (1' - *hydroxy* - 1' - p - *methoxyphenylmethyl*) - 4,4 - *dimethylpentan* - 2 - *one* (6) (61 mg, 12%); ν_{max} (film) 3380 (OH), 1705, 1690 (C=O), 1245 (=C–O–C), 1175, 1110, 1035, 870 (p-substituted aryl) cm^{-1}; NMR [100 MHz] δ 1.02 (9H, s, t-Bu), 1.99 (3H, s, $-COCH_3$), 2.89 (1H, d, J = 4.5 Hz, C-3 methine), 3.78 (3H, s, $-OCH_3$), 4.98 (1H, d, J = 4.5 Hz, $-CH$(OH)Ar), 6.84, 7.19 (4H, AB system, J_{AB} = 9 Hz, aromatic protons). The C-3 doublet at δ 2.89 collapsed to a singlet when the adjacent $-CH$(OH)Ar peak at δ 4.98 was irradiated and *vice versa*. *m/e* 250 (M^+), 152, 137, 136, 135 (base peak), 124, 109, 92, 77, 65, 43. (Found: C, 71.97; H, 8.51. $C_{15}H_{22}O_3$ requires: C, 71.97; H, 8.86%).

Repetition of the reaction at 0° gave, after plc *threo* (37 mg, 7%) and *erythro* (194 mg, 39%) isomers.

1 - p - *Methoxyphenyl* - 2 - *t* - *butyl* - 1,3 - *butanedione*. Oxidation of *threo* 6 (145 mg, 0.58 mmole) gave pure 1 - p - *methoxyphenyl* - 2 - *t* - *butyl* - 1,3 - *butanedione* (54 mg, 38%); ν_{max} (film) 1720, 1666, 1600 (enolic β-diketone), 1265 (=C–O–C), 1170, 1028, 835 (p-substituted C_6H_4) cm^{-1}; NMR [100 MHz] δ 1.13 (9H, s, t-Bu), 2.16 (3H, s, $-COCH_3$), 3.85 (3H, s, $-OCH_3$), 4.46 (1H, s, C-2 methine), 6.94, 7.95 (4H, AB system, J_{AB} = 9 Hz, aromatic protons); *m/e* 248 (M^+), 192 ($M^+-C_4H_8$), 135 (base peak), 107, 92, 84.81 (m* 135–107), 77, 65, 55.41 (m*, 107–77), 43.

Repetition of the oxidation using *erythro* 6 (22 mg, 0.09 mmole) also gave tlc pure diketone (17 mg, 76%).

Diastereoisomeric 3 - (1' - *hydroxypropyl*) - 4,4 - *dimethyloctan* - 2 - *one* (7). Mesityl oxide with Bu_2CuLi followed by propionaldehyde gave a mixture (198 mg) which after plc (30E:70H), gave in order of decreasing R_f: 4,4 - *Dimethyloctan* - 2 - *one* (25 mg, 12%); erythro 3 - (1' - *hydroxypropyl*) - 4,4 - *dimethyloctan* - 2 - *one* 7 (17 mg, 8%); ν_{max} (film) 3450 (OH), 1695 (C=O) cm^{-1}; NMR δ 0.98–1.07 (12H, m, C-4, C-8 methyls and $-CH$(OH)CH_2CH_3), 1.27 (8H, m, C-5, C-6, C-7 methylenes and $-CH$(OH)CH_2CH_3), 2.23 (3H, s, $-COCH_3$), 2.67 (1H, d, J_{MX} = 1.5 Hz, C-3 methine), 3.20 (1H, s, broad, OH), 3.73 (1H, d of t, J_{MX} = 1.5 Hz, J_{AX} = 6 Hz, $-CH$(OH)Et). *m/e* 214 (M^+), 116 ($M^+-C_7H_{14}$), 99 (base peak), 98, 97, 87, 83, 70.30 (m*, 98–83), 57. threo 3 - (1' - *Hydroxypropyl*) - 4,4 - *dimethyloctan* - 2 - *one* 7 (95 mg, 44%); ν_{max} (film) 3400 (OH), 1700 (C=O) cm^{-1}; NMR [100 MHz] δ 0.91, 0.96, 1.00, 1.06 (12H, m, C-4, C-8 methyls and $-CH$(OH)CH_2CH_3), 1.21–1.53 (8H, m, C-5, C-6, C-7 methylenes and $-CH$(OH)CH_2CH_3), 2.03 (1H, s, broad, OH), 2.17 (3H, s, $-COCH_3$), 2.74 (1H, d, J_{MX} = 8 Hz, C-3 methine), 3.87 (1H, d of d of d, J_{MX} = 8 Hz, J_{AX} = 8 Hz, J_{RX} = 3.5 Hz, $-CH$(OH)Et). The peak at δ 2.74 collapsed to a singlet when the peak at δ 3.87 was irradiated. When the peak at δ 2.74 was irradiated, the peak at δ 3.87 collapsed to 4 lines (d of d, J_{AX} = 8 Hz, J_{RX} = 3.5 Hz). ^{13}C NMR δ 10.4 (q), 14.3 (q), 23.5 (t), 25.7 (q), 26.1 (t + q), 29.4 (t), 35.4 (q), 36.2 (s), 41.2 (t), 65.2 (d), 73.2 (d), 212.5 (s).

Repetition of this reaction at 0° gave diastereoisomeric 7 (198 mg, 93%), as indicated by NMR and tlc. Purification by plc gave the *erythro* (34 mg) and *threo* (86 mg) isomers.

