73. Preparation of 4-(4'-Methyl-2'-oxo-cyclohex-3'-en-1'-yl)-pentan-1-ol and Derivatives of 3-(4'-Methyl-2'-oxo-cyclohex-3'-en-1'-yl)-butan-1-ol[1])

by **David G. Leppard**[2]), **Peter W. Raynolds**[3]), **Christopher B. Chapleo**[4]) and **André S. Dreiding**

Organisch-Chemisches Institut der Universität Zürich, Rämistrasse 76, 8001 Zürich

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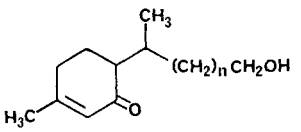
Zusammenfassung. Es wird über eine, bzw. zwei Methoden zur Herstellung von 4-(4'Methyl-2'-oxo-cyclohex-3'-en-1'-yl)-pentan-1-ol (*Schema 1*) bzw. 3-(4'-Methyl-2'-oxo-cyclohex-3'-en-1'-yl)-butan-1-ol[1])-Derivaten (*Schemata 2* und *3*) berichtet. Die Synthesen sind nicht spezifisch bezüglich Diastereoisomerie an den Zentren C(1') und C(4), bzw. C(1') und C(3). Als potentielles Terpenoid-Synthon kommt das Produkt der Synthese nach *Schema 1*, Schritte (1) bis (3), in Frage.

1. Introduction. – 6-Substituted 3-methyl-cyclohex-2-en-1-ones of the type shown below are potential synthons for certain terpenoid substances. We report here the exploration of three routes to this system with n = 1 or 2.



n = 1 or 2

The reaction sequences for the three routes are given in *Schemes 1* to *3*. The individual steps in each *Scheme* are indexed (numbers in brackets) and additional remarks such as unusual conditions, structure evidence and stereoisomerism are given in the text under the step index.

2. *Scheme 1.* – 2.1. *Routes (1) → (5).* To (1): The reagent is 2,2,2-triphenyl 1,2-oxaphosph(V)olane (**12**) made from (3-hydroxypropyl)-triphenyl-phosphonium bromide (**11**) with sodium hydride in diglyme according to the method described [1] for the corresponding iodide. In $CDCl_3$ solution the two hydrogen atoms at C(3) in **12** were replaced by deuterium atoms which permitted a better interpretation of its ^{1}H-NMR. spectrum (see Exper. Part). The condensation reaction at 180° between **1** and **12** (*cf.* [2]) gave 4-(2'-methoxy-4'-methyl-phenyl)-pent-3-en-1-ol (**2**) as a 3:1 mixture of stereoisomers **A** and **B** (configurations unassigned) which were separated chromatographically.

To (2): The *Birch* reduction [3] of **2** resulted not only in attack of the aromatic ring but also of the double bond in the side chain. The constitution of the product as

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1) The IUPAC-Nomenclature of these compounds is: *6-(4'-hydroxy-1'-methyl-butyl)-3-methyl-cyclohex-2-en-1-one* and 6-(3'-hydroxy-1'-mcthyl-propyl)-3-methyl-cyclohex-2-en-1-one.

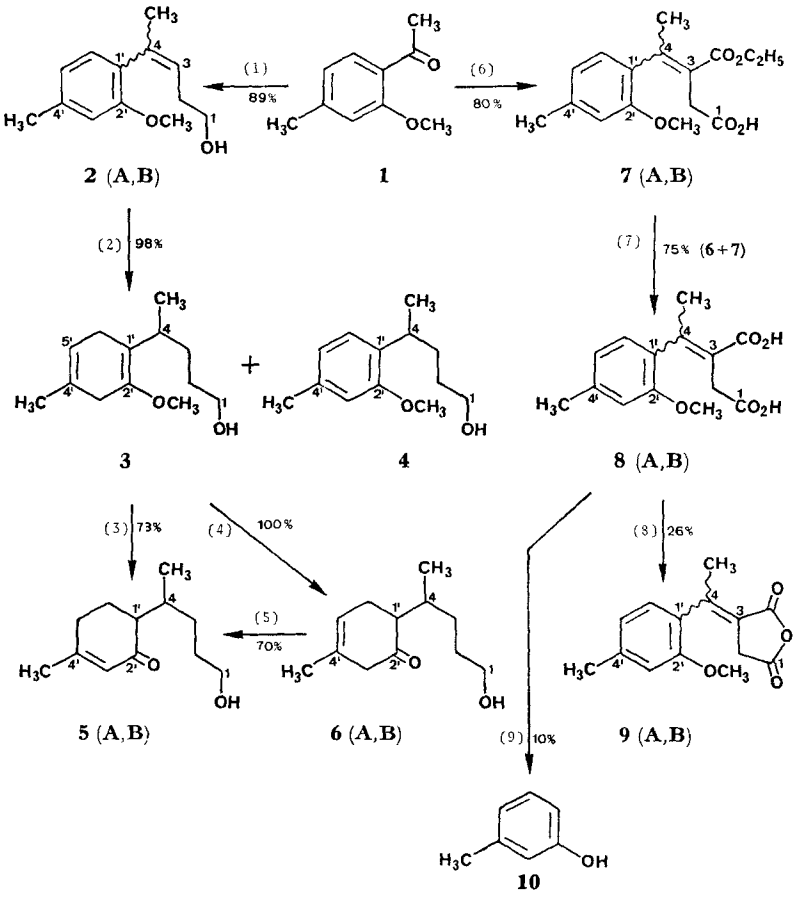
2) Royal Society Post-doctoral fellow 1972–1973. Present address: *Ciba-Geigy*, Photochemie, 1723 Marly, Switzerland.

3) Research assistant 1974. Present address: Department of Chemistry, Ohio State University Columbus, Ohio.

4) Post-doctoral fellow 1972–1975. Present address: Department of Chemistry, Salford University Salford, England.

4-(2'-methoxy-4'-methyl-cyclohexa-1',4'-dien-1'-yl)-pentan-1-ol (**3**) was derived from its properties in the following way: Elemental analysis and mass spectrum (M^+ 210 *m/e*) indicate the molecular formula $C_{13}H_{22}O_2$. IR. absorptions at 1705 and 1674 cm^{-1} suggest the presence of C=C–OCH_3 and C=C groups, respectively (compare [4]). That the double bond as well as the aromatic ring had been reduced can be seen in the ^{1}H-NMR. spectrum which shows the presence of a methyl group *geminal* to a hydrogen atom (H_3C–C(4), $\delta = 0.95$/d, $J = 7$), the absence of aromatic hydrogen atoms as well as the presence of a vinylic hydrogen atom (H–C(5'), $\delta = 5.4$–5.2). When the reduction time was reduced, 4-(2'-methoxy-4'-methyl-phenyl)-pentan-1-ol (**4**) was also isolated (after step (3)) indicating that the first stage in the conversion of **2** to **3** is the reduction of the C(3)–C(4) double bond of **2**.

Scheme 1



(1) Ph_3P=O 12
(2) Na, ammonia
(3) HCl, methanol
(4) HCl/ether 1:1
(5) HCl, methanol
(6) *t*-butanol, K, diethyl succinate
(7) KOH, H_2O
(8) pyrolysis
(9) conc. HCl or HBr, acetic acid

To (3): The one phase acidic hydrolysis [5] of **3** gave a 1:1 mixture of diastereoisomers (**A** and **B**) of 4-(4'-methyl-2'-oxo-cyclohex-3'-en-1'-yl)-pentan-1-ol (**5**)[5]) whose constitution was determined spectroscopically as follows: Elemental analysis and mass spectrum (M^+196 *m/e*) indicate the composition $C_{12}H_{20}O_2$. The IR. spectrum shows absorptions at 3460 and 1660 cm^{-1} for the OH and C=O groups, respectively. The presence of an α,β-unsaturated ketone is confirmed by the UV. maximum at 232 nm ($\varepsilon = 14850$). The ^{1}H-NMR. spectrum of **5** contains a one-proton signal at $\delta = 5.86$ attributed to H–C(3'), a three-proton signal at $\delta = 2.00$ (H_3C–C(4')), and two doublets ($J = 6$) of nearly equal intensity at $\delta = 1.04$ and 0.92 representing together the three hydrogen atoms of H_3C–C(4) of **A** and **B**.

To (4): A two phase acidic hydrolysis [6] of **3** resulted in the unconjugated ketone, namely 4-(4'-methyl-2'-oxo-cyclohex-4'-en-1'-yl)-pentan-1-ol (**6**)[5]), also as a 1:1 mixture of diastereoisomers **A** and **B**. Evidence for the constitution comes from the IR. spectrum which shows the unconjugated carbonyl group (1710 cm^{-1}) as well as from the ^{1}H-NMR. spectrum with its signal at $\delta = 5.57$ attributed to H–C(5') (*cf.* $\delta =$ 5.86 for H–C(3') in **5**) and its two equally intense doublets ($J = 6$) at $\delta = 0.88$ and 0.84 attributed to the methyl group at C(4) in the two (unassigned) configurations.

To (5): The one phase acidic hydrolysis of **6** caused the double bond to move into conjugation with the carbonyl group to give **5**.

2.2 *Attempt at another route, (6) → (9).* To (6): The *Stobbe* condensation of diethyl succinate with **1** gave a 1:1 mixture of two stereoisomers **A** and **B** (configuration unassigned) of 3-ethoxycarbonyl-4-(2'-methoxy-4'-methyl-phenyl)-pent-3-enoic acid (**7**). One isomer was isolated pure after fractional crystallisation.

To (7): Basic hydrolysis of the crude acid-ester **7** resulted in a 1:1 mixture (not separated) of stereoisomers **A** and **B** (configuration unassigned) of 3-carboxy-4-(2'-methoxy-4'-methyl-phenyl)-pent-3-enoic acid (**8**).

To (8): Thermolysis of **8** resulted in two stereoisomers **A** and **B** of the anhydride **9**, separated chromatographically. The anhydride function is evidenced by the IR. absorptions at 1838/1828 and 1770/1768 cm^{-1}.

To (9): Attempts to decarboxylate the diacid mixture **8** using a number of aqueous acids were unsuccessful. Only on treatment with concentrated mineral acids in acetic acid was a product isolated in very low yield, namely *m*-cresol (**10**).

3. ***Scheme 2.*** – To (1): That the reaction of *t*-butyl acetoacetate with a mixture of crotononitrile and isocrotononitrile (*cf.* [7]) gave 4-*t*-butoxycarbonyl-3-methyl-5-oxo-hexanenitrile (**13**) was confirmed by the IR. spectrum (2250, 1740 and 1715 cm^{-1} representing C≡N, COOR and C=O groupings, respectively) and the ^{1}H-NMR. spectrum which shows signals (ratio 1:3:1) for the three types of methyl groups, namely at $\delta = 2.20/s$ for CH_3C=O, 1.46/*s* for $COOC(CH_3)_3$, and 1.08/*d* ($J = 7$) for R_2CH–CH_3.

