Unsaturated Carboxylic Acid Dienolates. Reaction with Substituted Cyclohexanones and Unsubstituted Cycloalkanones. Regio- and Stereoselectivity

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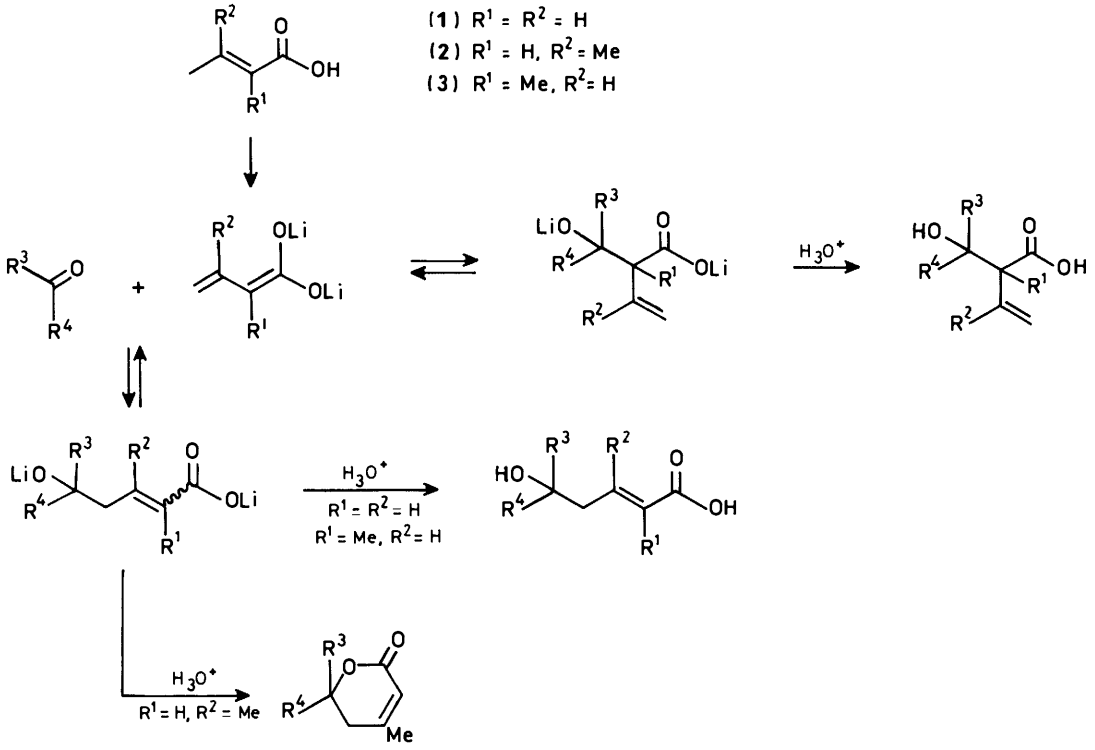
Regio- and stereo-selectivities for the reaction of lithium dienolates derived from crotonic and dimethylacrylic acids with substituted cyclohexanones (**4**)—(**6**) are found to depend on reaction time and temperature. α-Adducts resulting from equatorial attack predominate after a short time at −70 °C, but axial approach and γ-addition are favoured by longer reaction time and higher temperature. Inversion of axial/equatorial stereoselectivity is observed for some cyclohexanones. For unsubstituted cycloalkanones, regioselectivity is dependent on ring size. This effect can be explained on the basis of Brown's 'I-strain' rationalization. For C_5—C_{12} ketones, γ-adducts are found when reactions are carried out above room temperature, but at 0 °C, C_5, C_6, and C_{12} cycloalkanones yield α-isomers whereas mesocyclic ketones afford γ-isomers.

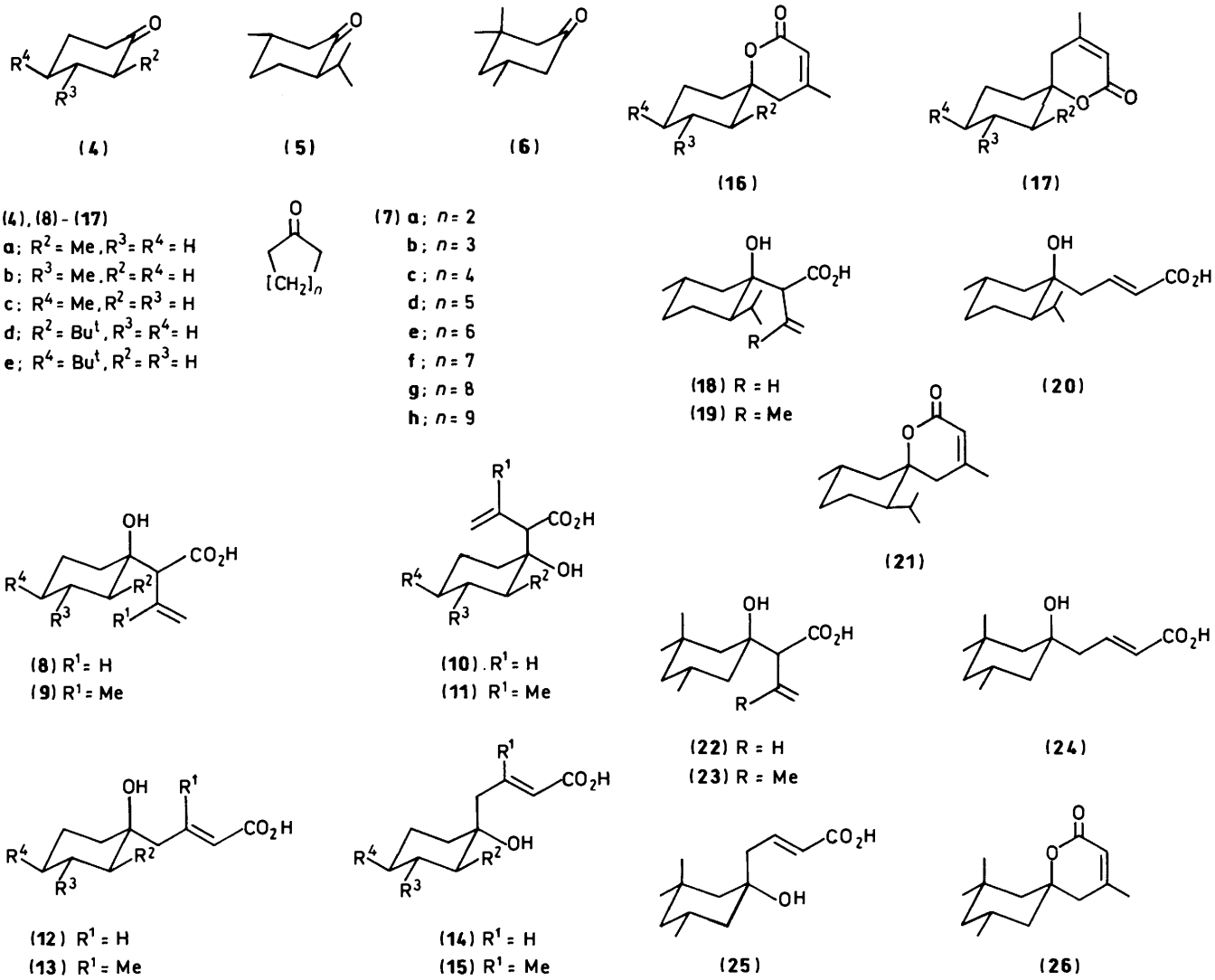
Lithium dienolates derived from unsaturated carboxlic acids have been the object of study as potential d^4 synthons by a number of authors [1,2] since the first report by Watanabe.[3] These dienolates react with electrophilic reagents at the α-carbon.[4–8] With carbonyl compounds, hydroxy acids resulting from α-addition are usually obtained in the cold, but the corresponding γ-adducts result on heating [9–13] (Scheme 1). Experimental conditions have been established for a convenient preparation of any of the regioisomeric (α- or γ-addition) hydroxy acids. The γ-adducts have proved valuable as intermediates for annelation, and eventual ring expansion, of cycloalkanones.[13]

The influence of temperature and reaction time on α:γ regioselectivity has been stated to be the result of a fast, but reversible, α-addition and a slower, though practically irreversible, γ-addition [5,9,10,12] which gives the more stable compound (Scheme 1). Steric crowding around the carbonyl group either hinders α-attack or accelerates decomposition of α-adducts, and is the cause of enhanced yields of γ-adducts.[10,12]

An interesting stereochemical selectivity is found for γ-addition. On the one hand, crotonic [(*E*)-but-2-enoic] and (*E*)-2-methylbut-2-enoic acids (**1**) and (**3**) lead to (*E*)-2-unsaturated 5-hydroxy acids, and on the other, dimethylacrylic acid (**2**)



Scheme 1.



affords the corresponding (*Z*)-2-unsaturated adducts.[10,12] Although these selectivities are high, the corresponding minor *E* and *Z* isomers are frequently observed, and occasionally isolated.[10,14]

Within a project for the synthesis of bicyclic and macrocyclic systems, we have studied the reaction of the lithium dienolates of crotonic and dimethylacrylic acids (**1**) and (**2**) with substituted cyclohexanones (**4**)—(**6**) and with C_5—C_{12} cycloalkanones (**7**). A preliminary account of part of this work has been reported.[15]

For each substituted cycloalkanone (**4**)—(**6**) and acid, four categories of isomer are to be considered as possible products. First of all, α and γ regioisomers can result. The latter regioisomers can be obtained as *E* or *Z* stereoisomers, whereas *erythro* and *threo* diastereoisomers (here referred to as *R,R* and *R,S*) are to be expected for the α-adducts derived from 2- and 3-substituted cyclohexanones. Finally, for both α- and γ-adducts, ring *cis* and *trans* isomers can be obtained as the result of axial or equatorial attack of the nucleophilic reagent to the cyclohexanone. Steric factors governing regiochemical and *E*:*Z* stereochemical selectivities for the dienolates were already known, as shown above, and *R,R*:*R,S* diastereoselectivity was a subsidiary question beyond our objectives. Our interest was instead directed to the study of the ring *cis*/*trans* selectivity, especially for the γ-addition, as this might determine axial or equatorial orientation of the alcoholic hydroxy group, and hence the direction of dehydrations and cyclizations to bicyclic compounds. For unsubstituted cycloalkanones, just the regioselectivity was the object of our interest.

The unsaturated acids (**1**) and (**2**) have been deprotonated, as described in former communications, by lithium diethylamide (LDE) at −70 °C.[10,13] The amide is usually prepared *in situ* from lithium metal, naphthalene, and diethylamine in an ultrasonic bath. The ketone was added at −70 °C, and the mixture allowed to react at 0 °C or 55 °C for the required time. Most experiments have been carried out under these conditions for 2 h for comparison of structural effects. Individual components of the reaction mixtures have been isolated as free acids by crystallization, or as esters by column chromatography. γ-Adducts derived from dimethylacrylic acid have usually been isolated as δ-lactones.