3 - (1',1' - *Dimethylpentyl*) - 2,4 - *hexanedione*. Oxidation of *threo* 7 (52 mg, 0.24 mmole) gave pure 3 - (1',1' - *dimethylpentyl*) - 2,4 - *hexanedione* (24 mg, 47%); ν_{max} (film) 1725, 1690 (β-diketone) cm^{-1}; NMR δ 1.03 (3H, t, J = 7 Hz, C-6 Me), 1.05 (9H, s, C-1', C-5' methyls), 1.3 (6H, m, C-2', C-3', C-4' methylenes), 2.20 (3H, s, $-COCH_3$), 2.50 (2H, q, J = 7 Hz, C-5 methylene), 3.74 (1H, s, C-3 methine). (Found: C, 73.82; H, 11.05. $C_{13}H_{24}O_2$ requires: C, 73.53; H, 11.39%).

Repetition of the oxidation with *erythro* 7 (21 mg, 0.1 mmole) gave the same product (17 mg, 80%).

Diastereoisomeric 3 - (1' - *hydroxybenzyl*) - 4,4 - *dimethyloctan* - 2 - *one* (8). Mesityl oxide with Bu_2CuLi followed by benzaldehyde gave a mixture of compounds which, on plc (30E:70H), gave in order of decreasing R_f: benzaldehyde (58 mg), 4,4 - dimethyloctan - 2 - one (21 mg), threo 3 - (1' - *hydroxybenzyl*) - 4,4 - *dimethyloctan* - 2 - *one* 8 (194 mg, 37%); ν_{max} (film) 3370 (OH), 1710 (C=O), 750, 700 (phenyl) cm^{-1}; NMR [100 MHz] δ 0.93 (3H, m, C-8 Me), 1.06, 1.15 (6H, s, C-4 methyls), 1.27–1.72 (6H, m, C-5, C-6, C-7 methylenes), 1.54 (3H, s, $-COCH_3$), 2.12 (1H, s broad, OH), 3.03 (1H, d, J = 10 Hz, C-3 methine), 4.93 (1H, d, J = 10 Hz, $-CH$(OH)Ph), 7.27 (5H, s, phenyl). The peak at δ 3.03 collapsed to a singlet when the adjacent peak at δ 4.93 was irradiated and *vice versa*. NMR (C_6D_6) δ 0.93 (3H, m, C-8 Me), 1.13–1.52 (6H, m, C-5, C-6, C-7 methylenes), 1.06, 1.20 (6H, s, C-4 methyls), 1.33 (3H, s, $-COCH_3$), 2.87 (1H, d, J = 10 Hz, C-3 methine), 4.83 (1H, d, J = 10 Hz, $-CH$(OH)Ph), 7.30 (5H, s, phenyl). ^{13}C NMR δ 14.2 (q), 23.5 (t), 25.5 (q), 26.0 (q), 26.1 (t), 34.6 (q), 36.9 (s), 41.2 (t), 66.2(d), 74.8 (d), 127.1 (2d), 127.8 (d), 128.4 (2d), 143.5 (s), 211.9 (s); and erythro 3 - (1' - *hydroxybenzyl*) - 4,4 - *dimethyloctan* - 2 - *one* 8 (252 mg, 48%); ν_{max} (film) 3390 (OH), 1700 (C=O), 760, 702 (phenyl) cm^{-1}; NMR δ 0.95 (6H, s, C-4 Me's), 1.37 (6H, m, C-5, C-6, C-7 methylenes), 1.80 (3H, s, $-COCH_3$), 2.95 (1H, d, J = 3 Hz, C-3 methine), 4.07 (1H, d, J = 8 Hz, OH), 5.07 (1H, d of d, J = 3 Hz, 8 Hz, $-CH$(OH)Ph), 7.25 (5H, s, phenyl). The peak at δ 2.95 collapsed to a singlet when the adjacent peak at δ 5.07 was irradiated and *vice versa*. NMR (C_6D_6) δ 0.85–1.20 (9H, m, C-8 methyl and C-5, C-6, C-7 methylenes), 0.93, 1.07 (6H, s, C-4 Me's), 1.58 (3H, s, $-COCH_3$), 2.77 (1H, d, J = 3.5 Hz, C-3 methine), 3.93 (1H, s broad, OH), 4.98 (1H, s broad, $-CH$(OH)Ph), 7.30 (5H, s, phenyl). ^{13}C NMR δ 14.1 (q), 23.4 (t), 25.7 (q), 26.0 (q), 26.1 (t), 35.9 (q), 36.9 (s), 41.2 (t), 64.8 (d), 72.4 (d), 125.3 (2d), 127.1 (d), 128.3 (2d), 144.3 (s), 215.8 (s).