To (2): A second *Michael* addition – this time with methyl vinyl ketone – converted **13**, presumably *via* **14**, in high yield to 3-(1'-*t*-butoxycarbonyl-4'-hydroxy-4'-methyl-2'-oxo-cyclohex-1'-yl)-butanenitrile (**15**). That cyclisation of **14** to **15** had occurred was indicated by the IR. spectrum of the product which shows an OH-absorption at 3500 cm^{-1}.

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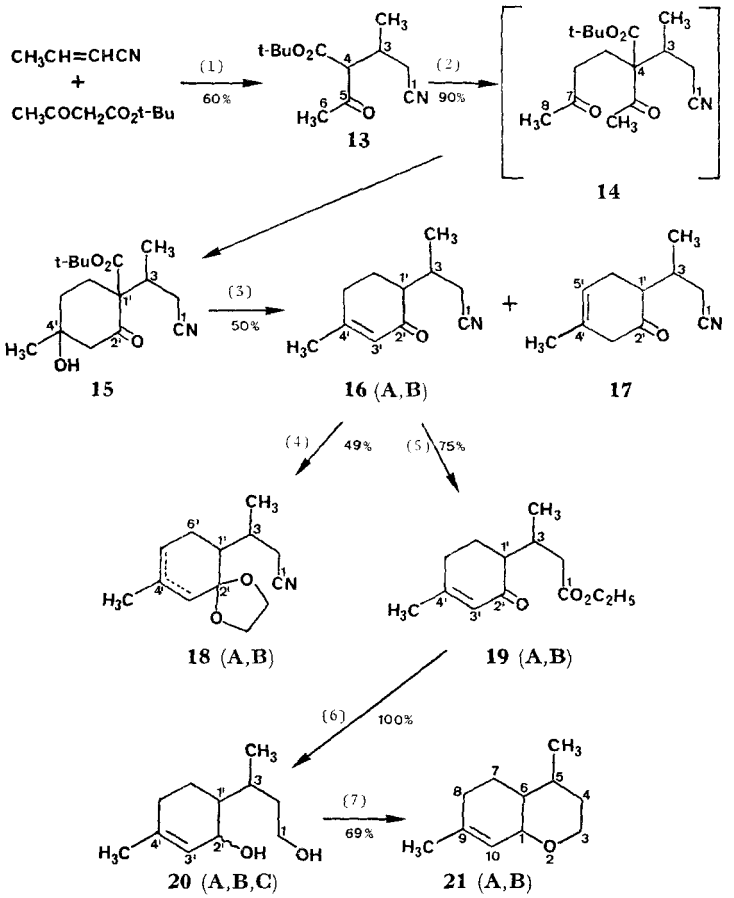
[5]) See footnote [1]).

Scheme 2



(1) KOH, ethanol
(2) Na, ethanol, methyl vinyl ketone
(3) *p*-toluenesulfonic acid
(4) ethylene glycol, *p*-toluenesulfonic acid
(5) HCl, ethanol
(6) $LiAlH_4$
(7) pyridine, *p*-toluenesulfonyl chloride

To (3): Dehydration and decarboxylative cleavage of nitrile **15** with *p*-toluenesulfonic acid gave a 1:1 mixture of diastereoisomers **A** and **B** of 3-(4′-methyl-2′-oxocyclohex-3′-en-1′-yl)-butanenitrile (**16**) as the major product. Evidence for the composition $C_{11}H_{15}NO$ comes from elemental analysis and mass spectrum (M^+ 177 *m/e*). The IR. spectrum shows the absorptions expected for an α,β-unsaturated ketone and a nitrile group, namely 1665, 1635 and 2245 cm^{-1}, respectively. In the ^{1}H-NMR. spectrum H–C(3′) appears at $\delta = 5.76$ and H_3C–C(4′) at 1.96, both signals being singlets with fine splitting. The two doublets ($J = 6$) at $\delta = 1.15$ and 1.04 of equal intensity and integrating together for three protons (H_3C–C(3)), show the stereoisomerism mentioned. A minor product, isolated in an impure form, is considered to be 3-(4′-methyl-2′-oxo-cyclohex-4′-en-1′-yl)-butanenitrile (**17**) because of its IR.

absorption at 1715 cm^{-1}, its lack of absorption in the OH region and its ^{1}H-NMR. multiplet at $\delta = 5.7–5.4$ (HC–C(5')).

To (4): The reaction of **16** with ethylene glycol in the presence of *p*-toluenesulfonic acid was not very efficient; up to 39% of starting material **16** was recovered. A diastereoisomeric mixture ($\sim$ 1:1) of **A** and **B** of 3-(2'-ethylenedioxy-4'-methyl-cyclohex-3'-(possibly-4')-en-1'-yl)-butanenitrile (**18**) was obtained. That the carbonyl group has been protected is evident from the IR. spectrum which shows no absorptions in the region 1800–1600 cm^{-1}, and from the four-proton singlet at $\delta = 3.93$ (ethylenedioxy group) in the ^{1}H-NMR. spectrum. The spectroscopic data of **18** are consistent with either of the constitutions shown for **18.**

To (5): Conversion of the nitrile group in **16** to an ester function was achieved by HCl in ethanol. The constitution of ethyl 3-(4'-methyl-2'-oxo-cyclohex-3'-en-1'-yl)-butanoate (**19**) (1:1 mixture of diastereoisomers **A** and **B**) was evident from the comparison of the spectral properties with those of the educt **16**: absence of a nitrile (IR.) but presence of an ethyl ester function (IR., ^{1}H-NMR.).

To (6): Reduction of **19** gave a mixture of diastereoisomers of 3-(2'-hydroxy-4'-methyl-cyclohex-3'-en-1'-yl)-butan-1-ol (**20**). Lack of IR. absorptions in the carbonyl region, but new bands at 3310 and 1050 cm^{-1} are evidence for the diol **20**.

To (7): Attempts to synthesize the *p*-toluenesulfonate of diol **20** caused cyclic ether formation. The constitution of the product as 5,9-dimethyl-2-oxa-bicyclo [4.4.0]dec-9-ene (**21**) was deduced from the spectroscopic data: The mass spectrum (M^+ 166 *m/e*) shows the composition $C_{11}H_{18}O$ and the IR. spectrum suggests the presence of an ether link (band at 1087 cm^{-1}, but none in the OH-region) as well as unsaturation (1678 cm^{-1}). Two low field signal groups ($\delta = 5.7–5.3$ and 4.3–3.2, ratio 1:3) in the ^{1}H-NMR. spectrum clearly belong to the vinylic H–C(10) and to the three hydrogen atoms in α-positions to the oxygen atom, namely H–C(1) and 2H–C(3), respectively. The three-proton singlet at $\delta = 1.73$ is assigned to H_3C–C(9), whilst H_3C–C(5) appears as two equally intense doublets ($J = 5.6$) at $\delta = 1.05$ and 0.95 indicating the product **21** to be a 1:1 mixture of two (**A** and **B**) of the four possible diastereoisomers.

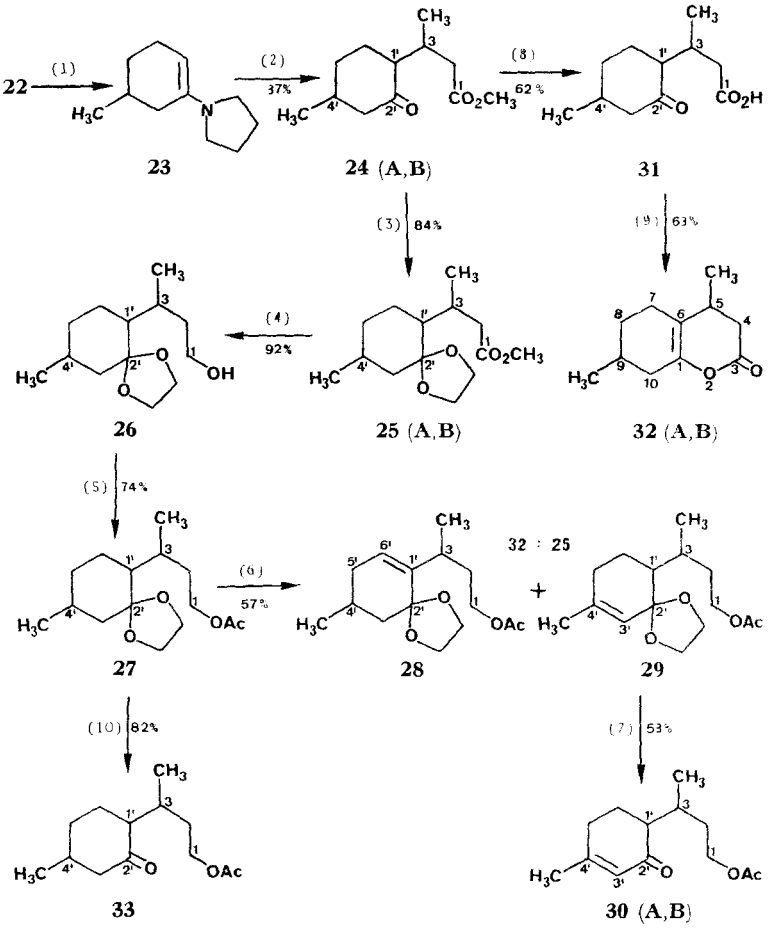
4. ***Scheme 3.*** – To (1): The pyrrolidine enamine (*cf.* [8]) **23** obtained from 3-methyl-cyclohexanone (**22**) was not purified.

To (2): Reaction of the enamine **23** with methyl crotonate, followed by hydrolysis gave after fractional distillation a product which according to capillary GC. consisted of two minor components (together 12%), and two major components (1:1 ratio, together 88%). The latter are considered to be two (**A** and **B**) of the four possible diastereoisomers of methyl 3-(4'-methyl-2'-oxo-cyclohex-1'-yl)-butanoate (**24**). The composition $C_{12}H_{20}O_3$ was confirmed by elemental analysis. The IR. spectrum exhibits the two expected carbonyl absorptions at 1740 and 1712 cm^{-1}.

To (3): Evidence for the formation of methyl 3-(2'-ethylenedioxy-4'-methyl-cyclohex-1'-yl)-butanoate (**25**) comes from the IR. spectrum which shows only one carbonyl absorption (1740 cm^{-1}; ester) and the ^{1}H-NMR. spectrum which possesses a four-proton signal at $\delta = 3.91$ (ethylenedioxy group). Capillary GC. shows 20% impurities and 80% of a $\sim$1:1 mixture of presumably two diastereoisomers **A** and **B** of **25.**

To (4): Reduction of the acetal-ester **25** with lithium aluminium hydride afforded 3-(2'-ethylenedioxy-4'-methyl-cyclohex-1'-yl)-butan-1-ol (**26**) which was not purified.