Compositions of crude reaction mixtures have been obtained from ^{1}H n.m.r. spectra and g.l.c. analyses of esterified aliquots. The ^{1}H n.m.r. spectra allowed estimation of α:γ ratios, and stereochemical axial:equatorial (*cis*:*trans*) ratios for adducts once these had been isolated and purified. G.l.c. allowed only the study of relative amounts of stereoisomeric γ-adducts (*E*:*Z* and *cis*:*trans* isomers), due to thermal instability of α-adducts. Configurations of ring stereochemical isomers (**8**)—(**26**) have been assigned through their ^{13}C n.m.r. and ^{1}H n.m.r. spectral data. When both *cis* and *trans* isomers were available, immediate assignment of configuration was possible by com-

Table 1. (a) ^{13}C and ^{1}H Chemical shifts (δ) for cyclohexane C-1 and chain α methine groups in α-cyclohexylbut-3-enoic acids

Compd.[a]	C-1	C_α	C_α-H	Compd.	C-1	C_α	C_α-H
(8a)	74.1	57.6	3.44				
(8b)	71.9	60.9	2.95	**(10b)**	72.3	53.7	3.43
(8c)	71.0	60.6	2.95	**(10c)**	71.7	54.1	3.40
(8d)	76.8	56.2	3.60				
(8e)[b]	71.8	61.1	2.92				
(9a)	73.9	58.0	3.40				
(9e)	71.7	62.0	2.94				
(18)	77.1	58.1	3.59				
(19)[b]	77.2	59.6	3.53				
(22)	73.1	61.2	2.94				
(23)	73.9	62.5	2.94				

(b) ^{13}C and ^{1}H Chemical shifts (δ) for cyclohexane C-1 and chain γ methylene groups in γ-cyclohexyl-but-2-enoic acids and spirolactones

Compd.[a]	C-1	C_γ	C_γ-H	Compd.	C-1	C_γ	C_γ-H
(12b)[b]	73.5	43.9		**(14b)**[b]	74.6	41.7	
(12a)	72.4	43.4	2.39	**(14a)**	74.1	41.3	2.33
(12b)	71.5	45.6	2.32	**(14b)**	72.3	40.0	2.45
(12c)	70.0	46.4	2.33	**(14c)**	71.4	40.1	2.43
(12d)	75.0	45.8	2.70				
(12e)	70.6	46.7	2.31	**(14e)**	71.9	39.2	2.43
(20)	75.0	48.5	2.45				
(24)	72.8	48.4	2.30	**(25)**	72.6	50.1	2.48
(16a)	80.8	36.6	2.73 1.92	**(17a)**			2.48 2.13
(16e)	81.6	35.7	2.40				
(26)	81.3	41.5	1.98				
(21)	83.2	37.4	2.80 2.12				

[a] As methyl ester (for acids). [b] As free acid.

parison of ^{13}C n.m.r. chemical shifts for the quaternary C-1 carbon ring atoms and the substituent carbon atom of the carboxylic acid chain (Table 1). It is well known,[16] and model cyclohexanols confirm,[17] that quaternary cyclohexane carbon atoms substituted by an axial hydroxy group resonate upfield when compared with their equatorial hydroxy stereoisomers. Similarly, signals due to equatorial substituent carbon atoms are found at lower field than those for axial substituents. In spite of the expected conformational mobility, axial orientation of the carboxylic substituent chain seems to predominate in adducts (**10**), (**11**), (**14**), (**15**), and (**17**) in agreement with estimations based on conformational *A* values,[18] and the above generalizations have been qualitatively fulfilled here. The stereoisomeric crotonic γ-adducts (**24**) and (**25**) of 3,3,5-trimethylcyclohexanone (**6**) are exceptional in that their ^{13}C n.m.r. data afford no distinction, probably because the 1,3-diaxial methyl–alkyl repulsion of the chair conformation of adduct (**25**) is relieved by attaining a boat conformation. Proton magnetic resonance chemical shifts for the methine and methylene protons of the chain are also useful for assignment of configurations, as equatorial substituents usually resonate upfield relative to axially oriented equivalent groups.[19] Configurations assigned when only one isomer has been isolated do not contradict their spectral data, and are in agreement with chemical behaviour.

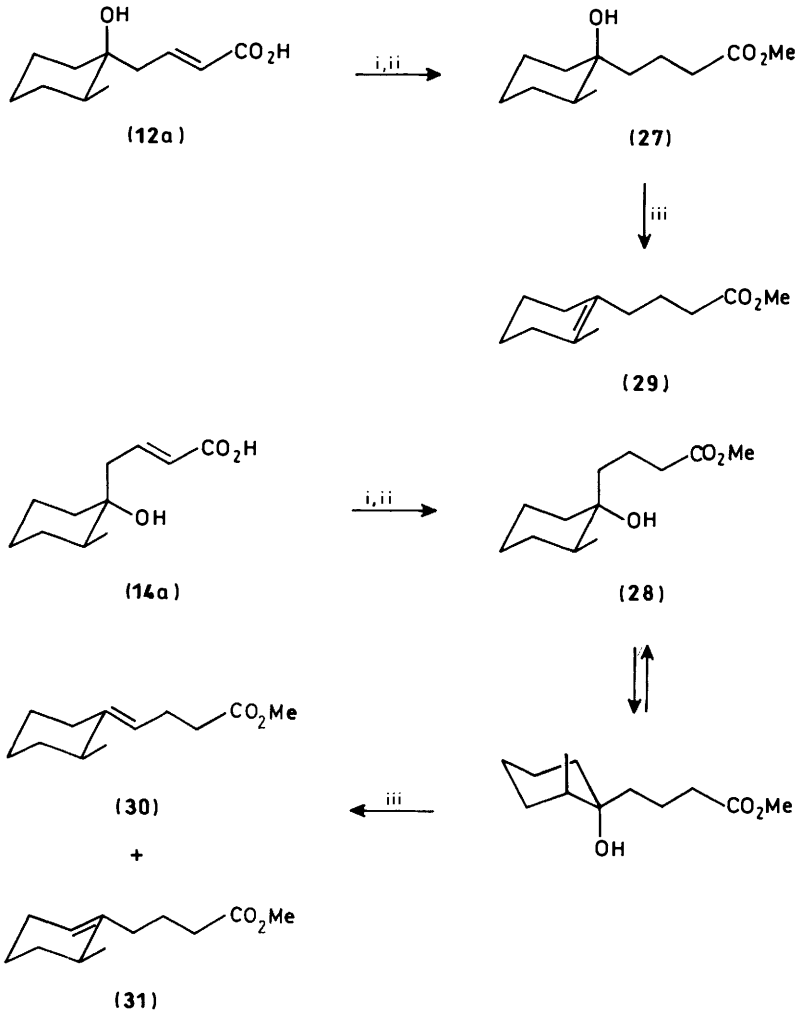
Configurations (**12a**) and (**14a**) have been confirmed chemically. Addition of crotonic acid dienolate of 2-methylcyclohexanone (**4a**) at 0 °C affords a 5-hydroxy acid, m.p. 111 °C, whereas a second acid, m.p. 140 °C, results at 55 °C. The hydroxy acids have been converted into the saturated hydroxy esters (**27**) and (**28**), and these have been dehydrated by treatment with methanesulphonyl chloride in the presence of triethylamine (Scheme 2). The ester deriving from the first hydroxy acid (m.p. 111 °C) afforded a crude unsaturated ester mixture whose ^{1}H n.m.r. spectrum showed an allylic methyl signal at δ 1.93, but no ethylenic protons, in agreement with structure (**29**). By the same treatment, the hydroxy ester resulting from the second hydroxy acid (m.p. 140 °C) gave a mixture of unsaturated esters (**30**) and (**31**), as could be ascertained from the g.l.c. analysis, which showed two main components in the mixture, and from the ^{1}H n.m.r. spectrum where methyl peaks at δ 0.9 and ethylenic protons at δ 4.35 were observed. These dehydrations are those expected respectively for the hydroxy esters (**27**) and (**28**), when the known stereoelectronic requirements of bimolecular eliminations and the commonly found orientation of eliminations (Saytzeff's rule) are considered. Consequently, configurations (**12a**) and (**14a**) should be assigned respectively to the first and second hydroxy acids (m.p. 111 °C and 140 °C) resulting from γ-addition of crotonic acid to 2-methylcyclohexanone (**4a**).

Ring *cis*:*trans* configurations of non-isolated *Z* and *E* isomers resulting from crotonic and dimethylacrylic acid have not been established.

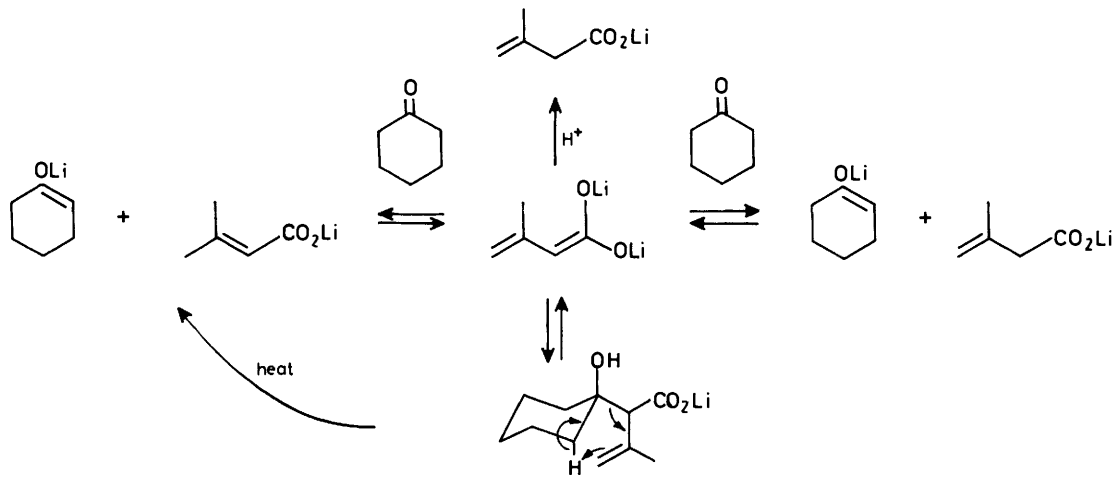
As expected, *R,R*:*R,S* mixtures result from some α-additions to some cyclohexanones which have prochiral carbonyl groups. However, configurations have not been established, as either a single isomer has been obtained, or the diastereoisomeric mixture has not been resolved.

Yields, as well as regio- and stereo-selectivities, for the reactions of the dienolates of crotonic and dimethylacrylic acids with cyclohexanones (**4**)—(**6**) are given in Table 2. Yields for crude acid mixtures are usually good. However, low yields result on heating for the addition of dimethylacrylic acid dienolate to 4-(t-butyl)cyclohexanone (**4e**), and, most strikingly, the starting acid (**2**) is recovered as the sole product when the dienolate is allowed to react with ketones (**4a**), (**5**), and (**6**) at 55 °C. The addition of crotonic acid dienolate to 2-(t-butyl)cyclohexanone (**4d**) at low temperature is slow, and but-3-enoic acid is obtained along with adducts after reaction at −70 °C, but recovery of the starting crotonic acid is observed after 2 h at 0 °C.

Deprotonation of the ketone would seem the most plausible cause of recovery of starting carboxylic acids, as well of the decreased yields resulting for most cyclohexanones after too prolonged heating. It should be stressed here that the starting carboxylic acid is recovered, instead of its deconjugated isomer. Protonation of dienolates is always found to occur with deconjugation,[4] whereas the conjugated acids are now obtained. This is not a temperature effect, as we have found that protonation of the dienolate by addition of water or methanol at 55 °C affords the deconjugated acid. The same result has been obtained on protonation by a carbon acid, namely indene (pK_a 20).[20] The surprising regioselectivity of this protonation might be due to acid–base equilibration with the enolate of the ketone (Scheme 3). Certainly, ketones exhibit C–H acidities *ca.* four pK_a units lower than acetate ions (pK_a 20—21, and 24, respectively),[1,20] but conjugation of the carboxylic salt should reduce this difference, and equilibration would then be feasible. Isomerization could also proceed through proton transfer between dianion dienolate and the lithium salt of the unconjugated acid. Baldwin has recently shown that in the presence of catalytic amounts of sodium hydride, β,γ-unsaturated esters undergo conjugative isomerization.[21] On the other hand, a [1,5]-sigmatropic shift of an α-adduct, according to a retroenic process, could also account for the present results. However, one experiment gave evidence against this mechanism. 2-Methylcyclohexanone (**4a**) and dimethylacrylic acid dienolate gave the corresponding γ-adducts (**13a**) at 0 °C, as was confirmed through an aliquot. An equivalent amount of benzophenone was added to the solution and this was heated under reflux for 20 min. The γ-adduct of benzophenone[14] was then obtained in 83% yield, and no dimethylacrylic acid or its unconjugated



Scheme 2. *Reagents:* i, CH_2N_2; ii, H_2, Pd; iii, $MeSO_2Cl$, Et_3N



Scheme 3.

isomer was observed in the crude mixture. Evidently, the decomposition of adduct (**13a**) on heating had afforded the dienolate, and not the dimethylacrylic salt.

