172. β-Cleavage of Bis(homoallylic) Potassium Alkoxides. Synthesis of γ-Damascone

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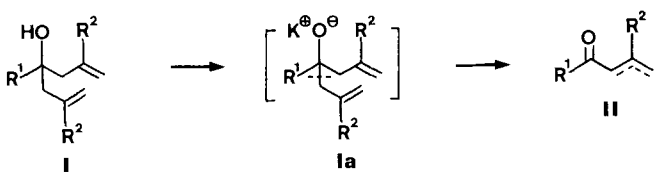
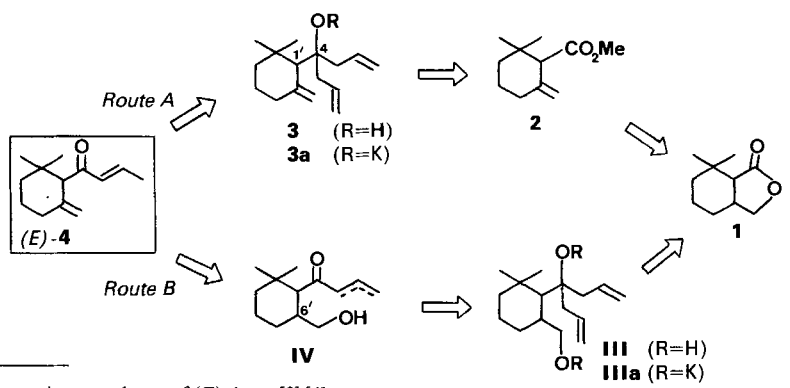
Starting from the γ-lactone *cis*-**1**, two new syntheses of γ-damascone ((*E*)-**4**) are described. In both syntheses, the key step involves the β-cleavage of a bis(homoallylic) potassium alkoxide, *viz.* the transformation of **3a** to **20** and (*E*/*Z*)-**4**, and the conversion of **21a** to **23** and (*E*/*Z*)-**24**.

Introduction. – Because of their extensive application in perfumery [1], the rose ketones have attracted widespread synthetic interest during the past twenty years [2]. We now report two novel syntheses of racemic γ-damascone ((*E*)-**4**)[1]), an important member of this family of odorants. Both syntheses apply a recently developed methodology which involves the transformation of bis(homoallylic) alcohols **I**, *via* β-cleavage of their potassium alkoxides **Ia** in dipolar aprotic solvents, to alkenones **II** *(cf. Scheme 1)* [5].

Scheme 1



Scheme 2 (retrosynthetic)

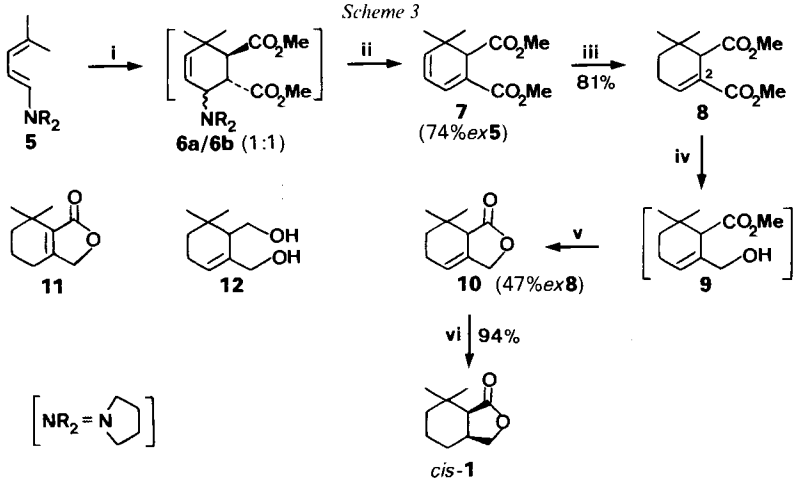


[1]) For previous syntheses of (*E*)-**4**, see [3] [4].

Synthetic Strategy *(cf. Scheme 2).* – Starting from the γ-lactone **1**[2]), retrosynthetic analysis envisaged two routes to (*E*)-**4**. *Route A* planned transformation of **1** to methyl γ-cyclogeranate (**2**) [6] and subsequently to the tris(homoallylic) alcohol **3**. From model studies [5], it was anticipated that the potassium alkoxide **3a** would undergo β-cleavage of one of the three allylic C–C bonds adjacent to the alkoxy group, β-cleavage of either one of the two allyl groups allowing access to (*E*)-**4**[3])[4]). In contrast, and in analogy to previous work [7], *Route B* envisaged conversion of **1** to the diol **III** followed by β-cleavage of the bis(homoallylic) potassium alkoxide moiety of its dipotassium dialkoxide **IIIa** to afford hydroxy ketone **IV**. Conversion of the C(6′)-hydroxymethyl group to a methylidene group would then complete the synthesis of (*E*)-**4**.

Results and Discussion. – *Synthesis of* **1**. A stereoselective synthesis of *cis*-**1** is described in *Scheme 3*. *Diels-Alder* reaction between (*E*)-4-methyl-1-pyrrolidino-1,3-pentadiene (**5**) [8] and dimethyl maleate (3 mol-equiv.)[5]) in refluxing toluene afforded a 1:1 mixture of two diastereoisomeric cycloadducts, **6a** and **6b**[5]), which, without purification[6]), was treated with Ac_2O at reflux to afford the cyclohexadiene dicarboxylate **7**[7]) in

Scheme 3



i) (*Z*)-$MeO_2C \cdot CH{=}CH \cdot CO_2Me$, toluene, reflux 72 h; *ii*) Ac_2O, reflux; *iii*) H_2, Pd/C, MeOH, r.t.; *iv*) DIBAH (2.5 mol-equiv.), toluene, −60° then aq. HCl; *v*) TsOH (cat.), toluene, 50°; *vi*) H_2, $(Ph_3P)_3RhCl$(cat.)/toluene, r.t.

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[2]) At this planning stage, the ring-junction configuration of **1** was left undefined.

[3]) For an analogous approach to α-damascone from methyl α-cyclogeranate, see [5].

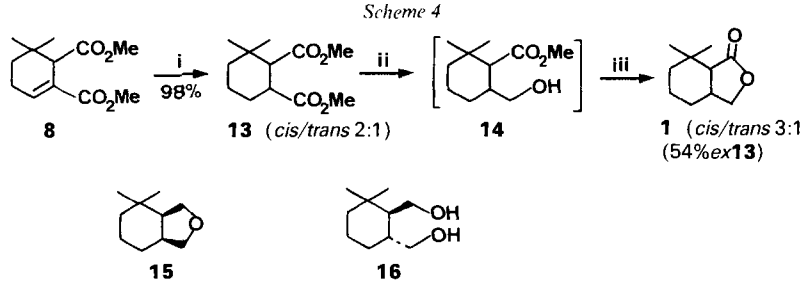
[4]) A direct access to (*E*)-**4** from **2** *via* mono-addition of an allylic organometallic reagent such as allyllithium or allylmagnesium chloride is inefficient because of competing di-addition to give **3**; for an elegant synthesis of (*E*)-**4** involving mono-addition of a *Grignard* reagent to an ester dienolate derived from methyl β-cyclogeranate, see [4].

[5]) The *Diels-Alder* reaction between **5** and diethyl maleate at 150° has been reported to afford a mixture of cycloadducts, of unspecified configuration, in 58% yield [8].

[6]) For characterisation purposes, pure samples of **6a** and **6b** were obtained by column chromatography *(cf. Exper. Part)*; in both these cycloadducts the C(1)- and C(2)-methoxycarbonyl groups are *trans*-diequatorial (J(H–C(1),H–C(2)) = 12 Hz), a result which is explained by a rapid, *in situ* isomerisation of dimethyl maleate to dimethyl fumarate, the more reactive dienophile.

[7]) Elimination of pyrrolidine from **6a** and **6b** to give **7** was partially effected (*ca.* 20% conversion) during the cycloaddition-reaction conditions *(cf. Exper. Part)*.

Scheme 4



i) H_2, Pd/C, MeOH, r.t., 60 h; *ii*) DIBAH (2.5 mol-equiv.), toluene, −60°, then aq. HCl; *iii*) TsOH (cat.), toluene, 50°.

74% overall yield from **5**. Catalytic mono-hydrogenation of **7** (10% Pd/C in MeOH) then regioselectively furnished the cyclohexene dicarboxylate **8** in 81% yield. Employing reaction conditions similar to those already reported for an analogous substrate [9], **8** was treated with diisobutylaluminium hydride (DIBAH) (2.5 mol-equiv.) in toluene at −60° in order to effect a site-selective reduction of the C(2)-methoxycarbonyl group[8]).