Diastereoisomeric 3 - (1' - *hydroxybenzyl*) - 4 - *methylpentan* - 2 - *one* (9). 3-Penten-2-one with Me_2CuLi followed by benzaldehyde at −78° gave a crude mixture, which on plc (50E:50H), gave in order of decreasing R_f: benzaldehyde (48 mg); threo 3 - (1' - *hydroxybenzyl*) - 4 - *methylpentan* - 2 - *one* 9 (93 mg, 45%); ν_{max} (film) 3320 (OH), 1700 (C=O), 755, 700 (phenyl) cm^{-1}; NMR δ 1.02 (6H, d, J = 7.4 Hz, C-4 Me's), 1.76 (3H, s, $-COCH_3$), 1.92–2.43 (1H, m, C-4 methine), 2.93 (1H, d of d, J_{MX} = 8.3 Hz,

J_{AM} = 4.4 Hz, C-3 methine), 4.85 (1H, d, J_{MX} = 8.3 Hz, –CH(OH)Ph), 6.59 (1H, s, OH), 7.24 (5H, s, phenyl). When the absorption at δ 1.02 was irradiated, the adjacent C-4 methine multiplet (δ 1.92–2.43) collapsed to a doublet δ 2.26 (J = 4.4 Hz). When the C-4 methine peak at δ 1.92–2.43 was irradiated, the adjacent peak at δ 2.93 collapsed to a doublet (J = 8.3 Hz) and the doublet at δ 1.02 collapsed to a singlet. When the peak at δ 2.93 was irradiated, the doublet at δ 4.85 collapsed to a singlet. When the peak at δ 4.85 was irradiated, the adjacent peak at δ 2.93 collapsed to a doublet (J = 4.4 Hz). NMR (C_6D_6) δ 0.88, 1.05 (6H, d, J = 7 Hz, C-4 methyls), 1.50 (3H, s, –$COCH_3$), 1.98–2.55 (1H, m, C-4 methine), 2.77 (1H, d of d, J_{MX} = 8.3 Hz, J_{AM} = 4.4 Hz, C-3 methine), 4.80 (1H, d, J_{MX} = 8.3 Hz, –CH(OH)Ph), 6.59 (1H, s, OH), 7.27 (5H, s, phenyl); NMR (acetone-d_6) δ 1.02 (6H, d, J = 7 Hz, C-4 Me's), 1.68 (3H, s, –$COCH_3$), 2.15–2.58 (1H, m, C-4 methine), 2.98 (1H, d of d, J_{MX} = 9.5 Hz, J_{AM} = 4.5 Hz, C-3 methine), 4.80 (1H, d, J_{MX} = 9.5 Hz, –CH(OH)Ph), 6.60 (1H, s, OH), 7.23 (5H, s, phenyl). (Found: C, 75.48; H, 8.54; $C_{13}H_{18}O_2$ requires: C, 75.69; H, 8.80%); erythro 3 - (1' - *hydroxybenzyl*) - 4 - *methylpentan* - 2 - *one* **9** (61 mg, 30%); ν_{max} (film) 3330 (OH), 1710 (C=O), 760, 700 (phenyl) cm^{-1}; NMR δ 0.92, 1.07 (6H, d, J = 7 Hz, C-4 Me's), 1.86 (3H, s, –$COCH_3$), 2.13 (1H, m, C-4 methine), 2.73 (1H, d of d, J_{MX} = 5 Hz, J_{AM} = 8 Hz, C-3 methine), 3.52 (1H, s broad, OH), 4.95 (1H, d, J_{MX} = 5 Hz, –CH(OH)Ph), 7.28 (5H, s, phenyl). When the peak at δ 4.95 was irradiated, the adjacent peak at δ 2.73 collapsed to a doublet (J = 8 Hz). NMR (C_6D_6) δ 0.75, 0.85 (6H, d, J = 6 Hz, C-4 Me's), 1.61 (3H, s, –$COCH_3$), 2.02 (1H, m, C-4 methine), 2.52 (1H, d of d, J_{MX} = 5 Hz, J_{AM} = 8 Hz, C-3 methine), 3.43 (1H, s broad, OH) 4.87 (1H, d, J_{MX} = 5 Hz, –CH(OH)Ph), 7.25 (5H, s, phenyl); NMR (acetone-d_6) δ 0.85, 0.92 (6H, d, J = 6.6 Hz, C-4 Me's), 1.84 (3H, s, –$COCH_3$), 2.68–3.03 (3H, m, C-3, C-4 methines and OH), 4.93 (1H, d, J = 7 Hz, –CH(OH)Ph), 7.31 (5H, s, phenyl). (Found: C, 75.25; H, 8.52. $C_{13}H_{18}O_2$ requires: C, 75.69; H, 8.80%).

2 - *Isopropyl* - 1 - *phenyl* - 1,3 - *butanedione*. Oxidation of *threo* **9** (41 mg, 0.2 mmole) gave pure 2 - *isopropyl* - 1 - *phenyl* - 1,3 - *butanedione* (24 mg, 59%); ν_{max} (film) 3350 (OH), 1735, 1720 (diketone), 1680 (enolic β-diketone), 762, 697 (phenyl) cm^{-1}; NMR δ 0.90, 0.98 (6H, d, J = 7 Hz, –$CH(CH_3)_2$), 2.14 (3H, s, –$COCH_3$), 2.50–2.92 (1H, m, –$CH(CH_3)_2$), 4.21 (1H, d, J = 10 Hz, C-2 methine), 7.23–7.53, 7.78–8.05 (5H, m, phenyl).

Repetition of the oxidation with *erythro* **9** (20 mg, 0.1 mmole) gave the same product.

Diastereoisomeric 3 - (1' - *hydroxyethyl*) - 4 - *phenylpentan* - 2 - *one* (**10**). Benzalacetone (4 mmoles) with Me_2CuLi (8 mmoles) followed by $ZnCl_2$ (8 mmoles) and acetaldehyde (40 mmoles), gave a diastereoisomeric mixture (3 spots tlc) of 3 - (1' - *hydroxyethyl*) - 4 - *phenylpentan* - 2 - *one* **10** (680 mg, 83%). Separation by plc (70E:30H) gave in order of decreasing R_f three diastereoisomers I, II and III.

