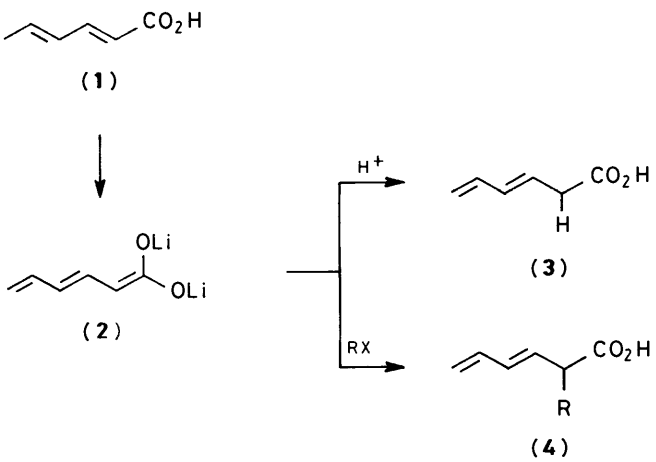
Unsaturated Carboxylic Acid Polyenolates. Lithium Trienolate of Sorbic Acid as a d^6 Synthon: Addition to Ketones and Unsaturated Ketones

Pablo Ballester, Antonio Costa, and Angel García-Raso
Departament de Química, Universitat de les Illes Balears, Palma de Mallorca, Spain
Ramon Mestres *
Departament de Química Orgànica, Universitat de València, València, Spain

Deprotonation of sorbic acid by two equivalents of lithium diethylamide, and aldol-type reaction of the resulting trienolate dianion (**2**) with carbonylic compounds affords the pentadienyl hydroxy acids (**6**) or 7-hydroxyhexa-2,4-dienoic acids (**7**) according to the duration and temperature of the reaction. The reaction of the dianion (**2**) with α,β-unsaturated ketones gives 1,4-ε-adducts for di- or tri-substituted enones, but either 1,4-γ- or 1,4-α-adducts for monosubstituted enones.

Lithium dienolates of unsaturated carboxylic acids are known to lead to the synthesis of 5-hydroxy- and 7-oxo-unsaturated carboxylic acids by reaction with ketones and enones, respectively.[1-4] Thus, the easily available crotonic, dimethylacrylic, and (*E*)-2-methylbut-2-enoic acids are useful d^4 synthons. With this in view, it was hoped that sorbic acid† might similarly constitute a useful d^6 synthon. Indeed, sorbic acid can be deprotonated to afford a dianion, the structure of which will be assumed here to be that of lithium trienolate (**2**). Protonation or alkylation of this dianion occurs at the α-carbon, and gives deconjugated hexadienoic acids (**3**) or (**4**) (Scheme 1). The same behaviour is found for equivalent



Scheme 1.

trienolates derived from other hexadienoic acids or their esters.[5-7] However, we have shown in a short communication that the addition of the trienolate (**2**) to the carbonyl group is reversible, and that the regioselectivity can be dramatically modified by time and temperature of the reaction.[8] The experimental details of these results, as well as the reaction of the trienolate with unsaturated ketones, are here described in full.

The trienolate was prepared by deprotonation of the free acid (**1**) by two equivalents of lithium diethylamide in THF at −70 °C. The carbonylic compounds were added at −70 °C, and the reaction mixture was stirred at this temperature and for the time established for each run. Quenching with aqueous sodium hydroxide, extraction of neutrals, and acidification of the aqueous solution allowed the isolation of a crude mixture of carboxylic acids.

Product compositions of mixtures were established by ^{1}H n.m.r. spectroscopy of esterified aliquots. Although the patterns of the ethylenic proton signals were rather complex (80 MHz), the presence of α,γ, or ε adducts was discernible from the multiplets centred at δ 5.25 ($C{=}CC{=}CH_2$), 6.90 (dd, $CH{=}CHCO_2Me$) and 7.45 ($C{=}CCH{=}CCO_2Me$), respectively. As the latter signal was sometimes obscured when phenyl groups were present, the multiplet at 5.75—6.2, common to all regioisomers, and the signals at 5.0—5.15 of both α and γ adducts were helpful as well.

When the reactions of the sorbic acid dianion (**2**) with aldehydes and ketones were monitored, α-adducts were found to predominate over short reaction times, whereas ε compounds were found with longer reaction times, at room temperature. This behaviour parallels that of the dienolates of crotonic and dimethylacrylic acids, but both α and ε additions to the carbonylic compounds are slower. The unconjugated hexadienoic acid (**3**) is found in the reaction mixture as the result of protonation of unchanged trienolate. The equivalent vinylacetic acids derived from dienolates of crotonic or dimethylacrylic acids are rarely detected when these dienolates are employed.[1-4] However, the hexadienoic acid (**3**) is frequently found after several hours. The unconjugated acid (**3**) also occurs in the mixtures resulting from runs carried out with heating after long reaction times, or when hexamethylphosphoric triamide (HMPA) or an excess of ketone were added. On these occasions lower total yields are obtained, and the presence of polymeric materials hampers the purification of adducts. These unwanted polymers probably arise from the deprotonation of the ketone by the trienolate, and polymerization of the resulting unconjugated carboxylic acid lithium salt during the reaction, or of the free acid during work-up.[8] The deleterious effect of HMPA has already been observed for dienolates of crotonic and dimethylacrylic acids.

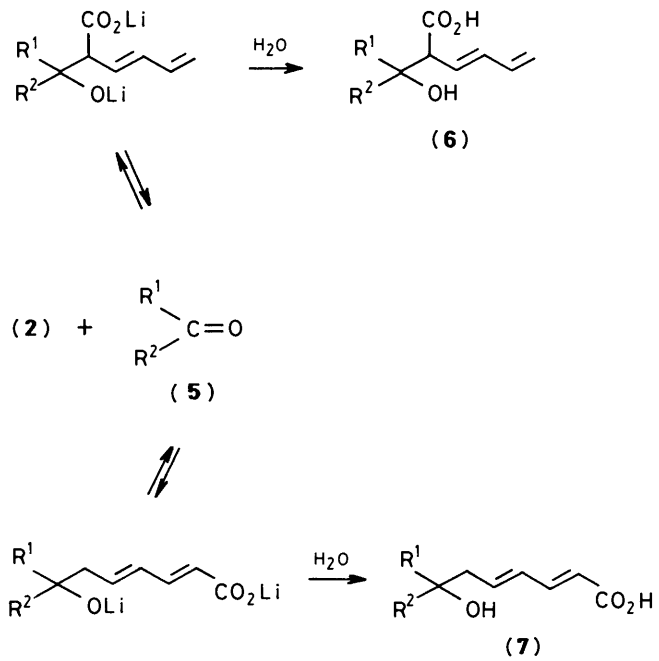
The results for the reaction of the trienolate (**2**) with aldehydes and ketones (**5**) are given in Table 1. Owing to the ease of polymerization, purification of the butadienyl hydroxy acids (**6**) is feasible only when the unconjugated acid (**3**) or the ε-adducts are not present in the reaction mixtures. For the same reason, these α-adducts have only being characterized spectroscopically, with the exception of (**6h**) which precipitates as a stable, crystalline material. On the other hand, the 7-hydroxy acids (**7**) are stable, and have been conveniently purified as acids or as esters by crystallization or column

† (2*E*,4*E*)-Hexa-2,4-dienoic acid.

