Tetrahedron Vol. 42, No. 2, pp. 561 to 572, 1986
Printed in Great Britain.

0040-4020/86 · $3.00 + .00

RADICAL ADDITION TO THE CARBONYL CARBON OF KETONES PROMOTED BY AQUEOS TITANIUM TRICHLORIDE IN ACIDIC MEDIUM. ONE STEP SYNTHESIS OF PINACOLS AND LACTONES.

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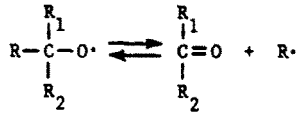
(*Received in UK* 28 *October* 1985)

Abstract - Carbon centered radical 1, generated by reduction of methyl phenylglyoxalate with Ti(III) ion, adds to the carbonyl carbon of ketones 2 to afford pinacols 3. Yields of 3 are remarkably influenced by the structure of 2, in that the reaction is very sensitive to steric factors. Many other functional groups present in 2 do not interfere with carbonyl addition, but lactonization of 3 occurs when the additional groups are COOH, $COOC_2H_5$, and OH.
Alkyl radical addition to ketones is a reversible process, but the rapid reduction of the resulting alkoxy radical 8 by Ti(III) ion makes the whole process practically irreversible and accounts for pinacol formation.

INTRODUCTION

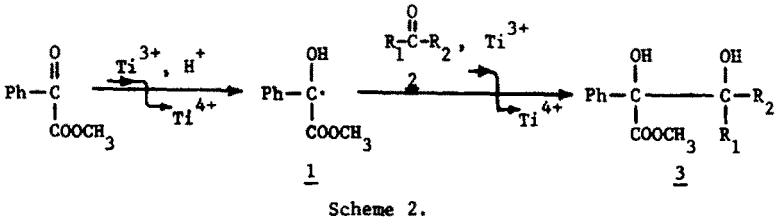
One of the characteristic reactions of t-alkoxy radicals is the β-scission[1] to give a carbonyl compound and a new carbon-centered radical (Scheme 1).



Scheme 1.

The reverse of this process, that is the addition of a carbon-centered radical to a carbonyl group, is rare and only few scattered examples can be found in the literature[2].

We now report that carbon-centered radical 1 generated from methyl phenylglyoxalate by uptake of an electron from Ti(III) ion[3], adds to ketones 2 at the carbonyl carbon affording the unsymmetrical pinacols 3 from respectable to excellent yields (Scheme 2).



Scheme 2.

The reaction is not limited to acetone[3] (R_1=R_2=CH_3) but is a generally applicable method for the synthesis of 3: only five out of the twentyfive ketones 2 examined failed to react for steric reasons.

Beyond the novelty of the process, which has to be considered exactly the reverse of the well known

cleavage reaction of t-alkoxy radical, these reactions are of interest in relation to the question of the direction of radical attack: a) carbonyl carbon instead of carbonyl oxygen with simple ketones; b) carbonyl carbon instead of double bond with ketones containing an isolated or conjugated double bond.

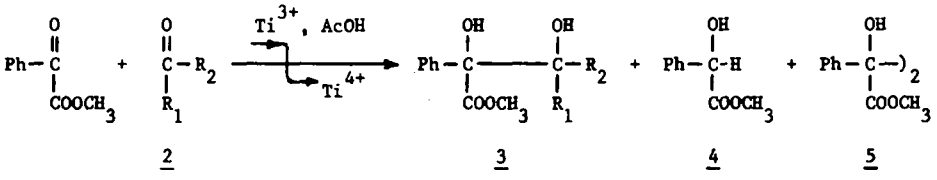
To evaluate the scope and limitation of the process, and to gain better understanding on both the sensitivity of the reaction to steric effects and the type of functional groups tolerated with the carbonyl addition, we have tested:

1) ketones with different steric environment around the reaction center;

2) ketones containing an additional functional group.

RESULTS

Reactions among titanium trichloride (30 mmol of an aqueous 15% solution), methyl phenylglyoxalate (15 mmol) and ketones 2a-zz (100-150 mmol) were carried out in acetic acid (10-15 ml) at room temperature under nitrogen. After workup, the results of product analysis could be described by Scheme 3.



Scheme 3.

Product isolated and NMR yields are listed in Tables 1 and 2. Unsymmetrical pinacols 3 and dimer 5 are obtained as a threo, erythro and meso, dl mixture, respectively.

The reaction conditions chosen are those under which consistent yields of 3 are obtained, that is: a) a great excess of ketone 2 has been utilized in order to minimize the formation of 5 in favour of 3[4]; b) rapid instead of dropwise addition of titanium trichloride solution has been adopted, for an excess of Ti(III) ion in the reaction medium improves the yield of 3 and reduces the formation of 5; c) acetic acid as the best co-solvent: use of methanol or ethanol favours the formation of 4 with respect to 3.

As for steric factors, the addition of radical 1 to the carbonyl group of 2 is remarkably influenced by the structure of the ketones investigated. The data of Table 1 clearly indicate that the yield of pinacols 3 decreases upon increasing the steric congestion around the carbonyl group of ketones 2.

The effect of steric hindrance is indeed clear in the series of methyl, n-alkyl ketones 2a-d: ^{1}H NMR yields of 3 decrease from 90 to 44% as the n-alkyl chain becomes longer ($CH_3 > C_2H_5 > C_3H_7 > C_4H_9$). With diethylketone 2e, yield of 3e drops to 18% indicating that n-dialkyl ketones are not suitable substrates for the addition of radical 1; with the less hindered cyclic ketones 2f-h, yields of 3 arise again to 68-80%.

The severely congested ketones 2i-ℓ fail to give 3 under our reaction conditions: radical 1 apparently does not attack the carbonyl group of these α-branched ketones, and both the competitive hydrogen atom abstraction from 2, or from the solvent, to give the carbinol 4 or its dimerization to afford 5 occur instead.

If the steric congestion is far away from the carbonyl group (cfr. methyl isobutyl- 2m with methyl isopropylketone 2i, and methyl benzylketone 2n with acetophenone 2ℓ) a respectable amount of 3 is again obtained: 43 and 52% ^{1}H NMR yields of 3m and 3n, respectively.

Table 1. Product isolated yields (%) in the reaction of $PhCOCOOCH_3$ with different sterically hindered ketones 2a-n.

Run	2 $R_1\overset{O}{\overset{\|}{C}}R_2$	Product isolated yields (%)[a] 3		Isomer ratio[b]	4	5	Unreacted $PhCOCOOCH_3$
a	$CH_3\overset{O}{\overset{\|}{C}}CH_3$	85	(90)[c]	-	traces	traces	-
b	$CH_3\overset{O}{\overset{\|}{C}}C_2H_5$	60	(68)	1 : 1	12	5	12
c	$CH_3\overset{O}{\overset{\|}{C}}C_3H_7$	51	(60)	1 : 1	12	7	15
d	$CH_3\overset{O}{\overset{\|}{C}}C_4H_9$	38	(44)	1 : 1	13	traces	33
e	$C_2H_5\overset{O}{\overset{\|}{C}}C_2H_5$	14	(18)	-	40	10	27
f	$(CH_2)_4C{=}O$	60	(68)	-	12	5	10
g	$(CH_2)_5C{=}O$	75	(80)	-	5	traces	5
h	$(CH_2)_6C{=}O$	71	(78)	-	5	5	5
i	$CH_3\overset{O}{\overset{\|}{C}}CH(CH_3)_2$	-			(49)	(41)	(10)
j	$CH_3\overset{O}{\overset{\|}{C}}C(CH_3)_3$	-			(56)	(36)	(8)
k	$CH_3\overset{O}{\overset{\|}{C}}cyC_6H_{11}$	-			(52)	(29)	(19)
l	$CH_3\overset{O}{\overset{\|}{C}}Ph$	-			(43)	(32)	(25)
m	$CH_3\overset{O}{\overset{\|}{C}}CH_2CH(CH_3)_2$	38	(43)	1 : 1	15	10	30
n	$CH_3\overset{O}{\overset{\|}{C}}CH_2Ph$	45	(52)	7 : 3	12	7	20