Isomer I (189 mg, 23%); ν_{max} (film) 3400 (OH), 1710, 1695 (C=O), 764, 700 (phenyl) cm^{-1}; NMR [100 MHz] δ 1.07 (3H, d, J = 7 Hz, –CH(OH)CH_3), 1.24 (3H, d, J = 7 Hz, C-5 methyl), 2.24 (3H, s, –$COCH_3$), 2.59 (1H, s broad, OH), 2.75 (1H, d of d, J = 4, 11 Hz, C-3 methine), 3.28 (1H, d of q, J = 11 Hz, J = 7 Hz, C-4 methine), 3.59 (1H, broad m, J = 4 Hz, J = 7 Hz, –CH(OH)CH_3), 7.23 (5H, s, phenyl). When the peak at δ 1.24 was irradiated, the adjacent peak at δ 3.28 collapsed to a doublet (J = 11 Hz). When the peak at δ 3.28 was irradiated, the doublet at δ 1.24 collapsed to a singlet. When the peak at δ 3.59 was irradiated, the adjacent d of d collapsed to a doublet (J = 11 Hz) and the doublet at δ 1.07 collapsed to a singlet. ^{13}C NMR δ 19.7 (q), 22.3 (q), 34.5 (q), 39.6 (d), 64.4 (d), 66.7 (d), 126.7 (d), 127.4 (2d), 128.6 (2d), 144.1 (s), 215.3(s); single frequency ^{13}C (^{1}H) experiments[20] showed the ^{1}H resonances at δ 3.6 and δ 3.28 were coupled to the ^{13}C peaks at δ 66.7 and 39.6 respectively enabling the assignments as shown; *m/e* 206 (M$^+$), 105 (base peak), 91, 77, 56.47 (m*, 105–77), 43.

Isomer II (270 mg, 33%); ν_{max} (film) 3350 (OH), 1710 (C=O), 764, 736, 704 (phenyl) cm^{-1}; NMR [100 MHz] δ 1.07 (3H, d, J = 6 Hz, –CH(OH)CH_3), 1.22 (3H, d, J = 6 Hz, C-5 methyl), 2.09 (3H, s, –$COCH_3$), 3.08–3.17 (2H, m, C-3 and C-4 methines), 3.76 (1H, m, 4 lines: 366, 373, 379, 384 Hz [relative intensities 1:2:2:1], –CH(OH)CH_3), 7.24 (5H, s, phenyl). When the absorption at δ 3.08–3.17 was irradiated, the doublet at δ 1.22 collapsed to a singlet. ^{13}C NMR δ 19.6 (2q), 34.6 (q), 39.1 (d), 64.5 (d), 67.9 (d), 126.7 (d), 127.3 (2d), 128.8 (2d), 144.5 (s), 212.1 (s); *m/e* 206 (M$^+$), 161, 105 (base peak), 43.

Isomer III (221 mg, 27%); ν_{max} (film) 3550 (OH), 1720 (C=O), 764, 708 (phenyl) cm^{-1}; NMR δ 1.30 (6H, d, J = 6 Hz, C-5 methyl and –CH(OH)CH_3), 1.80 (3H, s, –$COCH_3$), 2.17 (1H, s broad, OH), 3.07–3.17 (2H, m, C-3 and C-4 methines), 4.18 (1H, m, 7 lines: 238, 240, 245, 250, 251, 256, 262 Hz [relative intensity 1:1:2:3:3:2:1], –CH(OH)CH_3), 7.19 (5H, s, phenyl). When the absorption at δ 3.07–3.17 was irradiated, the doublet at δ 1.30 appeared as 3 lines (75, 78, 81 Hz [relative intensities 1.2:1.1:1]) and the multiplet at δ 4.18 collapsed to a quartet (J = 6 Hz). ^{13}C NMR δ 19.2 (q), 19.8 (q), 34.1 (q), 39.5 (d), 64.0 (d), 67.9 (d), 126.3 (d), 127.3 (2d), 128.4 (2d), 144.8 (s), 212.2 (s); *m/e* 206 (M$^+$), 161, 145, 105 (base peak), 43. (Found: C, 75.90; H, 8.43. $C_{13}H_{18}O_2$ requires: C, 75.69; H, 8.80%).

Diastereoisomeric 3 - (1' - *hydroxyethyl*) - 4 - *methyl* - 1 - *phenylpentan* - 2 - *one* (**11**). 1 - Phenyl - 3 - penten - 2 - one with Me_2CuLi followed by acetaldehyde gave *diastereoisomeric* 3 - (1' - *hydroxyethyl*) - 4 - *methyl* - 1 - *phenylpentan* - 2 - *one* **11** (2 spots on tlc) (200 mg); ν_{max} (film) 3315 (OH), 1705 (C=O), 732 (phenyl) cm^{-1}; NMR δ 0.85–1.27 (9H, m, C-4 Me's and –CH(OH)CH_3), 2.08–3.00 (3H, m, OH, C-3 and C-4 methines), 3.73 (2H, s, C-1 benzylic protons), 4.04 (1H, m, J = 7 Hz, –CH(OH)CH_3), 7.18 (5H, s, phenyl). Attempted separation by plc (50E:50H) resulted in decomposition.