Regiochemical $\alpha:\gamma$ ratios obtained in the cold and on heating for cyclohexanones without a 2-substituent, namely (**4b**), (**4c**), (**4e**), and (**6**) are all similar, and comparable to those previously obtained for cyclohexanone.[10,12] Lower $\alpha:\gamma$ ratios result for 2-substituted ketones (**4a**), (**4d**), and (**5**). All these observations are in keeping with the previously observed influence of steric congestion of the regiochemistry of the additions. No important differences are found when both dienolates are compared, in agreement with former observations.[10]

Table 2. Addition of crotonic and dimethylacrylic acid dienolates to substituted cyclohexanones (**4**)—(**6**)

Ketone	Carboxylic acid	Time (h)	Temp (°C)	Crude yield (%)	Selectivity[a] α_e	α_a	γ_e	γ_a	Isolated[b] compounds (%)
(**4a**)	(**1**)	0.5	−70	72	66		29	5	(**8a**) (5)
		2	0	96	15		60	20	(**12a**) (27)
		2	55	92			30	70	(**14a**) (27)
	(**2**)	0.5	−70	85	60		30	10	(**9a**) (10)
		2	0	90	10		70	10	(**16a**) (56)
		2	55	0	80	10	6	4	(**8b**) (42)
(**4b**)	(**1**)	0.5	−70	77	60	20	15	5	
		2	0		8	44	37	11	(**10b**) (9)
		16	20	89			48	52	(**12b**) (12), (**14b**) (11)
		2	55	79					
(**4c**)	(**1**)	1	−70	86	85		10	4	(**8c**) (51)
		14	20	83	24	60	12	4	(**10c**) (16), (**12c**) (4)
		2	55	77			52	48	(**12c**) (13), (**14c**) (16)
(**4d**)	(**1**)	0.5	−70	30	30		60		(**8d**) (5)
		1	−70	51			90		(**12d**) (12)
		2	0	0					
(**4e**)	(**1**)	2	0	84	75	10	15		(**8e**) (50)
		2	55	77			50	50	(**12e**) (10), (**14e**) (22)
		100	37	84			25	75	
	(**2**)	2	0	69	80	20			(**9e**) (8)
		2	55	43			80		(**16e**) (20)
(**6**)	(**1**)	0.5	−70	88	80		20		(**22**) (10)
		2	0	90	35		60	5	(**22**) (10), (**24**) (36)
		2	55	80			85	15	(**24**) (12), (**25**) (1)
	(**2**)	0.5	−70	68	70		20		(**23**) (15)
		2	0	81			85		(**26**) (49)
		2	55	0					
(**5**)	(**1**)	0.5	−70	70	50		45		(**18**) (10)
		2	0	65	20		60	5	(**20**) (10)
		2	55	65			70	30	(**19**) (10)
	(**2**)	0.5	−70	61	50		50		(**21**) (53)
		2	0	53			80		

[a] α_e And γ_e (α_a and γ_a) stand for α and γ adducts resulting from equatorial (axial) approach. [b] Yields (%) for pure samples.

When attention is paid to the ring *cis*:*trans* stereoselectivity of the additions, either α- or γ-adducts derived from equatorial attack are found to predominate under kinetic conditions, in keeping with many addition reactions of organometallic reagents with substituted cyclohexanones described in the literature.[22] A second observation is that no axial α-adducts are found for the 2-substituted ketones (**4a**), (**4d**), and (**5**). This is again in agreement with literature results, as, regardless of the precise mechanism, the steric requirements for the α-carbon atom of the dienolate on approaching the carbonyl group of the cyclohexanone should not be smaller than those shown by isopropenyl organometallics, and related isopropyl reagents are known to give very small amounts of adducts derived from axial attack on 2-substituted cyclohexanones. On the other hand, the γ-carbon of the dienolate should be sterically similar to an allylic reagent, and its approach from the axial site of 2-methylcyclohexanones is found to be feasible for these reagents.[22]

A more interesting finding is that *cis*:*trans* ratios depend on both the reaction and temperature time, and that for some ketones this change leads in the end to an inversion of stereochemical trends. Thus, α-adducts (**8b**) and (**8c**) derived from equatorial approach of crotonic acid dienolate to 3- and 4-methylcyclohexanone (**4b**) and (**4c**) predominate for runs carried out at −70 °C, whereas hydroxy acids (**10b**) and (**10c**) resulting from axial attack are obtained at 0 °C, with no substantial modification of yield of α-addition. Similar inversions are found for γ-additions to 2-methyl- and 4-(t-butyl)cyclohexanone (**4a**) and (**4e**). In fact, conditions for the convenient preparation of either *cis* or *trans* γ-stereoisomers can be established for the ketone (**4a**). Equilibration to *ca.* 1:1 equatorial:axial ratios for γ-additions to ketones (**4b**) and (**4c**) have been found, although these ratios probably correspond to intermediate situations in the inversions of trends. Other stereochemical ratios depending on temperatures and time have been reported for additions of *N*,*S*-dimethyl-*S*-phenylsulphoximine and dithiane carbanions,[23,24] but except for some additions of magnesium enolates to 3,3,5-trimethylcyclohexanone,[25] we have not found in the literature any other clearly inverted stereoselectivities as those reported here.

Within the study of the reactivity of dienolate dianions of unsaturated carboxylic acids, the present changes of *cis*:*trans* ratios for γ-adducts constitute the first clear evidence ever attained of the reversibility of γ-addition. Although this reversibility was presumed, some cross-over experiments starting from the γ-adducts of cyclohexanone had failed.

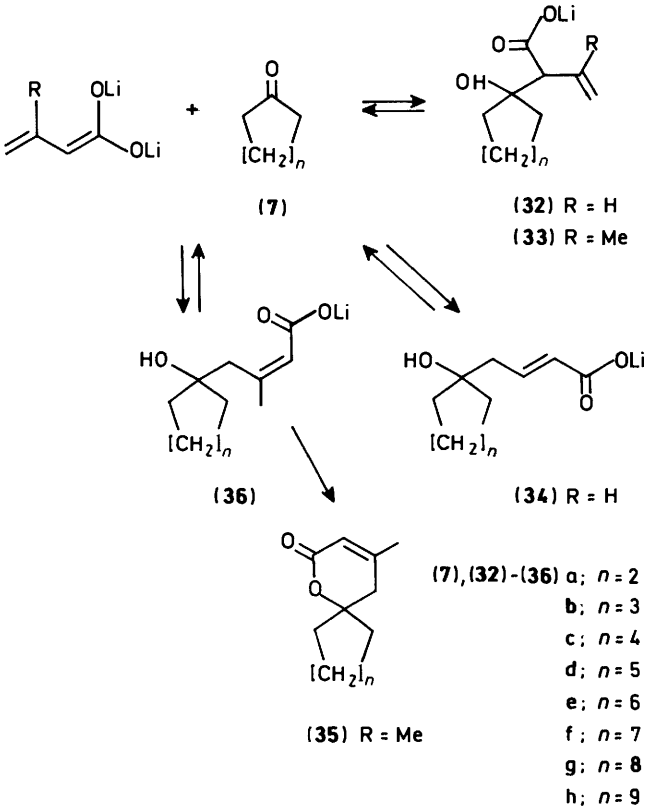
Another remarkable general observation in the present findings is that equilibration favours isolation of the adducts which should be considered the less thermodynamically stable. Thus, the diequatorially disubstituted cyclohexanols (**12**) are found to predominate after short reaction times (kinetic conditions), whereas the axial–equatorial isomers (**14**) are obtained after longer times or at higher temperatures (thermodynamic conditions). Evidently, these paradoxical results cannot be justified by the bulk of the hydroxy group of the free isolated alcohol, as the *A* value of a hydroxy group is smaller than that of any alkyl group.[18] An understanding rather requires the assumption that the effective volume of the lithiated alkoxide oxygen is larger than that of the substituent α or γ carboxylic chain. In view of the present results we suggest that

this effective volume should be larger than that of an isopropyl group.

Our final comment emerging from the present investigation is that the slow equilibration depicted by the dienolate of crotonic acid, especially on γ-addition to carbonyl groups, enables us clearly to discern kinetic from thermodynamic stereoselectivity trends. A reagent with these properties would have saved much confusion and long running discussions about the factors governing the stereoselectivity of alkylating additions to cyclohexanones. Arguments for or against the 'product development control' concept were frequently based on relative stabilities of the resulting cyclohexanols, by assuming that equatorial and axial alkylations led to the thermodynamically more and less stable cyclohexanols respectively. However, the present results show that under our reaction conditions relative stabilities for many alkylation products found in the literature are opposite to those previously assumed.

At present, the unambiguous distinction between kinetic and thermodynamic trends may be useful in order to establish whether early or late transitions states are involved in a process. Thus, comparison of the γ-addition of the dienolate of crotonic acid to 4-(t-butyl)cyclohexanone with irreversible additions of organometallic allylic reagents to the same ketone reveals that the present equatorial kinetic attack resembles the stereoselectivity trend depicted by aluminium, cadmium, and zinc reagents. On the other hand lithium, sodium and magnesium allylic reagents tend to parallel the stereoselectivities obtained now after equilibration.[26–28] Regardless of the precise mechanism involved, this observation suggests that the additions of the first group of organometallic reagents occur through an early transition state, and that a late transition state leads to the more stable alkoxides for the second group.

Yields and regiochemical ratios obtained for reactions of crotonic and dimethylacrylic acid dienolates with C_5—C_{12} cycloalkanones (Scheme 4) at different temperature and times



Scheme 4. R = H, crotonic acid (**1**); R = Me, dimethylacrylic acid (**2**)

Table 3. Addition of crotonic and dimethylacrylic acid dienolates to cycloalkanones (**7**)

Ketone	Carboxylic acid	Time (h)	Temp (°C)	Crude yield (%)	Regioselectivity α:γ	Isolated adducts (%)[a,b]
(**7a**)	(**1**)	2	0	85	95:5	(**32a**) (52)
		2	65	75	40:60	(**34a**) (29)
	(**2**)	2	0	80	95:5	(**33a**) (55)
		2	65	75	1:99	(**35a**) (55)
(**7b**)	(**1**)	2	0	90	80:20	(**32b**) (57)
		2	65	80	1:99	(**34b**) (45)
	(**2**)	2	0	90	95:5	(**33b**) (64)
		2	65	75	5:95	(**35b**) (64)
(**7c**)	(**1**)	2	0	90	85:15	(**32c**) (48)
		2	65	75	1:99	(**34c**) (20)
	(**2**)	2	0	90	25:75	
		2	65	75	1:99	(**35c**) (64)
(**7d**)	(**1**)	2	0	70	30:70	(**34d**) (22)
	(**2**)	2	0	70	20:80	(**35d**) (30)
(**7e**)	(**1**)	0.4	−70	*c*	40:60	
		2	0	51[b]	0:100	(**34e**) (51)
	(**2**)	2	0	73	0:100	(**35e**) (41)
(**7f**)	(**1**)	0.4	−70	*c*	60:40	(**32f**)[c]
		2	0	*c*	20:80	
		1.5	40	76	0:100	(**34f**) (22)
	(**2**)	0.4	−70	*c*	70:30	(**33f**)[c]
		2	0	*c*	10:90	
		25	25	40	0:100	(**35e**) (10)
(**7g**)	(**1**)	0.4	−70	*c*	60:40	(**32g**)[c]
		2	0	*c*	30:70	
		1.5	40	62	0:100	(**34g**) (18)
	(**2**)	0.4	−70	*c*	70:30	(**33g**)[c]
		2	0	*c*	20:80	
		16	25	73	10:90	(**35g**) (26)
(**7h**)	(**1**)	2	0	90	95:5	(**32h**) (70)
		2	65	80	5:95	(**34h**) (75)
	(**2**)	2	0	85	95:5	(**33h**) (52)
		2	65	80	0:100	(**35h**) (32)

[a] Adducts obtained from cycloalkanones (**7a**—**d**) and (**7h**) have been described elsewhere.[13] [b] Pure isolated yields. [c] Only an aliquot was taken.

are given in Table 3. No attempts to improve preparative conditions have been made. Yields for purified materials are frequently low due to poor crystallization recoveries, even for purified samples.