Scheme 3



(1) pyrrolidine, *p*-toluenesulfonic acid
(2) methyl crotonate, H_2O
(3) ethylene glycol, *p*-toluenesulfonic acid
(4) $LiAlH_4$
(5) acetic anhydride, pyridine
(6) phenyl-trimethyl-ammonium tribromide; 1,5-diaza-bicyclo[4.3.0]non-5-ene
(7) *p*-toluenesulfonic acid, H_2O
(8) NaOH, H_2O
(9) *p*-toluenesulfonic acid
(10) *p*-toluenesulfonic acid, H_2O

To (5): The crude acetal-alcohol **26** was converted to 1-acetoxy-3-(2'-ethylenedioxy-4'-methyl-cyclohex-1'-yl)-butane (**27**) (mixture of diastereoisomers **A** and **B** ~ 4:5) using the standard procedure. That the acetate **27** had been formed was evident from the mass spectrum, which shows the molecular ion peak (M^+ 270 *m/e*) as well as a fragment peak ($M - CH_3CO$). Confirmation comes from the IR. (carbonyl, 1745 cm^{-1}) and from the ^{1}H-NMR. spectrum (three-proton singlet at $\delta = 1.96$).

To (6): The acetate **27** was brominated with phenyl-trimethyl-ammonium tribromide to give a mixture of presumably the 3'-bromo and 1'-bromo ketones in high yield. Dehydrobromination of this mixture with (1,5-diaza-bicyclo[4.3.0]non-5-ene followed by purification *via* column chromatography resulted in the isolation of two products. The first, obtained in 32% yield, was 1-acetoxy-3-(2'-ethylenedioxy-4'-methyl-cyclohex-6'-en-1'-yl)-butane (**28**). In the ^{1}H-NMR. spectrum H–C(6') appears as a clearly defined doublet of doublets (J = 2 and 5) at δ = 5.68, the two different J arising from coupling with the two non equivalent H–C(5'), and the two methyl signals (H_3C–C(3) and H_3C–C(4')) are both doublets (δ = 1.02 and 0.96, J = 7 and 6). It is likely that **28** was obtained from an intermediate in which the bromine atom had been introduced into the 1'-position of **27**. The second product from the chromatography is probably the result of the bromination having taken place in the 3'-position of **27** since it was a mixture of diastereoisomers (1:1 of **A** and **B**) of 1-acetoxy-3-(2'-ethylenedioxy-4'-methyl-cyclohex-3'-en-1'-yl)-butane (**29**). Evidence for the constitution comes from the ^{1}H-NMR. spectrum in which the signal at δ = 5.24 (broadened singlet) must belong to H–C(3'). One of the three-proton signals (δ = 1.66) is a singlet (broadened) which is to be expected for H_3C–C(4'). The other methyl group H_3C–C(3)) appears as two doublets (J = 7) of equal intensity at higher field, namely at δ = 0.96 and 0.92, indicating the stereoisomerism mentioned.

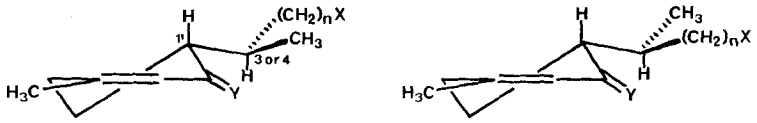
To (7): Mild acidic hydrolysis of the acetal grouping in **29** leads to 1-acetoxy-3-(4'-methyl-2'-oxo-cyclohex-3'-en-1'-yl)-butane (**30**). Elemental analysis and mass spectrum (M^+ 224 *m/e*) indicate the molecular formula $C_{13}H_{20}O_3$. The IR. spectrum shows the presence of two carbonyl groups (1740 and 1670 cm^{-1}) and of unsaturation (1640 cm^{-1}). That the product contains an α,β-unsaturated carbonyl function is confirmed by the UV. spectrum (maximum 233 nm, ε = 9000). The ^{1}H-NMR. spectrum of **30** shows the product to be a 1:1 mixture of two diastereoisomers **A** and **B** because H_3C–C(3) appears as two doublets of equal intensity at δ = 0.96 and 0.81 (J = 7). The other four interpretable signal groups in the intensity ratio of 1:2:3:3 are assigned as follows: the broad singlet at δ = 5.73 to H–C(3'), the triplet (J = 7) at δ = 4.02 to 2H–C(1), the broad singlet at δ = 1.90 to H_3C–C(4') and the singlet at δ = 1.94 to the acetoxy group.

To (8) and (9): 3-(4'-methyl-2'-oxo-cyclohex-1'-yl)-butanoic acid (**31**), obtained by hydrolysing **24**, was dehydrated to 5,9-dimethyl-2-oxa-bicyclo[4.4.0]dec-1(6)-en-3-one (**32**) whose constitution was confirmed spectroscopically in the following way: The composition $C_{11}H_{16}O_2$ is evident from the elemental analysis and the mass spectrum (M^+ 180 *m/e*). The presence of a lactone function and of an enolic double bond is indicated in the IR. spectrum by the absorptions at 1765 cm^{-1} and at 1710 cm^{-1}. The ^{1}H-NMR. spectrum, in the presence of Eu(fod)$_3$ shift reagent and with the help of spin decoupling experiments, could be completely interpreted to fit structure **32** (see Exper. Part) and showed the product to be an about 1:1 mixture of diastereoisomers **A** and **B**.

5. Configuration. – Several compounds on the way to the 6-substituted 3-methyl-cyclohex-2-en-1-ones (*Schemes 1* to *3*), were formed as stereoisomers. Because the isomers (in most cases two) show only minor differences in properties, configurations were not assigned. Compounds **2**, and **7** to **9** occurred as (E)- and (Z)-isomers in ratios of from 3:1 to 1:1, which were separated partially in three cases.

Of interest in connection with potential synthetic uses is the diastereoisomerism generated by the *adjacent* chirality centres C(1') and C(3) or C(4). This feature occurs in compounds **5**, **6**, **16** to **21**, **24** to **27**, **29** to **31** and **33**; in none of these cases the stereoisomers were separated. Some of them (**20**, **21**, **24** to **28** and **31**) have an additional centre of chirality which obscures the identification in the mixtures. Compounds **5**, **6**, **16** to **19**, **29** and **30** possess *only* the indicated centres of chirality (see *Scheme 4*) and were obtained sufficiently pure to permit recognition of the stereo-

Scheme 4



Diastereomerism due to chirality centres C(1') and C(3) or C(4)

isomers and estimation of their relative amounts by observing two doublets with $J = 6$–7 in the $\delta = 0.8$ to 1.2 region for H_3C–C(3) or H_3C–C(4). In these cases the two stereoisomers were invariably present in a ratio of $\sim 1:1$. The conditions of their formation suggest thermodynamic control of the isomer ratio. The value of $\sim 1:1$ is reasonable in view of the almost negligeable difference in bulk interaction between the two stereoisomers, as can be seen in *Scheme 4*.

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Experimental Part

1. General. – The designations, abbreviations and spectral data notations given in [9] were adhered to, apart from the following modifications or additions. *Working up*: the term 'dried' refers to the use of anhydrous magnesium or sodium sulfates. All compounds were analysed on thin layer chromatography (TLC.) plates prepared from *Macherey-Nagel* silica gel N-HR/UV_{254} or aluminium oxide N/UV_{254} or by analytical gas-liquid chromatography on an *Erba* Fractovap Model G1 and reported as capillary GC.

The mass spectra, ^{1}H-NMR. and IR. spectra were measured in our laboratories for mass spectrometry (under Prof. *M. Hesse*), for nuclear magnetic resonance (under Prof. *W. von Philipsborn*) and for micro-analysis (under Mr. *H. Frohofer*), respectively. Elemental analyses were performed in the last mentioned laboratory. Some ^{1}H-NMR. spectra were measured by Mr. *M. Karpf*.

Abreviations: RT. = room temperature.

2. *Scheme 1.* – *Step (1).* a) *2-Methoxy-4-methyl-acetophenone* (**1**) was made from *m*-cresol in 42% yield by the procedure of *Julia & Chastrette* [10], m.p. 35–36°, b.p. 80–82°/0.2 Torr, semicarbazone (EtOH) m.p. 195–198° (lit. [10] m.p. 35–36°, b.p. 100–103°/0,06 Torr, semicarbazone (EtOH) m.p. 194–198°). The product was homogeneous by GC. – ^{1}H-NMR. (60 MHz, $CDCl_3$): 7.70/*d* ($J = 8$), 1H (H–C(6)); 6,82/*d* ($J = 8$), 1H (H–C(5)); 6,78/br. *s*, 1H (H–C(3)); 3,92/*s*, 3H (OCH_3); 2,61/*s*, 3H (H_3C–C=O); 2.40/*s*, 3H (H_3C–C(4)). – IR. (Film): 1660 *s* (C=O), 1600 *m*, 1260–1230 *s* (C–O).

b) *(3-Hydroxypropyl)-triphenyl-phosphonium bromide* (**11**). The procedure of *Hands & Mercer* [1] for the preparation of the corresponding iodide was used. A solution of 131 g (0.5 mol) of triphenylphosphine and 80 g of 3-bromo-propan-1-ol '> 85% pure' (more than 0.5 mol) in 300 ml of toluene was refluxed for 20 h. The mixture was cooled and the solids were filtered and recrystallized from methanol/ethanol to give 160 g of **11** as white crystals, m.p. 232.5–233.5°.

More material (35 g), m.p. 231–232°, was recovered by concentrating the toluene filtrate and the alcoholic mother liquors. Total yield: 97%. – ^{1}H-NMR. (60 MHz, CD_3OD): 8.1–7.5/*m*, 15H (3 times 5 H–Ar); 3.9–3.4/*m*, partially covered by the CHD_2OD signal, 4H (2 H–C(1), 2 H–C(3)); 2.2–1.6/*m*, 2H (2 H–C(2)). – IR. (KBr): 3300*s* (OH), 1108*s*, 740*s*.

$C_{21}H_{22}BrOP$	Calc.	C 62.85	H 5.53	Br 19.91	P 7.72%
(401.29)	Found	C 62.74	H 5.50	Br 21.76	P 6.98%

c) *2,2,2-Triphenyl-1,2-oxaphosh(V)olane* (**12**). The procedure of *Hands & Mercer* [1] for the corresponding iodide was applied to (3-hydroxypropyl)-triphenyl-phosphonium bromide (**11**). **12** was obtained using both tetrahydrofuran and diglyme as solvent; the latter was preferred since it dissolved **11** better and higher reaction temperatures could be achieved. In a typical run, 13.2 g (33 mmol) of **11** was added to 1.6 g (66 mmol) of sodium hydride in 50 ml of diglyme. The mixture was heated under nitrogen for 16 h at 70–80° (slow evolution of gas). The solvent was removed under reduced pressure and the residue was extracted by warming with 6 × 100 ml of dry ether. The colourless organic extracts were concentrated to 75 ml from which a white crystalline solid precipitated at 6°. The liquid was decanted and the solid was recrystallized from ether to give 6.1 g (58%) of **12**, m.p. 111–113° (lit. [1] m.p. 116–117°). – ^{1}H-NMR. (60 MHz, $CDCl_3$): 7.6–7.0/*m*, 15H (3 times 5 H–Ar); 3,43/*d* × *t* (*J* = 10 and 7), 2H (2 H–C(5)); 1.90/br. *d* × *t* (*J* = 18 and 7), 2H (2 H–C(4)). This NMR. spectrum shows that the 2 H–C(3) had been replaced by deuterium atoms, presumably from the NMR. solvent $CDCl_3$ and perhaps under the influence of some base still present in the product. Otherwise the spectrum has the same features as the reported one [1], with the exception that we find the coupling between H–C(4) and H–C(5) to be 7 (and not 10.5) Hz. Due to this deuterium exchange the signal of the 2 H–C(4) can be seen more clearly and the coupling between H–C(4) and phosphorus can be recognized as 18 Hz. – IR. (Film): 1589*m*, 1435*s*, 1112*s*, 1053*s*, 1048*s*, 900*m*, 878*m*, 740*s*, 720*s*, 690*s*.