1 - *Phenyl* - 3 - *isopropyl* - 3 - *penten* - 2 - *one* (**21**). The diastereoisomeric mixture **11** (96 mg, 0.44 mmoles) was dehydrated (method II) to give a mixture (90 mg). Purification by chromatography was not successful as the compounds have very similar R_f values. From NMR of the mixture it could be deduced that the mixture contained: (*E*) - 1 - *Phenyl* - 3 - *isopropyl* - 3 - *penten* - 2 - *one* (**21**) (56%); ν_{max} (film) 1660 (C=O), 1620 (C=C), 665, 690 (phenyl) cm^{-1}; NMR δ 1.10 (6H, d, J = 7 Hz, C-4 Me's), 1.84 (3H, d, J = 7 Hz, =$CHCH_3$), 2.67–3.12 (1H, m, J = 7 Hz, C-4 methine), 3.87 (2H, s, C-1 benzylic protons), 6.57 (1H, q, J = 7 Hz, =$CHCH_3$), 7.17 (5H, s, phenyl); (*Z*) - 1 - *Phenyl* - 3 - *isopropyl* - 3 - *penten* - 2 - *one* (**21**) (12%); ν_{max} (film) 1660 (C=O), 1620 (C=C), 665, 690 (phenyl) cm^{-1}; NMR δ 1.10 (6H, d, J = 7 Hz, C-4 Me's), 1.65 (3H, d, J = 7 Hz, =$CHCH_3$), 2.67–3.12 (1H, m, J = 7 Hz, C-4 methine), 3.80 (2H, s, C-1 benzylic protons), 5.53 (1H, q, J = 2 Hz, 7Hz, =$CHCH_3$), 7.17 (5H, s, phenyl); and 4 - *methyl* - 1 - *phenylpentan* - 2 - *one*[45] (32%).

Repetition of the dehydration (method I) gave (E)-isomer (41%), (Z)-isomer (15%), diastereoisomeric **11** (37%) and 4 - methyl - 1 - phenylpentan - 2 - one (8%), as indicated by NMR.

erythro 2 - (1' - *Hydroxyethyl*) - 3 - *methylcyclohexan* - 1 - *one* (**12**). 2 - Cyclohexen - 1 - one (2 mmole) with Me_2CuLi (4 mmoles) followed by acetaldehyde (20 mmoles) gave tlc pure 2 - (1' - *hydroxyethyl*) - 3 - *methylcyclohexan* - 1 - *one* **12** (303 mg, 97%); ν_{max} (film) 3370 (OH), 1720 (C=O) cm^{-1}; NMR δ 1.04 (3H, d, J = 6 Hz, C-3 Me), 1.19 (3H, d, J = 3 Hz, –CH(OH)CH_3), 1.32–2.50 (8H, m, aliphatic CH), 4.00 (1H, m, –CH(OH)CH_3).

(*E*) - 2 - *Ethylidene* - 3 - *methylcyclohexan* - 1 - *one* (**22**). *Erythro* **12** (150 mg, 0.96 mmole) was dehydrated (method II) to give crude **22** (108 mg, 78%), which was separated by plc (25E:75H) to give (*E*) - 2 - *ethylidene* - 3 - *methylcyclohexan* - 1 - *one* **22**[46] (32 mg, 23%); ν_{max} (film) 1684 (C=O), 1613 (C=C) cm^{-1}; NMR δ 1.03 (3H, d, J = 7 Hz, C-3 methyl), 1.75 (3H, d, J = 7 Hz, =$CHCH_3$), 1.78 (4H, m, C-4, C-5 methyleneS), 2.35 (2H, m, C-6 methyleneS), 3.13 (1H, m, C-3 methine), 6.57 (1H, q, J = 7 Hz, =$CHCH_3$).

The 2,4-dinitrophenylhydrazone, bad m.p. 178°. (Found: C, 56.63; H, 5.56; N, 17.60. $C_{15}H_{18}N_4O_4$ requires: C, 56.60; H, 5.66; N, 17.61%).

Repetition of the dehydration (method I) gave pure (E)-(**22**) (30%).

threo 2 - (1' - *Hydroxyethyl*) - 3,3 - *dimethylcyclohexan* - 1 - *one* (**13**). 3 - Methyl - 2 - cyclohexen - 1 - one with Me_2CuLi followed by acetaldehyde gave tlc pure 2 - (1' - *hydroxyethyl*) - 3,3 - *dimethylcyclohexan* - 1 - *one* **13** (167 mg, 98%); ν_{max} (film) 3260 (OH), 1700 (C=O) cm^{-1}; NMR δ 1.03, 1.10 (2 × 3H, s, C-3 methyls), 1.28 (3H, d, J = 7 Hz, –CH(OH)CH_3), 1.60–2.00 (4H, m, C-4 and C-5 methyleneS), 2.17–2.50 (3H, m, C-2 methine and C-6 methylene), 4.13 (1H, m, J_{AB} = 7 Hz, J_{BX} = 6 Hz, –CH(OH)CH_3). Identical by NMR with an authentic sample.[20]

(*Z*) - 2 - *Ethylidene* - 3,3 - *dimethylcyclohexan* - 1 - *one* (23). *Threo* 13 (167 mg, 0.98 mmoles) was dehydrated (method II) to give tlc pure (*Z*) - 2 - *ethylidene* - 3,3 - *dimethylcyclohexan* - 1 - *one* 23 (148 mg, 98%); ν_{max} (film) 1685 (C=O), 1625 (C=C) cm^{-1}; NMR δ 1.07, 1.27 (2×3H, s, C-3 Me's), 1.77 (3H, d, J = 7 Hz, =CHCH_3), 1.50–2.10 (4H, m, C-4 and C-5 methylenes), 2.38 (2H, t, J = 6 Hz, C-6 methylene), 5.60 (1H, q, J = 7 Hz, =CHCH$_3$).