Table 1. Reaction of the lithium dianion of sorbic acid with aldehydes and ketones

Carbonyl compound	Temp. (°C)	Time (h)	Crude yield (%)	Isolated yield (6) (%)	Isolated yield (7) (%)
(5a)	30	72	64	54[b]	
(5b)	−70	0.5	87	75[a]	
(5c)	30	24	65		42[b]
(5d)	30	24	92		33[c]
(5e)	30	24	86		55[b]
(5f)	30	3	85		68[c]
(5g)	−70	0.5	83	80[a]	
	30	24	70		28[b]
(5h)	0	3	85	76[c]	
	30	72	64		15[b]

[a] Characterized spectroscopically. [b] Isolated as the methyl ester by column chromatography. [c] Isolated as the free acid by crystallization.



a; R^1 = Et, R^2 = H
b; R^1 = Ph, R^2 = H
c; R^1 = Me, R^2 = Bu^t
d; R^1 = Me, R^2 = Ph
e; R^1 = Me, R^2 = $(CH_2)_2CH{=}CMe_2$
f; R^1 = R^2 = Ph
g; R^1,R^2 = $-(CH_2)_6-$
h; R^1,R^2 = $-(CH_2)_{11}-$

Scheme 2.

chromatography. No improved preparative conditions have been attempted.

The effect of time and temperature on the mixture composition seems to be the result of two addition equilibria (Scheme 2), the α-addition occurring faster, but the ε-adducts being more stable. Fortunately the decomposition of the trienolate is slow at room temperature, and the satisfactory preparation of 7-hydroxy acids is possible, provided only moderate equilibration times are required. The steric bulk of the groups attached to the carbonyl groups affects the regioselectivity as well. Thus, aldehydes do not afford ε-adducts in practical amounts even after several days. Conversely, a ketone with a hindered carbonyl group, such as benzophenone, leads directly to the ε-adduct (**7f**). Takeda has observed *E,Z*-isomers resulting from the protonation of ester trienolates,[7] and the same could be expected for the electrophilic attack of the carbonyl group on the α-carbon of the trienolate. However, mixtures of *E,Z*-isomers have not been observed. The *E* configuration for all the ethylenic double bonds of some of the isolated compounds (**6**) and (**7**) was established by 200 MHz n.m.r. spectroscopy, and the same configuration is assumed for others, as the adducts were obtained as both chromatographically and spectroscopically homogeneous materials.

Table 2. Reaction of the sorbic acid dianion with unsaturated ketones

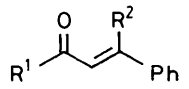
Ketone	Temp. (°C)	Time (h)	Crude yield (%)	Regioisomers Major	Regioisomers Minor	Isolated compound[a] (purified yield)
(8)	−70	0.5	81	1,4-γ		(15)[e] (40)
	25	12	82	1,4-α		(18)[d] (38)
	25	72	90	1,4-ε	1,4-ε	(18a), (18b)
(9)	−70	0.5	74	1,4-γ	1,2-ε	(16),[c,e] (22)
					1,4-ε	
	25	24	96	1,4-α		(19)[b] (73)
(10)	−70	0.5	53		1,2-ε	(3) (25), (23)[c]
					1,4-γ	(5)
						(17)[c] (5)
	25	36	94	1,4-α		(20)[c] (25)
				1,4-ε		(21)[c] (30)
(11)	0	3	95	1,4-γ		(24)[e] (65)
(12)	0	3	98	1,4-γ		(25)[e] (80)
(13)	25	24	78	1,4-ε		(26)[f] (42)
(14)	25	24	88	1,4-ε		(27)[f] (46)

[a] Isolated as methyl esters by column chromatography unless otherwise stated. [b] Isolated as the free acid by crystallization. [c] Fairly pure samples obtained for spectroscopic characterization. [d] One single diastereoisomer obtained. [e] Obtained as a mixture of diastereoisomers. [f] Obtained as a *E,E* + *Z,Z* mixture.

We have previously found that unsaturated ketones undergo addition with dienolates of unsaturated carboxylic acids to give 1,4-γ adducts.[4] Very few exceptions were found to this general regioselectivity. It has now been shown that the trienolate of sorbic acid parallels the behaviour of dienolates on reaction with aldehydes and ketones. From these observations we expected that the reaction of the sorbic acid trienolate (**2**) with enones would be fairly simple, and that 1,4-ε compounds would generally be obtained. In contrast, we found that the reaction is rather complex, and that its regioselectivity is very sensitive to structural effects and to reaction conditions. This can be seen in Table 2, in which the results obtained for the reaction of the trienolate (**2**) with enones (**8**)—(**14**) are summarized.

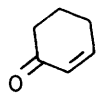
One general feature is that 1,2-adducts were not observed as the predominant components of the reaction mixtures obtained after short reaction times at −70 °C or at room temperature. Small amounts of 1,2-ε adducts are certainly present in the mixtures, and the hydroxy acids (**22**) and (**23**), arising from the enones (**9**) and (**10**), respectively, were isolated.

For the di- and tri-substituted enones (**10**), (**13**), and (**14**), the additions are slow, and hexa-3,5-dienoic acid (**3**), which is indicative of incomplete reaction, is still present after several hours, and no predominant intermediate adducts are observed. A mixture of the 1,4-α and 1,4-ε adducts (**20**) and (**21**) was finally obtained for the methyl(diphenyl)propenone (**10**), and only the 1,4-ε products (**26**) and (**27**) are obtained from the cyclic substrates (**13**) and (**14**). All these 1,4-ε products have been isolated as mixtures of *E,Z*-isomers, in contrast with the

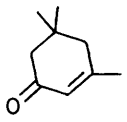


(**8**) R^1 = Me, R^2 = H
(**9**) R^1 = Ph, R^2 = H
(**10**) R^1 = Ph, R^2 = Me

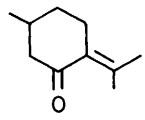
(**11**)



(**12**)



(**13**)



(**14**)