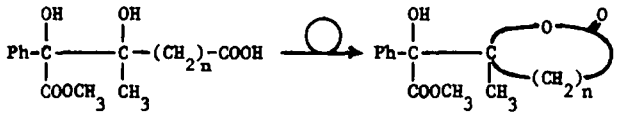
[a] Product isolated yields (%) are based on the starting $PhCOCOOCH_3$.
[b] Isomer ratios have been determined by ^1H NMR analysis of the crude reaction mixture.
[c] Yields in parentheses refer to ^1H NMR yield (%) determined on the crude reaction mixture.

The results of Table 2 address the chemoselectivity of radical 1 towards ketones 2o-zz containing additional functional groups: carboxylic acid, ester, hydroxy, methoxy, phenoxy, chloromethyl groups and isolated or conjugated double bonds do not interfere with the carbonyl addition.

The reaction of levulinic acid 2o with radical 1 affords γ-lactone 3o' in 51% yield indicating that carbon-carbon bond formation occurs solely at the keto function; the intermediate pinacol 3o undergoes lactonization to 3o' prior to distillation of unreacted 2o (Scheme 4).

A six membered δ-lactone 3p' (40% yield) is formed analogously from the corresponding acetylbutyric acid 2p (Scheme 4). The lower yield of 3p' with respect to that of 3o' may be interpreted in terms of steric factors due to the longer hydrocarbon chain of 2p. It remains to be seen whether larger

lactones can be synthesized as well.



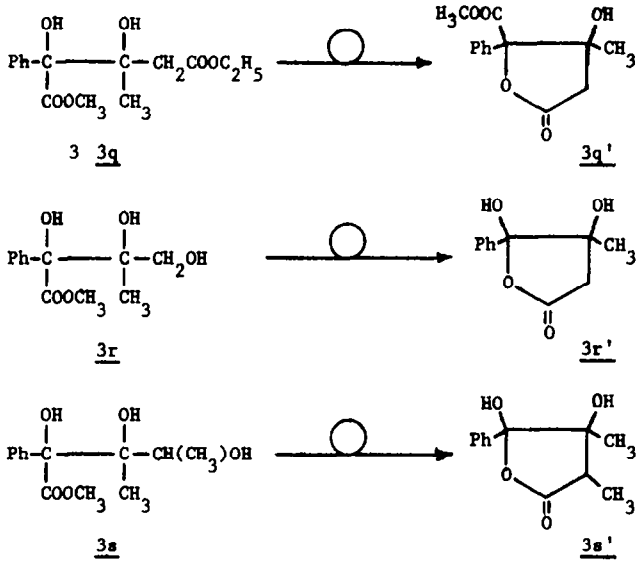
3o n= 2 3o' γ-lactone

3p n= 3 3p' δ-lactone

Scheme 4.

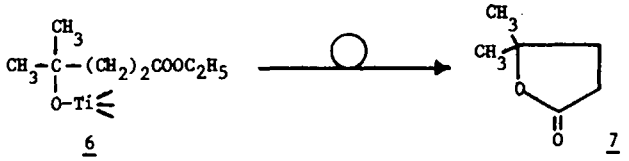
The reaction of ethylacetoacetate 2q with radical 1 occurs selectively at the ketone without attack to the ester group, but the intermediate pinacol 3q undergoes transesterification to γ-lactone 3q' (40% yield) prior to distillation of unreacted 2q (Scheme 5).

Transesterification does also occur with ketones containing an additional hydroxy group: addition of radical 1 to hydroxyacetone 2r and acetoin 2s affords γ-lactones 3r' and 3s' via intermediate pinacols 3r and 3s in 70 and 51% yields, respectively. With acetoin all four possible isomers 3s' were formed with only one highly favoured (60 : 24 : 8 : 8) (Scheme 5).



Scheme 5.

Since $Ti(OR)_4$ has been utilized as a catalyst in the alcoholysis of esters[5], and since it has recently been reported that the intermediate titanium compound 6 induces lactonization to 7[6] (Scheme 6), it is plausible to postulate in the case of the formation of 3q', 3r' and 3s' a specific interaction between Ti(IV) ion and both hydroxyl and carbonyl ester groups involved in the lactone formation.

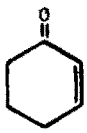


Scheme 6.

Neglecting minor electronic differences, the preferred addition of radical 1 to hydroxyacetone 2r with respect to acetoin 2s can be ascribed to steric effects; for the same reason 5-hydroxy-2-pentanone 2t fails to give 3t and hydrogen abstraction from 2t itself to form 4 in high yield (70%) seems the preferred path of radical 1.

Methoxy, phenoxy and chloro groups do not interfere with the carbonyl addition: in fact, 2u, 2v, and 2w react chemoselectively with radical 1 to give the corresponding pinacols. The higher yields obtained with methoxy- with respect to phenoxyacetone are once more due to steric factors.

Table 2. Product isolated yields (%) in the reaction of $PhCOCOOCH_3$ with ketones 2o-zz containing an additional functional group.

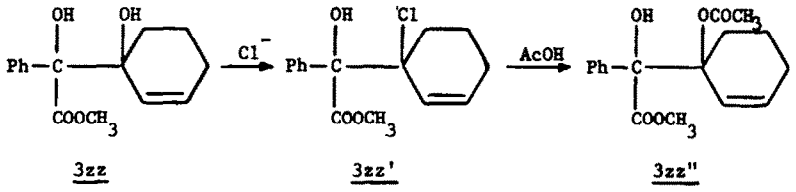
Run	2	Product isolated yields (%)[a] 3 or its derivatives	Isomer ratio[b]	4	5	Unreacted $PhCOCOOCH_3$
o	$CH_3C(=O)-(CH_2)_2COOH$	3o' (γ-lactone) 51	60:40	10	5	20
p	$CH_3C(=O)-(CH_2)_3COOH$	3p' (δ-lactone) 40	50:50	10	10	20
q	$CH_3C(=O)-CH_2COOC_2H_5$	3q' (γ-lactone) 46	63:37	15	14	14
r	$CH_3C(=O)-CH_2OH$	3r' (γ-lactone) 70	60:40	5	traces	10
s	$CH_3C(=O)-CH(CH_3)OH$	3s' (γ-lactone) 51	60:24:8:8	14	10	16
t	$CH_3C(=O)-(CH_2)_3OH$	-	-	(70)[c]	(10)	(20)
u	$CH_3C(=O)-CH_2OCH_3$	3u 71 (78)	70:30	10	traces	10
v	$CH_3C(=O)-CH_2OPh$	3v 40 (45)	55:45			
w	$CH_3C(=O)-CH_2Cl$	3w 54 (60)	50:50	8	12	20
z	$CH_3C(=O)-(CH_2)_2CH=CH_2$	3z 50 (58)	56:44	13	5	22
zz		3zz'(chlorinated) 35 3zz"(acetylated) 30 3zz 55[d] (65)	-	20	5	10

[a] Product isolated yields (%) are based on the starting $PhCOCOOCH_3$.
[b] Isomer ratios have been determined by ^1H NMR analysis of the crude reaction mixture.
[c] Yields in parentheses refer to ^1H NMR yields (%) determined on the crude reaction mixture.
[d] $Ti_2(SO_4)_3$ instead of $TiCl_3$ solution has been used as reducing agent.