threo 2 - (1' - *Hydroxyethyl*) - 3,3,5,5 - *tetramethylcyclo* - *hexan* - 1 - *one* (14). 3,5,5 - Trimethyl - 2 - cyclohexen - 1 - one with Me_2CuLi followed by acetaldehyde gave crude 2 - (1' - *hydroxyethyl*) - 3,3,5,5 - *tetramethylcyclohexan* - 1 - *one* 14 (162 mg, 82%) ν_{max} (film) 3335 (OH), 1700 (C=O) cm^{-1}; NMR δ 1.02, 1.12 (2×6H, s, C-3 and C-5 Me's), 1.27 (3H, d, J = 6 Hz, –CH(OH)CH_3), 1.59 (2H, s, C-4 methylene), 2.10–2.35 (3H, m, C-2 methine and C-6 methylene), 4.18 (1H, m, J = 6 Hz, –CH(OH)CH$_3$).

(*Z*) - 2 - *Ethylidene* - 3,3,5,5 - *tetramethylcyclohexan* - 1 - *one* (24). *Threo* 14 (162 mg, 0.82 mmoles) was dehydrated (method II) to give crude 2 - *ethylidene* - 3,3,5,5 - *tetramethylcyclohexan* - 1 - *one* 24 (142 mg, 96%). Purification of a sample (84 mg) by plc (15E:85H) gave pure (*Z*)-24 (30 mg, 36%); ν_{max} (film) 1690 (C=O), 1615 (C=C) cm^{-1}; NMR δ 1.03, 1.15 (2×6H, s, C-3, C-5 Me's), 1.59 (2H, s, C-4 methylene), 1.85 (3H, d, J = 7 Hz, =CHCH_3), 2.28 (2H, s, C-6 methylene), 5.80 (1H, q, J = 7 Hz, =CHCH$_3$).

The 2,4-dinitrophenylhydrazone had m.p. 118°. (Found: C, 59.54; H, 6.50; N, 15.26. $C_{18}H_{24}N_4O_4$ requires: C, 59.98; H, 6.71; N, 15.55%).

Repetition of the dehydration (method I) gave 24 (93%), as indicated by NMR and tlc.

threo - 1 - (1' - *Hydroxyethyl*) - 9,10 - cis - *dimethyldecal* - 2 - *one* (15). 10 - Methyl - 1(9) - octal - 2 - one with Me_2CuLi followed by acetaldehyde gave threo - 1 - (1' - *hydroxyethyl*) - 9,10 - cis - *dimethyldecal* - 2 - *one* 15 (170 mg, 76%); ν_{max} (film) 3460 (OH), 1700 (C=O) cm^{-1}; NMR δ 0.91, 1.04 (2×3H, s, C-9 and C-10 Me's), 1.32 (3H, d, J = 6 Hz, –CH(OH)CH_3), 1.48–2.34 (13H, m, aliphatic CH), 4.00 (1H, m, J = 6 Hz, –CH(OH)CH$_3$).

(*Z*) - 1 - *Ethylidene* - 9,10 - cis - *dimethyldecal* - 2 - *one* (25). Crude *threo* 15 (224 mg, 1 mmole) was dehydrated (method I) to give crude 1 - *ethylidene* - 9,10 - cis - *dimethyldecal* - 2 - *one* 25 (186 mg, 90%). Purification by plc (40E:60H) gave pure (*Z*)-(25) (52 mg, 25%); ν_{max} (film) 1685 (C=O), 1620 (C=C) cm^{-1}; NMR δ 1.00, 1.07 (2×3H, s, C-9, C-10 Me's), 1.53 (10H, m, aliphatic CH), 1.82 (3H, d, J = 7 Hz, =CHCH_3), 2.40 (2H, t, J = 5 Hz, C-3 methylene), 5.70 (1H, q, J = 7 Hz, =CHCH$_3$); ^{13}C NMR δ 15.3 (q), 21.1 (q), 21.2 (t), 21.8 (t), 23.9 (q), 33.6 (t), 34.7 (2t), 36.0 (s), 39.1 (t), 45.3 (s), 127.1 (d), 146.9 (s), 206.7 (s); *m/e* 206 (M^+), 191 (base peak), 150.

Repetition of the dehydration (method I) gave, after plc (40E:60H), pure (*Z*)-25 (124 mg, 60%), as indicated by tlc and NMR.

3 - *Methoxycarbonyl* - 4 - *phenylpentan* - 2 - *one* (29). Benzalacetone (292 mg, 2 mmoles) in ether (1 ml) was added to a soln of Me_2CuLi (4 mmoles) and stirred for 30 min at 0°. Dry CO_2 gas was then bubbled into the suspension for 1 hr at room temp. (flow rate = 1 ml s^{-1}). The mixture was diluted with water (100 ml) and, after washing with ether (2×), cooled with ice then acidified with 25% HCl. The white ppt which formed was extracted with ether.