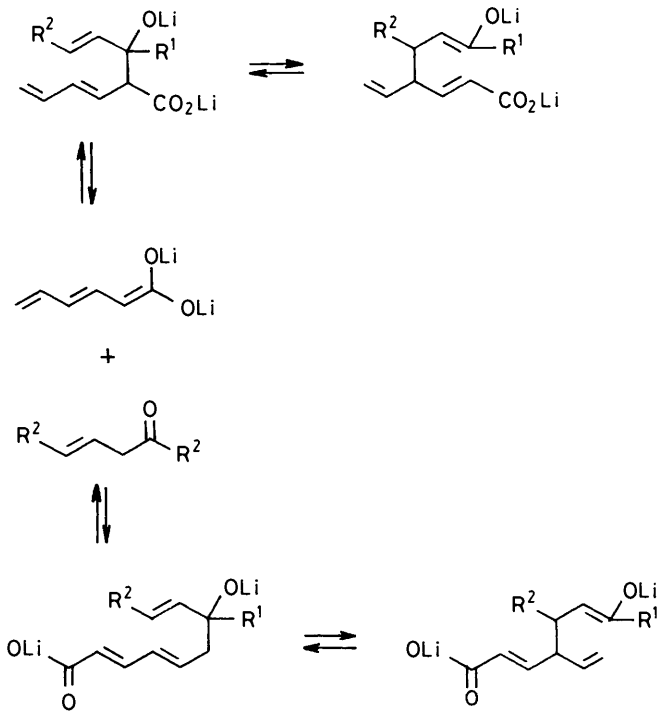
E,E-ε-adducts obtained on reaction of the trienolate with saturated ketones.

When the reactions with the monosubstituted enones (**8**), (**9**), (**11**), and (**12**) were carried out at −70 °C for 0.5 h, the corresponding 1,4-γ-adducts (**15**), (**16**), (**24**), and (**25**), respectively, were found to predominate in the reaction mixtures. A similar 1,4-γ-addition has been found by Haynes on reaction of the carbanion of a pentadienylic sulphoxide with a substituted cyclopentenone.[9]

The cyclic enones (**11**) and (**12**) afforded 1,4-γ-adducts (**24**) and (**25**) as single diastereoisomers, though their configuration has not been established. In contrast, the acyclic compounds (**15**) and (**16**) are obtained as isomeric mixtures.

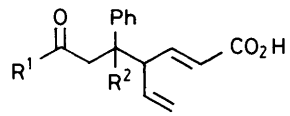
When the reactions are monitored, the 1,4-γ-adducts derived from the styryl ketones (**8**) and (**9**) are found to fade away gradually from the reaction mixtures on warming to room temperature and increasing amounts of the corresponding 1,4-α-adducts (**18**) and (**19**) are then observed. A similar change is not observed for the cyclic enones (**11**) and (**12**), most probably because of the insolubility of the corresponding lithium salts, and only the oxo acids (**24**) and (**25**) are found after 3 h at 0 °C.

Small amounts of 1,4-ε-adducts derived from the enones (**8**) and (**9**) were isolated as well, but were not fully characterized. The 1,4-γ-adducts may be the result of a 1,2-addition (α or ε), and a subsequent anionic oxy-Cope rearrangement (Scheme 3),

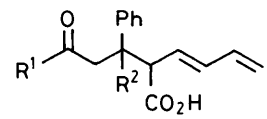


Scheme 3.

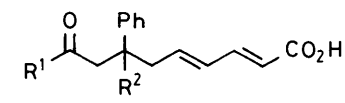
according to a similar mechanism found for additions of the dienolate of crotonic acid to some enones.[4] The slow progress of the addition of the trienolate to the methyl substituted styrylenone (**10**) after 0.5 h at −70 °C, and the poor yield of 1,4-adduct (**17**) obtained (see Table 2) might afford some



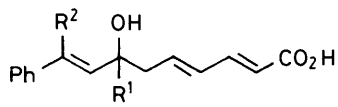
(**15**) R^1 = Me, R^2 = H
(**16**) R^1 = Ph, R^2 = H
(**17**) R^1 = Ph, R^2 = Me



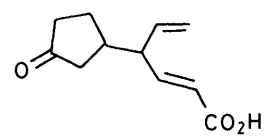
(**18**) R^1 = Me, R^2 = H
(**19**) R^1 = Ph, R^2 = H
(**20**) R^1 = Ph, R^2 = Me



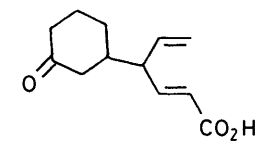
(**21**) a; R^1 = Ph, R^2 = Me
b; R^1 = Ph, R^2 = H



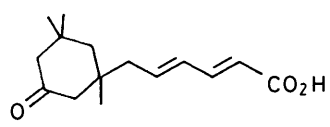
(**22**) R^1 = Ph, R^2 = H
(**23**) R^1 = Ph, R^2 = Me



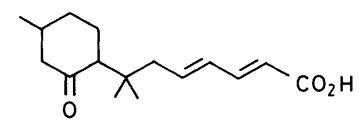
(**24**)



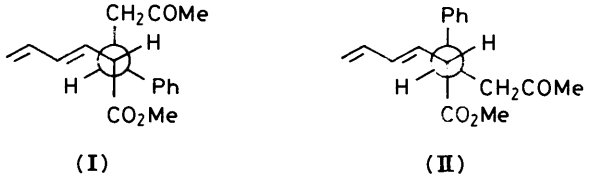
(**25**)



(**26**)

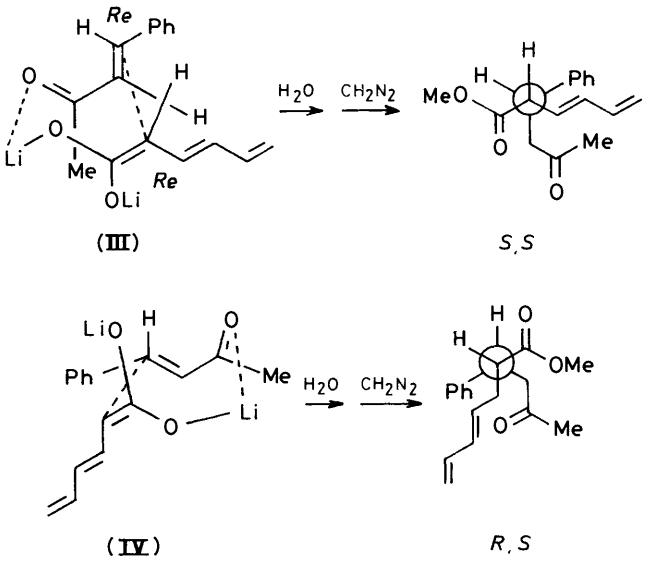


(**27**)



(I) (II)

Figure 1.



(III) S,S

(IV) R,S

Figure 2.

support to this interpretation, as the enone (**10**) has been found to add crotonic acid dienolate by reversible 1,2- and 1,4-additions, instead of through the aldol–oxy-Cope mechanism.[4] However, the instability of the present 1,4-γ-adducts under the reaction conditions throws some doubt upon the above mechanism, as the decomposition of these adducts implies a reversible anionic oxy-Cope rearrangement. Although [3,3]-sigmatropic processes are certainly reversible, we have not found any precedent for the reversibility of this rearrangement. On the other hand, a concerted conversion 1,4-γ- into the 1,4-α-adducts seems very unlikely to us, as a supra–antara [1,3]-sigmatropic shift would be required.