The present results confirm former findings, by showing that good yields of 5-hydroxy acids can be obtained by adequate choice of time and temperature, although for C_7—C_{11} cycloalkanones poor yields are obtained on heating above 40 °C, or on keeping the reaction mixture for long periods of time. It is interesting to find that the size of the ring affects dramatically the γ/α ratios obtained at 0 °C. Regiochemical γ/α ratios for reactions of crotonic and dimethylacrylic acids carried out at 0 °C for 2 h have been plotted against ring size of the cycloalkanone (Figure). Both diagrams are very similar, except for the reaction of cycloheptanone, where a much higher γ/α ratio is found for dimethylacrylic acid. High amounts of α-isomer are observed for C_5, C_6, and C_{12} ketones at 0 °C, whereas the γ-adduct strongly predominates for C_8—C_{11} cycloalkanones. The trends observed qualitatively parallel those described for decomposition constants of cyanohydrins and acetals and for other reactions of cycloalkane systems where an sp^3 carbon changes to sp^2 hybridization.[29] Cycloalkanones are known for their strong dependence of reactivity on ring size, which has been explained in Brown's '*I*-strain' rationalization on the basis of differences in torsional and nonbonded interactions in the sp^2 and sp^3 states of these molecules. Force field analysis has recently provided numerical basis for that explanation.[29]

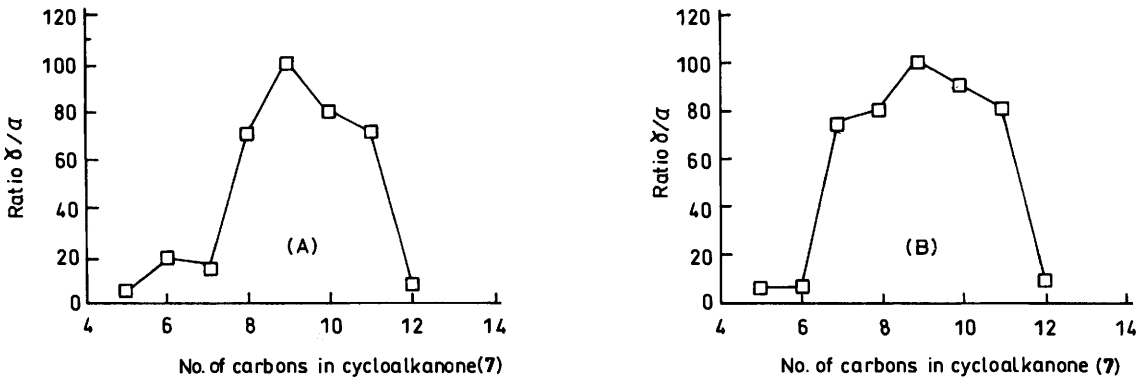


Figure. Plots of γ/α ratio *vs.* cycloalkanone ring size. (A) Crotonic acid (**1**). (B) Dimethylacrylic acid (**2**)

Earlier findings, as well as present ratios at both lower and higher temperatures, indicate that under the conditions established for comparison (0 °C), equilibration by conversion of the α-adduct into the γ-regioisomer is taking place. Thus, these regiochemical ratios give us an estimation of the relative rates of conversion of the α- into the γ-adduct, whereas the shape of the diagrams show that decomposition of α-adducts is the rate-determining step for the rearrangement, as this is the only step in the addition or in the conversion of α- into γ-adducts which implies change of sp^3 to sp^2 hybridization.

Experimental

Cyclononanone (**7e**), cyclodecanone (**7f**), and cycloundecanone (**7g**) were prepared by one-carbon contraction.[30] Substituted cyclohexanones (**4**)—(**6**) and most cycloalkanones (**7**) were commercially available. All additions were carried out under argon, using standard techniques for exclusion of moisture. Glassware was stored in an oven at 120 °C for several hours, and flame-dried with internal argon sweep. Tetrahydrofuran (THF) was distilled prior to use from sodium benzophenone ketyl; diethylamine was distilled from calcium hydride. Concentrated butyl-lithium (*ca.* 10M) was obtained by evaporation of commercial 1.5M hexane solutions under a stream of argon under reduced pressure (Method B). Unless otherwise stated, LDE was generated from lithium naphthalenide (Method A). Methyl esters were obtained by esterification of carboxylic acids with diazomethane. Reaction temperatures refer to bath temperatures. Solid CO_2–acetone was used for cooling to −70 °C.

M.p.s were determined with a Büchi SMP-20 apparatus. Bulb-to-bulb distillations were carried out with a Büchi GKR-50 rotatory oven. I.r. spectra were recorded using KBr discs, unless otherwise stated, on a Hitachi 268-10 spectrophotometer. ^1H and ^{13}C n.m.r. spectra were obtained on a Varian CFT-80A spectrometer, using $CDCl_3$ as solvent and Me_4Si as internal reference. Elemental analyses were determined by 'Servicio de Semimicroanálisis del Centro de Investigación y Desarrollo de Barcelona.' G.l.c. analyses were performed with Perkin-Elmer Sigma-2 or Hewlett-Packard 58320A chromatographs, with nitrogen as carrier gas, and a flame ionization detector, on UCC (10% UCC on Chromosorb P AW-DMCS 60—80) columns, and isothermal programs between 160 and 180 °C, as convenient.

All chiral compounds were obtained as racemic mixtures. Configurations (*R,R* or *R,S*) are given for one single enantiomer of each racemic mixture. Cyclohexanone ring *cis* and *trans* configurations are given for the hydroxy group as the reference.

General Procedure for Addition of Dienolates to Ketones.—*Method A.* A mixture of lithium (0.56 g, 80 mmol), naphthalene (5.12 g, 40 mmol), and THF (50 ml) was sonicated for 10 min at room temperature in an ultrasonic bath. Diethylamine (8.34 ml, 80 mmol) was added dropwise over 15 min and the mixture was sonicated for *ca.* 1.5 h until no lithium was observed. The solution was cooled to −70 °C, and a solution of the carboxylic acid (36 mmol) in THF was added dropwise over 0.5 h to the efficiently stirred mixture. The solution was stirred at 0 °C for 1 h and cooled again to −70 °C. A solution of the ketone (36 mmol) in THF (20 mmol) was added dropwise over 20 min and the solution was stirred at the temperature and times described for each particular run. 1M Sodium hydroxide (40 ml) was added, the solvent was partly evaporated off, and the residue was extracted with diethyl ether (3 × 25 ml). The aqueous solution was acidified under ice-cooling by careful addition of hydrochloric acid, then extracted with diethyl ether, and the combined organic layers were dried. Evaporation of the solvent afforded the crude reaction mixture.

Individual components of the mixture were isolated as free acids by crystallization, or as esters by esterification followed by column chromatography. γ-Adducts derived from 3-methylbut-2-enoic acid (**2**) were set aside for a few days and then isolated as lactones, by being stirred with 1M sodium hydroxide, extraction with diethyl ether, and distillation or chromatography.

Method B. THF (5 ml) was added to conc. butyl-lithium (10 mmol) at −70 °C; the mixture was stirred at 0 °C for 10 min and cooled again to −70 °C; a solution of diethylamine (0.73 g, 10 mmol) in THF (5 ml) was added, the solution was stirred for 1 h at 0 °C, and cooled to −70 °C. A solution of the carboxylic acid (4.5 mmol) in THF (5 ml) was added dropwise, and the same procedure was followed as in Method A.

Reaction of Crotonic Acid with 2-Methylcyclohexanone.—(A) Crotonic acid (**1**) (3.15 g, 36.6 mmol) and 2-methylcyclohexanone (**4a**) (4 g, 35.7 mmol) were allowed to react for 0.5 h at −70 °C. Usual work-up led to a syrup (5.1 g, 72%), which on crystallization from benzene afforded white prisms of (R,R or R,S)-cis-2-(1-*hydroxy*-2-*methylcyclohexyl*)*but*-3-*enoic acid* (**8a**), m.p. 144—145 °C (Found: C, 66.7; H, 9.15. $C_{11}H_{18}O_3$ requires C, 66.66; H, 9.09%); $\nu_{max.}$ 3 450 (OH), 1 700 (C=O), and 1 240 cm^{-1} (COO).

Methyl ester: $\nu_{max.}$(neat) 3 550 (OH), 1 735 (C=O), 1 635 (C=C), and 1 240 cm^{-1} (COO); δ_H 5.94 (1 H, ddd, *J* 18, 8, and 2 Hz, C=CH), 5.25 (1 H, dd, *J* 8 and 2 Hz, C=CH_c), 5.19 (1 H, dd, *J* 18 and 2 Hz, C=CH_t), 3.70 (3 H, s, CO_2Me), 3.44 (1 H, d, *J* 8 Hz, C*H*CO_2Me), 2.26 (1 H, s, OH), 1.44 (9 H, br s, C_6H_9), and 0.97 (3 H, d, *J* 5.8 Hz, ring Me); δ_C 173.1, 132.9, 119.8, 74.1, 57.6, 51.7, 36.7, 33.6, 30.5, 24.2, 21.6, and 14.8.

(B) Crotonic acid (6.3 g, 73 mmol) and 2-methylcyclohexanone (8 g, 71 mmol) were allowed to react for 2 h at 0 °C and the usual work-up gave a syrup (13.4 g, 96%), which when dissolved in acetonitrile yielded white prisms of (E)-cis-4-(1-

hydroxy-2-methylcyclohexyl)but-2-enoic acid (**12a**) (3.8 g, 27%), m.p. 109—111 °C (Found: C, 66.7; H, 9.1. $C_{11}H_{18}O_3$ requires C, 66.66; H, 9.09%); $\nu_{max.}$ 3 450 and 3 550 (OH), 1 680 (C=O), 1 630 (C=C), and 1 270 cm^{-1} (COO).

Methyl ester: $\nu_{max.}$(neat) 3 500 (OH), 1 720 (C=O), 1 642 (C=C), and 1 270 cm^{-1} (COO); δ_H 6.98 (1 H, dt, *J* 15.6 and 7.9 Hz, C*H*=CCO$_2$Me), 5.86 (1 H, d, *J* 15.6 Hz, C=C*H*CO$_2$Me), 3.73 (3 H, s, CO$_2$Me), 2.39 (2 H, d, *J* 7.9 Hz, CH$_2$C=C), 1.41 (9 H, m, C_6H_9), and 0.91 (3 H, d, *J* 5.1 Hz, ring Me); δ_C 166.3, 145.3, 122.8, 72.4, 50.8, 43.4, 38.2, 36.3, 29.9, 25.1, 21.15, and 14.4.

(C) The same reagents and amounts as for method B for 2 h but at 55 °C yielded a syrup (13 g, 92%). Crystallization from diethyl ether gave white prisms of (E)-trans-4-(1-*hydroxy*-2-*methylcyclohexyl*)*but-2-enoic acid* (**14a**), m.p. 139—140 °C (Found: C, 66.7; H, 9.1. $C_{11}H_{18}O_3$ requires C, 66.66; H, 9.09%); $\nu_{max.}$ 3 300 (OH), 1 700 (C=O), 1 650 (C=C), and 1 230 cm^{-1} (COO).