The pale yellow product 28 visibly decomposed on standing so it was treated with diazomethane for 1 hr at room temp. Excess diazomethane was destroyed with acetic acid and the product was isolated by ether extraction to give a residue (720 mg) which on plc (50E:50H) afforded crude 3 - *methoxycarbonyl* - 4 - *phenylpentan* - 2 - *one* 29 (232 mg), as an enolic mixture [44% keto, 56% enol by NMR], b.p. 62°/0.03 mm; ν_{max} (film) 1740 (saturated ester), 1715 (α,β-unsaturated ester), 765, 700 (phenyl) cm^{-1}. Keto isomer δ 2.26 (3H, s, –COCH_3), 3.40 (3H, s, COOCH_3), 3.54–3.90 (2H, m, C-3, C-4 methines), 7.18 (5H, s, phenyl). Enol isomer δ 1.90 (3H, s, =C(OH)CH_3), 3.72 (3H, s, COOCH_3), 4.36 (2H, s, C-4 methine and OH), 7.18 (5H, s, phenyl). Two three-proton doublets (δ 1.23, J = 6 Hz; δ 1.29, J = 7 Hz) are assigned to the Me protons at C-5. ^{13}C NMR (enolic mixture) δ 20.1 (q), 20.6 (q), 29.7 (2q), 39.8 (d), 40.1 (d), 52.3 (2q), 66.9 (d), 67.4 (d), 127.3, 128.6 (10d), 143.0 (2s), 168.7 (s), 169.0 (s), 202.2 (s), 203.0 (s). (Found: C, 70.86; H, 7.37. $C_{13}H_{16}O_3$ requires: C, 70.89; H, 7.32%).

2 - *Hydroxymethylene* - 3 - *methylcyclohexanone*. 2 - Cyclohexen - 1 - one (192 mg, 2 mmoles) in ether (1 ml) was added to a soln of Me_2CuLi (4 mmoles) as described previously. After stirring for 30 min at 0°, ethyl formate (1.62 ml, 20 mmoles) was added and the suspension stirred for 10 min at 0°. The mixture was poured into 10% NH_4Cl (100 ml), which was ether extracted. The green ether fraction was extracted with 10% NaOH, then the alkaline layer was acidified with ice-cold 50% HCl and extracted with ether. Evaporation of the ether gave tlc pure, very volatile 2 - *hydroxymethylene* - 3 - *methylcyclohexanone* (124 mg, 44%); ν_{max} (film) 3420 (OH), 1710 (C=O), 1630 (enolic β-diketone) cm^{-1}; NMR δ 1.15 (3H, d, J = 7 Hz, C-3 Me), 1.63–2.60 (7H, m, C-3 methine, C-4, C-5, C-6 methylenes), 8.00 (1H, s broad, OH), 8.67 (1H, d, J = 4 Hz, =CH(OH)). Spontaneous decarbonylation occurred at room temp., as indicated by loss in weight and IR.

Reaction of boron trifluoride-methanol complex with 2 - *hydroxymethylene* - 5 - *methoxy* - 1 - *tetralone* (30)

BF_3–MeOH complex (0.1 ml of 14%) was added to 30[10] (51 mg, 0.25 mmole) in dry MeOH (2 ml) and stirred for 1 day at room temp. under N_2. The mixture was then diluted with water (50 ml) and ether extracted.

Evaporation and plc (50E:50H) gave a pure liquid, 2 - *dimethoxymethyl* - 5 - *methoxy* - 1 - *tetralone* 32 (63 mg, 100%); ν_{max} (film) 1695 (C=O), 1120, 1075 (C–O–C), 1590, 806 (3 adjacent H atoms of aryl) cm^{-1}; NMR δ 2.00–3.10 (5H, m, C-2 methine and C-3, C-4 methylenes), 3.46 (6H, s, –CH(OCH_3)$_2$), 3.83 (3H, s, C-5 OCH_3), 4.92 (1H, d, J = 4 Hz, –CH(OCH$_3$)$_2$), 6.67–7.67 (3H, m, aromatic protons).

1,1 - *Dimethoxy* - 5 - *phenylhexan* - 3 - *one* (33). Benzalacetone with Me_2CuLi followed by freshly distilled ethyl formate as described for 2 - cyclohexen - 1 - one gave the crude α-formyl ketone (319 mg, 84%); ν_{max} (film) 3360 (OH), 1710 (C=O), 1620 (broad) (C=C), 760, 698 (phenyl) cm^{-1} which was treated immediately with BF_3–MeOH complex (0.67 ml of 14%) in MeOH (13 ml) as described for 30 to give 1,1 - *dimethoxy* - 5 - *phenylhexan* - 3 - *one* 33 (256 mg, 65%); ν_{max} (film) 1710 (C=O), 1190, 1115, 1060 (C–O–C–O–C), 760, 698 (phenyl) cm^{-1}; NMR δ 1.25 (3H, d, J = 6.5 Hz, C-6 Me), 2.61 (2H, d, J = 5.6 Hz, C-2 methylene), 2.72 (2H, d, J = 6.5 Hz, C-4 methylene), 3.03–3.61 (1H, m, C-5 methine), 3.27, 3.31 (2×3H, s, –OCH_3), 4.70 (1H, t, J = 5.6 Hz, C-1 methine), 7.19 (5H, s, phenyl); ^{13}C NMR 22.1 (q), 35.1 (d), 47.1 (t), 52.3 (t), 53.9 (q), 54.1 (q), 101.8 (d), 126.3 (d), 126.8 (2d), 128.6 (2d), 146.3 (s), 206.4 (s); *m/e* 205 (M^+–OCH$_3$), 118, 105, 75 (base peak). (Found: C, 71.43; H, 8.33. $C_{14}H_{20}O_3$ requires: C, 71.16; H, 8.53%).