The 1,4-α-adducts (**18**), (**19**), and (**20**) were obtained as single diastereoisomers. However, addition to 4-phenylbut-3-en-2-one (**8**) for 72 h afforded a second diastereoisomer (**18b**). This feature has enabled us to assign the *R,R* (*S,S*)-configuration to the predominant diastereoisomer (**18a**) through the 0.23 p.p.m. upfield shift found for the methoxy protons of the methyl ester (δ 3.42) of the *R,R* isomer (**18a**) [Figure 1, (**I**)], as compared with the equivalent signal (δ 3.65) of the *R,S* isomer (**18b**) [Figure 1, (**II**)], caused by the net shielding effect of the phenyl group.[10] The same *R,R* configuration has been assigned to the isolated adducts (**19**) and (**20**) on the basis of the chemical shift values (δ 3.42) of their methyl ester protons.

The high diastereoselectivity found for the 1,4-α-additions contrasts with the poor selectivities observed by Mulzer for the Michael addition of enolates of saturated carboxylic acids to acyclic enones.[11] Mulzer's findings are in agreement with Heathcock's open transition state model for selective Michael additions of *Z*- and *E*-ester enolates. According to this model, selectivity is based on steric control by the large enolate oxygen relative to the ester oxygen,[12–14] but in carboxylic acid enolates both oxygen atoms are equally large, and selectivities should be poor. For the present 1,4-α additions, an eight-membered transition state might be implied, similar to the cyclic models which have been invoked for diastereoselective reactions of dithioester enolthiolates[15] and carbanions of allylic sulphoxides.[9]

The resulting *R,R*-configurations require a *Re,Re* (*Si,Si*) (for R^2 = Ph) facial attack and could be explained by transition states such as (**III**) or (**IV**) (Figure 2). An s-*cis*-conformation for the enone and a chair–boat shape for the transition state are suggested here as these are the usually accepted conformations for acyclic enones,[16] and some eight-membered rings.[17]

Unfortunately, the present results can not be accounted for by a rationalization which might be coherent with the behaviour of equivalent enolates and dienolates. Further experimental studies and a better knowledge of the structures of the carbanionic species,[18,19] are required. From a synthetic point of view it can be concluded that sorbic acid is a potentially valuable d^6 synthon which provides a convenient entry to 7-hydroxy- and 9-oxo-carboxylic acids. In addition, sorbic acid also affords substituted 3,5-dienoic acids and functionalized divinyl methane structures, ready for inter- or intra-molecular Diels–Alder cyclizations and for photochemical rearrangements to vinyl cyclopropanes, respectively.

Experimental

M.p.s were determined with a Büchi SMP-20 apparatus and are uncorrected. I.r. spectra were recorded for potassium bromide discs, unless otherwise stated, with a Hitachi 269-10 spectrophotometer. N.m.r. spectra were obtained for $CDCl_3$ solutions, with $SiMe_4$ as the internal reference with a Varian FT-80A (80 MHz); unless otherwise stated. Elemental analyses were determined by Servicio de Semimicroanalisis del Instituto de Química Bio-organica de Barcelona.

Distillations of adducts were performed with a Büchi GKR-50 bulb-to-bulb distillation apparatus. Temperatures given are oven temperatures.

Silica gel HF254 (Merck) was used for column chromatography separations with hexane–diethyl ether (8:2 v/v) as the eluant.

Esterifications were with diazomethane. Tetrahydrofuran (THF) was distilled from sodium diphenylketyl immediately before use. Diethylamine was dried over CaH_2 and distilled before use.

Generation and reactions of the trienolate were carried out under an argon atmosphere, using standard conditions for the exclusion of moisture. The reaction temperature (−70 °C) was achieved by cooling with a CO_2–acetone bath.

2-(1-*Hydroxypropyl*)*hexa*-3,5-*dienoic Acid* (**6a**).—To lithium diethylamide [from lithium (0.28 g), naphthalene (2.56 g), and diethylamine (4.2 ml)] in THF (50 ml) at −70 °C, was added dropwise sorbic acid (2.02 g) in THF (20 ml) over 30 min. The cooling bath was removed after 15 min and the stirred solution was allowed to warm for 15 min. The solution was recooled to −70 °C, and propionaldehyde (1 g) in THF (20 ml) was added dropwise over 30 min. The mixture was stirred for 30 min at the same temperature and for 2 h at 30 °C. Aqueous sodium hydroxide (1M; 10 ml) was added, the solvent partially evaporated under reduced pressure, and the residue extracted with ether (3 × 10 ml). The aqueous layer was cooled in an ice–water bath and acidified, with stirring, by the slow addition of concentrated hydrochloric acid. The mixture was extracted with ether, and the organic layer was dried. Evaporation of the solvent led to an oil (3 g, 100%). An aliquot of this was esterified. Column chromatography gave hexa-3,5-dienoic acid (300 mg), and the methyl ester (**6a**) as a pale yellow oil (1.2 g); $\nu_{max.}$(neat) 3 500 (OH), 1 730 (C=O), and 1 650 and 1 600 cm^{-1} (C=C); δ_H 6.35—5.50 (3 H, m, CH=CHCH=), 5.30—5.05 (2 H, m, $=CH_2$),

3.74 (1 H, m, C*H*OH), 3.71 (3 H, s, CO_2Me), 3.10 (1 H, dd, *J* 8.9 and 4.4 Hz, C*H*CO_2Me), 1.42 (2 H, m, CH_2Me), and 0.95 (3 H, t, *J* 6.9 Hz, Me).

(2E,4E)-7-*Hydroxy*-7,8,8-*trimethylnona*-2,4-*dienoic Acid* (**7c**).—Hexadienoic acid (3.2 g) and 3,3-dimethylbutanone (2.90 g) were allowed to react at room temperature for 24 h. An oil (3.7 g, 65%) was isolated, which was esterified. Chromatography of the crude product led to the methyl ester of the acid (**7c**), m.p. 83—84 °C (Found: C, 67.8; H, 10.0. $C_{12}H_{22}O_3$ requires C, 67.28; H, 10.34%); $\nu_{max.}$ 3 520 (OH), 1 700 (C=O), and 1 640 and 1 620 cm^{-1} (C=C); δ_H 7.25 (1 H, dd, *J* 15.4 and 10.0 Hz, CH=CCO_2Me), 6.39 (1 H, ddd, *J* 15.4, 8.2, and 5.6 Hz, CH=CC=CCO_2Me), 6.27 (1 H, dd, *J* 15.4 and 10.5 Hz, C=CHC=CCO_2Me), 5.82 (1 H, d, *J* 15.4 Hz, C=CHCO_2Me), 3.80 (3 H, s, CO_2Me), 2.50 (1 H, dd, *J* 13.7 and 5.2 Hz, CH_2C=C), 2.28 (1 H, dd, 13.9 and 8.0 Hz, CH_2=C), 1.08 (3 H, s, Me), and 0.95 (9 H, s, CMe_3).