Methyl ester: $\nu_{max.}$(neat) 3 475 (OH), 1 720 (C=O), 1 650 (C=C), and 1 270 and 1 170 cm^{-1} (COO); δ_H 7.04 (1 H, dt, *J* 16 and 7.2 Hz, C*H*=CCO$_2$Me), 5.84 (1 H, d, *J* 16 Hz, C=C*H*CO$_2$Me), 3.72 (3 H, s, CO$_2$Me), 2.33 (2 H, d, *J* 7.2 Hz, CH$_2$C=C), 1.55 (9 H, m, C_6H_9), and 0.94 (3 H, d, *J* 6.4 Hz, ring Me); δ_C 166.6, 145.6, 123.6, 74.1, 51.3, 41.35, 37.0, 36.4, 30.8, 23.8, 22.8, and 15.0.

Reaction of 3-*Methylbut-2-enoic Acid with* 2-*Methylcyclohexanone*.—(A) 3-Methylbut-2-enoic acid (**2**) (3.6 g, 36 mmol) and 2-methylcyclohexanone (**4a**) (4.1 g, 36 mmol) for 0.5 h at −70 °C and the usual work-up led to a yellow oil (6.45 g, 85%). Crystallization from benzene gave white prisms of (*R,R* or *R,S*)-*cis*-2-(1-hydroxy-2-methylcyclohexyl)-3-methylbut-3-enoic acid (**9a**) (0.77 g, 10%), m.p. 112—114 °C, which proved to be chromatographically and spectroscopically homogeneous; $\nu_{max.}$ 3 440 (OH), 1 640 (C=O), and 1 460 cm^{-1} (C=C); δ_H 5.05 (2 H, s, C=CH$_2$), 3.48 (1 H, s, C*H*CO$_2$Me), 1.91 (3 H, s, C=CMe), 1.50 (9 H, br s, C_6H_9), and 0.96 (3 H, d, *J* 5.9 Hz, ring Me).

Methyl ester: $\nu_{max.}$(neat) 3 500 (OH), 1 710 (C=O), and 1 640 cm^{-1} (C=C); δ_H 4.94 (2 H, s, C=CH$_2$), 3.69 (3 H, s, CO$_2$Me), 3.40 (1 H, s, C*H*CO$_2$Me), 1.86 (3 H, d, *J* 1 Hz, C=CMe), 1.47 (9 H, m, C_6H_9), and 0.91 (3 H, d, *J* 4.7 Hz, ring Me); δ_C 174.6, 139.7, 116.9, 73.9, 57.9, 51.5, 39.1, 32.9, 30.6, 23.7, 21.9, 21.4, and 15.2.

(B) The same reagents on reaction for 2 h at 0 °C gave a yellow oil (7 g, 90%). An aliquot of this (4 g) was esterified. Chromatography on silica gel with hexane–diethyl ether (5:1) led to: (i) (R,R)-4,7-*dimethyl*-1-*oxaspiro*[5.5]*undec*-3-*en*-2-*one* (**16a**) as an oil (2.5 g) (Found: C, 74.35; H, 9.75. $C_{12}H_{18}O_3$ requires C, 74.18; H, 9.33%); $\nu_{max.}$ 1 710 (C=O), 1 650 (C=C), and 1 250 cm^{-1} (COO); δ_H 5.77 (1 H, s, 3-H), 2.73 (1 H, d, *J* 18 Hz, 5-H$_A$), 1.94 (3 H, d, *J* 1.4 Hz, C=CMe), 1.92 (1 H, d, *J* 18 Hz, 5-H$_B$), 1.53 (9 H, m, C_6H_9), and 0.98 (3 H, d, *J* 5.6 Hz, 7-Me); δ_C 163.2, 154.8, 114.2, 80.8, 38.3, 36.6, 34.7, 28.6, 24.0, 22.0, 20.1, and 14.9; and (ii) the oily (*R,S*)-epimer of the above spirolactone, compound (**17a**) (0.1 g); $\nu_{max.}$ 1 710 cm^{-1} (C=O); δ_H 5.77 (1 H, s, 3-H), 2.48 (1 H, d, *J* 18 Hz, 5-H$_A$), 2.13 (1 H, d, *J* 18 Hz, 5-H$_B$), 1.94 (3 H, s, C=CMe), 1.55 (9 H, m, C_6H_9), and 0.95 (3 H, d, *J* 5.5 Hz, 7-Me).

Another aliquot (2 g) was washed with 1M sodium hydroxide and extracted with ether. Evaporation of the extract afforded oily 4.7-dimethyl-1-oxaspiro[5.5]undec-3-en-2-one (**16a**) (1.2 g) as above.

The aqueous layer was acidified with hydrochloric acid and extracted with diethyl ether. The solvent was evaporated off and a syrup was obtained (0.7 g), which on crystallization from diethyl ether gave white prisms of (E)-cis- or -trans-4-(1-*hydroxy*-2-*methylcyclohexyl*)-3-*methylbut*-2-*enoic acid* (**13a**) or (**15a**), m.p. 119—120 °C (Found: C, 67.85; H, 9.45. $C_{12}H_{20}O_3$ requires C, 67.89; H, 9.49%).

Methyl ester: $\nu_{max.}$(neat) 3 525 (OH), 1 710 (C=O), 1 640 (C=C), and 1 220 cm^{-1} (COO); δ_H 5.7 (1 H, s, C=C*H*CO$_2$Me), 3.68 (3 H, s, CO$_2$Me), 2.63 (1 H, d, *J* 16 Hz, CH$_A$C=C), 2.25 (3 H, d, *J* 1.4 Hz, C=CMe), 2.03 (1 H, d, *J* 16 Hz, CH$_B$C=C), 1.27 (9 H, m, C_6H_9), and 0.93 (3 H, d, *J* 5 Hz, ring Me).

Reaction of Crotonic Acid with 3-*Methylcyclohexanone*.—(A) Crotonic acid (**1**) (1.6 g, 18 mmol) and 3-methylcyclohexanone (**4b**) (1.9 g, 17 mmol) were allowed to react to −70 °C for 0.5 h. Work-up as above gave a syrup (2.6 g, 77%). An aliquot (2 g) of this was esterfied; column chromatography allowed isolation of a mixture of isomers of (R,R)- and (R,S)-trans-2-(1-*hydroxy*-3-*methylcyclohexyl*)*but*-3-*enoic acid* (**8b**) *methyl ester* as an oil (Found: C, 67.45; H, 9.8. $C_{12}H_{20}O_3$ requires C, 67.92; H, 9.43%); $\nu_{max.}$(neat) 3 510 (OH), 1 720 (C=O), 1 635 (C=C), and 1 160 cm^{-1} (COO); δ_H 5.87 (1 H, ddd, *J* 18, 8, and 8 Hz, C*H*=CH$_2$), 5.23 (1 H, dd, *J* 8 and 2 Hz, C=CH$_c$), 5.16 (1 H, dd, *J* 18 and 2 Hz, C=CH$_t$), 3.71 (3 H, s, CO$_2$Me), 2.95 (1 H, d, *J* 8 Hz, C*H*CO$_2$Me), 1.62 (9 H, br s, C_6H_9), and 0.85 (3 H, d, *J* 5.8 Hz, ring Me); δ_C 173.4, 132.1, 119.0, 71.9, 60.9, 51.1, 44.4, 42.6, 35.3, 34.0, 33.6, 27.0, 26.8, 22.0, and 20.9.

(B) The same reagents as above were allowed to react for 16 h at room temperature. Usual work-up led to an oil (3 g, 89%); esterification and column chromatography of an aliquot (2 g) gave (R,R)- or (R,S)-cis-2-(1-*hydroxy*-3-*methylcyclohexyl*)*but*-3-*enoic acid* (**10b**) *methyl ester* (0.23 g, 9%) as an oil (Found: C, 67.4; H, 9.95%); $\nu_{max.}$(neat) 3 525 (OH), 1 720 (C=O), 1 640 (C=C), and 1 170 cm^{-1} (COO); δ_H 5.88 (1 H, m, C*H*=CH$_2$), 5.21 (1 H, d, *J* 8 Hz, C=CH$_c$), 5.17 (1 H, d, *J* 18 Hz, C=CH$_t$), 3.72 (3 H, s, CO$_2$Me), 3.43 (1 H, d, *J* 8 Hz, C*H*CO$_2$Me), 1.72—1.20 (9 H, m, C_6H_9), and 0.89 (3 H, d, *J* 6.4 Hz, ring Me); δ_C 173.5, 131.9, 119.1, 72.3, 53.7, 51.8, 43.0, 38.0, 33.9, 28.6, 23.0, and 22.5.

(C) Crotonic acid (3.2 g, 37 mmol) and 3-methylcyclohexanone (4.0 g, 35 mmol) were allowed to react at 55 °C for 2 h. A yellow oil (5.5 g, 79%) was obtained, which on esterification and column chromatography of an aliquot (1 g) led to isolation of: (i) (E)-trans-4-(1-*hydroxy*-3-*methylcyclohexyl*)*but*-2-*enoic acid* (**12b**) *methyl ester* as an oil (0.15 g, 11%) (Found: C, 67.6; H, 9.2%); $\nu_{max.}$(neat) 3 450 (OH), 1 720, (C=O), 1 650 (C=C), and 1 260 cm^{-1} (COO); δ_H 7.05 (1 H, dt, *J* 15.6 and 7.9 Hz, C*H*=CCO$_2$Me), 5.86 (1 H, d, *J* 15.6 Hz, C=C*H*CO$_2$Me), 3.73 (3 H, s, CO$_2$Me), 2.32 (2 H, d, *J* 7.9 Hz, CH$_2$C=C), 1.6 (9 H, m, C_6H_9), and 0.87 (3 H, d, *J* 6.1 Hz, ring Me); δ_C 166.5, 144.7, 123.6, 71.55, 51.1, 47.0, 45.6, 36.5, 34.2, 27.4, 22.1, and 21.1; and (ii) (E)-cis-4-(1-*hydroxy*-3-*methylcyclohexyl*)*but*-2-*enoic acid* (**14b**) *methyl ester* as an oil (0.16 g, 12%) (Found: C, 67.25; H, 9.25%); $\nu_{max.}$(neat) 3 420 (OH), 1 720 (C=O), 1 640 (C=C), and 1 265 cm^{-1} (COO); δ_H 7.00 (1 H, dt, *J* 15.7 and 7.6 Hz, C*H*=CCO$_2$Me), 5.80 (1 H, d, *J* 15.7 Hz, C=C*H*CO$_2$Me), 3.76 (3 H, s, CO$_2$Me), 2.45 (2 H, dd, *J* 7.6 and 1 Hz, CH$_2$C=C), 1.8—1.48 (9 H, m, C_6H_9), and 0.83 (3 H, d, *J* 5.3 Hz, ring Me); δ_C 166.4, 145.0, 123.5, 72.35, 51.1, 47.2, 40.0, 38.0, 33.9, 29.7, 22.8, and 22.2

Reaction of Crotonic Acid with 4-*Methylcyclohexanone*.—(A) From crotonic acid (**1**) (1.6 g, 18 mmol) and 4-methylcyclohexanone (**4c**) (2.0 g, 18 mmol) for 1 h at −70 °C according to the general procedure, an oil (3.1 g, 86%) was obtained. Crystallization from hexane afforded white prisms of cis-2-(1-*hydroxy*-4-*methylcyclohexyl*)*but*-3-*enoic acid* (**8c**), m.p. 96—98 °C (Found: C, 66.7; H, 9.1. $C_{11}H_{18}O_3$ requires C, 66.66; H, 9.09%).

Methyl ester: $\nu_{max.}$(neat) 3 525 (OH), 1 720 (C=O), 1 640 (C=C), and 1 175 cm^{-1} (COO); δ_H 5.90 (1 H, ddd, *J* 18.9, 9.5, and 8.7 Hz, C*H*=CH$_2$), 5.22 (1 H, d, *J* 8.5 Hz, C=CH$_c$), 5.16 (1 H, d, *J* 18.9 Hz, C=CH$_t$), 3.70 (3 H, s, CO$_2$Me), 2.95 (1 H, d, *J* 9.5 Hz, C*H*CO$_2$Me), 1.44 (9 H, m, C_6H_9), and 0.90 (3 H, br s, ring Me); δ_C 173.6, 132.1, 119.1, 71.0, 60.6, 51.3, 35.7, 34.0, 31.6, 29.5, 29.4, and 21.8.