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REFERENCES

[1]Part IV, R. A. J. Smith and A. R. Lal, *Aust. J. Chem.* submitted for publication.
[2]Preliminary report of this work; K. K. Heng and R. A. J. Smith, *Tetrahedron Letters* 589 (1975).
[3]G. H. Posner, *Organic Reactions* 19, 1 (1972).
[4]cf. H. O. House, *Accts. Chem. Res.* 9, 59 (1976).
[5]e.g. E. S. Brinkley and C. H. Heathcock, *J. Org. Chem.* 40, 2156 (1975).
[6]H. O. House and J. M. Wilkins, *Ibid.* 41, 4031 (1976).
[7]e.g. R. M. Coates and R. L. Sowerby, *J. Am. Chem. Soc.* 93, 1027 (1971).
[8]R. K. Boeckman Jr., *J. Org. Chem.* 38, 4450 (1973); R. M. Coates and L. O. Sandefur, *Ibid.* 39, 275 (1974); A. E. Greene and P. Crabbé, *Tetrahedron Letters* 4867 (1976).
[9]T. Tanaka, S. Kurozumi, T. Toru, M. Kobayashi, S. Miura and S. Ishimoto, *Ibid.* 1535 (1975).
[10]R. G. Salomon and M. F. Salomon, *J. Org. Chem.* 40, 1488 (1975); T. Toru, S. Kurozumi, T. Tanaka, S. Miura, M. Kobayashi and S. Ishimoto, *Tetrahedron Letters* 4087 (1976).

[11]S. Kurozumi, T. Toru, T. Tanaka, M. Kobayashi, S. Misra and S. Ishimoto, *Ibid.* 4091 (1976).
[12]H. J. Reich, I. L. Reich and J. M. Renga, *J. Org. Chem.* 39, 2133 (1974); *J. Am. Chem. Soc.* 97, 5434 (1975).
[13]R. K. Boeckman Jr., *Ibid.* 95, 6867 (1973).
[14]A. Rosan and M. Rosenblum, *J. Org. Chem.* 40, 3621 (1975).
[15]N. L. Holy and Y. F. Wang, *J. Am. Chem. Soc.* 99, 944 (1977).
[16]G. H. Posner, C. E. Whitten, J. J. Sterling and D. J. Brunelle, *Tetrahedron Letters* 2591 (1974).
[17]F. Näf, R. Decorzant and W. Thommen, *Helv. Chim. Acta* 58, 1808 (1975).
[18]J. E. McMurry and S. J. Isser, *J. Am. Chem. Soc.* 94, 7312 (1972).
[19]G. Stork and J. d'Angelo, *Ibid.* 96, 7114 (1974).
[20]F. Näf and R. Decorzant, *Helv. Chim. Acta* 57, 1317 (1974).
[21]R. W. Morris, B.Sc(Hons) Project Report, University of Otago (1972).
[22]H. O. House, D. S. Crumrine, A. Y. Teranishi and H. D. Olmstead, *J. Am. Chem. Soc.* 95, 3310 (1973).
[23]T. A. Spencer, R. W. Britton and D. S. Watt, *Ibid.* 89, 5727 (1967).
[24]S. N. Huckin and L. Weiler, *Can. J. Chem.* 52, 2157 (1974).
[25]For an example of enolate isomerisation prior to aldol condensation see: E. Piers and C. K. Lau, *Synthetic Communications* 495 (1977).
[26]E. A. Jeffery, A. Meisters and T. Mole, *J. Organometallic Chem.* 74, 373 (1974).
[27]J. Sicher, M. Cherest, Y. Gault and H. Felkin, *Coll. Czech. Chem. Comm.* 28, 72 (1963).
[28]H. Felkin and R. A. J. Smith, unpublished observations.
[29]Determined by Dr. R. T. C. Brownlee, La Trobe University.
[30]G. B. Porter and J. Simpson, *Angew. Chem. Intl. Ed.* 17, 49 (1978).
[31]L. M. Jackman and S. Sternhell, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry* (2nd Edn), p. 185. Pergamon, Oxford (1969).
[32]cf H. W. Whitlock, Jr. and L. E. Overman, *J. Org. Chem.* 34, 1962 (1969).
[33]T. Tsuda, Y. Chujo and T. Saegusa, *J. Chem. Soc.* Chem. Comm. 963 (1975).
[34]cf J. F. Normant, *J. Organometallic Chem. Library* 1, 219 (1976).
[35]A. McKillop and E. C. Taylor, *Accts. Chem. Res.* 3, 338 (1970).
[36]R. F. Borch, M. D. Bernstein and H. D. Durst, *J. Am. Chem. Soc.* 93, 2897 (1971).
[37]A. D. Harmon and C. R. Hutchinson, *J. Org. Chem.* 40, 3474 (1975).
[38]A. McKillop, *Proceedings Robert A. Welch Foundation Conference XVII*, p. 171.
[39]R. A. J. Smith and T. A. Spencer, *J. Org. Chem.* 35, 3220 (1970).
[40]G. B. Kauffman and L. A. Teter, *Inorg. Synth.* 7, 9 (1963).
[41]H. Gilman and F. K. Cartledge, *J. Organometallic Chem.* 2, 447 (1964).
[42]A. I. Meyers and E. M. Smith, *J. Org. Chem.* 37, 4289 (1972).
[43]I. M. Goldman, *Ibid.* 34, 1979 (1969).
[44]E. F. Pratt and S. P. Suskind, *Ibid.* 28, 638 (1963).
[45]D. Ivanov, M. Marekov and E. Zidarov, *Rev. Chim. Acad. Rep. Populaire Roumaine* 7, 985 (1962); *Chem. Abstr.* 61, 4254g.
[46]J. M. Conia, M. Bortolussi and R. Bloch, *Bull. Soc. Chim. Fr.* 2722 (1975).