(2E,4E)-7-*Hydroxy*-7-*phenylocta*-2,4-*dienoic Acid* (**7d**).—Sorbic acid (3.2 g) and acetophenone (4.44 g) were allowed to react by the above procedure for 24 h at 30 °C and the mixture was worked up as above to give a syrup (6.1 g, 92%). Crystallization of this from ethanol afforded white prisms (2.2 g, 33%) of the acid (**7d**), m.p. 97—100 °C (Found: 72.1; H, 6.95. $C_{14}H_{14}O_3$ requires C, 72.4; H, 6.95%); $\nu_{max.}$ 3 350 (OH), 1 680 (C=O), and 1 640 and 1 600 cm^{-1} (C=C).

The methyl ester showed $\nu_{max.}$ 3 470 (OH), 1 700 (C=O), and 1 640 and 1 600 (C=C) cm^{-1}; δ_H 7.50—7.00 (6 H, m, Ph and C*H*=CCO_2Me), 6.25—5.65 (3 H, m, CH=CHC=CHCO_2Me), 3.71 (3 H, s, Me), 2.65 (2 H, m, CH_2C=C), 1.95 (1 H, s, OH), and 1.56 (3 H, s, Me).

(2E,4E)-7-*Hydroxy*-7,11-*dimethyldodeca*-2,4,10-*trienoic Acid* (**7e**).—6-Methylhex-5-en-2-one (2.27 g) and hexadienoic acid (2.02 g) were allowed to react by the usual procedure for 24 h at room temperature. On work-up, a syrup (3.66 g, 86%) was obtained, which was esterified. Chromatography of the crude product gave the pure methyl ester of (**7e**) (Found: C, 71.0; H, 9.85. $C_{15}H_{24}O_3$ requires C, 71.4; H, 9.6%); $\nu_{max.}$(neat) 3 500 (OH), 1 720 (C=O), and 1 640 and 1 620 cm^{-1} (C=C); δ_H 7.40 (1 H, m, CH=CCO_2Me), 5.11 (1 H, m, CH=CMe_2), 3.74 (3 H, s, CO_2Me), 2.55—1.20 (7 H, m, 3 × CH_2 and OH), 1.69 and 1.62 (6 H, 2 × s, C=CMe_2), 1.19 (3 H, s, Me).

(2E,4E)-7-*Hydroxy*-7,7-*diphenylhepta*-2,4-*dienoic Acid* (**7f**).—Hexadienoic acid (3.2 g) and benzophenone (5.2 g) were allowed to react for 3 h at room temperature. The usual work-up led to a solid material (7.3 g, 85%), which on crystallization from benzene–ethanol yielded the acid (**7f**) (5.9 g, 68%), m.p. 188 °C (decomp.) (Found: C, 77.5; H, 6.15. $C_{19}H_{18}O_3$ requires C, 77.53; H, 6.16%); $\nu_{max.}$ 3 500 (OH), 1 650 (C=O), and 1 640—1 600 cm^{-1}; δ_H 7.5—6.9 (11 H, m, 2 × Ph and CH=CCO_2Me), 6.30—5.70 (3 H, m, C*H*=C*H*C=C*H*CO_2Me), 3.70 (3 H, s, CO_2Me), 3.17 (2 H, d, *J* 6.3 Hz, CH_2C=C), and 2.1 (1 H, s, OH).

Reaction of Sorbic Acid with Cyclohexanone (**5g**).—(*a*) The reaction between sorbic acid (1.6 g) and cyclohexanone (1.4 g) for 0.5 h at −70 °C led to a syrup (2.33 g, 78%) of (3E)-2-(1-*hydroxycyclohexyl*)*hexa*-3,5-*dienoic acid* (**6g**). The corresponding methyl ester showed δ_H 6.50—5.70 (3 H, m, C=CHCH=CCO_2Me), 5.30—4.95 (2 H, m, C=CH_2), 3.70 (3 H, s, CO_2Me), 3.08 (1 H, d, *J* 8.9 Hz, CHCO_2Me), 2.5 (1 H, s, OH), 1.49 (10 H, br s, C_6H_{10}).

(*b*) The same amounts of reagents were allowed to react for 24 h at room temperature, and an oil (2.1 g, 70%) was obtained, which on crystallization from ethanol afforded white prisms (0.9 g, 11%) of (2E,4E)-6-(1-*hydroxycyclohexyl*)*hexa*-2,4-*dienoic acid* (**7g**), m.p. 163—164 °C (Found: C, 68.6; H, 8.96. $C_{12}H_{18}O_3$ requires C, 68.54; H, 8.63%). The corresponding methyl ester; m.p. 58—59 °C (Found: 69.3; H, 9.05. $C_{13}H_{20}O_3$ requires C, 69.91; H, 8.99%); $\nu_{max.}$ 3 500 (OH), 1 700 (C=O), and 1 640 and 1 620 cm^{-1} (C=C); δ_H 7.26 (1 H, m, CH=CCO_2Me), 6.22 (2 H, m, CH=CHC=CCO_2Me), 5.81 (1 H, d, 15.3 Hz, C=CHCO_2Me), 3.74 (3 H, s, CO_2Me), 2.32 (2 H, d, *J* 6 Hz, CH_2C=C), and 1.50 (10 H, C_6H_{10}).

Reaction of Sorbic Acid with Cyclododecanone (**5h**).—(*a*) The reaction between sorbic acid (4.16 g) and cyclododecanone at 0 °C for 3 h led to a solid material (9.3 g, 85%), which on crystallization from hexane–diethyl ether afforded (3E)-2-(1-*hydroxycyclododecyl*)*hexa*-3,5-*dienoic acid* (**6h**), m.p. 159—161 °C (Found: C, 73.4; H, 10.7. $C_{18}H_{30}O_3$ requires C, 73.42; H, 10.27%); $\nu_{max.}$ 3 540 (OH), 1 680 (C=O), 1 640 and 1 600 (C=C), 1 240 and 1 220 (CO_2) cm^{-1}. The corresponding methyl ester showed δ_H(200 MHz) 6.29 (1 H, ddd, *J* 16.6, 10.1, and 10.1 Hz, C*H*=CH_2), 6.14 (1 H, dd, *J* 14.7 and 10.1 Hz, C=C*H*C=CH_2), 5.83 (1 H, dd, *J* 14.6 and 9.7 Hz, C*H*=CC=CH_2), 5.12 (1 H, dd, *J* 16.5 and 2.2 Hz, C=CH_2), 5.05 (1 H, dd, *J* 10.0 and 2.0 Hz, C=CH_2), 3.67 (3 H, s, CO_2Me), 3.55 (1 H, s, OH), 3.00 (1 H, d, *J* 9.7 Hz, C*H*CO_2Me), 1.1—1.5 (22 H, m, $C_{12}H_{22}$).