After an aqueous workup, the crude unsaturated hydroxy ester **9** was then treated with a catalytic amount of TsOH in toluene at 50° to afford the β,γ-unsaturated γ-lactone **10** in 47% overall yield from **8**. This only moderate yield is the consequence of two major factors. Firstly, the hydride reduction is not completely selective, and the excess of DIBAH employed results in over-reduction of **10** to the unsaturated diol **12** (10% yield from **8**). Secondly, **10** undergoes ready acid-catalysed isomerisation to its α,β-unsaturated isomer **11**[9]) (14% yield from **8**) which was resistant to catalytic hydrogenation under pressure (75 bars) using either 10% Pd/C in MeOH or PtO_2 in AcOH/AcOEt 3:1. In contrast, homogeneous catalytic hydrogenation of **10**, using *Wilkinson*'s catalyst ($(Ph_3P)_3RhCl$) in toluene, smoothly afforded *cis*-**1** in 94% yield[10]).

Scheme 4 describes a synthesis of **1** (*cis*/*trans* 3:1). Catalytic hydrogenation of **8** (10% Pd/C in MeOH) afforded the cyclohexane dicarboxylate **13** (*cis*/*trans* 2:1)[11]) which was then treated with DIBAH (2.5 mol-equiv.) in toluene at −60° to afford, after aqueous workup, the crude hydroxy ester **14**, which was subsequently cyclised (TsOH/toluene, reflux) to furnish **1** (*cis*/*trans* 3:1)[12]) in 54% overall yield. As was the case for the preparation of **10** from **8** *(vide supra)*, side-products resulting from the over-reduction of *cis*- and *trans*-**13** were isolated. Thus, the bicyclic ether **15**, presumably derived from the non-isolated *cis*-isomer of **16** or its dialkoxide, and **16** were isolated in 20% and 8% yields, respectively.

Synthesis of γ-Damascone ((*E*)-**4**). *Route A* (*cf. Scheme 5*). Treatment of *cis*-**1** with NaSePh in THF/HMPA 20:1 at reflux [12] resulted in alkyl–O cleavage of the γ-lactone

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[8]) The use of less DIBAH (*i.e.* 2 mol-equiv.) resulted in incomplete conversion of **8** (*ca.* 80%) and, although the formation of **12** was suppressed, the chromatographic separation of **10** from unreacted **8** was troublesome.

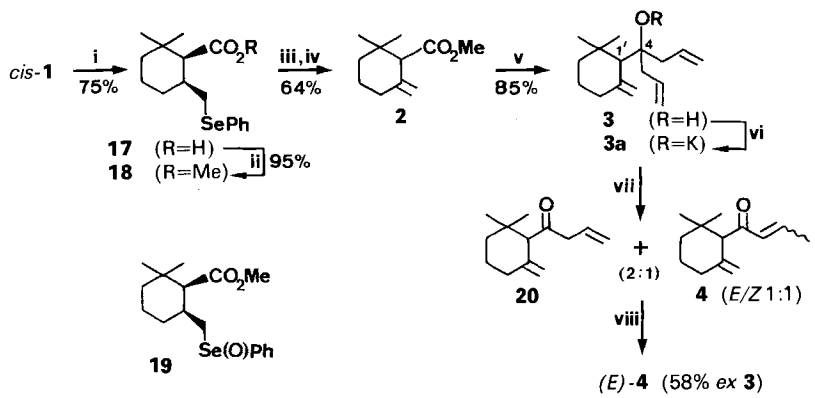
[9]) Butenolide **11** had previously been isolated as a minor side-product (*ca.* 10% yield) resulting from the oxidation (SeO_2, dioxan) of methyl β-cyclogeranate [10], for a recent synthesis, see [11].

[10]) Catalytic hydrogenation of **10** using Pd/C in MeOH resulted in extensive isomerisation of **10** to afford a 1:1 mixture (92% yield) *cis*-**1**/**11**.

[11]) Equilibration of **13** (*cis*/*trans* 2:1) under basic conditions (NaOMe/MeOH, r.t.) afforded **13** (*cis*/*trans* 1.5:1).

[12]) Equilibration of either **1** (*cis*/*trans* 3:1) or *cis*-**1** under basic conditions (NaOMe/MeOH, r.t.) afforded **1** (*cis*/*trans* 1.6:1).

Scheme 5



i) PhSeSePh, NaH, THF/HMPA, reflux; *ii*) CH_2N_2, Et_2O; *iii*) AcO_2H, $CHCl_3$; *iv*) CH_2Cl_2, reflux; *v*) ^{Cl}, Mg, THF, reflux; *vi*) KH (1.1 mol-equiv.), HMPA, r.t.; *vii*) HMPA, r.t. then aq. NH_4Cl soln.; *viii*) TsOH (cat.), THF, reflux.

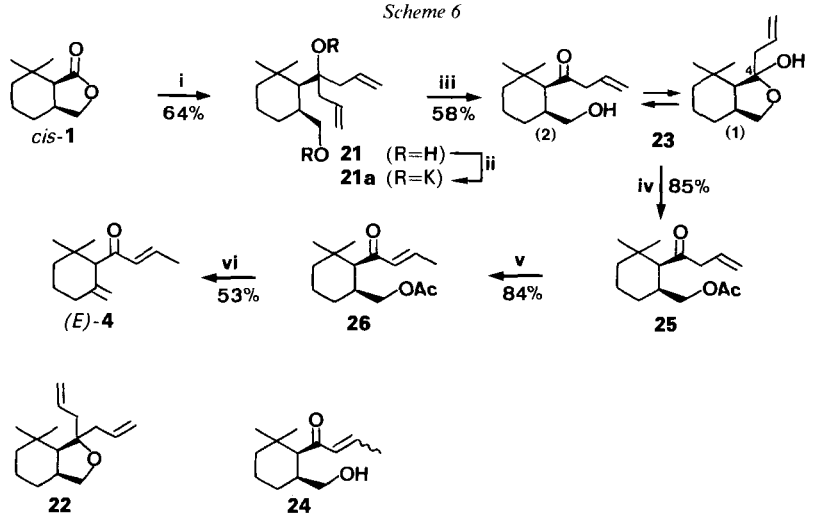
to afford the [(phenylselenenyl)methyl]cyclohexane carboxylic acid **17** (m.p. 115–116°) in 75% yield. Subjection of **1** (*cis*/*trans* 3:1) to identical conditions also furnished **17**, but in only 54% yield, with no trace of its putative *trans*-isomer. This result implies that, in contrast to *cis*-**1**, *trans*-**1** does not undergo alkyl–O bond cleavage[13]). Esterification of **17** with CH_2N_2 in Et_2O afforded the methyl carboxylate **18** (95% yield) which was then oxidised with peracetic acid in $CHCl_3$ at r.t. [13] to give the non-isolated intermediate selenoxide **19**. Thermal elimination of PhSeOH from **19** in refluxing CH_2Cl_2 [13] furnished **2** (64% yield from **18**) which was subsequently treated with an excess of allylmagnesium chloride, formed *in situ* using *Barbier* conditions, in refluxing THF, to afford the tertiary alcohol **3** in 85% yield. Reaction of **3** with KH (1.1 mol-equiv.) in HMPA at 25° gave, after aqueous workup and distillation *i.v.*, a crude 2:1 mixture of ketones **20** and **4** (*E*/*Z* 1:1) which was readily equilibrated (TsOH/THF, reflux) to afford (*E*)-**4** in 58% yield from **3**.

Analysis of the crude reaction mixture revealed the absence of products resulting from the putative β-cleavage of the C(4)–C(1′) bond, thus showing that the intermediate potassium alkoxide **3a** exclusively favours β-cleavage of either one of the two diastereotopic allyl groups. This result was gratifying but nevertheless unexpected as previous studies concerning the β-cleavage of tris(homoallylic) potassium alkoxides [5] had indicated that substitution of the C-atom next to the alkoxy group generally tends to favour β-cleavage of the allylic C–C bond. A possible explanation, involving a combination of steric and electronic factors, may be that the chair conformation of the cyclohexane ring in **3a** stabilises the C(4)–C(1′) bond by twisting it out of the plane of the adjacent C(6′)=CH_2 group.

Route B (*cf. Scheme 6*). Employing the reaction conditions used for the transformation of **2** to **3** (*vide supra*), *cis*-**1** was treated with allylmagnesium chloride in refluxing THF to afford the diol **21** in 64% yield. Other side-products isolated from this reaction

[13]) Careful analysis of this reaction indicates that *trans*-**1** undergoes acyl–O bond cleavage to afford an intermediate hydroxy-carboxylic acid which then lactonises back to *trans*-**1** during the isolation procedure.