When this unstable, hygroscopic product was titrated with 1 equivalent of methanolic hydrobromic acid, **11**, m.p. 229–231°, was obtained as identified by its ^{1}H-NMR. spectrum.

d) *4-(2'-Methoxy-4'-methyl-phenyl)-pent-3-en-1-ol* (**2**). 2-Methoxy-4-methyl-acetophenone (**1**) (1.64 g, 10 mmol) and 2,2,2-triphenyl-1,2-oxaphosph(V)olane (**12**) (3.4 g, 10.5 mmol) were sealed in a glass tube and heated in an oven at 180° for 68 h. The product was taken up in ether and the precipitated triphenyl-phosphine oxide was filtered off. Chromatography (2 × 60 cm silica gel, ether/hexane 1:4) afforded 1.83 g (89%) of an approximately 3:1 mixture (according to ^{1}H-NMR.) of the two stereoisomers **A** and **B** of **2** as a brown oil, which partially decomposed on attempted distillation. – IR. (Film): 3360*s* (OH), 1612*m* (C=C), 1281*s*, 1260*s* (C–O), 1040*s*. – UV. (CH_3OH): 282 (11600). – MS. (70 eV): 206 (31, *M*), 191 (5, *M* – CH_3), 188 (8, *M* – H_2O), 187 (8, *M* – H – H_2O), 175 (100, *M* – CH_3O).

$C_{13}H_{18}O_2$ (206,27) Calc. C 75.69 H 8.80% Found C 75.05 H 8.80%

The double bond isomers could be separated by the chromatographic procedure described above. The first few fractions afforded pure stereoisomer **A** as an oil. – ^{1}H-NMR. (100 MHz, $CDCl_3$): 6.95–6.65/*ABM*-system, 3H (3 H–Ar); 5.48/*t* × *q* (*J* = 7 and ~2), 1H (H–C(3)); 3.74/*s*, 3H (CH_3O–C(2')); 3.46/*t* (*J* = 7), 2 H (2 H–C(1)); 2.54/*s*, 1 H (HO–C(1)); 2.32/*s*, 3H (H_3C–C(4')); 2.08/br. *d* × *t*, partially covered by signal at 1.96, (*J* = 7 and 7), 2 H (2 H–C(2)); 1.96/br. *s*, 3H (H_3C–C(4)).

The last few fractions afforded the almost pure stereoisomer **B** as an oil. – ^{1}H-NMR. (60 MHz, $CDCl_3$): 7.2–6.6/*m*, 3H (3 H–Ar); 5.38/*t* × *q* (*J* = 7 and 1), 1H (H–C(3)); 3.78/*s*, 3H (CH_3O–C(2')); 3.72/*t*, partially covered by signal at 3.78 (*J* = 7), 2H (2 H–C(1)); 2.50/br. *t* × *d*, partially covered by signal at 2.34 (*J* = 7 and 7), 2H, (2 H–C(2)); 2.34/*s*, 3H (H_3C–C(4'); 2.23/*s*, 1 H (HO–C(1)); 2.00/br. *s*, 3H (H_3C–C(4)).

The 3,5-dinitrobenzoate of **2A** was prepared in the usual way, after crystallization from ether/hexane m.p. 68–69°. – ^{1}H-NMR. (60 MHz, $CDCl_3$): 9.3–9.0/*m*, 3H (3 H–Ar(NO_2)$_2$); 7.0–6.6/*m*, 3H (3 H–Ar); 5.52/*q* × *t* (*J* = ~2 and 7), 1H (H–C(3)); 4.36/*t* (*J* = 7), 2H (2 H–C(1)), 3.76/*s*, 3H (CH_3O–C(2')); 2.35/*s*, 3H (H_3C–C(4'), 2.6–2.1/*m* (partially covered by signal at 2.35), 2H (2 H–C(2)); 2.00/br. *s*, 3H (H_3C–C(4)). – IR. (KBr): 1723*s* (C=O), 1635*m*, 1612*w*, 1552*s* (NO_2), 1302*s* (C–O).

$C_{20}H_{20}N_2O_7$ (400.38) Calc. C 59.99 H5.04 N 7.00% Found C 59.90 H 4.96 N 6.75%

Step (2). a) *4-(2'-Methoxy-4'-methyl-cyclohexa-1',4'-dien-1'-yl)-pentan-1-ol* (**3**). Ammonia (about 30 ml) was distilled into a stirred solution of 0.914 g (4.43 mmol) of 4-(2'-methoxy-4'-methyl-phenyl)-pent-3-en-1-ol (**2**, **A** and **B**) in 6 ml of abs. ethanol, cooled to −75°. The solution was allowed to warm to reflux and 3.0 g (132 mmol) of clean sodium were added in 0.1 g portions over 1 h dissolving first with gas evolution and later giving a deep blue colour. The solution was stirred at reflux until the blue colour disappeared (about 9 h, having added another 3 ml of abs. ethanol after 6 h) and the ammonia was allowed to evaporate under a stream of nitrogen. The residue was taken up in 25 ml of water and 50 ml of ether; the aqueous layer was saturated with sodium chloride and extracted with 25 ml of ether, and the combined organic extracts were washed with 2 × 50 ml of water and once with saturated sodium chloride. Drying of the extracts and removal of solvent gave 0.918 g of **3** (98%) as an analytically pure, clear, colourless liquid. – ^{1}H-NMR. (100 MHz, $CDCl_3$): 5.4–5.2/*m*, 1 H (H–C(5')); 3.50/*t* (*J* = 6), 2 H (2 H–C(1)) and 3.50/*s*, 1 H (HO–C(1)), the latter two signals partly covered by the signal at 3.44; 3.44/*s*, 3 H (CH_3O–C(2')); 2.96/br. *q*, (*J* = 7), 1 H (H–C(4)); 2.60/br. *s*, 4 H (2 H–C(3'), 2 H–C(6')); 1.66/br. *s*, 3 H (H_3C–C(4')); 1.6–1.1/*m*, 4 H (2 H–C(2), 2 H–C(3)); 0.95/*d*, (*J* = 7), 3 H (H_3C–C(4)). – IR. (Film): 3350*s* (OH), 1705*m* (C=C–OCH_3), 1674*m* (C=C), 1120, 1060*s* (C–O). – MS. (70 eV): 210 (1, *M*), 208 (2, *M* – H_2), 178 (50, *M* – CH_3OH), 163 (100, *M* – CH_3OH – CH_3).

$C_{13}H_{22}O_2$ (210.31) Calc. C 74.24 H 10.54% Found C 74.04 H 10.32%

b) *4-(2'-Methoxy-4'-methyl-phenyl)-pentan-1-ol* (**4**). In one experiment the sodium/liquid ammonia reduction of **2** described above was worked-up after only 5 h destroying the excess sodium with abs. ethanol. The isolated residue was shown by its ^{1}H-NMR. spectrum to contain ~70% of **3** and ~30% of an aromatic product. The mixture was hydrolysed using the methanol/concentrated hydrochloric acid procedure (see step (3)) to give after extraction an oil which was purified by preparative TLC. on silica gel using ether/hexane 3:1. The major product was shown by its IR. and ^{1}H-NMR. spectra to be identical with **5** isolated in step (3). The minor product (~30 mg) was impure *4-(2'-methoxy-4'-methyl-phenyl)-pentan-1-ol* (**4**). – ^{1}H-NMR. (60 MHz, $CDCl_3$): 7.08/*d* (*J* = 7), 1 H (H–C(5') or H–C(6')); 6.75/*d* (*J* = 7), 1 H (H–C(6') or H–C(5')); 6.69/*s*, 1 H (H–C(3')); 3.80/*s*, 3 H (OCH_3); 3.60/*t* (*J* = 6), 2 H (2 H–C(1)); 3.4–3.0/*m*, 1 H (H–C(4)); 2.31/*s*, 3 H (H_3C–C(4')); 1.9–1.4/*m*, 4 H (2 H–C(2), 2 H–C(3)); 1.68/*s*, 1 H (OH); 1.18/*d* (*J* = 7), 3 H (H_3C–C(4)). – IR. ($CHCl_3$): 3420*w* br. (OH), 2930*s*, 1612*m*, 1580*w*, 1502*m*, 1465*m*, 1410*w*, 1285*w*, 1255*m*, 1040*m*, 925*w*. – MS. (70 eV): 208 (20, M^+), 150 (10), 149 (100, M^+ – C_3H_7O), 119 (6), 91 (5).

The 3,5-dinitrobenzoate of **4** was obtained after crystallization from hexane at −20°, m.p. 62–65°. – ^{1}H-NMR. (60 MHz, $CDCl_3$): 9.3–9.1/*m*, 3 H (3 H–Ar(NO_2)$_2$); 7.1–6.6/*ABM*-system, 3 H (3 H–Ar); 4.7–4.3/*m*, 2 H (2 H–C(1)); 3.80/*s*, 3 H (CH_3O–C(2')); 3.6–3.0/*m*, 1 H (H–C(4)); 2.30/*s*, 3 H (H_3C–C(4')); 1.73/*m*, with *J* = 4 visible, 4 H (2 H–C(2), 2 H–C(3)); 1.23/*d* (*J* = 7), 3 H (H_3C–C(4)). – IR. (KBr): 1729*s* (C=O), 1630*m*, 1610*m*, 1538*s* (NO_2), 1280*s*(C–O), 1160*s* (C–O).

$C_{20}H_{22}N_2O_7$ (402.39) Calc. C 59.69 H 5.51 N 6.96% Found C 59.86 H 5.53 N 6.72%

Step (3). *4-(4'-Methyl-2'-oxo-cyclohex-3'-en-1'-yl)-pentan-1-ol* (**5**)[6]. To a stirred solution of 0.365 (1.74 mmol) of 4-(2'-methoxy-4'-methyl-cyclohexa-1',4'-dien-1'-yl)pentan-1-ol (**3**) in 8 ml of methanol were added 2 ml of water/concentrated hydrochloric acid 2:1. After 2 h at RT. water was added and the mixture was extracted with chloroform. The combined extracts were washed with water, dried and evaporated to give 0.35 g of a brown oil. Purification by preparative TLC. on silica gel using ether/hexane 9:1 gave 0.25 g (73%) of an about 1:1 mixture of the two diastereomers **A** and **B** of **5** as a colourless oil, b.p. 85–90°/0.005 Torr. – ^{1}H-NMR. (100 MHz, $CDCl_3$): 5.86/finely split *s*, 1 H (H–C(3')); 3.66/*t* (*J* = 6), 2 H (2 H–C(1)); 3.08/*s*, 1 H (OH); 2.5–1.1/*m*, 10 H; 2.00/*s*, 3 H (H_3C–C(4')); 1.04 and 0.92/2 *d*, (each with *J* = 6), ~1.5 H and 1.5 H (H_3C–C(4) of **A** and **B**). – IR. ($CHCl_3$): 3460*s* (OH), 1660*s* (C=O), 1455*m*, 1430*m*, 1380*m*, 1055*m*, 1015*m* 878*m*. – UV. (EtOH): 232 (14850). – MS. (70 eV): 196 (1, *M*), 137 (30, *M* – C_3H_7O), 110 (100, *M* – $C_5H_{10}O$), 109 (30), 95 (75), 82 (76).

