Regio- and Stereoselective Transformations of 3,3,5,5-Tetramethylcyclohexane Derivatives
Oxygenations, Annulations, and S_N2'-Reactions

Winnfried Hasel[a,b] **and H. M. R. Hoffmann***[a]

Department of Organic Chemistry, University of Hannover[a],
Schneiderberg 1B, D-3000 Hannover
Department of Chemistry, Columbia University[b],
New York, N.Y. 10027

Received January 28, 1988

Hydroboration of TM-$\Delta^{1,7}$-methadiene (**4**) (TM = tetramethyl) with 9-BBN gave TM-*cis*-shisool (*cis*-**5**), which was converted into TM-*trans*-shisool (*trans*-**5**) via the aldehyde *cis*-**7**, base-catalyzed epimerization to *trans*-**7**, and finally $LiAlH_4$ reduction. Starting from TM-isocrypton (**8**) and spiroepoxide **6-E**, respectively, both stereoisomeric spiroannulated lactones **10-Z** and **10-E** as well as spiroannulated ethers **11-Z** and **11-E** were prepared by stereoselective 3-carbon and 2-carbon homologations. 1-Vinylcyclohexene derivative **16** and dimethyl acetylenedicarboxylate underwent Diels-Alder addition to **17**, which was formed in a 1:1 stereoisomeric ratio. TM-isocrypton (**8**) was annulated to give the cyclopentenone derivative **19** in a Rupe-Nazarov sequence. 1-Mesyloxy-2-methylenecyclohexane derivative **14** with its hindered and quasi-axial mesyloxy group is a useful system for studying S_N2' reactions, which in this case require temperatures in the range of 50–70°C. It is suggested that the S_N2' reactions are preceded by a slow ionization of **14** to a contact ion-pair. Above 70°C, mesylate **14** started to decompose.

Regio- und stereoselektive Transformationen von 3,3,5,5-Tetramethylcyclohexan-Derivaten. – Oxygenierungen, Anellierungen und S_N2'-Reaktionen

Hydroborierung von TM-$\Delta^{1,7}$-Menthadien (**4**) (TM = Tetramethyl) mit 9-BBN gab TM-*cis*-Shisool (*cis*-**5**), welches über den Aldehyd *cis*-**7**, basenkatalysierte Epimerisierung zu *trans*-**7** und schließlich $LiAlH_4$-Reduktion in TM-*trans*-Shisool (*trans*-**5**) umgewandelt wurde. Ausgehend von TM-Isocrypton (**8**) bzw. Spiroepoxid **6-E** erhielten wir, über stereoselektive 3-Kohlenstoff- und 2-Kohlenstoff-Homologisierungen, beide stereoisomeren, spiro-anellierten Lactone **10-Z** und **10-E** sowie die spiro-anellierten Ether **11-Z** und **11-E**. – Das 1-Vinylcyclohexenderivat **16** und Dimethyl-acetylendicarboxylat bildeten in einer Diels-Alder-Reaktion das Addukt **17**, das in einem Stereoisomerenverhältnis von 1:1 entstand. Durch eine Rupe-Nazarov-Sequenz wurde TM-Isocrypton (**8**) zum Cyclopentenonderivat **19** anelliert. Das 1-Mesyloxy-2-methylencyclohexan-Derivat **14** besitzt eine gehinderte, quasiaxiale Mesylat-Fluchtgruppe und ist deshalb ein nützliches System zum Studium von S_N2'-Reaktionen, die im vorliegenden Beispiel Temperaturen im Bereich von 50–70°C erfordern. Es wird vorgeschlagen, daß den S_N2'-Reaktionen eine langsame Ionisierung von **14** zum Kontakt-Ionenpaar vorausgeht. Oberhalb von 70°C begann das Mesylat **14** sich zu zersetzen.