Scheme 6



i) ⌒Cl, Mg, THF, reflux; *ii*) KH (2.2 mol-equiv.), HMPA, r.t.; *iii*) HMPA, 65° then aq. NH_4Cl soln., *iv*) Ac_2O, pyridine, r.t.; *v*) TsOH (cat.), toluene, r.t.; *vi*) pyrolysis, 450°.

included the products of mono-*Grignard* addition[14]), *i.e.* the hydroxy ketones **23** and **24** (*E*/*Z* 1:1), in 18% and 1% yields, respectively, together with the bicyclic ether **22** (14% yield) which is presumably formed from a facile acid-catalysed cyclisation of **21**. Reaction of **21** with KH (2.2 mol-equiv.) in HMPA at r.t. followed by heating the thus-formed dipotassium dialkoxide **21a** at 65° resulted in β-cleavage of the bis(homoallylic)-potassium-alkoxide moiety to afford **23** (58% yield), shown by ^{1}H-NMR analysis ($CDCl_3$, r.t.) to consist of a 2:1 mixture of hydroxy ketone and lactol tautomers. Also isolated from this reaction were **22** (3% yield) and **24** (*E*/*Z* 1:1) (2% yield): the former product probably results from the cyclisation of small amounts of unreacted **21**, whilst the latter product is either the consequence of γ-protonation of the intermediate potassium dienolate formed after the β-cleavage of **21a** or due to partial isomerisation of **23** during the isolation procedure. Subsequent treatment of **23** with Ac_2O in pyridine smoothly gave the acetoxy ketone **25** (85% yield) which was then isomerised to its (*E*)-α,β-unsaturated isomer **26** (84% yield) prior to thermal elimination of AcOH *via* pyrolysis at 450° to finally afford (*E*)-**4** in 53% yield[15])[16]).

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[14]) The formation of **23** and **24** from this *Grignard* reaction is doubtless due to the low solubility of the intermediate halomagnesium alkoxide of **23** in THF which effectively protects it from a second attack by allylmagnesium chloride.

[15]) This yield was calculated taking into account recovered **26** (31% yield); side-products included **20** (6% yield) and (*Z*)-**4** (11% yield).

[16]) It should be noted that pyrolysis of **25** (450°→500°) did not afford **20** but gave rise to the formation of a mixture of unidentified products.

Experimental Part

(with the valuable collaboration of *M. Wüst*)

General. See [5].

Dimethyl 6,6-Dimethyl-2,4-cyclohexadiene-1,2-dicarboxylate (**7**). A soln. of *(E)-4-methyl-1-pyrrolidino-1,3-pentadiene* (**5**)[17]) (90 g, 0.6 mol) and dimethyl maleate (247 g, 1.7 mol) in toluene (1.5 l) containing hydroquinone (1.5 g) was refluxed under N_2 for 68 h. The mixture was then cooled to 50° and AcOEt (1 l) added before further cooling to r.t. The mixture was then poured into cold 10% aq. HCl soln. (1 l). The phases were separated and the org. phase washed with 10% aq. HCl soln. (2 × 200 ml) and H_2O. The aq. phase was extracted with AcOEt and the org. phase washed with sat. aq. $NaHCO_3$ and sat. aq. NaCl soln., dried (Na_2SO_4), and concentrated *i.v.* (15 Torr) until turbidity was observed. This soln. was then cooled to −60° and the precipitate (dimethyl fumarate, *ca.* 110 g) isolated by filtration; the filtrate was concentrated *i.v.* to afford crude **7** (28 g). The aq. phase was basified with 20% aq. NaOH soln. and extracted with AcOEt. The org. phase was washed with sat. aq. NaCl soln., dried (Na_2SO_4), and concentrated *i.v.* to afford a brown oil (152 g), which contained **7** (7%) and the *Diels-Alder* cycloadducts **6a** and **6b** (*ca.* 1:1 mixture) (59%)[18]). To this oil was added Ac_2O (40 g, 0.4 mol), and the mixture was refluxed for 3 h (oil bath temp.: 170°). The cooled mixture was then diluted with Et_2O (500 ml) and poured into cold 10% aq. HCl soln. The org. phase was then washed with 10% aq. HCl soln., H_2O, sat. aq. $NaHCO_3$, and sat. aq. NaCl soln. prior to drying (Na_2SO_4). Concentration of the filtered org. soln. afforded crude **7** (112 g) which was combined with the previously isolated crude **7** *(vide supra)*; fractional distillation *i.v.* furnished pure **7** as a pale-yellow oil (99 g, 74%). B.p. 88–91°/0.1 Torr. R_f (cyclohexane/AcOEt 1:1) 0.55. IR: 1740, 1720, 1650, 1584, 1440, 1270, 1200, 1090, 790, 750, 736, 660. ^{1}H-NMR: 1.11 (*s*, 3 H); 1.14 (*s*, 3 H); 3.45 (*s*, 1 H); 3.66 (*s*, 3 H); 3.75 (*s*, 3 H); 5.82 (*d*, J = 9, 1 H); 6.01 (*dd*, J = 9, 5.5, 1 H); 7.14 (*d*, J = 5.5, 1 H). MS: 224 (5, $M^{+\cdot}$), 209 (23), 169 (84), 165 (60), 121 (55), 105 (60), 91 (81), 86 (100), 77 (57), 59 (81).

Dimethyl 6,6-Dimethyl-2-cyclohexene-1,2-dicarboxylate (**8**). A soln. of **7** (47 g, 0.21 mol) in MeOH (500 ml) containing 10% Pd/C (0.7 g) was hydrogenated at r.t. under atmospheric pressure. After 25 min (absorption of H_2: 5 l), the mixture was filtered through *Hyflo* and the filtrate concentrated *i.v.* The residual oil was distilled *i.v.* to afford **8** as a colourless oil (38.4 g, 81%). B.p. 71–78°/0.05 Torr. R_f (cyclohexane/AcOEt 1:1) 0.56. IR: 1740, 1660, 1440, 1260, 1200, 1160, 1092, 1062, 990, 780, 720. ^{1}H-NMR: 0.97 (*s*, 6 H); 1.27 (*m*, 1 H); 1.72 (*m*, 1 H); 2.22 (*m*, 1 H); 2.36 (*m*, 1 H); 3.16 (*s*, 1 H); 3.68 (*s*, 3 H); 3.72 (*s*, 3 H); 7.18 (br. *t*, J = 3.5, 1 H). MS: 226 (0, $M^{+\cdot}$), 194 (21), 166 (85), 151 (30), 135 (19), 107 (100), 91 (40), 79 (20), 59 (29), 41 (22).

7,7-Dimethyl-5,6,7,7a-tetrahydro-1(3H)-isobenzofuranone (**10**). A soln. of diisobutylaluminium hydride (DIBAH) in toluene (167 ml of a 1.2M soln.: 0.2 mol) was added dropwise within 4 h to a mechanically stirred soln. of **8** (17.5 g, 0.08 mol) in toluene (350 ml) at −65° under N_2, and the mixture was allowed to attain −45° during a further 16 h. The mixture was then re-cooled to −65°, and conc. aq. HCl soln. (75 ml) was added dropwise within 15 min. After dilution with Et_2O, the phases were separated and the org. phase washed with H_2O, sat. aq. $NaHCO_3$, and sat. aq. NaCl soln. The org. soln. was then dried (Na_2SO_4), filtered, and concentrated *i.v.* to afford crude *methyl 6,6-dimethyl-2-(hydroxymethyl)-2-cyclohexene-1-carboxylate* (**9**) as a pale-yellow oil (19 g)[19]) which was

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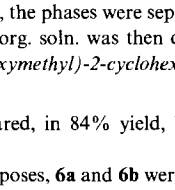
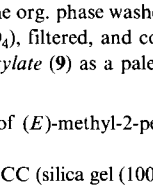
[17]) Compound **1** was prepared, in 84% yield, by reaction of (*E*)-methyl-2-pentenal with pyrrolidine in the presence of K_2CO_3 [8].

[18]) For characterisation purposes, **6a** and **6b** were purified by CC (silica gel (100 g), cyclohexane/AcOEt 3:2) of an aliquot (2 g).



6a



6b [NR$_2$=N⟨ ⟩]

Data of **6a**: R_f (cyclohexane/AcOEt 7:3) 0.26. ^{1}H-NMR: 0.86 (*s*, 3 H); 1.20 (*s*, 3 H); 1.64 (4 H); 2.65 (4 H); 2.93 (br. *d*, J = 12, 1 H); 3.15 (*dd*, J = 12, 7, 1 H); 3.65 (*s*, 3 H); 3.68 (*s*, 3 H); 3.76 (*m*, 1 H); 5.58 (*dd*, J = 11, 5, 1 H); 5.65 (*d*, J = 11, 1 H).