(B) The same reagents were allowed to react for 14 h at room temperature. Usual work-up led to an oil (3 g, 83%), which on crystallization from diethyl ether afforded white needles (0.15 g) of (*E*)-*cis*-4-(1-hydroxy-4-methylcyclohexyl)but-2-enoic acid (**12c**), m.p. 178—179 °C.

Methyl ester: oil (Found: C, 67.75; H, 9.5. $C_{12}H_{20}O_3$ requires C, 67.92; H, 9.43%); $\nu_{max.}$(neat) 3 460 (OH), 1 720 (C=O), 1 660 (C=C), and 1 280 cm^{-1}; (COO); δ_H 7.95 (1 H, dt, *J* 15.3 and 7.7 Hz, C*H*=CCO$_2$Me), 5.86 (1 H, d, *J* 15.3 Hz, C=C*H*CO$_2$Me), 3.72 (3 H, s, CO$_2$Me), 2.33 (2 H, d, *J* 7.7 Hz, CH$_2$C=C), 1.65—1.25 (9 H, m, C_6H_9), and 0.92 (3 H, br s, ring Me); δ_H 166.3, 145.1, 123.1, 70.0, 50.8, 46.4, 36.4, 31.5, 29.5, and 21.7.

Crystallization of the residue of the supernatant mother liquors from hexane–dichloromethane gave fine needles of *trans*-2-(1-*hydroxy*-4-*methylcyclohexyl*)*but*-3-*enoic acid* (**10c**), m.p. 117—118 °C (Found: C, 66.65; H, 9.1. $C_{11}H_{18}O_3$ requires C, 66.66; H, 9.09%).

Methyl ester: $\nu_{max.}$(neat) 3 500 (OH), 1 720 (C=O), 1 635 (C=C), and 1 180 cm^{-1} (COO); δ_H 5.90 (1 H, m, C*H*=CH$_2$), 5.25 (1 H, d, *J* 9.2 Hz, C=CH$_c$), 5.20 (1 H, d, *J* 18 Hz, C=CH$_t$), 3.72 (3 H, s, CO$_2$Me), 3.40 (1 H, d, *J* 9 Hz, C*H*CO$_2$Me), 1.62 (9 H, m, C_6H_9), and 0.92 (3 H, d, *J* 5.3 Hz, ring Me); δ_C 173.9, 131.9, 119.0, 71.7, 54.1, 51.3, 36.33, 32.8, 30.5, 30.3, 29.6, and 20.4.

(C) Crotonic acid (1.6 g, 18 mmol) and 4-methylcyclohexanone (2 g, 18 mmol) were allowed to react for 2 h at 55 °C. Work-up gave a solid (2.8 g, 77%). A sample (2 g) of this was esterified; chromatography gave an oil (0.42 g) of (*E*)-*cis*-4-(1-hydroxy-4-methylcyclohexyl)but-2-enoic acid (**12c**) methyl ester as above. Further elution afforded oily (E)-trans-4-(1-*hydroxy*-4-*methylcyclohexyl*)*but*-2-*enoic acid* (**14c**) *methyl ester* (0.35 g) (Found: C, 67.85; H, 9.6. $C_{12}H_{20}O_3$ requires C, 67.92; H, 9.43%); $\nu_{max.}$(neat) 3 475 (OH), 1 720 (C=O), 1 655 (C=C), and 1 275 cm^{-1} (COO); δ_H 7.06 (1 H, dt, *J* 15.7 and 7.6 Hz, C*H*=CCO$_2$Me), 5.89 (1 H, d, *J* 15.7 Hz, C=C*H*CO$_2$Me), 3.73 (3 H, s, CO$_2$Me), 2.43 (2 H, d, *J* 7.6 Hz, CH$_2$C=C), 1.7—1.1 (9 H, m, C_6H_9), and 0.91 (3 H, d, *J* 5.1 Hz, ring Me); δ_C 166.3, 145.1, 123.1, 71.4, 50.9, 40.1, 37.0, 31.0 30.8, and 20.8.

Reaction of Crotonic Acid with 2-(*t-Butyl*)*cyclohexanone*.—(A) Crotonic acid (**1**) (1.6 g, 18 mmol) and 2-(t-butyl)cyclohexanone (**4d**) (2.7 g, 18 mmol) on reaction for 0.5 h at −70 °C, work-up, and esterification gave an oil (1.43 g, 30%). Chromatography gave an oil (0.3 g), which was characterized spectroscopically as *cis*-2-[1-hydroxy-2-(t-butyl)cyclohexyl]-but-3-enoic acid (**8d**) methyl ester; $\nu_{max.}$ 3 500 (OH), 1 710 (C=O), 1 630 (C=C), and 1 165 cm^{-1} (COO); δ_H 5.92 (1 H, ddd, *J* 16.7, 7.8, and 7.3 Hz, C*H*=CH$_2$), 5.27 (1 H, d, *J* 7.8 Hz, C=CH$_c$), 5.21 (1 H, d, *J* 16 Hz, C=CH$_t$), 3.71 (3 H, s, CO$_2$Me), 3.60 (1 H, d, *J* 7.3 Hz, C*H*CO$_2$Me), 1.97—1.05 (9 H, m, C_6H_9), and 1.18 (9 H, s, Bu^t); δ_C 175.0, 132.5, 119.4, 76.8, 56.2, 49.7, 34.7, 32.1, 31.9, 31.3, 26.1, 21.9, and 21.8.

(B) The same reagents on reaction for 1 h at the same temperature afforded an oil (2.2 g, 51%). Esterification and chromatography of this allowed isolation of a fairly pure sample (0.5 g) of (*E*)-*cis*-4-[1-hydroxy-2-(t-butyl)cyclohexyl]but-2-enoic acid (**12d**) methyl ester; $\nu_{max.}$ 3 525 (OH), 1 720 (C=O), 1 640 (C=C), and 1 260 cm^{-1} (COO); δ_H 7.09 (1 H, dt, *J* 15.6 and 7.9 Hz, C*H*=CCO$_2$Me), 5.89 (1 H, d, *J* 15.6 Hz, C=CHCO$_2$Me), 3.75 (3 H, s, CO$_2$Me), 2.70 (2 H, d, *J* 7.9 Hz, CH$_2$C=C), 2.0—1.1 (9 H, m, C_6H_9), and 1.09 (9 H, s, Bu^t); δ_C 166.0, 145.8, 122.4, 75.0, 52.0, 50.6, 45.8, 39.6, 34.1, 30.6, 25.7, 23.9, and 21.0.

Reaction of Crotonic Acid with 4-(*t-Butyl*)*cyclohexanone*.—(A) Crotonic acid (**1**) (3 g, 35 mmol) and 4-(t-butyl)cyclohexanone (**4e**) (5.6 g, 42 mmol) for 2 h at 0 °C and usual work-up afforded a solid material (7.1 g, 84%), which on crystallization from benzene gave cis-2-[1-*hydroxy*-4-(*t-butyl*)*cyclohexyl*]*but*-3-*enoic acid* (**8e**) as white prisms, m.p. 139—140 °C (Found: C, 69.7; H, 10.0. $C_{14}H_{24}O_3$ requires C, 69.96; H, 10.06%); $\nu_{max.}$ 3 540 (OH), 1 680 (C=O), 1 630 (C=C), and 1 220 cm^{-1} (COO); δ_C 131.8, 120.4, 71.8, 61.1, 46.6, 36.3, 34.8, 32.3, 27.5, and 22.6.

Methyl ester: (Found: C, 70.7; H, 10.2. $C_{15}H_{26}O_3$ requires C, 70.86; H, 10.23%); δ_H 6.1 (1 H, ddd, *J* 17.3, 8.1, and 7.3 Hz, CH=CH$_2$), 5.22 (1 H, d, *J* 7.3 Hz, C=CH$_c$), 5.15 (1 H, d, *J* 17.3 Hz, C=CH$_t$), 3.71 (3 H, s, CO$_2$Me), 2.94 (1 H, d, *J* 9 Hz, C*H*CO$_2$Me), 2.33 (1 H, s, OH), 1.50 (9 H, br s, C_6H_9), and 0.85 (9 H, s, Bu^t).

(B) The same reagents were heated for 2 h at 55 °C. A solid (6.5 g, 77%) was obtained, which was crystallized from benzene–diethyl ether to give small prisms, m.p. 160—162 °C, of a mixture of (*E*)-*cis*- and -*trans*-4-[1-hydroxy-4-(t-butyl)cyclohexyl]but-2-enoic acid, (**12e**) and (**14e**).

A sample of this mixture (1 g) was esterified; chromatography gave (E)-cis-4-[1-*hydroxy*-4-(*t-butyl*)*cyclohexyl*]*but*-2-*enoic acid* (**12e**) *methyl ester* (0.15 g) as a solid, m.p. 60—62 °C (Found: C, 70.65; H, 10.23. $C_{15}H_{26}O_3$ requires C, 70.86; H, 10.35%); $\nu_{max.}$ 3 400 (OH), 1 720 (C=O), 1 650 (C=C), and 1 220 cm^{-1} (COO); δ_H 7.04 (1 H, dt, *J* 15.6 and 7.9 Hz, C*H*=CCO$_2$Me), 5.86 (1 H, d, *J* 15.6 Hz, C=C*H*CO$_2$Me), 3.73 (3 H, s, CO$_2$Me), 2.31 (2 H, d, *J* 7.9 Hz, CH$_2$C=C), 1.63—1.25 (9 H, m, C_6H_9), and 0.85 (9 H, s, Bu^t); δ_C 166.5, 144.7, 123.7, 70.6, 51.2, 47.5, 46.7, 37.4, 32.4, 27.3, and 22.2.

Further elution gave (E)-trans-4-[1-*hydroxy*-4-(*t-butyl*)*cyclohexyl*]*but*-2-*enoic acid* (**14e**) *methyl ester* as a solid (0.33 g), m.p. 55—56 °C (Found: C, 70.65; H, 10.4%); $\nu_{max.}$ 3 300 (OH), 1 725 (C=O), 1 650 (C=C), 1 270 cm^{-1}; (COO); δ_H 7.06 (1 H, dt, *J* 15.6 and 7.7 Hz, C*H*=CCO$_2$Me), 5.89 (1 H, d, *J* 15.6 Hz, C=C*H*CO$_2$Me), 3.73 (3 H, s, CO$_2$Me), 2.43 (2 H, d, *J* 7.7 Hz, CH$_2$C=C), 1.77—1.0 (9 H, m, C_6H_9), and 0.86 (9 H, s, Bu^t); δ_C 166.5, 145.0, 123.5, 72.0, 51.1, 47.2, 39.2, 38.5, 32.0, 27.3, and 24.1.

Reaction of Dimethylacrylic Acid with 4-(*t-Butyl*)*cyclohexanone*.—(A) Dimethylacrylic acid (**2**) (1.8 g, 18 mmol) and 4-(t-butyl)cyclohexanone (**4e**) (2.8 g, 18 mmol) were allowed to react for 15 min at −70 °C and 2 h at 0 °C. An oil was isolated (3.2 g, 69%), which on crystallization from acetonitrile gave white prisms of cis-2-[1-*hydroxy*-4-(*t-butyl*)*cyclohexyl*]*but*-3-*enoic acid* (**9e**), m.p. 168—170 °C (Found: C, 70.85; H, 10.4%).

Methyl ester: (Found: C, 71.55; H, 10.45. $C_{16}H_{28}O_3$ requires C, 71.64; H, 10.44%); $\nu_{max.}$(neat) 3 520 (OH), 1 705 (C=O), 1 630 (C=C), and 1 160 cm^{-1} (COO); δ_H 5.02 (2 H, s, C=CH$_2$), 3.70 (3 H, s, CO$_2$Me), 2.94 (1 H, s, C*H*CO$_2$Me), 1.87 (3 H, d, *J* 1 Hz, C=CMe), 1.7—1.2 (9 H, m, C_6H_9), and 0.86 (9 H, s, Bu^t); δ_C 172.9, 139.7, 116.7, 71.7, 62.0, 51.7, 47.8, 38.2, 35.3, 32.3, 27.5, 22.6, and 22.2.