A very interesting example of chemoselectivity is shown by the reaction of radical 1 with ketones 2z and 2zz containing an additional double bond. In the case of 2z addition occurs exclusively at the keto function, the position of the double bond being unaffected. With α,β-unsaturated cyclohexanone 2zz solely the 1,2-addition mode is observed, but pinacol 3zz was not isolated because a

subsequent nucleophilic substitution of 3zz takes place to give the chlorinated 3zz' (35% yield) and acetylated 3zz" (30% yield) products.

When titanium sulphate is used instead of titanium trichloride as a precursor of radical 1, pinacol 3zz is obtained in 55% yield while acetylated product 3zz" is not formed even if acetic acid is still present as co-solvent. This means that with titanium trichloride in acetic medium the sequence of nucleophilic substitution operating is 3zz ⟶ 3zz' ⟶ 3zz" (Scheme 7).



3zz 3zz' 3zz"

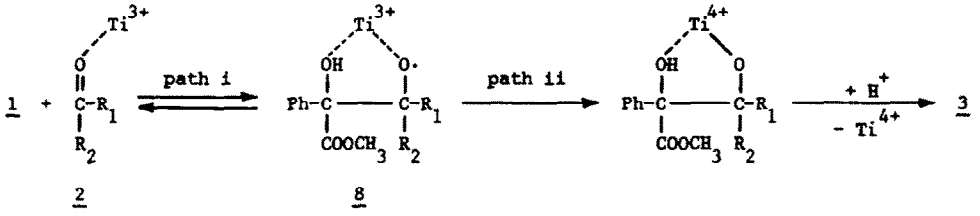
Scheme 7.

The Ti(III) or Ti(IV) ions present can act as "catalyst" or "promoter" in the latter type of reaction in assisting the chlorination of the allylic mojety 3zz. The "push-pull" mechanism of Swain[7a] emphasizes the importance of an electrophile in assisting the departure of a leaving group while a nucleophile attacks the carbon atom at the reaction center. The allylic system might be a special case because the structure is a very favourable one for the operation of a concerted mechanism. Many reactions of alkyl halides are known[7b] to be catalyzed by Lewis acids, but usually the metal-catalyzed reaction is the method used for preparing an alcohol from alkyl halides and not viceversa. In our case, the inverse transformation R-OH ⟶ R-Cl may well be due to the stronger electrophilicity of titanium ion towards oxygen with respect to halogen atom: in fact the π donor ability towards titanium ion seems to increase in the series Cl < OR[8].

In conclusion, the present results demonstrate that this type of reaction is highly sensitive to steric effects in the carbonyl substrate and highly chemoselective with ketones containing an additional functional group. This means that application in more complex systems, e.g., natural product syntheses, is likely to be successful.

DISCUSSION

A mechanism that explains the formation of pinacols 3 and is consistent with our previous reports[4,9] involves the addition of radical 1 to the carbonyl carbon of ketones 2 to give the intermediate alkoxy radical 8 (Scheme 8).



1 + 2 ⟶ 8 ⟶ 3

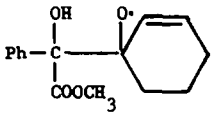
Scheme 8.

The success of addition to the carbonyl carbon depends on several factors, including the electronic character of the attacking radical and the reactivity of the radical resulting from addition. This latter is particularly important since path i is exactly the reverse of the well-known alkoxy radical cleavage. In our case, rapid reduction of the strong electrophilic alkoxy radical 8, path ii, by Ti(III) ion makes path i practically irreversible and accounts eventually for the significant yields of 3.

Ti(III) ion is able to give stable complexes with carbonyl compounds[10] also in aqueous solution[11]

and the complexation effect enhances the electrophilicity of the carbonyl group by increasing the positive carbon charge. A preexistent Ti(III) ion-carbonyl oxygen complexation favours the addition of radical 1 to ketones 2[12] and further on contributes to the easy reduction of alkoxy radical 8, being the Ti(III) ion already coordinated to the center which is going to be reduced.

The exclusive 1,2-addition of radical 1 to cyclohexanone 2zz stresses the twofold role played by Ti(III) ion in determining both the success and direction of the addition. The capability of Ti(III) ion to strongly coordinate with the carbonyl oxygen of enones[13] rather than with the π system of the double bond would favour the 1,2-addition mode. The direction of addition will be determined by the ease with which the radicals formed by carbonyl and double bond addition (9 and 10, respectively) are subsequently reduced by Ti(III) ion since both modes are reversible.



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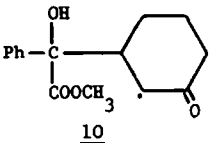

10

The stronger electrophilic nature of radical 9 with respect to 10 and therefore its easier reduction[14] accounts for the 1,2-addition product.

A question that requires an answer concerns the high yield of monomeric reduction product 4 obtained in the presence of the severely congested ketones 2i-ℓ, the hydroxy ketone 2t that fails to give the addition product, and ketone 2e that affords 3e in poor yield.

Formation of 4 from radical 1 could take several paths: a) disproportionation of 1 to form 4 and starting $PhCOCOOCH_3$; b) further reduction of 1 by a second electron uptake from Ti(III) ion; c) competitive hydrogen atom abstraction from ketones 2i-ℓ, 2t, and 2e which being used in great excess (10-15 ml) act both as co-solvents and hydrogen donors. Because in blank reactions (e.g., in absence of 2) the ratio 4 to 5 is markedly influenced by the H-donor ability of the solvent used but independent of Ti(III) ion concentration, we feel that the formation of 4 could be the result of hydrogen atom abstraction from the ketones that fail to give the addition product for steric reasons.

Nevertheless, to better elucidate this hypothesis subsequent more detailed studies, which are beyond the scope of this report, are underway.

EXPERIMENTAL

The physical data were obtained as follows: melting points in a Koffler apparatus (uncorrected); IR spectra on a Perkin-Elmer E 177; Mass spectra on a Hitachi-Perkin-Elmer RMU 6D at 70 eV; ^1H NMR spectra on a Varian A-90 and HA-300 with Me_4Si as an internal standard. Column and preparative TLC were carried out by using Merk silica gel 60 (0.06-0.24 mm) and Merk kieselgel GF-254 (2mm) plates, respectively. All starting materials were commercially available research grade chemicals and used as received. $TiCl_3$ and $Ti_2(SO_4)_3$ solutions (15% w/v) were standardized against Ce(IV) 0.1 N solution. All compounds were isolated and their structural assignments are completely consistent with the spectral data given below.

General procedure. To a well stirred solution of the substrate ($PhCOCOOCH_3$, 15 mmol) and the ketones (2a-zz, 100-150 mmol) in glacial acetic acid (15-20 ml), a 15% $TiCl_3$ aqueous solution (30 mmol) was added all at once. The reaction mixtures were allowed to react for 1 hr at room temperature under nitrogen.