Data of **6b**: R_f (cyclohexane/AcOEt 7:3) 0.11. ^{1}H-NMR: 0.95 (*s*, 3 H); 1.19 (*s*, 3 H); 1.71 (4 H); 2.57 (2 H); 2.77 (2 H); 2.83 (*d*, J = 12, 1 H); 2.95 (*dd*, J = 12, 11, 1 H); 3.67 (*m*, 1 H); 3.68 (2*s*, 6 H); 5.51 (*dd*, J = 10, 2, 1 H); 5.59 (*dd*, J = 10, 2, 1 H).

[19]) For characterisation purposes, a 0.5-g aliquot of **9** was purified by CC (silica gel (20 g), cyclohexane/AcOEt 3:2). R_f (cyclohexane/AcOEt 3:2) 0.26. IR: 3450 (br.), 1730, 1440, 1394, 1370, 1030, 772. ^{1}H-NMR (+D_2O): 0.95 (*s*, 6 H); 1.22 (*m*, 1 H); 1.84 (*m*, 1 H); 2.13 (*m*, 2 H); 2.83 (*s*, 1 H); 3.68 (*s*, 3 H); 3.99 (*AB*, J = 14, 2 H); 5.88 (*m*, 1 H).

dissolved in toluene (200 ml), and TsOH·H_2O (100 mg) was added. The mixture was then heated at 50° during 18 h, cooled to r.t., and diluted with Et_2O (150 ml). The org. soln. was washed with sat. aq. $NaHCO_3$ and sat. aq. NaCl soln., dried (Na_2SO_4), and concentrated *i.v.* to afford a yellow oil (17.5 g). CC (silica gel (370 g), cyclohexane/AcOEt 4:1) afforded **10** as a colourless oil (6.2 g, 47%). B.p. 71–72°/0.1 Torr. R_f (cyclohexane/AcOEt 1:1) 0.58. R_f (CH_2Cl_2) 0.32. IR: 1765, 1370, 1300, 1220, 1158, 1040, 938, 850, 830, 718. ^{1}H-NMR: 0.87 (*s*, 3 H); 1.32 (*s*, 3 H); 1.48 (*t*, *J* = 6, 2 H); 2.15 (2 H); 2.81 (br. *s*, 1 H); 4.60–4.75 (*m*, 2 H); 5.72 (br. *s*, 1 H). ^{13}C-NMR: 175.3 (*s*); 130.5 (*s*); 120.6 (*d*); 70.1 (*t*); 48.2 (*d*); 36.8 (*t*); 30.3 (*s*); 28.6 (*q*); 22.5 (*t*); 18.8 (*q*). MS: 166 (10, $M^{+\cdot}$), 122 (41), 111 (77), 107 (94), 93 (52), 79 (49), 67 (27), 56 (100), 53 (26), 41 (65).

Also isolated were *7,7-dimethyl-4,5,6,7-tetrahydro-1(3*H*)-isobenzofuranone* (**11**) [11] (colourless oil, 1.9 g, 14%) and *[5,5-dimethyl-6-(hydroxymethyl)-1-cyclohexenyl]methanol* (**12**) (colourless oil, 1.4 g, 10%).

Data of **11**: B.p. 81–82°/0.1 Torr. R_f (cyclohexane/AcOEt 1:1) 0.49. R_f (CH_2Cl_2) 0.26. IR: 1755, 1670, 1430, 1342, 1320, 1215, 1140, 788, 740. ^{1}H-NMR: 1.23 (*s*, 6 H); 1.55 (*m*, 2 H); 1.78 (*m*, 2 H); 2.27 (*t*, *J* = 6, 2 H); 4.61 (*s*, 2 H). ^{13}C-NMR: 172.9 (*s*); 160.0 (*s*); 132.6 (*s*); 71.0 (*t*); 38.9 (*t*); 30.4 (*s*); 26.4 (2 *q*); 24.2 (*t*); 19.0 (*t*). MS: 166 (80, $M^{+\cdot}$), 151 (82), 138 (24), 123 (99), 95 (100), 77 (48), 67 (52), 39 (61).

Data of **12**: B.p. (bulb-to-bulb distillation) 180–200°/0.05 Torr. R_f (cyclohexane/AcOEt 1:1) 0.15. IR: 3350 (br.), 1390, 1370, 1139, 940, 838. ^{1}H-NMR (+D_2O): 0.94 (2 *s*, 6 H); 1.27 (*ddd*, *J* = 14, 5.5, 5.5, 1 H); 1.47 (*ddd*, *J* = 14, 7, 7, 1 H); 1.96 (br. *s*, 1 H); 2.07 (br. *s*, 2 H); 3.57 (*dd*, *J* = 11, 7, 1 H); 3.88 (*dd*, *J* = 11, 3.5, 1 H); 3.97 (*d*, *J* = 11, 1 H); 4.17 (*d*, *J* = 11, 1 H); 5.76 (br. *s*, 1 H). MS: 170 (0.5, $M^{+\cdot}$), 152 (18), 122 (29), 107 (100), 91 (70), 83 (53), 79 (45), 67 (42).

*(3a*RS*,7a*SR*)-7,7-Dimethyl-3a,4,5,6,7,7a-hexahydro-1(3*H*)-isobenzofuranone* (*cis*-**1**). A soln. of **10** (3.6 g, 0.022 mol) in toluene (40 ml) containing tris(triphenylphosphine)rhodium (I) chloride (0.5 g, 0.54 mmol) was hydrogenated at r.t. under atmospheric pressure. After 9 h (absorption of H_2: 500 ml), concentration and distillation *i.v.* afforded *cis*-**1** (3.5 g, 94%). B.p. 69–71°/0.1 Torr. R_f (cyclohexane/AcOEt 1:1) 0.54. IR: 2910, 1760, 1360, 1180, 1134, 1030, 982, 972, 958, 922. ^{1}H-NMR: 1.04 (*s*, 3 H); 1.30 (*s*, 3 H); 1.18–1.43 (3 H); 1.43–1.62 (2 H); 1.77 (*m*, 1 H); 2.25 (*d*, *J* = 6, 1 H); 2.57 (*m*, 1 H); 3.87 (*dd*, *J* = 9, 1.5, 1 H); 4.12 (*dd*, *J* = 9, 5, 1 H). ^{13}C-NMR: 175.9 (*s*); 70.8 (*t*); 49.2 (*d*); 35.6 (*t*); 34.7 (*d*); 31.0 (*q*); 28.9 (*q*); 27.0 (*q*); 26.2 (*t*); 19.6 (*t*). MS: 168 (2, $M^{+\cdot}$), 125 (6), 108 (100), 93 (20), 85 (42), 67 (32), 55 (18).

Catalytic Hydrogenation of **10** *using 10% Pd/C*. A soln. of **10** (5.3 g, 0.032 mol) in MeOH (100 ml) containing 10% Pd/C (150 mg) was hydrogenated at r.t. under atmospheric pressure. After 1.5 h (absorption of H_2: 400 ml), the mixture was filtered through *Hyflo* and concentrated *i.v.* to afford a pale-yellow oil (5.6 g). CC (silica gel (350 g), cyclohexane/AcOEt 4:1) gave two major fractions: *cis*-**1** (2.1 g, 39%) and **11** (2.1 g, 40%), identical in all respects with authentic samples *(vide supra)*.

Attempted Catalytic Hydrogenation of **11**. A soln. of **11** (0.6 g, 3.6 mmol) in MeOH (15 ml) containing 10% Pd/C (40 mg) was submitted to hydrogenation conditions (r.t., 75 bars, 2 h) without any observed reaction (GC).

A similar experiment using PtO_2 (30 mg) with AcOH/AcOEt 3:1 as solvent (r.t., 75 bars, 2 h) also gave no detectable hydrogenation.

Dimethyl 3,3-Dimethylcyclohexane-1,2-dicarboxylate (**13**; *cis*/*trans* 2:1). A soln. of **8** (18 g, 0.08 mol) in MeOH (300 ml) containing 10% Pd/C (3 g) was hydrogenated at r.t. under atmospheric pressure. After 60 h (absorption of H_2: 1.9 l), the mixture was filtered through *Hyflo* and the filtrate concentrated and distilled *i.v.* to afford **13** (*cis*/*trans* 2:1) as a colourless oil (17.9 g, 98%). B.p. 63–65°/0.06 Torr. R_f (cyclohexane/AcOEt 1:1) 0.58.

Data of cis-**13**: ^{1}H-NMR: 0.93 (*s*, 3 H); 1.03 (*s*, 3 H); 0.90–1.90 (5 H); 2.09 (*ddd*, *J* = 12.5, 12.5, 4.5, 1 H); 2.63 (*d*, *J* = 4.5, 1 H); 2.76 (*ddd*, *J* = 12.5, 4.5, 4.5, 1 H); 3.65 (*s*, 6 H). MS: 228 (2, $M^{+\cdot}$), 196 (44), 168 (56), 136 (30), 114 (32), 109 (100), 93 (35), 82 (54).