(*b*) When sorbic acid (2.15 g) and cyclododecanone (3.3 g) were allowed to react for 72 h at room temperature a syrup (3.50 g) was obtained, which was esterified. Column chromatography and crystallization of the crude product led to white prisms (0.8 g) of (2E,4E)-6-(1-*hydroxycyclododecyl*)*hexa*-2,4-*dienoic acid* (**7h**). The corresponding methyl ester had m.p. 102—103 °C (Found: 74.1; H, 10.0. $C_{19}H_{32}O_3$ requires C, 74.45; H, 9.87%); $\nu_{max.}$ 3 540 (OH), 1 710 (C=O), and 1 650 and 1 630 cm^{-1} (C=C); δ_H 7.26 (1 H, m, CH=CCO_2Me), 6.22 (2 H, m, CH=CHC=CCO_2Me), 5.81 (1 H, d, *J* 15 Hz, CH_2C=C), and 1.36 (22 H, m, $C_{12}H_{22}$).

Reaction of Sorbic Acid with 4-*Phenylbut*-3-*enone* (**8**).—(*a*) The reaction between sorbic acid (2.02 g) and 4-phenylbut-3-enone (2.37 g) for 0.5 h at −70 °C led to a syrup (3.35 g, 81%), which was esterified. Chromatography of this gave a 9:1 *R,R*:*R,S* mixture of (E)-4-*ethenyl*-7-*oxo*-5-*phenyloct*-2-*enoic acid* (**15**) methyl esters, as a colourless oil (1.65 g), b.p. 135 °C (0.04 mmHg) (Found: C, 74.7; H, 7.4. $C_{17}H_{20}O_3$ requires C, 74.97; H, 7.40%); $\nu_{max.}$(neat) 1 720 (C=O), 1 645 (C=C), and 1 280 (CO_2) cm^{-1}; δ_H 6.90 (1 H, dd, *J* 15.5 and 8.1 Hz, CH=CCO_2Me), 5.80 (1 H, d, *J* 15.5 Hz, C=CHCO_2Me), 6.1—5.4 (1 H, m, CH_2), 5.05—4.78 (2 H, m, C=CH_2), 3.70 (3 H, s, CO_2Me), 3.30 (2 H, m, PhC*H* and CHC=), 2.77 (2 H, d, *J* 6.7 Hz, CH_2CO), and 1.97 (3 H, s, COMe); δ_C 166.3, 148.9, 141.2, 136.5, 128.5, 128.4, 128.3, 126.7, 122.1, 117.1, 51.8, 51.3, 47.2, 44.5, and 30.4.

(*b*) The same reaction when allowed to proceed for 12 h at 25 °C gave an oil (3.6 g, 82%), which led, as above, to a solid material. On crystallization fron hexane–benzene this afforded white prisms of (4R,5R)-(6E)-4-*phenyl*-2-*oxonona*-6,8-*diene*-5-*carboxylic acid* (**18a**) (1.59 g, 38%). The methyl ester had m.p. 69—70 °C (Found: C, 75.1; H, 7.15. $C_{17}H_{20}O_3$ requires C, 74.97; H, 7.40%); $\nu_{max.}$ 1 730 and 1 705 (C=O), 1 600 (C=C), and 1 260 (CO_2) cm^{-1}; δ_H 7.22 (5 H, s br, Ph), 5.4—5.05 (5 H, m, CH=CHCH=CH_2), 3.40—3.26 (2 H, m, CHCO_2Me and PhC*H*), 3.42 (3 H, s, CO_2Me), 2.7—2.85 (2 H, m, CH_2CO), and 1.97 (3 H, s, COMe); δ_C 206.5, 172.4, 141.4, 136.0, 135.2, 129.7, 128.4, 127.9, 127.0, 118.0, 56.2, 51.5, 47.3, 43.4, and 30.5.

(*c*) Sorbic acid (1 g) and the same ketone (**8**) (1.3 g) were allowed to react for 72 h at 25 °C. Work-up gave a syrup (2.1 g, 90%). Esterification of this and chromatography of an aliquot (1.5 g) led to isolation of the above (*R,R*)-oxodienecarboxylic acid (**18a**) methyl ester along with fairly pure samples of the (4R,5S)-(6E)-4-*phenyl*-2-*oxonona*-6,8-*diene*-5-*carboxylic acid* (**18b**) methyl ester (0.23 g); $\nu_{max.}$(neat) 1 730 (C=O) and 1 600

(C=C) cm^{-1}; δ_H 7.2 (5 H, br s, Ph), 6.1—5.6 (3 H, m, CH=CHCH=C), 5.17—4.94 (2 H, m, C=CH_2), 3.65 (3 H, s, CO_2Me), 3.65 (1 H, m, PhC*H*), 3.47 (1 H, dd, *J* 17.3 and 8.9 Hz, $CHCO_2Me$), 2.82 (2 H, d, *J* 7 Hz, CH_2CO), and 2.01 (3 H, s, COMe).

Reaction with 1,3-*Diphenylprop*-3-*en*-2-*one* (**9**).—(*a*) Sorbic acid (2.02 g) was allowed to react with the title ketone for 0.5 h at −70 °C. Usual work-up gave a syrup (4 g). Esterification and chromatography of this gave fractions of crude methyl esters of (E)-4-*ethenyl*-7-*oxo*-5,5-*diphenylhept*-2-*enoic acid* (**16**) (1.2 g) which could not be purified and characterized properly. The methyl ester of (**19**) (0.7 g), and of (2E,4E,8E)-7-*hydroxy*-7,9-*diphenylnona*-2,4,8-*trienoic acid* (**22**) (0.3 g) crystallized from hexane–diethyl ether. The latter had m.p. 85—86 °C (Found: C, 79.0; H, 6.37. $C_{22}H_{22}O_3$ requires C, 79.04; H, 6.58%); $\nu_{max.}$ 3 450 (OH), 1 690 (C=O), 1 640 and 1 620 (C=C), and 1 240 (CO_2) cm^{-1}; δ_H 7.30 (10 H, m, 2 × Ph), 7.02 (1 H, m, CH=CCO_2Me), 6.69 and 6.56 (2 H, 2 × d, *J* 15 Hz, PhC*H*=C*H*), 6.1 (3 H, m, CH=CHC=$CHCO_2Me$), 3.70 (3 H, s, CO_2Me), and 2.88 (2 H, d, *J* 6.3 Hz, CH_2C=C).