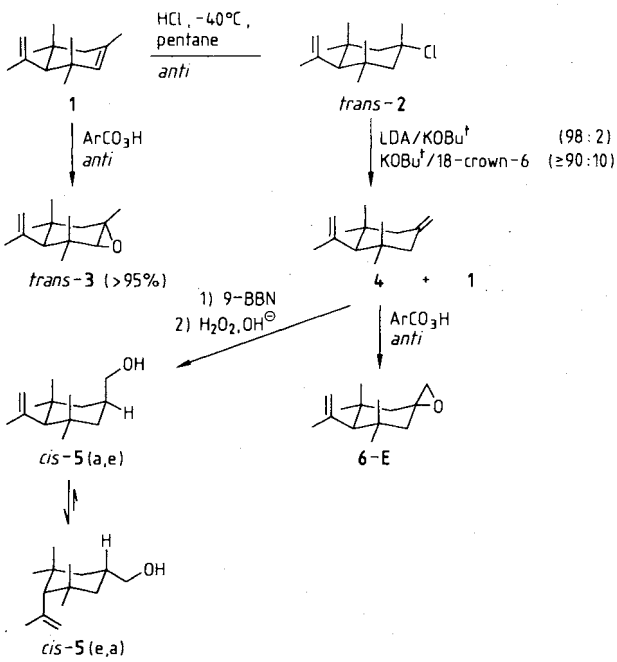
Tetramethyllimonene (**1**) can be regarded as an artificial terpene, and we have described a simple and efficient synthesis of it, which starts from mesityl oxide[1]. The formation of **1** has been suggested to mimic the biosynthesis of a number of terpenes, including complex polycyclic derivatives occurring in nature[2a]. Microbial oxygenation of **1** gives anguidine, a polyoxygenated sesquiterpene belonging to the trichothecene class, as a major byproduct[2]. In its chemical reaction **1** has shown unusual stereochemical features.

Epoxidation of **1** gave the *trans* epoxide *trans*-**3**, with less than 5% of the *cis* isomer[1]. The electrophilic hydrochlorination with HCl gas in pentane at −40°C yielded *trans*-**2**[3], which must have arisen by regio- and chemoselective protonation of the endocyclic double bond, giving a tertiary carbenium ion, which is trapped by stereoselective attack of chloride ion from the face *anti* to the isopropenyl group. *trans*-**2** was previously converted into TM-$\Delta^{1,7}$-menthadiene (**4**) (TM = tetramethyl) with LDA/KOBu^t. Alternatively, we have now used the simpler combination KOBu^t/18-crown-6 in refluxing heptane[4], although the regioselectivity was slightly less ($\leqq$ 90:10).

Oxygenations: Previously, **4** was transformed into spiroepoxide **6-E**, an ambergris-like odourant[2,5]. **4** has now been hydroborated selectively (chemo-, regio-, and stereo-) to give the *cis*-1,4-disubstituted cyclohexane *cis*-**5**, i.e. the hydrogen has been delivered *anti* to the isopropenyl group. As it turned out, conformer *cis*-**5** (e,a) was populated exclusively, as judged by X-ray crystallography[6].

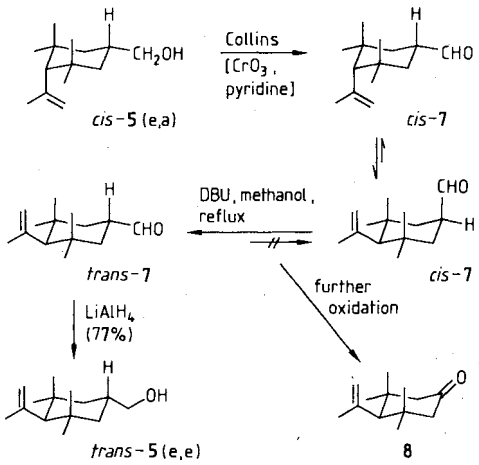
The *trans*-1,4-disubstituted alcohol *trans*-**5** (TM-shisool) was prepared as follows: Oxidation of *cis*-**5** was tried with several oxidizing agents. Collins oxidation gave mainly aldehyde *cis*-**7** (ca. 90%) (Scheme 1) with some leakage into *trans*-**7** (5%) and also ketone **8**. Milder oxidizing agents, which required longer reaction times (PCC, Swern, PDC), gave progressively more consecutive products, i.e. *trans*-**7** and **8**. Treatment of *cis*-**7** with DBU in refluxing methanol