General workup procedure. The crude reaction mixtures were extracted with ethyl acetate (3x100 ml). The combined organic layers were washed with water and then dried over anhydrous Na_2SO_4. Ethyl acetate and the low-boiling ketones were removed by rotary evaporator; the excess of unreacted high boiling ketones (b.p. > 120°C) were distilled off under reduced pressure in a water bath owing to the high temperature sensitive pinacols 3. The residue obtained were dissolved in a little ethyl acetate or chloroform and chromatographed on a silica gel column (50x2.5 cm) with the appropriate eluant. The unreacted $PhCOCOOCH_3$ was in all cases eluted first. Compounds 3 or their derivatives,

4 and 5 were the only reaction products. Yields given in Tables 1 and 2 are based on the starting $PhCOCOOCH_3$. Yields in parentheses and isomer ratios of 3 in Tables 1 and 2 were determined by ^1H NMR spectroscopy on an aliquot of the crude reaction mixture added to a suitable internal standard.

Spectroscopic data. All compounds of Tables 1 and 2 were isolated and their structural assignments were deduced from the following data:
Methyl dl-mandelate (4) was identified by comparison with an authentic sample.

Methyl meso-diphenyltartrate and Methyl dl-diphenyltartrate (5) see Ref. 3.

Methyl 2-phenyl-2,3-dihydroxy-3-methylbutanoate (3a) see Ref. 3.

Methyl 2-phenyl-2,3-dihydroxy-3-methylpentanoate (3b)
After workup of the crude residue (3.2 g) was chromatographed on a silica gel column and eluted with hexane-ethyl acetate (9:1). The elution order was: 3b (2.2 g, 60%), 5 and 4. By ^1H NMR analysis, 3b resulted to be a 1:1 mixture of isomers; m.p. 48-56 C. The higher melting point isomer was obtained pure by fractional crystallization of the isomeric mixture from petroleum ether-ether (9:1): m.p. 54-56 C; ^1H NMR ($CDCl_3$) δ 0.84 (t, J=7.2 Hz, 3H, CH_3), 1.20 (s, 3H, $CH_3C(OH)$), 1.50 (q, J=7.2 Hz, 2H, CH_2), 2.9 (s, 1H, OH, D_2O exch), 3.72 (s, 1H, OH, D_2O exch), 3.85 (s, 3H, $COOCH_3$), 7.3 (m, 3H, Ph-H), 7.7 (m, 2H, Ph-H_α). The lower melting point isomer was always contaminated with the higher melting point isomer: ^1H NMR ($CDCl_3$) δ 0.87 (t, J=7.2 Hz, 3H, CH_3), 1.08 (s, 3H, $CH_3CH(OH)$), 1.53 (q, J=7.2 Hz, 2H, CH_2), 2.8 (s, 1H, OH, D_2O exch), 3.7 (s, 1H, OH, D_2O exch), 3.85 (s, 3H, $COOCH_3$), 7.3 (m, 3H, Ph-H), 7.7 (m, 2H, Ph-H_α); MS m/e 223 (M-CH_3, 0.1), 221 (M-H_2O, 0.1), 209 (M-C_2H_5, 0.5), 166 (44), 151 (4), 134 (10), 107 (64), 106 (41), 105 (100), 79 (46), 77 (69), 73 (42), 55 (21), 51 (23); IR (nujol) ν_{max} 3500-3300 (OH), 1700 (C=O), 1250 (C-O-C) cm^{-1}.

Methyl 2-phenyl-2,3-dihydroxy-3-methylhexanoate (3c)
Workup as usual afforded 3.1 g of yellow thick syrup. This material was chromatographed on a silica gel column and eluted with hexane-chloroform-ether (5:4:1). The main fraction, collected and evaporated to dryness, afforded 2 g (51% yield) of pure 3c. ^1H NMR analysis of this product revealed to be a mixture of two isomers (1:1); m.p. 56-74 C. Any attempt to resolve the isomeric mixture by preparative TLC or fractionated recrystallization was unsuccessful. Isomeric mixture: ^1H NMR ($CDCl_3$) δ 0.83 (t, 3H, CH_3, one isomer), 0.86 (t, 3H, CH_3, the other isomer), 1.1 (s, 3H, $CH_3C(OH)$), one isomer), 1.25 (s, 3H, $CH_3C(OH)$), the other isomer), 1.4 (m, 4H, $2CH_2$), 2.9 (s, 1H, OH, D_2O exch), 3.7 (s, 1H, OH, D_2O exch), 3.83 (s, 3H, $COOCH_3$), 7.35 (m, 3H, Ph-H), 7.75 (m, 2H, Ph-H_α); MS m/e 237 (M-CH_3, 0.1), 235 (M-OH, 0.1), 219 (M-CH_3-H_2O, 0.4), 209 (M-C_3H_7, 0.9), 191 (M-C_3H_7-H_2O, 2), 166 (48), 151 (7), 134 (9), 107 (25), 106 (33), 105 (100), 87 (13), 79 (27), 77 (56), 51 (16), 45 (34), 43 (55); IR (nujol) ν_{max} 3480, 3380, 3300 (OH), 1730 (C=O), 1250 (C-O-C) cm^{-1}.

Methyl 2-phenyl-2,3-dihydroxy-3-methylheptanoate (3d)
After workup, the crude residue (3.2 g) was chromatographed on a silica gel column using as eluant the system hexane-chloroform-ether (5:4:1). Unreacted $PhCOCOOCH_3$ (33%) was eluted first. The second fraction collected was 3d (1.5 g, 42%) as a mixture of two isomers (1:1); m.p. 55-67 C. Recrystallization from petroleum ether did not change the isomers distribution and any further attempt to have the pure isomers was unsuccessful. Isomeric mixture: ^1H NMR ($CDCl_3$) δ 0.86 (2t, 3H, CH_3), 1.1 (s, 3H, $CH_3C(OH)$, one isomer), 1.2 (s, 3H, $CH_3C(OH)$, the other isomer), 1.2-1.6 (m, 6H, $(CH_2)_3$), 2.9 (s, br, 1H, OH, D_2O exch), 3.76 (s, 1H, OH, D_2O exch), 3.83 (s, 3H, $COOCH_3$), 7.3 (m, 3H, Ph-H), 7.75 (m, Ph-H_α, 2H); MS m/e 251 (M-CH_3, 0.1), 233 (0.5), 209 (M-C_4H_9, 2), 191 (3.6), 166 (100), 151 (6.4), 134 (10), 107 (42), 105 (43), 101 (9.5), 100 (6.6), 79 (20), 77 (24), 58 (20), 57 (7.6), 55 (5.4), 51 (6), 45 (8), 43 (49); IR (nujol) ν_{max} 3470 and 3350 (OH), 1700 (C=O), 1250 (C-O-C) cm^{-1}.

Methyl 2-phenyl-2,3-dihydroxy-3-ethylpentanoate (3e)
The crude reaction mixture was chromatographed on a silica gel column. Elution with hexane-chloroform-ether (5:4:1) gave in the order: unreacted $PhCOCOOCH_3$ (0.7 g, 28%), 3e (0.5 g, 14%), 4 (1 g, 40%). Recrystallization from petroleum ether-ether (1:1) gave colourless needles which melted at 77-78 C. ^1H NMR ($CDCl_3$) δ 0.78 (t, 3H, CH_3), 0.98 (t, 3H, CH_3), 1.3-2.0 (m, 4H, $2CH_2$), 3.15 (s, 1H, OH, D_2O exch), 3.65 (s, 1H, OH, D_2O exch), 3.80 (s, 3H , $COOCH_3$), 7.35 (m, 3H, Ph-H), 7.75 (m, 2H, Ph-H_α); MS m/e 253 (M+1, < 0.1)[15], 235 (0.1) 223 (M-C_2H_5, 2.5), 205 (11), 193 (M-$COOCH_3$, 0.5), 173 (4), 166 (100), 151 (6), 139 (9), 107 (57), 106 (29), 105 (74), 87 (21), 79 (35), 77 (47), 57 (45), 51 (12), 45 (16); IR (nujol) ν_{max} 3450, 3300 (OH), 1700 (C=O), 1250 (C-O-C) cm^{-1}.