(*b*) The reaction was allowed to proceed for 24 h at 25 °C. A syrup (5.22 g, 96%) was obtained, which on crystallization from hexane–benzene afforded white prisms of (R,R)-1-*oxo*-1,3-*diphenylocta*-5,7-*diene*-4-*carboxylic acid* (**19**) (3.97 g), m.p. 146—147 °C (Found: C, 78.5; H, 6.35. $C_{21}H_{20}O_3$ requires C, 78.73; H, 6.29%). Methyl ester: m.p. 90—92 °C; $\nu_{max.}$ 1 730 (C=O), 1 680 (C=O), and 1 260 cm^{-1} (CO_2); δ_H(200 MHz) 7.8 and 7.1 (10 H, 2 × m, Ph and PhCO), 6.31 (1 H, ddd, *J* 16.3, 10.3, and 10.3, C*H*=CH_2), 5.75 (1 H, dd, *J* 14.7 and 9.5 Hz, 5-H), 6.23 (1 H, dd, *J* 14.7 and 8.3 Hz, 6-H), 5.19 (1 H, dd, *J* 15.9 and 1.1 Hz, C=CH), 5.09 (1 H, dd, *J* 8.3 and 1.6 Hz, C=CH), 3.85 (1 H, m, PhCH), 3.42 (3 H, s, CO_2Me), and 3.3 (3 H, m, $CHCO_2$ and CH_2COPh); δ_C 198.0, 172.25, 141.20, 135.71, 135.06, 135.29, 130.34, 129.94, 129.55, 128.18, 128.06, 127.78, 127.66, 126.62, 117.67, 55.78, 51.26, 43.37, and 42.00.

Reaction with 1,3-*Diphenylbut*-2-*en*-1-*one* (**10**).—(*a*) Sorbic acid (**1g**) and the title ketone (1.45 g) were allowed to react for 0.5 h at −70 °C and work-up of the reaction mixture led to an oil (1.3 g, 53%). Esterification of this and chromatography of an aliquot (0.2 g) afforded fairly pure samples of (*E*)-4-ethenyl-5-methyl-7-oxo-5,7-diphenylhept-2-enoic acid (**17**) methyl ester (0.008 g) [δ_H 8.3 and 7.5 (10 H, 2 × br s, 2 × Ph), 7.04 (1 H, dd, *J* 16 and 9.6 Hz, CH=CCO_2Me), 6.00 (1 H, d, *J* 16 Hz, C=$CHCO_2Me$), 5.3 (2 H, m, C=CH_2), 3.80 (3 H, s, CO_2Me), 3.52 (2 H, m, CH_2CO), 1.64 (3 H, s, PhC*Me*)] and (2E,4E,8E)-7-*hydroxy*-9-*methyl*-7,9-*diphenyldeca*-2,4,8-*trienoic acid* (**23**) methyl ester (0.024 g); $\nu_{max.}$ 3 475 (OH), 1 700 (C=O), 1 640 and 1 620 (C=C), and 1 260 cm^{-1} (CO_2); δ_H 7.33 (11 H, 2 × Ph and PhC=CH), 6.24—6.1 (3 H, m, C*H*=C*H*C*H*=CCO_2Me), 5.60 (1 H, d, *J* 15.2 Hz, CH_2C=C), 3.70 (3 H, s, CO_2Me), 2.77 (2 H, d, *J* 6 Hz, CH_2C=C), and 1.9 (3 H, *J* 1 Hz, C=CMe).

(*b*) Sorbic acid (2.02 g) and 1,3-diphenylbut-2-en-1-one (3.9 g) were allowed to react for 36 h at 25 °C. The resulting syrup (5.7 g, 94%) was esterified (5 g). Column chromatography of the product led to the isolation of fairly pure samples of each: (3R,4R)-(5E)-3-*methyl*-1-*oxo*-1,3-*diphenylocta*-5,7-*diene*-4-*carboxylic acid* (**20**) methyl ester (1.3 g); $\nu_{max.}$ 1 730 and 1 690 (C=O), 1 600 and 1 590 (C=C), 1 220 cm^{-1} (CO_2); δ_H 7.9 and 7.3 (10 H, 2 × m, 2 × Ph), 6.1 (3 H, m, C=CHCH=CH), 5.16 (2 H, m, C=CH_2), 4.24 (1 H, d, *J* 17.6 Hz, $PhCOCH_A$), 3.42 (3 H, s, CO_2Me), 3.3 (1 H, d, *J* 3.8 Hz, $CHCO_2Me$), 3.15 (1 H, d, *J* 17.6-Hz, $PhCOCH_B$), and 1.70 (3 H, s, CMe); (E,E)- and (Z,E)-7-*methyl*-9-*oxo*-7,9-*diphenylnona*-2,4-*dienoic acid* (**21b**) methyl ester (1.6 g); $\nu_{max.}$(neat) 1 710 and 1 690 (C=O), 1 640 and 1 600 (C=C), and 1 260 cm^{-1} (CO_2); δ_H 7.7 and 7.3 (10 H, 2 × m, 2 × Ph), 7.18 (1 H, m, CH=CCO_2Me), 6.14—5.83 (3 H, m, CH=CHC= $CHCO_2Me$), 3.75 and 3.36 (3 H, 2 × s, *Z*- and *E*-CO_2Me), 2.81 (2 H, m, CH_2C=C), and 1.54 and 1.51 (3 H, 2 × s, *E*- and *Z*-CMe).

Reaction with Cyclopent-2-*enone* (**11**).—Sorbic acid (2.02 g) and cyclopentenone (1.33 g) were allowed to react for 15 min at 70 °C and 3 h at 0 °C to yield an oil (3.2 g, 95%). Esterification and column chromatography of this gave (E)-4-(3-*oxocyclopentyl*)*hexa*-2,5-*dienoic acid* (**24**) methyl ester, b.p. 124 °C (0.03 mmHg) (Found: C, 69.45; H, 7.8. $C_{12}H_{16}O_3$ requires C, 69.15; H, 7.74%); $\nu_{max.}$(neat) 1 730 (C=O), 1 655 (C=C), and 1 250 cm^{-1} (CO_2); δ_H 6.91 (1 H, dd, *J* 15.7 and 8.2 Hz, CH=CCO_2Me), 5.90—5.53 (1 H, m, CH=C), 5.87 (1 H, d, *J* 15.7 Hz, C=$CHCO_2Me$), 5.00—5.23 (2 H, m, C=CH_2), 3.74 (3 H, s, CO_2Me), 2.84 (1 H, m, CHC=C), and 2.4—1.8 (7 H, m, C_5H_7); δ_C 217.2, 166.4, 148.3, 137.0, 121.8, 117.1, 51.8, 51.4, 42.8, 40.3 38.2, and 27.4.

Reaction with Cyclohex-2-*enone* (**12**).—Hexa-2,4-dienoic acid (2.02 g) and cyclohex-2-enone (1.73 g) were allowed to react at −70 °C for 15 min and at 0 °C for 3 h. Work-up as usual led to an oil (3.75 g, 100%), which by esterification and column chromatography afforded (E)-4-(3-*oxocyclohexyl*)*hexa*-2,5-*dienoic acid* (**25**) methyl ester as a colourless oil (3.19 g, 80%), b.p. 130 °C (0.03 mmHg) (Found: C, 70.2; H, 8.15. $C_{13}H_{18}O_3$ requires C, 70.25; H, 8.16%); $\nu_{max.}$(neat) 1 730 (C=O), 1 655 (C=C), and 1 280 and 1 250 cm^{-1} (CO_2); δ_H 6.91 (1 H, dd, *J* 15.7 and 8.6 Hz, CH=CCO_2Me), 5.79 (1 H, d, *J* 15.7 Hz, C=$CHCO_2Me$), 5.98—5.3 (1 H, m, CH=CH_2), 5.25—4.95 (2 H, m, C=CH_2), 3.74 (3 H, s, CO_2Me), 2.77 (1 H, m, CHC=C), and 2.5—1.25 (9 H, m, C_6H_9); δ_C 210.2, 166.4, 148.2, 136.4, 122.2, 117.6, 51.3, 52.2, 45.5, 42.2, 41.2, 28.3, and 24.9.