Data of trans-**13**: ^{1}H-NMR: 0.89 (*s*, 3 H); 1.05 (*s*, 3 H); 0.90–1.90 (5 H); 2.13 (*ddd*, *J* = 12.5, 12.5, 4.5, 1 H); 2.46 (*d*, *J* = 12.5, 1 H); 2.84 (*ddd*, *J* = 12.5, 12.5, 4.5, 1 H); 3.65 (*s*, 3 H); 3.67 (*s*, 3 H). MS: 228 (1, $M^{+\cdot}$), 196 (60), 168 (34), 146 (43), 114 (48), 109 (100), 93 (42), 82 (58).

*3a,4,5,6,7,7a-Hexahydro-1(3*H*)-isobenzofuranone* (**1**; *cis*/*trans* 3:1). A soln. of DIBAH in toluene (183 ml of a 1.2M soln.: 0.22 mol) was added dropwise within 4 h to a mechanically stirred soln. of **13** (*cis*/*trans* 2:1) *(vide supra)* (19.5 g, 0.086 mol) in toluene (300 ml) at −65° under N_2, and the mixture was allowed to attain 0° during a further 16 h. The mixture was then re-cooled to −30° and conc. aq. HCl soln. (70 ml) added dropwise within 5 min. The phases were separated and the aq. phase extracted with Et_2O (2 × 250 ml). The org. phase was washed with H_2O, sat. aq. $NaHCO_3$, and sat. aq. NaCl soln., dried (Na_2SO_4), filtered, and concentrated *i.v.* to afford crude *methyl 6,6-dimethyl-2-(hydroxymethyl)cyclohexane-1-carboxylate* (**14**; *cis*/*trans* mixture) as a pale-yellow oil (15 g) which, without purification, was dissolved in toluene (180 ml), and TsOH·H_2O (200 mg) was added. The mixture was then refluxed for 1.5 h, cooled to r.t. and diluted with Et_2O (100 ml). The org. soln. was washed with sat. aq. $NaHCO_3$ and sat. aq. NaCl soln., dried (Na_2SO_4), and concentrated *i.v.* to afford a yellow oil which was purified by CC (silica

gel (360 g), cyclohexane/AcOEt 4:1) to afford **1** (*cis/trans* 3:1) as a colourless oil (7.7 g, 53% yield from **13** (*cis/trans* 2:1)). B.p. (bulb-to-bulb distillation) 120–140°/0.1 Torr.

Data of trans-**1**: R_f (cyclohexane/AcOEt 1:1) 0.53. ^{1}H-NMR: 0.98 (*s*, 3 H); 1.26 (*s*, 3 H); 1.08–1.74 (5 H); 1.74 (*d*, *J* = 14, 1 H); 1.91 (*m*, 1 H); 2.24 (*m*, 1 H); 3.72 (*dd*, *J* = 11, 8, 1 H); 4.30 (*dd*, *J* = 8, 7, 1 H). ^{13}C-NMR: 176.3 (*s*); 71.2 (*t*); 53.1 (*d*); 41.0 (*t*); 38.4 (*d*); 31.5 (*q*); 28.9 (*q*); 28.3 (*t*); 21.8 (*t*); 19.3 (*q*). MS: 168 (11, M^+), 125 (42), 108 (100), 95 (31), 81 (76), 67 (67), 55 (32).

Also isolated were *(3a*RS*,7a*RS*)-7,7-dimethyl-1,3,3a,4,5,6,7,7a-octahydroisobenzofuran* (**15**; colourless oil, 2.6 g, 20%) and *(1*RS*,2*RS*)-[3,3-dimethyl-2-(hydroxymethyl)-1-cyclohexyl]methanol* (**16**; colourless oil, 1.2 g, 8%).

Data of **15**: B.p. (bulb-to-bulb distillation) 40–60°/0.04 Torr. R_f (cyclohexane/AcOEt 1:1) 0.56. IR: 2860, 1450, 1360, 1196, 1060, 972, 896, 718. ^{1}H-NMR: 0.84 (*s*, 3 H); 1.03 (*s*, 3 H); 1.19 (*m*, 1 H); 1.26 (*m*, 1 H); 1.35 (*m*, 1 H); 1.44 (*m*, 1 H); 1.51 (*m*, 1 H); 1.55 (*m*, 1 H); 2.01 (*m*, 1 H); 2.13 (*m*, 1 H); 3.60 (*d*, *J* = 7, 1 H); 3.68 (*dd*, *J* = 11, 7, 1 H); 3.78 (*d*, *J* = 7, 1 H); 3.79 (*dd*, *J* = 11, 7, 1 H). ^{13}C-NMR: 75.0 (*t*); 67.8 (*t*); 49.3 (*d*); 36.9 (*d*); 34.1 (*t*); 30.7 (*s*); 29.8 (*q*); 28.8 (*q*); 26.6 (*t*); 21.1 (*t*). MS: 154 (18, M^+), 139 (12), 126 (39), 109 (80), 95 (50), 81 (78), 69 (82), 67 (100), 55 (56).

Data of **16**: B.p. (bulb-to-bulb distillation) 160–180°/0.01 Torr. R_f (cyclohexane/AcOEt 1:1) 0.16. IR: 3300 (br.), 2860, 1440, 1030, 940. ^{1}H-NMR (+D_2O): 0.80 (*s*, 3 H); 1.02 (*s*, 3 H); 1.05–1.65 (8 H); 3.50 (*dd*, *J* = 11, 6, 1 H); 3.54 (*dd*, *J* = 11, 7, 1 H); 3.73 (*dd*, *J* = 11, 3.5, 1 H); 3.90 (br. *d*, *J* = 11, 1 H). MS: 172 (0, M^+), 124 (43), 109 (36), 95 (33), 82 (100), 67 (57), 55 (54), 41 (50).

*(1*RS*,2*SR*)-2,2-Dimethyl-6-(phenylselenenyl)methylcyclohexane-1-carboxylic Acid* (**17**). A stirred mixture of NaH (0.4 g of a 55% oil dispersion, 9.2 mmol) and PhSeSePh (1.4 g, 4.5 mmol) in THF (20 ml) was refluxed under N_2 for 50 min (formation of a fine-yellow precipitate). The mixture was cooled to r.t. and HMPA (1 g) added to afford a clear orange soln. *cis*-**1** (1 g, 6 mmol) was then added and the mixture stirred under reflux for 45 h. The dark-red mixture was cooled to r.t. and, after the dropwise addition of MeOH (4 ml), concentrated *i.v.* To the residue was added H_2O (15 ml), and the mixture was then extracted with Et_2O (3 × 40 ml). The aq. phase was acidified with 10% aq. HCl soln. and then extracted with Et_2O (2 × 50 ml). The org. phase was washed with sat. aq. NaCl soln., dried (Na_2SO_4), filtered and concentrated *i.v.* to afford a reddish-brown oil (1.7 g). CC (silica gel (45 g), cyclohexane/AcOEt 7:3) separated PhSeSePh (0.4 g) from the mixture, and subsequent elution with cyclohexane/AcOEt 2:3 and recrystallisation from petroleum ether at −50°, afforded **17** (1.45 g, 75%). M.p. 115–116°. R_f (CH_2Cl_2) 0.16. IR (KBr): 3020 (br.), 1700, 1470, 1430, 1240, 1212, 1184, 1169, 730, 685. ^{1}H-NMR (+ D_2O): 0.96 (*s*, 3 H); 1.00 (*s*, 3 H); 1.14 (br. *d*, *J* = 12.5, 1 H); 1.44 (*m*, 1 H); 1.55–1.70 (3 H); 1.77 (*ddd*, *J* = 12.5, 12.5, 4, 1 H); 2.00 (*m*, 1 H); 2.56 (*d*, *J* = 4, 1 H); 2.83 (*m*, 2 H); 7.25 (3 H); 7.49 (2 H). MS: 325 (0, M^+), 169 (95), 123 (100), 109 (33), 91 (36), 81 (51), 69 (63).

Treatment of **1** (*cis/trans* 3:1; 1 g, 6 mmol) using the same experimental procedure afforded **17** (1.05 g, 54%).