Methyl 2-(1-cyclopentanol)mandelate (3f)
After workup and distillation under reduced pressure of the unreacted ketone, the residue was chromatographed with hexane-ethyl acetate (7:3); the elution order was: unreacted $PhCOCOOCH_3$, 4 and 3f. The main fraction, evaporated to dryness, afforded 2.2 g (60%) of pure 3f as white solid. Recrystallization from petroleum ether-ether: m.p. 52-54 C; ^1H NMR ($CDCl_3$) δ 1.3-2.0 (m, 8H, cy-C_4H_8), 2.75 (s, 1H, OH, D_2O exch), 3.7 (s, 1H, OH, D_2O exch), 3.83 (s, 3H, $COOCH_3$), 7.3 (m, 3H, Ph-H), 7.7 (m, 2H, Ph-H_α); MS m/e 233 (M-OH, 0.1), 215 (M-OH-H_2O, 1), 200 (0.2), 191 (M-$COOCH_3$, 1), 173 (2), 167 (10), 166 (97), 151 (6), 134 (11), 107 (43), 106 (39), 105 (100), 85 (23), 79 (28), 77 (59), 67 (16); IR (nujol) ν_{max} 3500, 3400 (OH), 1700 (C=O), 1250 (C-O-C) cm^{-1}.

Methyl 2-(1-cyclohexanol)mandelate (3g)
After workup and distillation under reduced pressure of the unreacted ketone 2g, a pale coloured solid was obtained as a residue. The solid was dissolved in hot hexane and, during evaporation, crystallization of 3g occurred. The product was collected upon filtration to give 2.9 g (73%) of pure 3g: m.p. 104-5 C; ^{1}H NMR ($CDCl_3$) δ 1.4-1.7 (m, 10H, cy-C_5H_{10}), 2.5-3.5 (s, br, 2H, 2OH, D_2O exch), 3.85 (s, 3H , $COOCH_3$), 7.35 (m, 3H, Ph-H), 7.75 (m, 2H, Ph-H_α); MS m/e 246 (M-H_2O, 0.1), 229 (M-OH-H_2O, 0.5), 205 (M-$COOCH_3$, 1), 187 (1), 166 (100), 151 (6), 134 (10), 107 (42), 106 (36), 105 (94), 99 (34), 81 (37), 79 (32), 77 (58), 55 (33); IR (nujol) ν_{max} 3440, 3420 (OH), 1700 (C=O),1250 (C-O-C) cm^{-1}.

Methyl 2-(1-cycloheptanol)mandelate (3h)
After workup and distillation under reduced pressure of the high boiling point ketone 2h, 3.6 g of a semisolid product was obtained. The crude material was dissolved in hexane-ether (1:1) and stored in refrigerator for 2 days; 3 g (71%) of pure 3h were obtained upon filtration as colourless needles: m.p. 100-2 C; ^{1}H NMR ($CDCl_3$) δ 1.3-1.9 (s, br, 12H, cy-C_6H_{12}), 2.8 (s, br, 1H, OH, D_2O exch), 3.7 (s, 1H, OH, D_2O exch), 3.83 (s, 3H, $COOCH_3$),7.35 (m, 3H, Ph-H), 7.75 (m, 2H, Ph-H_α); MS m/e 261 (M-OH, 0.1), 244 (M-2OH, 0.2), 219 (M-$COOCH_3$, 2), 166 (100), 151 (9), 134 (12), 113 (25), 107 (82), 105 (58), 95 (22), 84 (10), 79 (55), 77 (48), 68 (25), 55 (26), 51 (13); IR (nujol) ν_{max} 3560, 3540 (OH), 1725 (C=O), 1240 (C-O-C) cm^{-1}.

Methyl 2-phenyl-2,3- dihydroxy-3,5-dimethylhexanoate (3m)
After workup, the solution was evaporated to dryness and the crude residue was chromatographed on a silica gel column and eluted with hexane-chloroform-ether (5:4:1). The elution order was: Unreacted $PhCOCOOCH_3$, 3m and 4. The main fraction was collected and evaporated to dryness to give 1.45 g (38%) of pure 3m as a colourless solid-liquid material. ^{1}H NMR analysis revealed the presence of two isomers in equal amount. The higher melting point isomer was recovered pure upon twofold recrystallization from hexane as white needles: m.p. 87-90 C; ^{1}H NMR ($CDCl_3$) on a HA-300 δ 0.90 (d, J=6.5 Hz, 3H, CH_3), 0.89 (d, J=6.5 Hz, 3H, CH_3), 1.11 (s, 3H, $CH_3C(OH)$), 1.25 (dd, J_{AB}=14.5 Hz, J_{AC}=8 Hz, H_A-C-H_B), 1.72 (dd, J_{AB}=14.5 Hz, J_{BC}=4.5 Hz, H_B, H_A-C-H_B), 1.86 (m, H_C, >C-H_C), 2.86 (s, 1H, OH, D_2O exch), 3.69 (s, 1H, OH, D_2O exch), 3.86 (s, 3H, $COOCH_3$), 7.33 (m, 3H, Ph-H), 7.71 (m, 2H, Ph-H_α); MS m/e 248 (M-H_2O, 0.1), 233 (M-C_4H_9, 3), 231 (M-H_2O-OH, 0.5), 209 (3), 191 (5.5), 166 (100), 151 (6), 134 (8), 107 (15),106 (22), 105 (51), 101 (11), 79 (7.5), 77 (22), 59 (11), 57 (11), 43 (23); IR (nujol) ν_{max} 3490, 3300 (OH), 1700 (C=O), 1235 (C-O-C) cm^{-1}. The mother liquors of the above recrystallizations afforded, after removal of the solvent, a thick colourless oil. This latter was treated with hexane and stored in refrigerator for 3 days. Thereafter the lower melting point isomer was isolated as white crystals: m.p. 48-52 C; ^{1}H NMR ($CDCl_3$) δ 0.86 (d, 6H, $2CH_3$), 1.26 (s, 3H, $CH_3C(OH)$), 1.33 (dd, J_{AB}=13.5 Hz, J_{AC}=4.5 Hz, H_A, H_A-C-H_B), 1.6-2.0 (m, H_C, >C-H_C), 2.85 (s, 1H, OH, D_2O exch), 3.76 (s, 1H, OH, D_2O exch), 3.87 (s, 3H, $COOCH_3$), 7.33 (m, 3H, Ph-H), 7.71 (m, 2H, Ph-H_α).