(B) Dimethylacrylic acid (0.9 g, 9 mmol) and 4-(t-butyl)cyclohexanone (1.4 g, 9 mmol) for 15 min at −70 °C and 2 h at 55 °C led to an oil (1 g, 43%), which was set aside for 3 days, dissolved in ether, and extracted with 1M sodium hydroxide. The ethereal layer was evaporated, and a solid was obtained (0.52 g, 24%), which on crystallization from hexane yielded white prisms of *cis*-4-*methyl*-9-(*t-butyl*)-1-*oxaspiro*[5.5]*undec*-3-*en*-2-*one* (**16e**), m.p. 80—82 °C (Found: C, 75.9; H, 10.65. $C_{15}H_{24}O_2$ requires C, 76.27; H, 10.16%); $\nu_{max.}$ 1 700 cm^{-1} (C=O); δ_H 5.79 (1 H, s, 3-H), 2.40 (2 H, s, 5-H$_2$), 1.95 (3 H, s, C=CMe), 2.1—1.37 (9 H, m, C_6H_9), and 0.86 (9 H, s, Bu^t); δ_C 164.7, 154.6, 116.2, 81.6, 47.3, 36.5, 35.7, 32.2, 27.5, 24.0, and 23.3.

Reaction of Crotonic Acid with 2-*Isopropyl*-5-*methylcyclohexanone*.—(A) Crotonic acid (**1**) (1.6 g, 18 mmol) and 2-isopropyl-5-methylcyclohexanone (**5**) (2.8 g, 18 mmol) for 0.5 h at −70 °C led to an oil (3 g, 70%), which on esterification and chromatography gave a mixture of (*R*,*R*)- and (*R*,*S*)-2′-*cis*-5′-*trans*-2-(1-hydroxy-2-isopropyl-5-methylcyclohexyl)but-3-enoic acid (**18**) methyl ester; $\nu_{max.}$(neat) 3 500 (OH), 1 730 (C=O), 1 630 (C=C), and 1 240 cm^{-1} (COO); δ_H 5.87 (1 H, ddd, *J* 18.7, 10, and 8.7 Hz, C*H*=CH$_2$), 5.22 (1 H, dd, *J* 8.7 and 1.7 Hz,

C=CH_c), 5.15 (1 H, *J* 18.7 and 1.7 Hz, C=CH_t), 3.72 (3 H, s, CO_2Me), 3.59 (1 H, *J* 10 Hz, C*H*CO_2Me), 3.04 (1 H, s, OH), 2.0—1.2 (9 H, m, C_7H_9), and 0.89 (9 H, m, 3 × Me); δ_C 174.6, 133.0, 119.4, 77.0, 58.1, 52.1, 46.6, 43.8, 35.2, 27.9, 25.5, 23.1, 22.6, 20.8, and 18.2.

(B) The same reagents on reaction for 2 h at 0 °C led to an oil (2.8 g, 65%). Esterification and chromatography allowed isolation of an oil, which was characterized spectroscopically as (*E*)-2′-*cis*-5′-*trans*-4-(1-hydroxy-2-isopropyl-5-methylcyclohexyl)but-2-enoic acid (**20**) methyl ester; $\nu_{max.}$ 3 510 (OH), 1 720 (C=O), 1 650 (C=C), and 1 270 cm^{-1} (COO); δ_H 6.97 (1 H, dt, *J* 15.6 and 7.9 Hz, C*H*=CCO_2Me), 5.86 (1 H, d, *J* 15.6 Hz, C=C*H*CO_2Me), 3.74 (3 H, s, CO_2Me), 2.45 (2 H, d, *J* 7.9 Hz, CH_2C=C), 2.2—1.1 (8 H, m, C_6H_8), 0.95 (3 H, s, 5-Me), and 0.86 (6 H, m, 2 × Me); δ_C 166.6, 145.3, 123.5, 75.0, 51.2, 48.5, 48.0, 47.4, 44.0, 34.8, 27.8, 25.7, 23.4, 22.1, 20.5, and 17.9.

Reaction of Dimethylacrylic Acid with 2-*Isopropyl*-5-*methylcyclohexanone*.—(A) Dimethylacrylic acid (**2**) (1.8 g, 18 mmol), and 2-isopropyl-5-methylcyclohexanone (**5**) (2.7 g, 18 mmol) for 0.5 h at −70 °C gave a syrup (2.8 g, 61%), which on crystallization from hexane–diethyl ether gave white needles of (R,R)- or (R,S)-2′-cis-5′-trans-2-(1-*hydroxy*-2-*isopropyl*-5-*methylcyclohexyl*)-3-*methylbut*-3-*enoic acid* (**19**), m.p. 136—138 °C (Found: C, 70.5; H, 9.95. $C_{15}H_{26}O_3$ requires C, 70.86; H, 10.23%); $\nu_{max.}$ 3 520 (OH), 1 670 (C=O), 1 630 (C=C), and 1 200 cm^{-1} (COO); δ_H 5.10 and 5.00 (2 H, 2 s, C=CH_2), 3.53 (1 H, s, C*H*CO_2H), 1.90 (3 H, d, *J* 1 Hz, C=CMe), 1.8—1.2 (9 H, m, C_7H_9), 0.92 (6 H, s, 2 × Me), and 0.83 (3 H, s, 5-Me); δ_C 178.6, 139.4, 118.4, 77.2, 59.6, 49.1, 44.6, 34.8, 27.7, 26.3, 23.3, 22.5, 22.3, 20.6, and 17.6.

(B) The same reagents for 2 h at 0 °C gave an oil (3.5 g, 77%), which was set aside for a few days, and then stirred with 1M sodium hydroxide, and extracted with diethyl ether. Evaporation of the solvent led to a solid (2.3 g, 53%), which on crystallization from hexane yielded prisms of (6S,7R,10S)-7-*isopropyl*-4,10-*dimethyl*-1-*oxaspiro*[5.5]*undec*-3-*en*-2-*one* (**21**), m.p. 97—99 °C (Found: C, 76.1; H, 10.4. $C_{15}H_{24}O_3$ requires C, 76.22; H, 10.23%); $\nu_{max.}$ 1 700 cm^{-1} (C=O); δ_H 5.75 (1 H, s, 3-H), 2.80 (1 H, s, 5-H), 2.12 (1 H, s, 5-H), 1.94 (3 H, d, *J* 1 Hz, C=CMe), 2.05—1.25 (9 H, m, C_7H_9), 0.95 (3 H, d, *J* 5.2 Hz, 10-Me), 0.86 (3 H, d, *J* 5.1 Hz, CH*Me*), and 0.81 (3 H, d, *J* 6.2 Hz, CH*Me*); δ_C 164.0, 155.6, 115.2, 83.2, 49.4, 45.8, 37.4, 34.6, 26.9, 26.4, 23.5, 23.0 21.8, 20.0, and 17.4.

Reaction of Crotonic Acid with 3,3,5-*Trimethylcyclohexanone*.—(A) Crotonic acid (**1**) (1.6 g, 18 mmol) and 3,3,5-trimethylcyclohexanone (**6**) (2.4 g, 17 mmol) were allowed to react for 0.5 h at −70 °C. Usual work-up led to isolation of an oil (3.4 g, 88%), which on crystallization from benzene gave white prisms of a mixture of (R,R)- and (R,S)-trans-2-(1-*hydroxy*-3,3,5-*trimethylcyclohexyl*)*but*-3-*enoic acid* (**22**), m.p. 119—120 °C (Found: C, 68.7; H, 9.8; $C_{13}H_{22}O_3$ requires C, 68.99; H, 9.79%); $\nu_{max.}$ 3 540 (OH), 1 685 (C=O), 1 635 (C=C), and 1 220 cm^{-1} (COO); δ_H 5.80 (1 H, m, C*H*=CH_2), 5.27 (1 H, d, *J* 8 Hz, C=CH_c), 5.19 (1 H, d, *J* 17.6 Hz, C=CH_t), 2.94 (1 H, d, *J* 8 Hz, C*H*COO), 1.54—0.9 (7 H, m, C_6H_7), 1.10 (3 H, s, ring Me), and 0.89 (6 H, br s, 2 × ring Me); δ_C 173.5, 131.8, 119.1, 73.1, 61.2, 51.2, 47.9, 47.1, 47.4, 44.7, 42.8, 33.8, 30.8, 30.7, 26.7, 23.3, and 23.2.

(B) The same reagents as above were allowed to react for 2 h at 0 °C. An oil was obtained (3.5 g, 90%) which was esterified. Chromatography led to isolation of the methyl ester of the above (*R,R*) and (*R,S*) mixture of acid (**22**).

Further elution gave (E)-trans-4-(1-*hydroxy*-3,3,5-*trimethylcyclohexyl*)*but*-2-*enoic acid* (**24**) *methyl ester*, m.p. 49—51 °C (Found: C, 69.65; H, 10.0. $C_{14}H_{24}O_3$ requires C, 69.96; H, 10.06%); $\nu_{max.}$ 3 550 (OH), 1 720 (C=O), 1 650 (C=C), and 1 265 cm^{-1} (COO); δ_H 7.03 (1 H, dt, *J* 15.6 and 7.9 Hz, C*H*=CCO_2Me), 5.86 (1 H, d, *J* 15.6 Hz, C=C*H*CO_2Me), 3.74 (3 H, s, CO_2Me), 2.30 (2 H, d, *J* 7.9 Hz, CH_2C=C), 1.60—0.80 (7 H, m, C_6H_7), 0.92 (3 H, s, ring Me), and 0.89 (6 H, m, 2 × ring Me); δ_C 166.4, 144.7, 123.6, 72.8, 51.0, 48.4, 48.0, 45.7, 34.0, 31.0, 26.9, 23.7, and 22.0.

(C) The same amounts of the reagents as above on reaction for 2 h at 55 °C and work-up as usual gave an oil (3.08 g, 80%). An aliquot (1 g) of this was esterified. Chromatography gave the aforementioned methyl ester of acid (**24**) (0.5 g) and a small amount (0.05 g) of (E)-cis-4-(1-*hydroxy*-3,3,5-*dimethylcyclohexyl*)*but*-2-*enoic acid* (**25**) *methyl ester* (Found: C, 70.15; H, 10.15%); $\nu_{max.}$ 3 480 (OH), 1 720 (C=O), 1 655 (C=C), and 1 270 cm^{-1} (COO); δ_H 7.03 (1 H, dt, *J* 15.6 and 7.5 Hz, C*H*=CCO_2Me), 5.82 (1 H, *J* 15.6 Hz, C=C*H*CO_2Me), 3.73 (3 H, s, CO_2Me), 2.48 (2 H, d, *J* 7.9 Hz, CH_2C=C), 1.77—1.1 (7 H, m, C_6H_7), 0.94 (6 H, m, 2 × ring Me), and 0.87 (3 H, s, ring Me); δ_C 166.5, 145.3, 123.7, 72.6, 51.2, 50.1, 48.0, 47.9, 42.5, 34.5, 31.9, 26.7, 26.3, and 22.1.

Reaction of Dimethylacrylic Acid with 3,3,5-*Trimethylcyclohexanone*.—(A) Dimethylacrylic acid (**2**) (1.8 g, 18 mmol) and 3,3,5-trimethylcyclohexanone (**6**) (2.52 g, 18 mmol) were allowed to react for 0.5 h at −70 °C. Work-up led to a thick oil (2.93 g, 68%), which on crystallization from benzene yielded small white prisms of (R,R)- or (R,S)-trans-2-(1-*hydroxy*-3,3,5-*trimethylcyclohexyl*)-3-*methylbut*-3-*enoic acid* (**23**), m.p. 174—175 °C (Found: C, 69.7; H, 10.05. $C_{14}H_{24}O_3$ requires C, 69.7; H, 10.06%); $\nu_{max.}$ 3 350 (OH), 1 690 (C=O), and 1 630 cm^{-1} (COO); δ_H 5.08 and 5.02 (2 H, 2 s, C=CH_2), 2.94 (1 H, s, CHCOO), 1.91 (3 H, d, *J* 1 Hz, C=CMe), 1.9—0.8 (7 H, m, C_6H_7), 1.11 (3 H, s, ring Me), and 0.88 (6 H, s + d, 2 × ring Me).