*(1*RS*,2*SR*)-Methyl 2,2-Dimethyl-6-[(phenylselenenyl)methyl]cyclohexane-1-carboxylate* (**18**). A freshly-prepared soln. of CH_2N_2 (*ca.* 10 mmol)[20]) in Et_2O (20 ml) was added dropwise to a stirred soln. of **17** (2 g, 6.2 mmol) in MeOH/H_2O (10:1; 40 ml) at r.t. Concentration *i.v.* afforded an oily residue which was dissolved in Et_2O (20 ml) and washed with 10% aq. NaOH and sat. aq. NaCl soln. The org. phase was dried (Na_2SO_4), filtered, concentrated, and distilled *i.v.* to afford **18** as a pale-yellow oil (2 g, 95%). B.p. (bulb-to-bulb distillation) 180–220°/0.05 Torr. R_f (CH_2Cl_2) 0.53. IR ($CDCl_3$): 2990, 1718, 1574, 1472, 1430, 1370, 1145, 1018, 992, 683. ^{1}H-NMR: 0.90 (*s*, 3 H); 0.95 (*s*, 3 H); 1.12 (br. *d*, *J* = 12.5, 1 H); 1.43 (*m*, 1 H); 1.55–1.70 (3 H); 1.78 (*ddd*, *J* = 12.5, 12.5, 4, 1 H); 1.98 (*m*, 1 H); 2.56 (*d*, *J* = 4, 1 H); 2.74 (*m*, 2 H); 3.61 (*s*, 3 H); 7.24 (3 H); 7.48 (2 H). MS: 339 (0, M^+), 183 (85), 123 (100), 109 (23), 81 (40), 69 (33).

Methyl 2,2-Dimethyl-6-methylidenecyclohexane-1-carboxylate (= *Methyl γ-Cyclogeranate*; **2**). Peracetic acid (48% soln. in AcOH, 0.8 g, 6 mmol) was added dropwise to a stirred soln. of **18** (1.9 g, 5.6 mmol) in $CHCl_3$ (20 ml) at r.t. After 10 min, the mixture was poured into sat. aq. $NaHCO_3$ soln. and extracted with CH_2Cl_2 (2 × 20 ml). The org. phase was washed with sat. aq. NaCl soln. and concentrated *i.v.* to give the crude selenoxide **19** as a pale-yellow residue which was dissolved in CH_2Cl_2 (25 ml) and refluxed for 3 h. The mixture was then cooled, concentrated *i.v.* and the residue purified by CC (silica gel (45 g), cyclohexane/AcOEt 25:1) to furnish **2** as a colourless oil (0.65 g, 64%). B.p. (bulb-to-bulb distillation) 40–50°/0.05 Torr ([6]: 95°/12 Torr). R_f (CH_2Cl_2) 0.53. IR: 1730, 1640, 1430, 1360, 1330, 1242, 1140, 1052, 1020, 892. ^{1}H-NMR: 0.93 (*s*, 3 H); 0.97 (*s*, 3 H); 1.24 (*ddd*, *J* = 12.5, 5, 5, 1 H); 1.59 (*m*, 2 H); 1.84 (*m*, 1 H); 2.11 (*ddd*, *J* = 12.5, 5, 5, 1 H); 2.47 (*m*, 1 H); 2.88 (*s*, 1 H); 3.65 (*s*, 3 H); 4.73 (*s*, 1 H); 4.85 (*s*, 1 H). ^{13}C-NMR: 173.0 (*s*); 144.6 (*s*); 111.5 (*t*); 59.9 (*d*); 51.1 (*q*); 35.8 (*t*); 34.6 (*s*); 32.1 (*t*); 27.5 (*q*); 26.5 (*q*); 22.8 (*t*). MS: 182 (13, M^+), 167 (20), 122 (83), 114 (37), 107 (56), 91 (24), 81 (41), 69 (100).

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[20]) Prepared from *N*-nitrosomethylurea [14].

4-(2',2'-Dimethyl-6'-methylidenecyclohexyl)-1,6-heptadien-4-ol (**3**). A soln. of **2** (3 g, 0.015 mol) and allyl chloride (4 g, 0.052 mol) in THF (55 ml) was added dropwise within 20 min to a stirred suspension of Mg turnings (1 g, 0.041 mol) in THF (10 ml) at 50° under N_2. After the addition, the mixture was refluxed for a further 1.5 h, cooled to r.t., poured into cold sat. aq. NH_4Cl soln., and extracted with Et_2O (2 × 60 ml). The org. phase was washed with sat. aq. $NaHCO_3$ and sat. aq. NaCl soln., dried (Na_2SO_4), filtered, concentrated, and distilled *i.v.* to afford **3** as a colourless oil (3 g, 85%). B.p. 73–74°/0.03 Torr. R_f (CH_2Cl_2) 0.53. IR: 3550 (br.), 3060, 2915, 1632, 1440, 1380, 1355, 1020, 990, 904, 860. ^{1}H-NMR (+D_2O): 0.92 (*s*, 3 H); 1.08 (br. *d*, *J* = 12.5, 1 H); 1.23 (*s*, 3 H); 1.45–1.70 (3 H); 2.02 (*ddd*, *J* = 12.5, 12.5, 5, 1 H); 2.07 (*s*, 1 H); 2.10–2.25 (3 H); 2.32 (*dd*, *J* = 14.5, 7, 1 H); 2.47 (*ABX*, *J* = 14.5, 7, 2 H); 4.56 (br. *s*, 1 H); 4.86 (*s*, 1 H); 5.03–5.17 (4 H); 5.84 (2 H). MS: 234 (0, M^+), 193 (2), 151 (4), 123 (17), 109 (55), 91 (9), 81 (15), 69 (100).

β-Cleavage of Potassium Alkoxide **3a**. *Preparation of (E)-1-(2',2'-Dimethyl-6'-methylidenecyclohexyl)-2-buten-1-one (= γ-Damascone; (E)-***4**). A soln. of **3** (1.5 g, 6.4 mmol) in HMPA (10 ml) was added dropwise within 20 min to a stirred slurry of KH (*ca.* 9 mmol) in HMPA (20 ml) under N_2. The mixture was then stirred at r.t. for a further 1.5 h, cooled to 5°, cautiously poured into cold sat. aq. NH_4Cl soln. (100 ml), and extracted with Et_2O (2 × 80 ml). The org. phase was washed with sat. aq. NaCl soln., dried (Na_2SO_4), filtered, and concentrated *i.v.* to afford an orange oil (1.8 g), a crude 2:1 mixture of *1-(2'-2'-dimethyl-6'-methylidenecyclohexyl)-3-buten-1-one* (**20**) and **4** (*E*/*Z* 1:1). B.p. (bulb-to-bulb distillation) 120–140°/0.1 Torr. Purification of an aliquot (0.3 g) was effected by CC (silica gel (20 g), cyclohexane/AcOEt 9:1).

Data of **20**: R_f (CH_2Cl_2) 0.59. IR: 3060, 2920, 1710, 1640, 1380, 1360, 1060, 990, 910, 890. ^{1}H-NMR: 0.89 (*s*, 3 H); 0.95 (*s*, 3 H); 1.18 (*ddd*, *J* = 12.5, 4.5, 4.5, 1 H); 1.51 (*m*, 1 H); 1.64 (*m*, 1 H); 1.98 (*ddd*, *J* = 12.5, 12.5, 4.5, 1 H); 2.09 (*ddd*, *J* = 12.5, 4.5, 4.5, 1 H); 2.22 (*ddd*, *J* = 12.5, 12.5, 4.5, 1 H); 3.12 (*s*, 1 H); 3.23 (*ABX*, *J* = 17, 7, 2 H); 4.73 (*s*, 1 H); 4.88 (*s*, 1 H); 5.11 (br. *d*, *J* = 18, 1 H); 5.17 (br. *d*, *J* = 11, 1 H); 5.89 (*m*, 1 H). ^{13}C-NMR: 208.3 (*s*); 144.9 (*s*); 130.9 (*d*); 118.7 (*t*); 112.2 (*t*); 65.6 (*d*); 48.9 (*t*); 35.3 (*t*); 35.0 (*s*); 31.7 (*t*); 27.6 (*q*); 26.9 (*q*); 22.9 (*t*). MS: 192, (1, M^+), 151 (7), 123 (100), 95 (11), 81 (64), 69 (35).

*Data of (E)-***4**: R_f (CH_2Cl_2) 0.47. IR: 2900, 1680, 1660, 1620, 1434, 1340, 1272, 1180, 1062, 960, 880. ^{1}H-NMR: 0.91 (*s*, 3 H); 0.95 (*s*, 3 H); 1.20 (*ddd*, *J* = 12.5, 4.5, 4.5, 1 H); 1.51 (*m*, 1 H); 1.64 (*m*, 1 H); 1.87 (*dd*, *J* = 7, 1.5, 3 H); 1.99 (*ddd*, *J* = 12.5, 12.5, 4.5, 1 H); 2.09 (*ddd*, *J* = 12.5, 4.5, 4.5, 1 H); 2.27 (*ddd*, *J* = 12.5, 12.5, 4.5, 1 H); 3.22 (*s*, 1 H); 4.70 (*s*, 1 H); 4.86 (*s*, 1 H); 6.17 (br. *d*, *J* = 15, 1 H); 6.83 (*dq*, *J* = 15, 7, 1 H). MS: 192 (2, M^+), 122 (8), 109 (6), 81 (10), 69 (100).