Methyl 2-phenyl-2,3-dihydroxy-3-benzylbutanoate (3n)
The higher melting point isomer precipitates directly from the reaction mixture. After filtration 1.4 g (31%) were recovered. Recrystallization from ether gave colourless crystals: m.p. 138-9 C; ^{1}H NMR ($CDCl_3$) δ 1.0 (s, 3H CH_3), 2.86 and 3.03 (2d, 2H, AB system, J_{AB}=12 Hz, H_A-C-H_B), 3.15 (s, 1H, OH, D_2O exch), 3.70 (s, 3H, $COOCH_3$), 3.85 (s, 1H, OH, D_2O exch), 7.2 (s, 5H, Ph-H), 7.35 (m, 3H, Ph-H), 7.75 (m, 2H, Ph-H_α); MS m/e 223 (M-Ph, <1, 209 (M-CH_2Ph, 8), 191 (M-H_2O-CH_2Ph, 6), 166 (32), 135 (10), 134 (11), 107 (45), 105 (22), 92 (12), 91 (35), 79 (25), 77 (25), 66 (10), 51 (12), 43 (100); IR (nujol) ν_{max} 3410, 3300 (OH), 1710 (C=O), 1240 (C-O-C) cm^{-1}. After workup of the crude reaction mixture, the unreacted ketone 2e was distilled off under reduced pressure and the residue was chromatographed on a silica gel column with hexane-chloroform-ether (5:4:1). The main fraction was collected and gave, upon evaporation, the lower melting point isomer (0.6 g, 14%) which after recrystallization from petroleum ether-ether (8:2) melted at 90-94 C: ^{1}H NMR ($CDCl_3$) δ 1.15 (s, 3H, CH_3), 2.75 (s, 2H, CH_2), 3.7 (s, br, 2H, 2OH, D_2O exch), 3.82 (s, 3H, $COOCH_3$), 7.2 (s, 5H, Ph-H), 7.35 (m, 3H, Ph-H), 7.75 (m, 2H, Ph-H_α).

Methyl 2-(γ-valerolactone)mandelate (3o')
Workup as usual afforded the crude γ-lactone (2.5 g) that was purified by a silica gel column using hexane-chloroform-ether (5:4:1) as eluant to give in the order: 4 and pure 3o' (2 g, 51%) as white powder; ^{1}H NMR analysis revealed the presence of two isomers (60:40). In spite of our effort, separation of the isomeric mixture was not achieved. Upon recrystallization from petroleum ether-ether (8:2) the isomer ratio remained unchanged: m.p. 102-5 C; ^{1}H NMR ($CDCl_3$) δ 1.5 (s, 3H, CH_3), 1.7-2.0 (m, 2H, CH_2), 2.2-2.7 (m, 2H, CH_2), 3.9 (s, 3H, $COOCH_3$, the more abundant isomer), 3.93 (s, 3H, $COOCH_3$, the less abundant isomer), 4.0 (s, 1H, OH, D_2O exch, the less abundant isomer), 4.1 (s, 1H, OH, D_2O exch, the more abundant isomer), 7.35 (m, 3H, Ph-H), 7.75 (m, 2H, Ph-H_α); MS m/e 264 (M, 1), 205 (M-$COOCH_3$, 0.7), 187 (M-$COOCH_3$-H_2O, 0.9), 166 (8), 105 (15), 99 (100), 77 (11), 71 (6), 55 (2), 51 (3), 43 (21); IR (nujol) ν_{max} 3450 (OH), 1760 (C=O, γ-lactone), 1730 (C=O, ester), 1250 cm^{-1}.

Methyl 2-(δ-caprolactone)mandelate (3p')
Workup as usual afforded 1.8 g of crude δ-lactone 3p'. ^{1}H NMR analysis of a suitable aliquot revealed the presence of two isomers in equal amount. Twofold crystallization of crude 3p' from ether-ethyl acetate (9:1) afforded 0.8 g (20%) of the pure higher melting point isomer: m.p. 139-41 C;

^{1}H NMR ($CDCl_3$) δ 1.38 (s, 3H, CH_3), 1.85 (m, 4H, $2CH_2$), 2.45 (m, 2H, CH_2), 3.85 (s, 3H, $COOCH_3$), 4.05 (s, 1H, OH, D_2O exch), 7.35 (m, 3H, Ph-H), 7.85 (m, 2H, Ph-H_α). The combined mother liquors, concentrated to dryness in vacuo, afforded upon recrystallization from ether, 0.8 g (20%) of the pure lower melting point isomer: m.p. 94-7 C.; ^{1}H NMR ($CDCl_3$) δ 1.41 (s, 3H, CH_3), 1.85 (m, 4H, $2CH_2$), 2.45 (m, 2H, CH_2), 3.85 (s, 3H, $COOCH_3$), 3.98 (s, 1H, OH, D_2O exch), 7.35 (m, 3H, Ph-H), 7.85 (m, 2H, Ph-H_α); MS m/e 278 (M, 1), 261 (M-OH, 0.1), 246 (M-CH_3OH, 0.4), 219 (M-$COOCH_3$, 0.9), 201 (1.3), 183 (0.6), 166 (6), 113 (100), 105 (22), 85 (48), 77 (15), 55 (13), 43 (47); IR (nujol) ν_{max} 3420 (OH), 1735 (C=O, δ-lactone), 1730 (C=O, ester), 1240 (C-O-C) cm^{-1}.

β-Methyl-β-hydroxy-γ-phenyl-γ- carbomethoxybutyrolactone (3q')
After distillation under reduced pressure of the unreacted 2q, 3.2 g of yellow thick oil was obtained. The latter was purified on a silica gel column using hexane-chloform-ether (5:4:1) as eluant; elution order: 4, 5 and 3q'. The main fraction corresponding to 3q', upon evapoartion in vacuo, gave 1.7 (46%) of a pale yellow oil which resulted to be a mixture of two isomers in the ratio 63:37 by ^{1}H NMR analysis. Separation of the isomeric mixture was not achieved. ^{1}H NMR ($CDCl_3$) δ 1.25 (s, 3H, CH_3, the more abundant isomer), 1.6 (s, 3H, CH_3, the less abundant isomer), 2.53 and 2.75 (2d, 2H, AB system, J=16.5 Hz, H_A-C-H_B, the more abundant isomer), 2.66 and 2.83 (2d, 2H, AB system, J=17.5 Hz, H_A-C-H_B, the less abundant isomer), 3.5 (s, 1H, OH, D_2O exch), 3.78 (s, 3H, $COOCH_3$, the less abundant isomer), 3.80 (s, 3H, $COOCH_3$, the more abundant isomer), 7.5 (m, 5H, Ph-H); MS m/e 250 (M, 5), 218 (24), 191 (M-$COOCH_3$, 8), 173 (M-Ph, 7), 166 (62), 149 (8), 105 (100), 85 (26), 77 (43), 58 (28), 51 (14), 43 (75); IR (film) ν_{max} 3450 (OH), 1790 (C=O, γ-lactone), 1735 (C=O, ester), 1260 (C-O-C) cm^{-1}.

β-Methyl-β,γ-dihydroxy-γ-phenylbutyrolactone (3r')
After distillation of unreacted 2r, 3.5 g of a yellow thick liquid was obtained as a residue which was further purified on a silica gel column with hexane-ether (3:7) as eluant. The first eluted fraction afforded, upon evaporation of the solvent, 2.2 g(70%) of lactone 3r' as a mixture of two isomers (60:40), separation of which was not achieved. ^{1}H NMR ($CDCl_3$) δ 0.93 (s, 3H, CH_3, the more abundant isomer), 1.3 (s, 3H, CH_3, the less abundant isomer), 3.5-4.0 (s, br, 2H, 2OH, D_2O exch), 4.03 and 4.28 (2d, 2H, AB system, J=9.9 Hz, H_A-C-H_B, the more abundant isomer), 4.16 and 4.33 (2d, 2H, AB system, J=9 Hz, H_A-C-H_B, the less abundant isomer), 7.35 (m, 5H, Ph-H); MS m/e 208 (M, 12), 190 (M-H_2O, 42), 166 (10), 151 (M-$COOCH_3$, 25), 134 (48), 107 (40), 106 (56), 105 (98), 79 (68), 77 (56), 58 (CH_2=C(OH)CH_3, 100), 51 (22), 43 (58); IR (film) ν_{max} 3450 (OH), 1775 (C=O), 1250 (C-O-C) cm^{-1}.