Reaction with 3,5,5-*Trimethylcyclohex*-2-*enone* (**13**).—Sorbic acid (2.02 g) was allowed to react with the title ketone (2.48 g) at room temperature for 24 h. Usual work-up gave an oil (3.51 g, 78%). This finally gave a mixture (2E,4E)- *and* (2E,4Z)- 6-(1,5,5-*trimethyl*-3-*oxocyclohexyl*)*hexa*-2,4-*dienoic acid* (**26**) methyl ester as a yellow oil (1.4 g, 42%), b.p. 145 °C (0.03 mmHg) (Found: C, 72.35; H, 9.35. $C_{16}H_{24}O_3$ requires C, 72.69; H, 9.15%); $\nu_{max.}$ 1 720 (C=O), 1 640 C=C), and 1 270 and 1 200 cm^{-1} (CO_2); δ_H 7.45 (1 H, m, CH=CCO_2Me), 3.75 and 3.74 (3 H, 2 × s, *E*- and *Z*-CO_2Me), 2.3 (2 H, m, CH_2C=C), 2.17 (4 H, br s, CH_2COCH_2), 1.6 (2 H, m, CH_2), and 1.04 (9 H, s, 3 × Me); δ_C(for major isomer) 211.1, 167.2, 144.4, 139.3, 131.6, 119.8, 54.0, 52.2, 51.3, 49.1, 42.6, 39.3, 32.4, 30.4, and 27.6.

Reaction with Pulegone (**14**).—Reaction of the usual amount of sorbic acid with pulegone (2.44 g) for 24 h at 25 °C gave a mixture of 2E,4E- and 2E,4Z-7-*methyl*-7-(4-*methyl*-2-*oxocyclohexyl*-*octa*-2,4-dienoic acid (**27**) (methyl esters) (1.6 g, 46%), b.p. 140 °C (0.03 mmHg) (Found: C, 73.2; H, 9.8. $C_{17}H_{26}O_3$ requires 73.34; H, 9.41%); $\nu_{max.}$(neat) 1 720 (C=O), and 1 640 (C=C), and 1 270 cm^{-1} (CO_2); δ_H 6.59 (1 H, dd, *J* 15.7 and 8.2 Hz, CH=CCO_2Me), 6.36—5.69 (3 H, m, CH=CHC=CH-CO_2Me), 3.75 (3 H, s, CO_2Me), and 2.4—1.6 (10 H, m, C_6H_8 and CH_2C=C); δ_C(for major isomer) 211.2, 167.3, 139.5, 137.9, 128.4, 121.2, 57.2, 52.2, 51.3, 38.3, 36.3, 35.3, 34.7, 26.2, 25.3, 24.2, and 22.2.

Acknowledgements

The present work was financed by Comisión Asesora de Investigación Científica y Técnica. One of us (P. B.) acknowledges a grant from the Ministerio de Educación y Ciencia.

References

1 I. Casinos and R. Mestres, *J. Chem. Soc., Perkin Trans. 1*, 1978, 1651.
2 P. R. Johnson and J. D. White, *J. Org. Chem.*, 1984, **49**, 4424.
3 P. Ballester, A. Garcia-Raso, and R. Mestres, *Synthesis*, 1985, 802.
4 P. Ballester, A. García-Raso, A. Gómez-Solivellas, and R. Mestres, *Tetrahedron Lett.*, 1985, 2485; P. Ballester, A. Costa, A. García-Raso, A. Gómez-Solivellas, and R. Mestres, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1711.
5 K. Yoshida and P. A. Grieco, *J. Org. Chem.*, 1984, **49**, 5527.
6 M. L. Bremmer and S. M. Weinreb, *Tetrahedron Lett.*, 1983, **24**, 261; R. P. Joyce, J. A. Gaynor, and S. M. Weinreb, *J. Org. Chem.*, 1987, **52**, 1177; B. B. Snider, G. B. Phillips, and R. Cordova, *ibid.*, 1983, **48**, 3003.
7 S. Tsuboi, A. Kuroda, T. Masuda, and Akira Takeda, *Chem. Lett.*, 1984, 1541.
8 P. Ballester, A. Costa, A. García-Raso, A. Gómez-Solivellas, and R. Mestres, *Tetrahedron Lett.*, 1985, **26**, 3625.
9 M. R. Brinns, R. K. Haynes, A. A. Katsifis, P. A. Schober, and S. C. Vonwiller, *Tetrahedron Lett.*, 1985, **26**, 1565; M. R. Binns, O. L. Chai, R. K. Haynes, A. A. Katsifis, P. A. Schober, and S. C. Vonwiller, *ibid.*, p. 1569.
10 C. A. Heathcock, S. Kiyooka, and T. A. Blumenkopf, *J. Org. Chem.*, 1984, **49**, 4214.
11 J. Mulzer, G. Bruntrup, G. Harty, U. Kuhl, U. Blascheck, and G. Bohrer, *Chem. Ber.*, 1981, **114**, 3701.
12 M. Yamaguchi, M. Tsukamoto, S. Tanaka, and I. Hirao, *Tetrahedron Lett.*, 1984, **25**, 5661.
13 C. H. Heathcock, M. A. Henderson, D. A. Oare, and M. A. Sahner, *J. Org. Chem.*, 1985, **50**, 3019.
14 C. H. Heathcock and D. A. Oare, *J. Org. Chem.*, 1985, **50**, 3022.
15 K. Kpegba, P. Metzner, and R. Rakotonirina, *Tetrahedron Lett.*, 1986, **27**, 1505.
16 P. Baas and H. Cerfontain, *Tetrahedron*, 1977, **33**, 1509; V. D. Orlov, S. V. Tukerman, and V. F. Lavrushin, *Vop. Stereochim.*, 1971, 89 (*Chem. Abstr.*, 1972, **77**, 151343e).
17 W. Clark Still and I. Galynker, *Tetrahedron*, 1981, **37**, 3996.
18 J. Kaneti, P. Von Ragué Schleyer, and A. J. Kos, *J. Chem. Soc., Chem. Commun.*, 1985, 1014.
19 A. Bonguini, M. Orena, and S. Sandri, *J. Chem. Soc., Chem. Commun.*, 1986, 50.

Received 14*th December* 1987; *Paper* 7/2182