Methyl ester: δ_C 174.6, 139.3, 116.7, 73.9, 62.5, 51.6, 48.8, 48.3, 43.45, 34.27, 31.4, 27.05, 23.7, 22.6, and 22.3.

(B) The same reagents as above for 2 h at 0 °C led to a solid product (3.5 g, 81%). This was set aside for a few days, and then stirred with 1M sodium hydroxide, and extracted with diethyl ether. Evaporation of the extract gave a solid (2.1 g, 51%), which on crystallization from hexane–diethyl ether gave (R,R)-4,8,8,10-*tetramethyl*-1-*oxaspiro*[5.5]*undec*-3-*en*-2-*one* (**26**), m.p. 62—63 °C (Found: C, 74.25; H, 10.35. $C_{14}H_{22}O_3$ requires C, 74.24; H, 10.54%); $\nu_{max.}$ 1 720 (C=O); δ_H 5.76 (1 H, s, 3-H), 1.98 (2 H, s, CH_2C=C), 1.97—1.1 (7 H, m, C_6H_7), 1.93 (3 H, d, *J* 1 Hz, 4-Me), 1.11 (3 H, s, ring Me), and 0.88 (6 H, s + d, 2 × ring Me); δ_C 163.8, 154.8, 115.3, 81.3, 47.7, 46.6, 44.7, 41.5, 33.7, 30.85, 26.8, 23.2, 22.8, and 21.7.

Reaction of Crotonic Acid with Cyclononanone.—LDE (from butyl-lithium, *ca.* 5 mmol), crotonic acid (**1**) (0.4 g), and cyclononanone (**7e**) (0.63 g) (Method B) for 2 h at 0 °C gave, after work-up according to the general procedure, a solid, which on crystallization from diethyl ether gave white prisms (0.52 g, 51%) of (E)-4-(1-*hydroxycyclononyl*)*but*-2-*enoic acid* (**34e**; H for Li) m.p. 148—149 °C (Found: C, 69.15; H, 9.8. $C_{13}H_{22}O_3$ requires C, 69.03; H, 9.73%); $\nu_{max.}$ 3 250 (OH), 1 700 (CO), and 1 630 cm^{-1} (C=C); methyl ester: δ_H 7.06 (1 H, dt, *J* 15.8 and 7.6 Hz, C*H*=CCO_2Me), 5.86 (1 H, d, *J* 15.8 Hz, C=C*H*CO_2Me), 3.73 (3 H, s, CO_2Me), 2.32 (2 H, dd, *J* 7.6 and 1 Hz, CH_2C=C), and 1.48 (16 H, s, $[CH_2]_8$).

Reaction of Dimethylacrylic Acid with Cyclononanone.—LDE (from butyl-lithium, *ca.* 5 mmol), dimethylacrylic acid (**2**) (0.45 g), and cyclononanone (**7e**) (0.63 g) (Method B), for 2 h at 0 °C, gave a viscous oil (0.73 g, 73%), which was set aside for 2 days, washed with 1M sodium hydroxide, and extracted with ether. Evaporation of the extract and distillation under reduced pressure (185 °C/1 mmHg) gave an oil, which was spectroscopically characterized as 4-methyl-1-oxaspiro[5.8]tetradec-3-ene-2-one (**35e**) (0.41 g, 41%); $\nu_{max.}$ 1 700 (CO) and 1 660 cm^{-1}

(C=C); 5.80 (1 H, s, 3-H), 2.28 (2 H, s, CH_2C=C), 1.94 (3 H, s, C=CMe), and 1.50 (16 H, s, $[CH_2]_8$).

Reaction of Crotonic Acid with Cyclodecanone.—Crotonic acid (**1**) (3.2 g) and cyclodecanone (**7f**) (5.5 g) were allowed to react for 20 min while being stirred at −70 °C, and an aliquot was taken. The remaining solution was heated at 40 °C for 1.5 h. Work-up of the aliquot, esterification of the acidic mixture, and column chromatography gave 2-(1-*hydroxycyclodecyl*)*but*-3-*enoic acid methyl ester* (**32f**; Me for Li) (0.1 g), m.p. 53—55 °C (Found: C, 70.75; H, 10.45. $C_{15}H_{26}O_3$ requires C, 70.82; H, 10.38%); $\nu_{max.}$ 3 500 (OH), 1 700 (CO), and 1 625 cm^{-1} (C=C); δ_H 6.00 (1 H, ddd, *J* 16.1, 10.2, and 9.3 Hz, C*H*=CH_2), 5.21 (1 H, d, *J* 10 Hz, C=CH_c), 5.16 (1 H, d, *J* 16 Hz, C–CH_t), 3.71 (3 H, s, CO_2Me), 3.06 (1 H, d, *J* 9.3 Hz, $CHCO_2Me$), and 1.52 (18 H, s, $[CH_2]_9$).

The main reaction mixture gave a yellow oil (6.4 g, 76%), which on crystallization from diethyl ether gave white prisms of (E)-4-(1-*hydroxycyclodecyl*)*but*-2-*enoic acid* (**34e**; H for Li) (1.9 g, 22%), m.p. 161—163 °C (Found: C, 69.4; H, 10.1. $C_{14}H_{14}O_3$ requires C, 69.96; H, 10.06%); $\nu_{max.}$ 3 350 (OH), 1 690 (CO), and 1 655 cm^{-1} (C=C); methyl ester: δ_H 7.07 (1 H, dt, *J* 15.6 and 7.6 Hz, CH=CCO_2Me), 5.87 (1 H, d, *J* 15.6 Hz, C=$CHCO_2Me$), 3.73 (3 H, s, CO_2Me), 2.30 (2 H, dd, *J* 7.6 and 1 Hz, CH_2C=C), and 1.43 (18 H, $[CH_2]_9$).

Reaction of Dimethylacrylic Acid with Cyclodecanone.—Dimethylacrylic acid (**2**) (1 g), was allowed to react with LDE (from butyl-lithium, *ca.* 12 mmol) and then with cyclodecanone (**7f**) (1.5 g) for 20 min at −70 °C. An aliquot was withdrawn, and the remaining reaction mixture was stirred for 24 h at room temperature. The aliquot was worked up as usual, and a yellow oil (0.36 g, 14%) was obtained, which on crystallization from benzene afforded white prisms of 2-(1-*hydroxycyclodecyl*)-3-*methylbut*-3-*enoic acid* (**33e**; H for Li), m.p. 147—148 °C (Found: C, 70.7; H, 10.2. $C_{15}H_{26}O_3$ requires C, 70.82, H, 10.30%); $\nu_{max.}$ 3 550 (OH), 1 680 (CO), and 1 630 cm^{-1} (C=C); methyl ester: δ_H 5.00 (2 H, s, C=CH_2), 3.71 (3 H, s, CO_2Me), 3.11 (1 H, s, $CHCO_2Me$), 1.89 (3 H, s, C=CMe), and 1.53 (18 H, s, $[CH_2]_9$).

The main reaction mixture afforded an oil (1 g, 40%), which after being washed with 1M sodium hydroxide and distilled gave an oil, characterized spectroscopically as 4-methyl-1-oxaspiro-[5.9]pentadec-3-en-2-one (**35e**) (0.3 g, 10%), b.p. 190 °C/1 mmHg; $\nu_{max.}$ 1 705 cm^{-1} (CO); δ_H 5.79 (1 H, s, 3-H), 2.28 (2 H, s, CH_2C=C), 1.94 (3 H, s, C=CMe), and 1.54 (18 H, s, $[CH_2]_9$).

Reaction of Crotonic Acid with Cycloundecanone.—Crotonic acid (**1**) (3.5 g) was allowed to react with cycloundecanone (**7g**) (6.2 g) for 20 min at −70 °C. An aliquot was taken, and the remaining reaction mixture was stirred for 1.5 h at 40 °C. The aliquot gave an oil, which was esterified. Chromatography led to a solid (0.14 g, 14%), 2-(1-*hydroxycycloundecyl*)*but*-3-*enoic acid methyl ester* (**32g**; Me for Li), m.p. 55—57 °C (Found: C, 71.75; H, 10.35; $C_{16}H_{28}O_3$ requires C, 71.60; H, 10.51%); $\nu_{max.}$ 3 500 (OH), 1 705 (CO), and 1 630 cm^{-1} (C=C); δ_H 6.00 (1 H, ddd, *J* 17.6, 10.5, and 9.3 Hz, C*H*=CH_2), 5.21 (1 H, d, *J* 10 Hz, C=CH_c), 5.17 (1 H, d, *J* 17.6 Hz, C=CH_t), 3.71 (3 H, s, CO_2Me), 3.06 (1 H, d, *J* 9.3 Hz, C*H*CO_2Me), and 1.42 (20 H, s, $[CH_2]_{10}$).

The main reaction mixture gave an oil (5.9 g, 62%), which on crystallization from hexane–diethyl ether afforded white prisms (1.7 g, 18%) of (E)-4-(1-*hydroxycycloundecyl*)*but*-2-*enoic acid* (**34g**; H for Li), m.p. 133—134 °C (Found: C, 70.7; H, 10.65. $C_{15}H_{26}O_3$ requires C, 70.82; H, 10.31%); $\nu_{max.}$ 3 550 (OH), 1 690 (CO), and 1 660 cm^{-1} (C=C); methyl ester: δ_H 6.97 (1 H, dt, *J* 15.6 and 7.6 Hz, C*H*=CCO_2Me), 5.87 (1 H, d, *J* 15.6 Hz, C=C*H*CO_2Me), 3.73 (3 H, s, CO_2Me), 2.32 (2 H, dd, *J* 7 and 1 Hz, CH_2C=C), and 1.43 (20 H, s, $[CH_2]_{10}$).

Reaction of Dimethylacrylic Acid with Cycloundecanone.—Dimethylacrylic acid (**2**) (3.5 g) was allowed to react with cycloundecanone (**7g**) (6 g) for 20 min at −70 °C. A sample was withdrawn, and the remaining reaction mixture was stirred for 16 h at room temperature. The aliquot sample gave a solid, which on crystallization from benzene gave white prisms of 2-(1-*hydroxycycloundecyl*)-3-*methylbut*-3-*enoic acid* (**33g**; H for Li), m.p. 132—133 °C (Found: C, 71.65; H, 10.55. $C_{16}H_{28}O_3$ requires C, 71.67; H, 10.55%); $\nu_{max.}$ 3 550 (OH), 1 690 (CO), and 1 630 cm^{-1} (C=C); methyl ester: δ_H 4.99 (2 H, s, C=CH_2), 3.71 (3 H, s, CO_2Me), 3.12 (1 H, s, $HCCO_2Me$), 1.88 (3 H, s, C=CMe), and 1.42 (20 H, s, $[CH_2]_{10}$).

The main reaction mixture gave an oil (5 g, 73%) on work-up. This was washed with 1M sodium hydroxide and the neutral products were distilled to afford a white solid (2.3 g, 26%), 4-*methyl*-1-*oxaspiro*[5.10]*hexadec*-3-*en*-2-*one* (**35g**), m.p. 44—45 °C (Found: C, 76.55; H, 10.75. $C_{16}H_{26}O_2$ requires C, 76.82; H, 10.39%); $\nu_{max.}$ 1 700 (CO) and 1 645 cm^{-1} (C=C); δ_H 5.78 (1 H, s, 3-H), 2.28 (2 H, s, CH_2C=C), 1.94 (3 H, s, C=CMe), and 1.44 (20 H, s, $[CH_2]_{10}$).

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