α,β-Dimethyl-β,γ-dihydroxy-γ-phenylbutyrolactone (3s')
The unreacted 2s remained in the aqueous layer. The combined organic extracts, evaporated to dryness by rotary evaporator, afforded 3.3 g of a syrup oil which was further purified on a silica gel column using ether-hexane (3:7) as eluant. All four possible isomers of 3s' were obtained; elution order: isomer A (0.4 g, 12%), isomer B (1 g, 30%), isomers C and D in equal amount (0.3 g, 9%). Upon recrystallization from petroleum ether-ether (1:1), isomer A was obtained as colourless needles: m.p. 126-9 C; ^{1}H NMR ($CDCl_3$) δ 0.8 (s, 3H, $CH_3C(OH)$), 1.25 (d, J=6.3 Hz, 3H, CH_3), 2.5-3.5 (2H, br, 2OH, D_2O exch), 4.6 (q, J=6.3 Hz, 1H, CH), 7.4 (s, 5H, Ph-H); IR (nujol) ν_{max} 3440, 3230 (OH), 1775 (C=O), 1215 (C-O-C) cm^{-1}. Isomer B, recrystallized from petroleum ether-ether (3:7), was obtained as white crystals: m.p. 120-3 C; ^{1}H NMR ($CDCl_3$) δ (s, 3H, $CH_3C(OH)$), 1.4 (d, J=6 Hz, 3H, CH_3), 3.2 (s, 1H, OH, D_2O exch), 3.7-4.2 (1H, br, OH, D_2O exch), 4.35 (q, J=6 Hz, 1H, CH), 7.4 (s, 5H, Ph-H); MS m/e 222 (M, 11), 166 (3.5), 134 (12), 106 (30), 105 (49), 89 (52), 77 (31), 72 (100), 71 (14), 57 (7), 51 (11), 43 (50). Separation of isomer C from D was not achieved: ^{1}H NMR ($CDCl_3$) 0.9(s, 3H, CH_3, one isomer), 1.3 (s, 3H, CH_3, the other isomer), 3.3 and 3.9 (2s, 2H, 2OH, D_2O exch), 4.1 (q, J=6 Hz, 1H, CH, one isomer), 4.33 (dq, J=6 Hz, 1.8 Hz, 1H, CH, the other isomer), 7.35 and 7.4 (s, 5H, Ph-H).

Methyl 2-phenyl-2,3-dihydroxy-3-methoxymethylbutanoate (3u)
After evaporation to dryness of the organic extracts, 3.5 g of residue were obtained as a thick oil. ^{1}H NMR analysis of the crude mixture revealed the presence of two isomers 3u in the ratio 70:30. By purification on a silica gel column with hexane-chloroform-ether (5:4:1) as eluant, the less abundant isomer was eluted first (0.8 g, 21%) as an oil : ^{1}H NMR ($CDCl_3$) δ 0.9 (s, 3H, CH_3), 3.28 and 3.75 (2d, AB system, J=9.3 Hz, 2H, H_A-C-H_B), 3.35 (s, 3H, OCH_3), 3.8 (s, 3H, $COOCH_3$), 4.3 (s, br, 2H, 2OH, D_2O exch), 7.35 (m, 3H, Ph-H), 7.85 (m, 2H, Ph-H_α). The more abundant isomer was eluted afterward (1.9 g, 50%) as an oil: ^{1}H NMR ($CDCl_3$) δ 1.3 (s, 3H, CH_3), 3.28 and 3.4 (2d, AB system, J=9.3 Hz, 2H, H_A-C-H_B), 3.3 (s, 3H, OCH_3), 3.83 (s, 3H, $COOCH_3$), 4.5 (s, 2H, 2OH, D_2O exch), 7.35 (m, 3H, Ph-H), 7.75 (m, 2H, Ph-H_α); MS m/e 254 (M, 0.5) 209 (M-CH_2OCH_3, 1.5), 191 (5.5), 166 (100), 134 (9.5), 107 (35), 106 (24), 105 (65), 89 (25), 88 (12), 79 (18), 77 (30), 59 (19), 51 (10), 45 (25), 43 (40); IR (film) ν_{max} 3480 (OH), 1725 (C=O), 1250 and 1100 (C-O-C) cm^{-1}.

Methyl 2-phenyl-2,3-dihydroxy-3-phenoxymethylbutanoate (3v)
Upon distillation under reduced pressure of unreacted 2v, 2 g of yellowish solid were recovered. Recrystallization from ether-chloroform (8:2) afforded the more abundant isomer 3v (1 g, 22%) as white crystals: m.p. 134-5 C; ^{1}H NMR ($CDCl_3$) δ 1.0 (s, 3H, CH_3), 3.86 and 4.4 (2d, AB system, J=9 Hz, H_A-C-H_B), 3.93 (s, 3H, $COOCH_3$), 4.03 (s, 1H, OH, D_2O exch), 4.15 (s, 1H, OH, D_2O exch), 6.9

(m, 3H, Ph-H), 7.35 (m, 5H, Ph-H), 7.9 (m, 2H, Ph-H_α); MS m/e 316 (M, 0.6), 257 (M-$COOCH_3$), 0.1), 239 (0.4), 209 (M-CH_2OPh, 1), 191 (5), 166 (100), 151 (14), 150 (34), 134 (9), 107 (CH_2OPh, 90), 105 (65), 94 (12), 79 (42), 77 (80), 57 (10), 51 (20), 43 (45); IR (nujol) ν_{max} 3460, 3370 (OH), 1720 (C=O), 1600 and 1500 (C=C, benzene ring), 1250, 1100 (C-O-C) cm^{-1}. The less abundant isomer was recovered (0.9 g, 18%) from the mother liquor of the above crystallization by dissolving the residue in petroleum ether-ether (1:1): ^1H NMR ($CDCl_3$) δ 1.4 (s, 3H, CH_3), 3.85 (s, 3H, $COOCH_3$), 3.98 (s, 2H, CH_2), 4.0-4.3 (s, br, 2H, 2OH, D_2O exch), 6.85 (m, 3H, Ph-H), 7.35 (m, 5H, Ph-H), 7.95 (m, 2H, Ph-H_α).