*Data of (Z)-***4**: R_f (CH_2Cl_2) 0.58. ^{1}H-NMR: 0.90 (*s*, 3 H); 0.99 (*s*, 3 H); 1.20 (*m*, 1 H); 1.51 (*m*, 1 H); 1.64 (*m*, 1 H); 1.99 (*m*, 1 H); 2.08 (*dd*, *J* = 7, 1.5, 3 H); 2.09 (*m*, 1 H); 2.27 (*m*, 1 H); 3.06 (*s*, 1 H); 4.72 (*s*, 1 H); 4.86 (*s*, 1 H); 6.14 (*dq*, *J* = 11, 7, 1 H); 6.21 (br. *d*, *J* = 11, 1 H). MS: 192 (2, M^+), 122 (7), 109 (6), 81 (11), 69 (100), 41 (10).

The foregoing crude mixture (1.5 g) was dissolved in THF (10 ml) containing TsOH·H_2O (35 mg) and the soln. refluxed for 55 h under N_2. The cooled mixture was poured into cold sat. aq. $NaHCO_3$ soln. and extracted with Et_2O (2 × 70 ml). The org. phase was washed with sat. aq. NaCl soln., dried (Na_2SO_4), filtered, and concentrated *i.v.* to give an orange oil which was purified by CC (silica gel (50 g), cyclohexane/AcOEt 4:1) to afford **4** (*E*/*Z* 13:1) as a colourless oil (0.71 g, 58%).

4-[2',2'-Dimethyl-6'-(hydroxymethyl)cyclohexyl]-1,6-heptadien-4-ol (**21**). A soln. of *cis*-**1** (3.5 g, 0.021 mol) and allyl chloride (4.6 g, 0.06 mol) in THF (150 ml) was added dropwise within 1 h to a stirred slurry of Mg turnings (1.3 g, 0.055 mol) in THF (30 ml) at 40° under N_2. After the addition, the mixture was refluxed for 3.5 h, cooled to r.t., and sat. aq. NH_4Cl soln. (10 ml) added dropwise. The mixture was then diluted with Et_2O (100 ml), and the phases were separated. The org. phase was washed with sat. aq. NaCl soln. (3 × 50 ml), dried (Na_2SO_4), and concentrated *i.v.* to afford a yellow oil which consisted of a crude 3:1 mixture of **21** and **23** (*vide infra*). Rapid CC (silica gel (100 g), cyclohexane/AcOEt 5:1) afforded **21** (3.4 g, 64%) as a colourless oil. R_f (CH_2Cl_2) 0.10. R_f (cyclohexane/AcOEt 1:1) 0.45. IR: 3440 (br.), 1632, 1462, 1000, 912. ^{1}H-NMR (+D_2O): 1.14 (*s*, 3 H); 1.16 (*s*, 3 H); 1.20–1.57 (6 H); 1.67 (*d*, *J* = 4, 1 H); 2.35 (*m*, 1 H); 2.49 (3 H); 2.66 (*dd*, *J* = 14.5, 7, 1 H); 3.64 (*dd*, *J* = 11, 5.5, 1 H); 4.11 (*dd*, *J* = 11, 6.5, 1 H); 5.07–5.19 (4 H); 5.88 (*m*, 2 H). MS: 252 (0, M^+), 193 (21), 123 (56), 109 (66), 82 (40), 69 (100), 41 (59).

Also isolated were *(3aRS,7aSR)-1,1-bis(2'-propenyl)-7,7-dimethyl-3a,4,5,6,7,7a-hexahydro-3H-isobenzofuran* (**22**; colourless oil, 0.7 g, 14%), *(1RS,6SR)-1-[2',2'-dimethyl-6'-(hydroxymethyl)cyclohexyl]-3-buten-1-one*, *(3aRS,7aSR)-7,7-dimethyl-1-(2'-propenyl)-3a,4,5,6,7,7a-hexahydro-1(3H)-isobenzofuranol*[21] (tautomeric mixture (**23**; white crystalline solid, 0.8 g, 18%), and *(1RS,6SR)-1-[2',2'-dimethyl-6'-(hydroxymethyl)cyclohexyl]-2-buten-1-one* (**24**; *E*/*Z* 1:1; pale-yellow oil, 50 mg, 1%).

[21]) The C(1)-configuration of the lactol tautomer is unassigned.

Data of **22**: b.p. (bulb-to-bulb distillation) 150–170°/0.1 Torr. R_f (CH_2Cl_2) 0.70. IR: 3062, 2920, 2860, 1632, 1484, 1460, 1050, 1000, 910, 720. ^{1}H-NMR: 1.04 (*s*, 3 H); 1.08 (*s*, 3 H); 1.16 (br. *d*, *J* = 7, 1 H); 1.42–1.68 (5 H); 2.02 (*d*, *J* = 7, 1 H); 2.09 (*dd*, *J* = 14.5, 9.5, 1 H); 2.31 (*dd*, *J* = 14.5, 8, 1 H); 2.31 (*m*, 1 H); 2.67 (*m*, 1 H); 2.82 (*m*, 1 H); 3.55 (*d*, *J* = 7, 1 H); 3.78 (*dd*, *J* = 7, 6.5, 1 H); 5.04 (br. *d*, *J* = 18, 2 H); 5.10 (*m*, 2 H); 5.82 (*m*, 1 H); 6.00 (*m*, 1 H). ^{13}C-NMR: 135.9 (*d*); 135.3 (*d*); 117.7 (*t*); 117.0 (*t*); 85.2 (*s*); 72.4 (*t*); 50.9 (*d*); 44.3 (*t*); 44.1 (*t*); 38.4 (*d*); 35.3 (*t*); 32.0 (*s*); 31.9 (*q*); 28.7 (*q*); 28.2 (*t*); 21.0 (*t*). MS: 234 (0, M^+), 193 (39), 123 (40), 109 (100), 81 (29), 69 (33), 41 (39).

Data of **23**: m.p. 57–59°. R_f (CH_2Cl_2) 0.10. R_f (cyclohexane/AcOEt 1:1) 0.53. IR ($CHCl_3$): 3340 (br.), 2900, 1700, 1640, 1440, 1300, 1040, 990, 920. ^{1}H-NMR (+D_2O; hydroxy-ketone tautomer (67%)): 0.89 (*s*, 3 H); 1.02 (*s*, 3 H); 1.10 (br. *d*, *J* = 12, 1 H); 1.30–1.90 (5 H); 2.02 (*m*, 1 H); 2.78 (br. *d*, *J* = 4.5, 1 H); 3.20 (*dd*, *J* = 18, 7, 1 H); 3.32 (*dd*, *J* = 11, 8, 1 H); 3.35 (*dd*, *J* = 18, 7, 1 H); 3.51 (*dd*, *J* = 11, 5.5, 1 H); 5.09 (br. *d*, *J* = 18, 1 H); 5.17 (br. *d*, *J* = 11, 1 H); 5.91 (*m* = 1 H); (lactol tautomer (33%)): 1.02 (*s* 3 H); 1.12 (*s*, 3 H); 1.10 (br. *d*, *J* = 12, 1 H); 1.30–1.90 (6 H); 2.24 (*m*, 1 H); 2.46 (*dd*, *J* = 13.5, 7, 1 H); 2.58 (*dd*, *J* = 13.5, 7, 1 H); 3.66 (*d*, *J* = 8, 1 H); 3.73 (*dd*, *J* = 8, 6, 1 H); 5.09 (br. *d*, *J* = 18, 1 H); 5.20 (br. *d*, *J* = 11, 1 H); 5.91 (*m*, 1 H). MS: 210 (0, M^+), 192 (20), 177 (47), 169 (30), 123 (80), 109 (100), 81 (85), 69 (78), 55 (70), 41 (85).

Data of (E)-**24**: R_f (cyclohexane/AcOEt 1:1) 0.30. ^{1}H-NMR (+D_2O): 0.85 (*s*, 3 H); 1.05 (*s*, 3 H); 1.12 (br. *d*, *J* = 12, 1 H); 1.20–1.75 (4 H); 1.84 (*dd*, *J* = 14, 4, 1 H); 1.88 (*dd*, *J* = 7, 1.5, 3 H); 2.07 (*m*, 1 H); 2.95 (br. *d*, *J* = 4.5, 1 H); 3.33 (*dd*, *J* = 11, 8, 1 H); 3.44 (*dd*, *J* = 11, 6, 1 H); 6.19 (*dd*, *J* = 15, 1.5, 1 H); 6.81 (*dq*, *J* = 15, 7, 1 H).