$C_{12}H_{20}O_2$ (196.292) Calc. C 73.43 H 10.27% Found C 73.17 H 10.54%

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[6] The IUPAC nomenclature for compound **5** is: 6-(4'-hydroxy-1'-methyl-butyl)-3-methyl-cyclohex-2-en-1-one.

Step (4). 4-(4'-Methyl-2'-oxo-cyclohex-4'-en-1'-yl)-pentan-1-ol (**6**)[7]. Acidic hydrolysis of 0.06 g **3** in 10 ml of ether/2N hydrochloric acid 1:1 for 1 h gave in nearly quantitative yield an about 1:1 mixture of the two diastereoisomers **A** and **B** of **6** (pure by ^{1}H-NMR.). – ^{1}H-NMR. (60 MHz, $CDCl_3$): 5.57/br. *s*, 1H (H–C(5')); 3.65/*t* (*J* = 6), 2H (2 H–C(1)); 2.76/*s*, 1H (OH); 2.7–1.1/*m*, 10H, 1.70/*s*, 3H (H_3C–C(4')); 0.88 and 0.84/2*d*, (each with *J* = 6), ~1.5H and 1.5H (H_3C–C(4) of **A** and **B**). – IR. ($CHCl_3$): 3470*s* (OH), 1710*s* (C=O), 1660*w*, 1440*m*, 1380*m*, 1230–1195*m*; a very weak band at 1660 suggests the conjugated ketone **5** as a minor impurity.

Step (5). The ketone **6** from step (4) was treated with the methanol/conc. hydrochloric acid solution for 2 h at RT. The product, *4-(4'-methyl-2'-oxo-cyclohex-3'-en-1'-yl)-pentan-1-ol* (**5**)[6], was isolated and purified as described in step (3), yield ~70%, identical by its IR. and ^{1}H-NMR. spectra with **5** isolated in step (3).

Step (6). 3-Ethoxycarbonyl-4-(2'-methoxy-4'-methyl-phenyl)-pent-3-enoic acid (**7**). Diethyl succinate (4.0 g, 23 mmol) and 3.0 g (18 mmol) of 2-methoxy-4-methyl-acetophenone (**1**) were added to a solution of 0.8 g (20 mmol) of potassium in 100 ml of *t*-butyl alcohol. After 4 h at reflux the mixture was cooled to 20°, acidified with concentrated hydrochloric acid and the solvent removed. The residue was taken up in 300 ml of ether and extracted with 5 × 100 ml of aqueous 5% potassium hydroxide. The aqueous phase was washed with 3 × 100 ml of ether, acidified with hydrochloric acid and extracted with 4 × 100 ml of ether. The combined extracts were dried and evaporated to give an about 1:1 mixture (^{1}H-NMR., see below) of the stereoisomers **A** and **B** of **7** as a brown oil which partially crystallized over the period of a week. Column chromatography (3 × 20 cm silica gel, ether/hexane 1:1) gave 4.9 g (80%) of a colourless oil. Distillation resulted in partial decomposition. Pure stereoisomer **A** was obtained by two crystallizations from ether/hexane and drying for 8 h at 80°/0.01 Torr, m.p. 108–112°. – IR. (KBr): 3200–2500*m* (COOH), 1695*s* (COOH and $COOC_2H_5$), 1610*w* (C=C), 1268*m* (C–O). – UV. (CH_3OH): 270 (12600). – MS. (70 eV): 292 (25, *M*), 261 (15, *M* – OCH_3), 246 (30, *M* – OCH_2CH_3 – H), 159 (100, *M* – CH_2CO_2H – $CO_2CH_2CH_3$ – H). – ^{1}H-NMR. of **A** (60 MHz, $CDCl_3$): 11.25/*s*, 1H (COOH); 7.1–6.7/*m*, 3H (H–C(3'), H–C(5'), H–C(6')); 3.91/*q* (*J* = 7), 2H ($COOCH_2CH_3$); 3.81/*s*, 3H (CH_3O–C(2')), 3.58/*s*, 2H (2 H–C(2)); 2.35/*s*, 3H (H_3C–C(4')); 2.14/*s*, 3H (H_3C–C(4)); 0.90/*t* (*J* = 7), 3H ($COOCH_2CH_3$).

$C_{16}H_{20}O_5$ (292.32) Calc. C 65.74 H 6.87% Found C 65.57 H 6.87%

From the ^{1}H-NMR.-spectrum of the 1:1 mixture of stereoisomers **A** and **B** it was possible to read out the following signals due to isomer **B**: ^{1}H-NMR. of **B** (60 MHz, $CDCl_3$): 4.29/*q* (*J* = 7), 2H ($COOCH_2CH_3$); 3.18/br. *s*, 2H (2 H–C(2)); 2.19/*s*, 3H (H_3C–C(4)); the other signals coincide or overlap with the corresponding signals of stereoisomer **A**.

Steps (6+7). 3-Carboxy-4-(2'-methoxy-4'-methyl-phenyl)-pent-3-enoic acid (**8**). The procedure for the synthesis of **7** described in step (6) was followed, using 20.0 g (115 mmol) of diethyl succinate, 15.0 g (90 mmol) of 2-methoxy-4-methyl-acetophenone (**1**) and 4.0 g (100 mmol) of potassium, up to and including the point where the crude product was taken up in 5% potassium hydroxide and washed with ether. The alkaline solution was allowed to stand at RT. overnight, washed with 2 × 100 ml of ether, acidified with hydrochloric acid, saturated with sodium chloride and extracted with 3 × 200 ml of ether. The extracts were dried and concentrated to give a brown oil, which was chromatographed on silica gel (3 × 10 cm, ether/hexane 1:1). A yield of 14.1 g (75%) of an about 1:1 mixture of stereoisomers **A** and **B** of **8** was recovered as a white amorphous solid, m.p. 95–100° with formation of bubbles. – ^{1}H-NMR. (60 MHz, $CDCl_3$): 11.98/br. *s*, 2H (2 COOH); 7.0–6.5/*m*, 3H (3 H–Ar); 3.71/*s*, 3H (CH_3O–C(2')); 3.52 and 3.13/2 br. *s*, ~1H and 1H (2 H–C(2) of **A** and **B**); 2.35 and 2.04/2*s*, ~1.5H and 1.5H (H_3C–C(4)) of **A** and **B**); 2.32/*s*, 3H (H_3C–C(4')). – IR. (KBr): 3700–2300*m* (COOH), 1708*s* (COOH), 1623, 1613*m*, 1285*m* (C–O).

$C_{14}H_{16}O_5$ (264.27) Calc. C 63.62 H 6.10% Found C 63.52 H 6.36%

Step (8). Anhydride of 3-Carboxy-4-(2'-methoxy-4'-methyl-phenyl)-pent-3-enoic acid (**9**). Thermolysis of previously dried 3-carboxy-4-(2'-methoxy-4'-methyl-phenyl)-pent-3-enoic acid (**8**) (0.29 g) was carried out in a flask, equipped with an argon filled balloon, by heating in a 190° oil bath until the bubbling ceased (about 15 min). A condensate, presumably water, which was

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[7] The IUPAC nomenclature for compound **6** is: 6-(4'-hydroxy-1'-methyl-(butyl)-3-methyl-cyclohex-3-en-1-one.

insoluble in ether was observed. After drying at 25°/0.01 Torr, a weight loss of 0.0375 g was recorded. TLC. (silica gel, ether/hexane 1:3) showed in addition to a minor amount of starting material two spots of Rf 0.4 and 0.6. Preparative TLC. using the above solvent followed by extraction with ether gave 32 mg (11%) of stereoisomer **9B** from the band of Rf 0.6 and 41.0 mg (15%) of stereoisomer **9A** from the band of Rf 0.4.

Stereoisomer **A** was a solid which was recrystallized from ether/hexane, m.p. 124–128°. – ^{1}H-NMR. (60 MHz, $CDCl_3$): 7.1–6.6/*m*, 3H (3 H–Ar); 3.76/*s*, 3H (CH_3O–C(2')); 3.60/*q* (*J* = ~2), 2H (2 H–C(2)); 2.37/*s*, 3H (H_3C–C(4')); 2.13/*t* (*J* = ~2), 3H (H_3C–C(4)). – IR. (KBr): 1828*s* and 1768*s* (C=O's); 1640*s*, 1605*m*). – MS. (70 eV): 246 (78, *M*), 215 (13, *M* – CH_3O), 203 (19, *M* + H – CO_2), 187 (42, *M* + H – CH_3O – CO), 173 (20, *M* + H – CO_2 – CO), 159 (100, *M* – H – CO_2 – CH_2CO), 115 (20, C_9H_7).

Stereoisomer **B** was an impure oil. Neglecting peaks at 4.63/br. *s*, and 2.67/*s*, 2.30/*s* and 1.30/*s*, the ^{1}H-NMR. spectrum (60 MHz, $CDCl_3$) could be interpreted as follows: 7.1–6.7/*m*, 3H (3 H–Ar); 3.87/*s*, 3H (CH_3O–C(2')); 3.33/*q*, (*J* = ~2), 2H (2 H–C(2)); 2.60/*t* (*J* = ~2), 3H (H_3C–C(4)); 2.41/*s*, 3H (H_3C–C(4')). – IR. (Film): 1838*s* and 1770*s* (C=O's).

Step (9). Attempts to decarboxylate 3-carboxy-4-(2'-methoxy-4'-methyl-phenyl)-pent-3-enoic acid (**8**). The action of dilute aqueous acetic acid, glacial acetic acid, 10% aqueous hydrochloric and hydrobromic acids on the mixture of stereoisomers **8** at RT. or at reflux for less than 10 h failed to cause the appearance of new spots on the TLC. of the crude reaction mixture.

Heating of the mixture **8** with concentrated hydrochloric or hydrobromic acid in acetic acid for 5 to 10 h resulted in the cleavage of the side chain from the aromatic ring: 1.0 g of **8** was heated for 5 h in a boiling mixture of 5 ml of acetic acid and 10 ml of 48% aqueous hydrobromic acid under nitrogen. The reaction was followed by TLC.: a major spot (Rf 0.8 with ether/hexane 6:1) appeared along with several minor spots. Evaporation under reduced pressure yielded a liquid residue with a phenolic odour which was chromatographed (1 × 10 cm silica gel, ether/hexane 1:1) to give 0.037 g (10%) of **10**, identified by comparison of the ^{1}H-NMR. and IR. spectra. The low yield of **10** may be due to loss during evaporation of solvents.