Methyl 2-phenyl-2,3-dihydroxy-3-chloromethylbutanoate (3w)
After usual workup, 3.3 g of thick oil were obtained. Purification on a silica gel column with hexane-ether (1:1) as eluant afforded a first fraction of 2.1 g (54%) of pure 3w in 1:1 mixture of two isomers. The isomeric mixture was further chromatographed on a silica gel plate and developed in hexane-ether (6:4). The band that moved first afforded one pure isomer as an oil: ^1H NMR ($CDCl_3$) δ 1.1 (s, 3H, CH_3), 3.0 (s, 1H, OH, D_2O exch), 3.6 and 3.96 (2d, AB system, J=11 Hz, H_A-C-H_B), 3.9 (s, 3H, $COOCH_3$), 4.0 (s, 1H, OH, D_2O exch), 7.35 (m, 3H, Ph-H), 7.75 (m, 2H, Ph-H_α). The band that moved less gave the other pure isomer as an oil: ^1H NMR ($CDCl_3$) δ 1.4 (s, 3H, CH_3), 3.0 (s, br, 2H, 2OH, D_2O exch), 3.61 (s, 2H, CH_2Cl), 3.86 (s, 3H, $COOCH_3$), 7.35 (m, 3H, Ph-H), 7.75 (m, 2H, Ph-H_α); MS m/e 209 (M-CH_2Cl, 2.4), 201 (0.9), 199 (M-$COOCH_3$, 2.7), 191 (10.6), 166 (98), 151 (11), 134 (15), 107 (40), 106 (35), 105 (100), 95 (3.1), 93 ($CH_3C(OH)CH_2Cl$, 9.3), 79 (18), 78 (10), 77 (50), 58 (8.6), 51 (17), 43 (75); IR (film) ν_{max} 3480 (OH), 1725 (C=O), 1250 (C-O-C), 740 (C-Cl) cm^{-1}.

Methyl 2-phenyl-2,3-dihydroxy-3-methyl-6-heptanoate (3z)
After workup, the crude residue (3 g) was purified on a silica gel column by using hexane-chloroform-ether (5:4:1); the elution order was: 5, 3z and 4. The main fraction was collected and gave, upon evaporation, 2 g of pure 3z (50%) which by ^1H NMR analysis resulted to be a mixture of two isomers (56:44). Twofold recrystallization from petroleum ether gave the less abundant isomer: m.p. 83-5 C; ^1H NMR ($CDCl_3$) δ 1.22 (s, 3H, CH_3), 1.6 (m, 2H, CH_2), 2.15 (m, 2H, CH_2), 3.0 (s, 1H, OH, D_2O exch), 3.75 (s, 1H, OH, D_2O exch), 3.85 (s, 3H, $COOCH_3$), 4.9 (m, 2H, H_2C=C), 5.75 (m, 1H, HC=C), 7.3 (m, 3H, Ph-H), 7.75 (m, 2H, Ph-H_α); MS m/e 265 (M+1, 0.1)[15], 247 (M-H_2O, 0.2), 219 (0.2), 206 (0.1), 187 (0.3), 166 (11), 151 (1.3), 149 (0.9), 134 (1.2), 107 (14), 106 (13), 105 (47), 99 (1.3), 79 (32), 77 (48), 55 (12), 51 (19), 43 (100), 41 (15), 39 (20); IR (nujol) ν_{max} 3500, 3400 (OH), 1700 (C=O), 1640 (C=C), 1250 (C-O-C) cm^{-1}. The mother liquors of the above recrystallizations, evaporated to small volume, were chromatographed on a silica gel plate and developed in hexane-chloroform-ether (5:3:1). The main band had minor R_f and gave, upon evaporation of the solvents, the more abundant low melting point isomer: ^1H NMR ($CDCl_3$) δ 1.1 (s, 3H, CH_2) 1.6 (m, 2H, CH_2), 2.1 (m, 2H, CH_2), 2.9 (s, 1H, OH, D_2O exch), 3.7 (s, 1H, OH, D_2O exch), 3.85 (s, 3H, $COOCH_3$), 4.9 (m, 2H, H_2C=C), 5.75 (m, 1H, HC=C), 7.3 (m, 3H, Ph-H), 7.75 (m, 2H, Ph-H_α).

Methyl 2-(2-cyclohexen-1-ol)mandelate (3zz)
When $TiCl_3$ was used as precursor of radical 1, 3zz was not obtained because its subsequent chlorination to 3zz' and acetylation to 3zz" occurred (see Results). $Ti_2(SO_4)_3$ afforded instead 3zz (2.2 g, 55%) after usual workup and purification over a silica gel column, eluant hexane-chloroform-ether (5:4:1). Recrystallization of 3zz from ether gave colourless crystals: m.p. 82-3 C; ^1H NMR ($CDCl_3$) δ 1.3-2.0 (m, 6H cy$(CH_2)_3$), 2.5-3.0 (s, br, 1H, OH, D_2O exch), 3.83 (s, 3H, $COOCH_3$), 4.0 (s, 1H, OH, D_2O exch), 6.0 (s, br, 2H, HC=CH), 7.35 (m, 3H, Ph-H), 7.75 (m, 2H, Ph-H_α); MS m/e 262 (M, 0.1), 245 (M-OH, 1), 203 (M-$COOCH_3$, 1.5), 185 (2), 166 (50), 107 (42), 105 (43), 97 (100), 79 (27), 77 (38), 68 (30), 55 (15), 51 (12); IR (nujol) ν_{max} 3480, 3340 (OH), 1710 (C=O), 1250 (C-O-C) cm^{-1}.

Methyl 2-(1-chloro-2-cyclohexene)mandelate (3zz') and
Methyl 2-(1-acethoxy-2-cyclohexene)mandelate (3zz")
When $TiCl_3$ was used as reducing agent, 3zz' and 3zz" were formed in 35 (1.5 g) and 30% (1.4 g) yield, respectively. After workup, the crude reaction residue (3.8 g) was fractionated on a silica gel column with hexane-chloroform-ether (5:4:1) as eluant. Products elution followed the order: 3zz', 3zz" and 4. Upon recrystallization from petroleum ether-ether (1:1) the chlorinated product 3zz' melted at 92-4 C; ^1H NMR ($CDCl_3$) δ 1.3-2.2 (m, 6H, cy$(CH_2)_3$), 3.75 (s, 1H, OH, D_2O exch), 3.85 (s, 3H, $COOCH_3$), 4.7 (m, 1H, HC=C), 5.8 (dd, 1H, C=CH), 7.35 (m, 3H, Ph-H), 7.55 (m, 2H, Ph-H_α); MS m/e 280 (M, 1.1), 262 (M-H_2O, 2), 244 (M-HCl, 3), 227 (M-HOCl, 10), 223 (35), 221 (M-$COOCH_3$, 85), 186 (21), 185 (94), 167 (24), 157 (22), 143 (21), 129 (12), 115 (11), 111 (9), 105 (100), 91 (18), 79 (26), 77 (81), 51 (18); IR (nujol) ν_{max} 3480 (OH), 1720 (C=O), 1650 (C=C), 1250 (C-O-C) cm^{-1}. The acetylated product 3zz" was obtained as a thick yellow liquid: ^1H NMR ($CDCl_3$) δ 1.4-1.9 (m, 6H, cy$(CH_2)_3$), 2.0 (s, 3H, CH_3COO), 3.8 (s, 3H, $COOCH_3$), 4.0 (s, 1H, OH, D_2O exch), 5.35 (m, 1H, HC=C), 5.65 (m, 1H, C=CH), 7.35 (m, 3H, Ph-H), 7.55 (m, 2H, Ph-H_α); MS m/e 304 (M, 0.8), 286 (M-H_2O, 3), 244 (M-CH_3COOH, 17), 216 (6), 185 (M-CH_3COOH-$COOCH_3$, 100), 166 (10), 157 (12), 105 (93), 97 (8), 91 (9), 85 (18), 83 (27), 77 (26), 55 (6), 51 (5), 47 (7), 43 (25); IR (film) ν_{max} 3500 (OH), 1730 (C=O), 1600 (C=C), 1240 (C-O-C) cm^{-1}.

Acknowledgements- Financial support from Ministero Pubblica Istruzione 60% is gratefully acknowledged.

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