Data of (Z)-**24**: R_f (cyclohexane/AcOEt 1:1) 0.35. ^{1}H-NMR (+D_2O): 0.89 (*s*, 3 H); 1.02 (*s*, 3 H); 1.10–2.05 (7 H); 2.07 (*dd*, *J* = 7, 1.5, 3 H); 2.75 (*d*, *J* = 4.5, 1 H); 3.38 (*dd*, *J* = 11, 8, 1 H); 3.49 (*dd*, *J* = 11, 6, 1 H); 6.08 (*dq*, *J* = 12, 7, 1 H); 6.24 (*dd*, *J* = 12, 1.5, 1 H).

β-Cleavage of Dipotassium Dialkoxide **21a**. *Preparation of* **23**. A soln. of **21** (1.4 g, 5 mmol) in HMPA (10 ml) was added dropwise within 10 min to a stirred slurry of KH (11 mmol) in HMPA (30 ml) at r.t. under N_2. The mixture was then heated at 65° during 1 h, cooled to 20° and cautiously poured into cold sat. aq. NH_4Cl soln. (100 ml) and extracted with Et_2O. The org. phase was washed with sat. aq. NaCl soln., dried (Na_2SO_4), filtered, and concentrated *i.v.* to give a yellow oil whose purification by CC (silica gel (50 g), cyclohexane/AcOEt 7:3) and recrystallisation from petroleum ether at −60° afforded **23** as a white, crystalline solid (0.61 g, 58%). *Vide supra* for physical and spectral data.

Also isolated were **22** (40 mg, 3%) and **24** (*E*/*Z* 1:1) (30 mg, 2%), spectrally identical with authentic samples *(vide supra)*.

(1′RS,2′SR)-[3′,3′-Dimethyl-2′-(1″-oxo-3″-butenyl)cyclohexyl]methyl Acetate (**25**). A soln. of **23** (0.54 g, 2.6 mmol) and Ac_2O (0.4 ml) in pyridine (6 ml) was stirred for 1 h at r.t. The soln. was then poured into cold 10% aq. HCl soln. (100 ml) and extracted with Et_2O. The org. phase was washed with H_2O, sat. aq. $NaHCO_3$, and sat. aq. NaCl soln., and dried (Na_2SO_4). Concentration and distillation *i.v.* afforded **25** as a pale-yellow oil (0.56 g, 85%). B.p. (bulb-to-bulb distillation) 160–180°/0.03 Torr. R_f (CH_2Cl_2) 0.27. IR: 2900, 1730, 1700, 1640, 1446, 1360, 1220, 1030, 916, 600. ^{1}H-NMR: 0.90 (*s*, 3 H); 1.02 (*s*, 3 H); 1.10 (br. *d*, *J* = 12, 1 H); 1.35–1.85 (5 H); 2.06 (*s*, 3 H); 2.13 (*m*, 1 H); 2.67 (br. *d*, *J* = 4.5, 1 H); 3.20 (*d*, *J* = 6.5, 2 H); 3.72 (*dd*, *J* = 11, 8, 1 H); 3.97 (*dd*, *J* = 11, 5.5, 1 H); 5.07 (br. *d*, *J* = 18, 1 H); 5.17 (br. *d*, *J* = 11, 1 H); 5.91 (*m*, 1 H). MS: 252 (0, M^+), 192 (5), 177 (8), 169 (12), 123 (21), 109 (20), 81 (25), 69 (100).

Pyrolysis of **25**. A 5% xylene soln. of **25** (50 mg) was passed through a heated 2-m glass column at 450° (carrier gas: N_2). GC of the resulting pyrolysate showed the absence of either **20** or (*E*/*Z*)-**4**. The experiment was, thus, abandoned.

(1′RS,2′SR)-[3′,3′-Dimethyl-2′-(1″-oxo-2″-butenyl)cyclohexyl]methyl Acetate (**26**). A soln. of **25** (0.25 g, 1 mmol) in toluene (5 ml) containing TsOH·H_2O (40 mg) was stirred for 120 h at r.t. under N_2. The mixture was then diluted with Et_2O (50 ml) and the org. soln. washed with sat. aq. $NaHCO_3$ and sat. aq. NaCl soln., and dried (Na_2SO_4). Concentration and distillation *i.v.* afforded **26** as a colourless oil (0.21 g, 84%). B.p. (bulb-to-bulb distillation) 160–190°/0.06 Torr. R_f (CH_2Cl_2) 0.20. IR: 2900, 1720, 1684, 1650, 1620, 1440, 1360, 1220, 1025, 962, 600. ^{1}H-NMR: 0.84 (*s*, 3 H); 1.03 (*s*, 3 H); 1.12 (br. *d*, *J* = 12, 1 H); 1.40–1.56 (2 H); 1.60–1.73 (2 H); 1.82 (*dd*, *J* = 14, 4, 1 H); 1.87 (*dd*, *J* = 7, 1.5, 3 H); 2.02 (*s*, 3 H); 2.17 (*m*, 1 H); 2.87 (br. *d*, *J* = 4.5, 1 H); 3.71 (*dd*, *J* = 11, 8, 1 H); 3.86 (*dd*, *J* = 11, 6.5, 1 H); 6.12 (*dd*, *J* = 15, 1.5, 1 H); 6.78 (*dq*, *J* = 15, 7, 1 H). MS: 252 (0, M^+), 192 (26), 177 (45), 149 (24), 136 (25), 123 (47), 109 (36), 69 (100).

Pyrolysis of **26**. A soln. of **26** (75 mg, 0.3 mmol) in xylene (2 ml) was passed through a heated 2-m glass column at 450° (carrier gas: N_2). GC of the resulting pyrolysate showed the formation of **4** (*E*/*Z* 4:1; 46% yield) and **20** (6% yield) together with unreacted **26** (31% yield, *i.e.* 69% conversion).

REFERENCES

[1] E. Demole, P. Enggist, U. Säuberli, M. Stoll, E. sz. Kovats, *Helv. Chim. Acta* **1970**, *53*, 541; E. Demole, D. Berthet, *ibid.* **1971**, *54*, 681; W. Renold, R. Näf-Müller, U. Keller, B. Willhalm, G. Ohloff, *ibid.* **1974**, *57*, 1301; E. sz. Kovats,E. Demole, G. Ohloff, M. Stoll, to *Firmenich SA*, U.S. Pat. 3,928,456 (prior. 9.11.1967) (*CA*: **1976**, *85*, 46082m).

[2] C. Fehr, J. Galindo, *Helv. Chim. Acta* **1986**, *69*, 228, and ref. cit. therein.

[3] K. H. Schulte-Elte, V. Rautenstrauch, G. Ohloff, *Helv. Chim. Acta* **1971**, *54*, 1805; K. H. Schulte-Elte, B. L. Muller, G. Ohloff, *ibid.* **1973**, *56*, 310; F. Näf, R. Decorzant, *ibid.* **1974**, *57*, 1317; O. Takazawa, K. Saigo, K. Narasaka, *Chem. Lett.* **1977**, 757; M. Zaidlewicz, *Tetrahedron Lett.* **1986**, *27*, 5135; P. Gosselin, *ibid.* **1986**, *27*, 5495; A. Amrollah-Madjdabadi, L. Stella, *Bull. Soc. Chim. Fr.* **1987**, 350; P. Gosselin, *Tetrahedron* **1988**, *44*, 1979.

[4] C. Fehr, J. Galindo, *J. Org. Chem.* **1988**, *53*, 1828.

[5] R. L. Snowden, S. M. Linder, B. L. Muller, K. H. Schulte-Elte, *Helv. Chim. Acta* **1987**, *70*, 1858.

[6] B. Willhalm, U. Steiner, H. Schinz, *Helv. Chim. Acta* **1958**, *41*, 1359; R. J. Armstrong, L. Weiler, *Can. J. Chem.* **1983**, *61*, 2530.

[7] R. L. Snowden, S. M. Linder, B. L. Muller, K. H. Schulte-Elte, *Helv. Chim. Acta* **1987**, *70*, 1879.

[8] H. Leotte, *Rev. Port. Quim.* **1965**, *7*, 214; F. Kienzle, I. Mergelsberg, J. Stadlwieser, W. Arnold, *Helv. Chim. Acta* **1985**, *68*, 1133.

[9] M. Jalali-Naini, D. Guillerm, J.-Y. Lallemand, *Tetrahedron* **1983**, *39*, 749.

[10] E. P. Demole, personal communication (*Firmenich SA*, CH–1211 Geneva 8).

[11] A. de Groot, B. J. M. Jansen, *J. Org.Chem.* **1984**, *49*, 2034.

[12] P. Dowd, P. Kennedy, *Synth. Commun.* **1981**, 935; D. Liotta, U. Sunay, H. Santiesteban, W. Markiewicz, *J. Org. Chem.* **1981**, *46*, 2605.

[13] T. R. Hoye, A. J. Caruso, *Tetrahedron Lett.* **1978**, 4611.

[14] F. Arndt, *Org. Synth., Coll. Vol. 2* **1943**, 461; *ibid.* **1943**, 165.