3. *Scheme 2.* – *Step (1). 4-t-Butoxycarbonyl-3-methyl-5-oxo-hexanenitrile* (**13**). To a solution of 47.4 g (0.3 mol) of *t*-butyl acetoacetate in 150 ml of ethanol, warmed to 40°, were added dropwise over $^1/_2$ h 40.2 g (0.6 mol) of a mixture of crotononitrile and isocrotononitrile. Simultaneously 1.0 ml portions of a 30% solution of potassium hydroxide in methanol were added every 5 min and the temperature was maintained at 45°. Having added a last portion of 4 ml (total 10 ml) of the base solution the mixture was stirred at 50° for 18 h, cooled, poured into 500 ml of water and extracted with 2 × 200 ml of ether. The extracts were washed thoroughly (8 × 100 ml) with water, dried and evaporated under reduced pressure to give 59.2 g of a yellow liquid. Distillation removed 5.1 g of unreacted *t*-butyl acetoacetate, b.p. 70–75°/8 Torr, 2.1 g of a liquid, b.p. 98–99°/0.2 Torr, and gave 40.5 g (60%) of **13** as a colourless oil, b.p. 103°/0.2 Torr. – ^{1}H-NMR. (60 MHz, CCl_4): 3.33/*d* (*J* = 8), 1H (H–C(4)); 2.6–2.3/*m*, 3H (H–C(3) and 2H–C(2)); 2.20/*s*, 3H (H_3C–C=O); 1.46/*s*, 9H ($COOC(CH_3)_3$); 1.08/*d* (*J* = 7), 3H (H_3C–C(3)). – IR. (Film): 2250*w* (C≡N), 1740*s* (COOR), 1715*s* (C=O), 1371*m*, 1282*m*, 1260*m*, 1150*s* br., 850*m*.

Steps (2+3). 3-(4'-Methyl-2'-oxo-cyclohex-3'-en-1'-yl)-butanenitrile (**16**). To a solution of 0.04 g (1.7 mmol) of sodium in 20 ml of abs. ethanol were added 22.5 g (100 mmol) of 4-*t*-butoxycarbonyl-3-methyl-5-oxo-hexanenitrile (**13**). The solution was cooled to 0° before adding 7.0 g (100 mmol) of methyl vinyl ketone over $^3/_4$ h. When the temperature was constant the ice bath was removed and the solution stirred at RT. for 18 h. The mixture was poured into 100 ml of water and extracted with 3 × 100 ml of ether. The extracts were washed with 5 × 100 ml of water, dried and evaporated under reduced pressure to give 27.27 g (92%) of crude *3-(1'-t-butoxycarbonyl-4'-hydroxy-4'-methyl-2'-oxo-cyclohex-1'-yl)-butanenitrile* (**15**) as a yellow viscous oil. – IR. (Film): 3500*s* br. (OH), 2250*w* (C≡N), 1712*s* (COOR and C=O), 1371*s*, 1250*s*, 1150*s*, 840*m*, 700*m*.

The crude ester **15** was heated for 2 h at 170° under reduced pressure with 0.05 g of *p*-toluenesulfonic acid. Distillation of the mixture gave 1.71 g of a forerun, b.p. 80–138°/2 × 10^{-4} Torr, and 10.28 g of a colourless oil, b.p. 140–145°/2 × 10^{-4} Torr, which was purified by column chromatography over 300 g of silica gel using ethyl acetate/pentane 1:9. The less polar fraction (0.8 g) is described below. The major fraction, 9.03 g of an oil, was distilled to give 8.82 g (50%) of an about 1:1 mixture of the two diastereoisomers **A** and **B** of *3-(4'-methyl-2'-oxo-cyclohex-3'-en-1'-yl)-butanenitrile* (**16**) as a colourless oil, b.p. 123–125°/8 × 10^{-5} Torr. – ^{1}H-NMR. (100 MHz, CCl_4):

5.76/*s* (with fine splitting), 1H (H–C(3')); 2.8–1.5/*m*, 8H (H–C(1'), H–C(3), 2 H–C(2), 2 H–C(5') and 2 H–C(6')); 1.96/*s* (with fine splitting), 3H (H_3C–C(4')); 1.15 and 1.04/2*d*, (each with $J = 6$) ~1.5H and 1.5H (H_3C–C(3) of **A** and **B**). – IR. (Film): 2245*w* (C≡N), 1665*s* (C=O), 1635*m* (C=C), 1430*m*, 1382*m*, 1210*s*, 1020*w*, 870*w*. – UV. (C_2H_5OH): 247. – MS. (70 eV): 177 (4, *M*), 137 (6), 110 (48), 95 (8), 82 (100).

$C_{11}H_{15}NO$ (177,23) Calc. C 74.54 H 8.53 N 7.90% Found C 74.26 H 8.42 N 7.76%

The above mentioned less polar fraction is considered to consist mainly of *3-(4'-methyl-2'-oxo-cyclohex-4'-en-1'-yl)-butanenitrile* (**17**). The following spectral aspects of the sample are attributed to **17**. – ^{1}H-NMR. ($CDCl_3$, 60 MHz): 5.7–5.4/br. *s*, assumed 1H (H–C(5')); 2.9–2.6/br. *s*, assumed 2H (2 H–C(3')); 1.70/br. *s*, 3H (H_3C–C(4')). – IR. (Film): 2248*w* (C≡N), 1715*s* (C=O); the carbonyl absorption at 1665 due to **16** in the sample is less than one fifth the intensity of the absorption at 1715.

Step (4). 3-Ethylenedioxy-4'-methyl-cyclohex-3'-(2'(possibly-4'-)-en-1'-yl)-butanenitrile (**18**). 4.60 g (26 mmol) of 3-(4'-methyl-2'-oxo-cyclohex-3'-en-1'-yl)-butanenitrile (**16**), 3.10 g (50 mmol) of ethylene glycol and 0.1 g of *p*-toluenesulfonic acid in 100 ml of anhydrous benzene were heated under reflux for 48 h with removal of water. The mixture was cooled, poured into 200 ml of saturated sodium hydrogen carbonate solution and extracted with 3 × 200 ml of ether. The extracts were washed with 100 ml of saturated sodium hydrogen carbonate solution and 3 × 100 ml of water, dried and evaporated under reduced pressure to give 5.20 g of a colourless oil which was purified by column chromatography over 150 g of basic alumina using ethyl acetate/pentane 1:9. After discarding 0.2 g of a less polar impurity, 2.87 g of an oil were collected and distilled to give 2.80 g (49%) of an about 1:1 mixture of the two diastereoisomers **A** and **B** of **18**, b.p. 110°/3 × 10^{-4} Torr, as a colourless oil. – ^{1}H-NMR. (60 MHz, CCl_4): 5.5–5.1/br. *s*, 1H (H–C(3')); 3.93/*s*, 4H (O–CH_2–CH_2–O); 2.8–1.4/*m*, 8H (H–C(1'), H–C(3), 2 H–C(2), 2 H–C(5'), 2 H–C(6')); 1.60/br. *s*, 3H (H_3C–C(4')); 1.13 and 1.03/2*d* (each with $J = 6$), ~1.5H and 1.5H (H_3C–C(3) of **A** and **B**). – IR. (Film): 2248*m* (C≡N), 1178*m*, 1085*s*, 950*m*, 870*m*, 700*m*. – MS. (70 eV): 221 (2, *M*), 181 (2), 153 (5), 139 (12), 126 (14), 113 (75), 91 (25), 77 (30), 69 (35), 41 (100).

The next fraction from the chromatography consisted of 1.8 g (39%) of recovered starting material **16**.

Step (5). Ethyl 3-(4'-methyl-2'-oxo-cyclohex-3'-en-1'-yl)-butanoate (**19**). A mixture of 5.0 g (28 mmol) of 3-(4'-methyl-2'-oxo-cyclohex-3'-en-1'-yl)butanenitrile (**16**), 0.50 g (28 mmol) of water and 50 ml of abs. ethanol was saturated with hydrogen chloride and refluxed under nitrogen for 42 h. The mixture was cooled, ammonium chloride was removed by filtration and reflux was continued for 24 h. After cooling, the ethanol was removed under reduced pressure and the residue (5.3 g) was distilled to give 4.8 g (77%) of a clear liquid, b.p. 81–90°/5 × 10^{-5} Torr. Filtration through a 2 × 10 cm column of silica gel with ethyl acetate/hexane 3:10 gave 4.7 g (75%) of an about 1:1 mixture of the two diastereoisomers **A** and **B** of **19**. – ^{1}H-NMR. (60 MHz, $CDCl_3$): 5,85/br. *s* with fine splitting ($J = 1.5$), 1H (H–C(3')); 4.10/*q* ($J = 7$), 2H (COOC$H_2$$CH_3$); 3.0–1.8/*m*, 8H (2 H–C(5'), 2 H–C(6'), 2 H–C(2), H–C(1'), H–C(3)); 1.95/br. *s*, 3H (H_3C–C(4')); 1.22/*t* ($J = 7$), 3H (COOCH_2CH_3); 0.98 and 0.89/2*d* (each with $J = 6$), ~1.5H and 1.5H (H_3C–C(3) of **A** and **B**). – IR. (Film): 2975*s*, 2935*s*, 2878*s*, 1731*s* (COOR), 1668*s* (C=O), 1640*m* (C=C), 1380*m* (CH_3), 1189*m*. – UV. (CH_3OH): 234 (14800).

$C_{13}H_{20}O_3$ (224.29) Calc. C 69.61 H 8.99% Found C 69.91 H 9.00%

Step (6). 3-(2'-Hydroxy-4'-methyl-cyclohex-3'-en-1'-yl)-butan-1-ol (**20**). A solution of 0.6 g (2.7 mmol) of ethyl 3-(4'-methyl-2'-oxo-cyclohex-3'-en-1'-yl)-butanoate (**19**) was added dropwise to a stirred solution of 0.204 g (5.7 mmol) of lithium aluminium hydride in 50 ml of ether at RT. and after 10 min the reaction was quenched with 2 ml of ethyl acetate. After stirring with 10 ml of a saturated aqueous solution of sodium sulfate the ether was decanted and dried. Removal of the solvent gave 0.50 g (100%) of a mixture of stereoisomers of **20** as a viscous oil, single spot on TLC. (silica gel, ethyl acetate/hexane 1:4, Rf 0.2). – ^{1}H-NMR. (60 MHz, $CDCl_3$): 5.75–5.45/*m* and 5.36/br. *s*, 1H (H–C(3')); 4.3–3.9/*m*, 1H (H–C(2')); 3.66/*t* with fine splitting ($J = 7$), 2H (2 H–C(1)); 2.8–2.3/*m*, 2H (2 H–C(5')); 1.8–1.1/*m*, 6H (H–C(3), 2 H–C(2), 2 H–C(6'), H–C(1')); 1.70/br. *s*, 3H (H_3C–C(4')); ~1.0/several *d* (each with $J = 6$), 3H (H_3C–C(3)). The signals of H–C(3') and H_3C–C(3) indicate the product to be a mixture of at least 3 diastereoisomers. – IR. (Film); 3310*s* br. (OH), 1050*s* (C–O).

Step (**7**). *5,9-Dimethyl-2-oxa-bicyclo[4.4.0]dec-9-ene* (**21**). A solution of 0.35 g (1.9 mmol) of 3-(2'-hydroxy-4'-methyl-cyclohex-3'-en-1'-yl)-butan-1-ol (**20**), 0.37 g (1.9 mmol) of *p*-toluenesulfonyl chloride and 25 ml anhydrous pyridine was stirred for 1 h below −10°, stored at 6° for 14 h and at RT. for 1 h. Sodium acetate (5.0 g) was added and the solution was stirred for 2 h. After the addition of 25 ml of methanol the solution was refluxed for 3 h, cooled and poured into 200 ml of 10% hydrochloric acid. Extraction with 3 × 100 ml of ether, drying and removal of solvent under reduced pressure gave 0.30 g of an oil. Chromatography (1 × 10 cm silica gel, ether/hexane 1:3) gave 0.23 g of an impure mixture of two (**A** and **B**) of the four possible diastereoisomers of **21** as a colourless liquid with a menthol-like odour, single spot on TLC. (silica gel, ethyl acetate/hexane 1:3, Rf 0.7). – ^{1}H-NMR. (60 MHz, $CDCl_3$): 5.7–5.3/*m*, 1H (H–C(10)); 4.3–3.2 and 3.62/*m* and *t*, the latter with (J = 5), 3H (H–C(1) and 2H–C(3)); 2.2–1.1/*m*, ~8H (2H–C(4), H–C(5), H–C(6), 2H–C(7), 2H–C(8)); 1.73/br. *s*, 3H (H_3C–C(9)); 1.05 and 0.95/2*d* (each with J = 5.6), ~1.5H and 1.5H (H_3C–C(5) of **A** and **B**). – IR. (Film): 1678*w* (C=C), 1087*s* (C–O). – MS.: 166 (17, *M*), 151 (100, *M* – CH_3), 123 (12).

4. *Scheme 3.* – *Steps* (*1+2*). *Methyl 3-(4'-methyl-2'-oxo-cyclohex-1'-yl)-butanoate* (**24**). 112.2 g (1 mol) of 3-methyl-cyclohexanone (**22**), 108.4 g (1,52 mol) of pyrrolidine and 0.22 g of *p*-toluenesulfonic acid were refluxed in 300 ml of toluene under nitrogen with removal of water (20 ml in all). After 4 h no more water was collected, the solvent and excess pyrrolidine were distilled off under reduced pressure leaving 155.3 g (94%) of a yellow liquid. A solution of this unpurified pyrrolidine enamine of 3-methyl-cyclohexanone (**23**) and 150 g (1.5 mol) of methyl crotonate in 1 l of N,N-dimethylformamide was refluxed for 36 h under nitrogen. The cooled mixture was treated with 100 ml of water and refluxed for 1 h, cooled, poured into 2 l of ice/water and extracted with 5 × 500 ml of ether. The organic phase was washed with 3 × 500 ml of 2% hydrochloric acid, 2 × 500 ml of saturated sodium hydrogen carbonate and 2 × 500 ml of water, dried and evaporated to give 163.8 g of an oil, which was fractionally distilled. After a forerun of 9.85 g, b.p. 27–43°/12 Torr, the crude keto-ester **24** was collected at 99–118°/0.04 Torr as a colourless liquid (137.6 g). TLC. on silica gel with ethyl acetate/pentane 1:19 showed the presence of less-polar material. The distillate was chromatographed over 1 kg of silica gel using ethyl acetate/pentane 1:19. After discarding 12.39 g of the less-polar fraction, 95.93 g of a main fraction was eluted which according to capillary GC. consisted predominantly of two very similar compounds in the ratio 1:1. A later fraction of 8.00 g which was shown by capillary GC. to contain three similar compounds in approximately equal amounts was discarded. The main chromatography fraction was again fractionally distilled. After discarding 4.91 g of a forerun, b.p. 80–87°/0.04 Torr, 78.64 g (37%) of product were collected at b.p. 87–90°/0.04 Torr as a colourless liquid. According to capillary GC. this product consisted of 12% of two impurities and 88% of two (**A** and **B**) of the possible four diastereoisomers of methyl *3-(4'-methyl-2'-oxo-cyclohex-1'-yl)-butanoate* (**24**) in about equal amounts. – ^{1}H-NMR. (60 MHz, CCl_4): 3.63/*s*, 3H (OCH_3); 2.7–1.2/*m*, 11H (H–C(1'), H–C(4'), H–C(3), 2H–C(3'), 2H–C(5'), 2H–C(6') and 2H–C(2)); 1.2–0.7/*m*, 6H (H_3C–C(4') and H_3C–C(3)). – IR. (Film): 1740*s* (COOR), 1712*s* (C=O), 1205*m*, 1175*m*, 1014*m*.

$C_{12}H_{20}O_3$ (212.32) Calc. C 67.92 H 9.43% Found C 67.92 H 9.45%

Step (*3*). *Methyl 3-(2'-ethylenedioxy-4'-methyl-cyclohex-1'-yl)-butanoate* (**25**). A solution of 42.4 g (200 mmol) of methyl 3-(4'-methyl-2'-oxo-cyclohex-1'-yl)-butanoate (**24**), 18.0 g (290 mmol) of ethylene glycol and 0.30 g of *p*-toluenesulfonic acid in 260 ml of benzene was refluxed under nitrogen with removal of water. After 6 h no more water was collected (total 3.6 ml), and the solvent was distilled off under reduced pressure leaving an oil which was taken up in 500 ml of ether. This solution was washed with 4 × 200 ml of saturated sodium hydrogen carbonate solution, dried and evaporated to give 50.53 g of a yellow oil. Fractional distillation, after a forerun of 1.69 g, b.p. 78–88°/0.08 Torr, yielded 42.63 g which according to capillary GC. consisted of 20% of two impurities and ~80% of two (**A** and **B**, 66%) of the possible four diastereoisomers of **25** in about equal amounts, b.p. 89–94°/0.08 Torr, as a colourless oil. – ^{1}H-NMR. (60 MHz, CCl_4): 3.91 br. *s* with fine splitting, 4H (OCH_2CH_2O); 3.60/*s*, 3H (OCH_3); 2.9–1.0/*m*, 11H (2H–C(2), 2H–C(3'), 2H–C(5'), 2H–C(6'), H–C(3), H–C(1') and H–C(4')); 1.0–0.7/*m*, 6H (H_3C–C(3), H_3C–C(4')). – IR. (Film): 1740*s* (COOR), 1640*w*, 1170*m*, 850*w*.

$C_{14}H_{24}O_4$ (256.35) Calc. C 65.62 H 9.37% Found C 65.63 H 9.59%

Steps (4+5). 3-(2'-Ethylenedioxy-4'-methyl-cyclohex-1'-yl)-butan-1-ol (**26**) *and its acetate* **27**. A suspension of 0.72 g (19 mmol) of lithium aluminium hydride in 70 ml of anhydrous ether was heated under reflux. After cooling a solution of 8.50 g (33 mmol) of methyl 3-(2'-ethylenedioxy-4'-methyl-cyclohex-1'-yl)-butanoate (**25**) in 10 ml of anhydrous ether was added dropwise at such a rate as to maintain refluxing. After refluxing for 1/2 h 2 ml of ethyl acetate followed by 10 ml of water were added slowly. The mixture was diluted with 50 ml of ether, the ether fraction washed with 3 × 100 ml of saturated sodium hydrogen carbonate solution, dried and evaporated to give 7.02 (92%) of crude *3-(2'-ethylenedioxy-4'-methyl-cyclohex-1'-yl)-butan-1-ol* (**26**) as a yellow oil. – ^{1}H-NMR. (60 MHz, CCl_4): 3.91/*s*, 4H (OCH_2CH_2O); 3.7–3.3/*m*, 2H (2 H–C(1)); 2.97/*s*, 1H (OH); 2.2–1.0/*m*, 11H (2 H–C(2), 2 H–C(3'), 2 H–C(5'), 2 H–C(6'), H–C(3), H–C(4'), H–C(1')); 1.0–0.7/*m*, 6H (H_3C–C(3), H_3C–C(4')).

A solution of this unpurified acetal-alcohol **26** in 30 ml of pyridine and 30 ml of acetic anhydride was heated under nitrogen at 50° for 2 h and then allowed to stand at RT. for 20 h. The mixture was poured into 2 l of an ice/saturated sodium hydrogen carbonate mixture and extracted with 3 × 500 ml of ether. The extract was washed with 3 × 500 ml of saturated sodium hydrogen carbonate solution and 2 × 200 ml of water, dried and evaporated under reduced pressure to give 7.92 g of crude acetal-ester **27** as an oil which was chromatographed over 600 g of silica gel using ethyl acetate/pentane 1:9. After discarding 0.42 g of a less-polar impurity 7.10 g of a major fraction were collected and distilled under vacuum. After a forerun of 0.22 g, b.p. 85–90°/0.06 Torr, 6.71 g (74%) of *1-acetoxy-3-(2'-ethylenedioxy-4'-methyl-cyclohex-1'-yl)-butane* (**27**) distilled at 92°/0.06 Torr as a colourless oil. Capillary GC. showed about 10% of impurity and an about 4:5 mixture (90%) of presumably two diastereoisomers **A** and **B** of **27**. – ^{1}H-NMR. (100 MHz, CCl_4): 4.2–3.8/*m*, 6H (OCH_2CH_2O and 2 H–C(1)); 1.96/*s*, 3H ($COCH_3$); 2.3–1.0/*m*, 11H (2 H–C(2), 2 H–C(3'), 2 H–C(5'), 2 H–C(6'), H–C(3), H–C(1'), H–C(4')); 1.0–0.8/2*d* (each with $J = \sim 6$), 6H (H_3C–C(3), H_3C–C(4')). – IR. (Film): 1745*s* (OAc), 1250*s*, 1045*m*, 850*w*. – MS. (70 eV): 270 (12, *M*), 255 (2, *M* – CH_3), 227 (2, *M* – CH_3CO), 213 (3), 183 (16), 113 (100), 99 (20).

$C_{15}H_{26}O_4$ (270.38) Calc. C 66.67 H 9.63% Found C 66.20 H 9.90%

Step (6). 1-Acetoxy-3-(2'-ethylenedioxy-4'-methyl-cyclohex-3'-en-1'-yl)-butane (**29**) and *1-acetoxy-3-(2'-ethylenedioxy-4'-methyl-cyclohex-6'-en-1'-yl)-butane* (**28**). A solution of 4.0 g (15 mmol) of 1-acetoxy-3-(2'-ethylenedioxy-4'-methyl-cyclohex-1'-yl)-butane (**27**) in 130 ml of tetrahydrofuran at – 5° to 0° under nitrogen was treated with 6.15 g (17 mmol) of phenyl-trimethyl-ammonium tribromide. After 3 h a colourless solid had deposited and the solution became colourless. The suspension was poured into a mixture of 50 ml of 5% sodium thiosulfate and 100 ml of saturated sodium hydrogen carbonate and extracted with 2 × 200 ml of ether. The extracts were washed with 8 × 200 ml of saturated sodium hydrogen carbonate, dried and evaporated under reduced pressure to give 4.67 g (90%) of a mixture consisting presumably of *1-acetoxy-3-(3'-bromo-2'-ethylenedioxy-4'-methyl-cyclohex-1'-yl)-butane* and *1-acetoxy-3-(1'-bromo-2'-ethylenedioxy-4'-methyl-cyclohex-1'-yl)-butane*. A solution of this mixture and 30 ml of 1,5-diaza-bicyclo[4.3.0]non-5-ene in 20 ml of benzene was stirred and heated at 90° under nitrogen for 24 h. The cooled mixture was poured into 200 ml of saturated sodium hydrogen carbonate and extracted with 3 × 200 ml of ether. The extracts were washed with 4 × 100 ml of saturated sodium hydrogen carbonate, dried, and evaporated under reduced pressure to give 3.20 g of an oil which was chromatographed over 400 g of basic alumina using ethyl acetate/pentane 1:19. After discarding a first fraction (0.22 g) of a less polar impurity a second fraction was collected which contained 1.14 g (32%) of **28** as a yellow oil. – ^{1}H-NMR. (100 MHz, CCl_4): 5.68/*d* × *d* ($J = 2$ and 5), (H–C(6')); 4.2–3.7/*m*, 6H (OCH_2CH_2O, 2 H–C(1)); 1.92/*s*, 3H ($COCH_3$); 2.5–1.15/*m*, 8H (2 H–C(2), 2 H–C(3'), 2 H–C(5'), H–C(3), H–C(4')); 1.02 and 0.96/2*d*, ($J = 7$ and 6), 6H (H_3C–C(3), H_3C–C(4')). – IR. (Film): 1740*s* (OAc), 1245*s*, 1035*s*, 970*m*, 850*m*.

The third chromatography fraction contained 0.9 g (25%) of an about 1:1 mixture of the two diastereomers **A** and **B** of **29**. – ^{1}H-NMR. (100 MHz, CCl_4): 5.24/br. *s*, 1H (H–C(3')); 4.1–3.6/*m*, 6H (OCH_2CH_2O, 2 H–C(1)); 1.94/*s*, 3H ($COCH_3$); 1.66/br. *s*, 3H (H_3C–C(4')); 2.4–1.4/*m*, 8H (2 H–C(2), 2 H–C(5'), 2 H–C(6'), H–C(3), H–C(1')); 0.96 and 0.92/2*d*, (each with $J = 7$), ~1.5H and 1.5H (H_3C–C(3) of **A** and **B**). – IR. (Film) 1740*s* (OAc), 1680*w* (C=C), 1250*s*, 1100*m*, 1050*m*, 1030*m*, 950*m*, 930*m*.

Step (7). 1-Acetoxy-3-(4'-methyl-2'-oxo-cyclohex-3'-en-1'-yl)-butane (**30**). A mixture of 0.25 g (0.93 mmol) of 1-acetoxy-3-(2'-ethylenedioxy-4'-methyl-cyclohex-3'-en-1'-yl)-butane (**29**) and

0.03 g of *p*-toluenesulfonic acid in 5 ml of acetone and 1 ml of water was allowed to stand at RT. for 2 h. Most of the acetone was removed under reduced pressure before the residue was poured into 50 ml of water and extracted with 2 × 50 ml of ether. The ether fraction was washed with 20 ml of water, dried and evaporated to give 0.20 g of an oil which was purified by preparative TLC. on silica gel using ethyl acetate/pentane 1:3, followed by distillation, to yield 0.11 g (53%) of an about 1:1 mixture of the two diastereoisomers **A** and **B** (as suggested by capillary GC.) of **30** as a yellow oil, b.p. 88–90°/0.02 Torr. – ^{1}H-NMR. (100 MHz, CCl_4): 5.73/br. *s*, 1H (H–C(3')); 4.02/*t* (*J* = 7), 2H (2 H–C(1)); 1.94/*s*, 3H (–$COCH_3$); 1.90/br. *s*, 3H (H_3C–C(4')); 2.6–1.2/*m*, 8H (2 H–C(2), 2 H–C(5'), 2 H–C(6'), H–C(3), H–C(1')); 0.96 and 0.81/2*d* (each with *J* = 7), ~1.5H and 1.5H, H_3C–C(3) of **A** and **B**). – IR. (Film): 1740*s* (OAc), 1670*s* (C=O), 1640*m* (C=C), 1245*s*, 1050*m*, 1030*m*, 875*m*. – UV. (EtOH): 233 (9000). – MS. (70 eV): 224 (1, *M*), 164 (100, *M* – CH_3COOH), 149 (45), 122 (20), 107 (12), 94 (16), 78 (20), 67 (12), 55 (16), 43 (70).

$C_{13}H_{20}O_3$ (224.30) Calc. C 69.61 H 8.99% Found C 69.57 H 8.81%

Steps (*8*+*9*). *5,9-Dimethyl-2-oxa-bicyclo[4.4.0]dec-1(6)-en-3-one* (**32**). 10.0 g (47 mmol) of methyl 3-(4'-methyl-2'-oxo-cyclohex-1'-yl)-butanoate (**24**) were refluxed with 60 ml of 10% (81 mmol) sodium hydroxide for $^3/_4$ h. The cooled mixture was extracted with 100 ml of ether and the alkaline fraction was acidified with 5% hydrochloric acid and extracted with 2 × 100 ml of ether. The extracts were washed with 100 ml of water, dried and concentrated under reduced pressure to give 9.26 g of a residue which was fractionally distilled. After a forerun of 1.7 g, b.p. 100–130°/0.06 Torr, *3-(4'-methyl-2'-oxo-cyclohex-1'-yl)-butanoic acid* (**31**) was collected at 132–135°/0.08 Torr as a colourless liquid, yield 5.77 g (62%). – IR. (CCl_4): 3500–2300*s* br. (OH); 1715*s* br. (C=O), 1290*m*, 945*m*.

A solution of 5.70 g (21 mmol) of the keto-acid **31** and 0.2 g of *p*-toluenesulfonic acid in 200 ml of toluene was refluxed with removal of water. After 24 h no more water was collected and the solvent was removed under reduced pressure leaving an oil which was taken up in 200 ml of ether. This solution was washed with 2 × 100 ml of water, dried and evaporated under reduced pressure to give 4.56 g of an oil which was chromatographed over 200 g of silica gel using ethyl acetate/pentane. The solvent mixture 1:19 eluted 0.31 g of a less-polar fraction (discarded), and 1:9 eluted 3.49 g of a yellow oil which was distilled to give 3.26 g (63%) of an about 1:1 mixture of the two diastereoisomers **A** and **B** of **32**, b.p. 75°/0.06 Torr, as a colourless oil. – ^{1}H-NMR. (100 MHz, CCl_4): 2.8–1.0/*m* with fine structure, 10H (H–C(5), H–C(9), 2 H–C(4), 2 H–C(7), 2 H–C(8), 2H–C(10)); 1.1–1.0/2*d* (each with *J* = ~6), 6H (H_3C–C(5) and H_3C–C(9)). – ^{1}H-NMR. (100 MHz, CCl_4 + Eu(fod)$_3$): 8.1–7.3/*m*, 2H (2 H–C(4)); 4.5–4.0/*m*, 1H (H–C(5)); 3.82/*d* × *d* (*J* = 14 and 5), 1H (H–C(10)); 3.44/br. *d*, (*J* = 14), 1H (H–C(10)); 3.4–3.0/*m*, 2H (2 H–C(7)); 2.7–2.4/*m*, 1H (H–C(9)); 2.71 and 2.60/2*d*, (each with *J* = 7), 1.5H and 1.5H (H_3C–C(5)), 2.55–1.9/*m*, 2H (2 H–C(8)); 1.52 and 1.47/2*d* (each with *J* = 7), 1.5H and 1.5H (H_3C–C(9)). Decoupling experiments using Eu(fod)$_3$ shifted spectrum: Irradiation at 4.12: part of 8.1–7.3/*m* simplifies, and 2.71/*d* becomes *s*; irradiation at 4.41: other part of 8.1–7.3/*m* simplifies, and 2.60/*d* becomes *s*; irradiation at 2.66: 1.52/*d* and 1.47/*d* become *s*, and the further coupled *AB* system between 4.0 and 3.3 becomes a clean *AB*. – IR. (Film): 1765*s* (C=O), 1710*m* (C=C–O), 1238*m*, 1155*s*, 1126*s*, 988*m*, 906*m*, 840*m*. – MS. (70 eV): 180 (100, *M*), 165 (68, *M* – CH_3), 152 (7, *M* – CO), 137 (42, *M* – CH_3 – CO), 123 (49), 110 (28), 109 (28), 95 (42), 81 (56), 67 (18), 41 (70).

$C_{11}H_{16}O_2$ (180.25) Calc. C 73.30 H 8.95% Found C 73.56 H 8.90%

Step (*10*). *1-Acetoxy-3-(4'-methyl-2'-oxo-cyclohex-1'-yl)-butane* (**33**). A solution of 4.12 g (15 mmol) of 1-acetoxy-3-(2'-ethylenedioxy-4'-methyl-cyclohex-1'-yl)-butane (**27**) and 0.3 g of *p*-toluenesulfonic acid in 60 ml of acetone and 20 ml of water was warmed to 40° for 2 h and then allowed to stand at RT. for 18 h. After most of the acetone had been removed under reduced pressure the mixture was poured into 100 ml of water and extracted with 2 × 100 ml of ether. The extracts were washed with 2 × 50 ml of water, dried and evaporated under reduced pressure to give 3.24 g of an oil which was chromatographed over 150 g of silica gel using ethyl acetate/pentane 1:9. After discarding a forerun of 0.05 g of a less-polar impurity, 2.92 g of a colourless oil was collected and distilled under vacuum. An about 3:2:1 diastereoisomer mixture of **33** distilled at 90°/0.04 Torr as colourless oil, yield 2.81 g (82%). – ^{1}H-NMR. (100 MHz, CCl_4): 4.2–3.8/*m*, 2H (2 H–C(1)); 2.4–1.2/*m*, 11H (2 H–C(2), 2 H–C(3'), 2 H–C(5'), 2 H–C(6'), H–C(3), H–C(1'), H–C(4')); 1.93/*s*, 3H ($COCH_3$); 1.0, 0.94 and 0.83/3*d*, (each with *J* = ~6), 3H, 2H and 1H

(H_3C–C(3) and H_3C–C(4')). – IR. (Film): 1740*s* (OAc), 1712*s* (C=O), 1245*s*, 1050*s*. – MS. (70 eV): 266 (3, *M*), 166 (40), 151 (80), 137 (45), 123 (70), 112 (100), 69 (47), 55 (67), 43 (100).

$C_{13}H_{22}O_3$ (226.32) Calc. C 68.99 H 9.80% Found C 68.70 H 9.74%

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