  0009–2940/88/0808–1461 $ 02.50/0

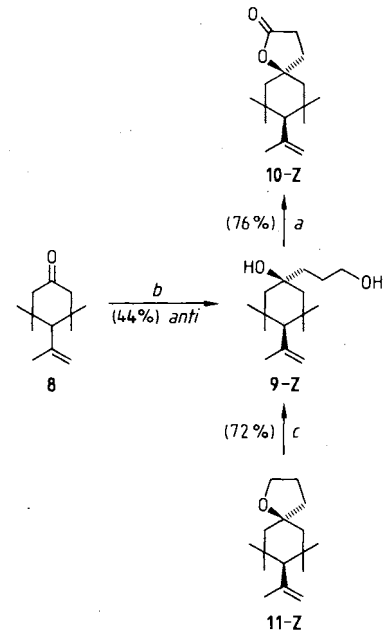


(Scheme 1) gave *trans*-**7** in an irreversible reaction. Not only chemical evidence points to the reactivity of *cis*-**7**. On the basis of the structural data and force-field calculations there is also reason to assume that *cis*-**7** is comparatively energy rich. Of course, *cis*-**5** and *trans*-**5** must be related similarly[6]. Reduction of aldehyde *trans*-**7** with $LiAlH_4$ afforded alcohol *trans*-**5** (e,e)[6].

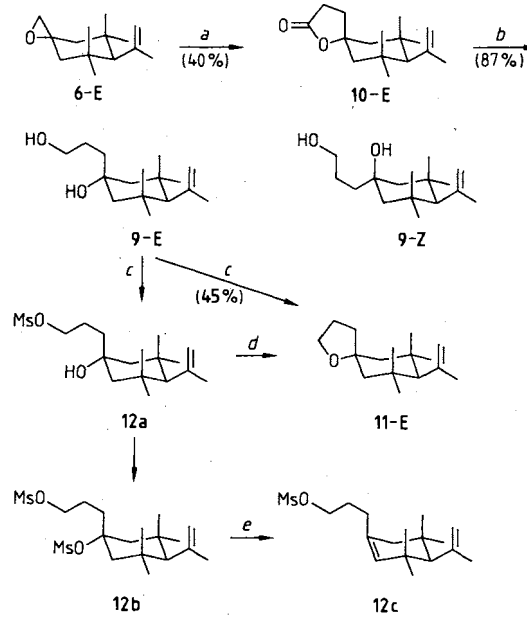
Scheme 1



Spiroannulations: Tetramethylisocrypton **8** reacted with the 3C-homologation reagent of Eaton[7] to give **9-Z** after deprotection. It was advantageous to use ultrasound and Barbier conditions to effect carbon–carbon bond formation. Since the tertiary alcohol formed in the first step was easily dehydrated, it was important to deprotect under as mild conditions as possible. Again, attack of the carbonyl group in **8** proceeded stereoselectively *anti* to the isopropenyl group. Spirolactonization of the diol **9-Z** was carried out with Collins reagent and was straightforward. The spiroannulated ether **11-Z** was obtained by chemoselective mesylation of the primary hydroxyl group and spontaneous spirocyclization.



a: $CrO_3 \cdot 2Py$, CH_2Cl_2, 15 min, r.t. —*b*: 1) Br, Li, Et_2O, ultrasound (Barbier), 4 h, 0 °C; 2) PyHOTs, 3 h, 55 °C, EtOH.—*c*: MsCl, DABCO, DMAP, $CHCl_3$, 18 h, r.t.

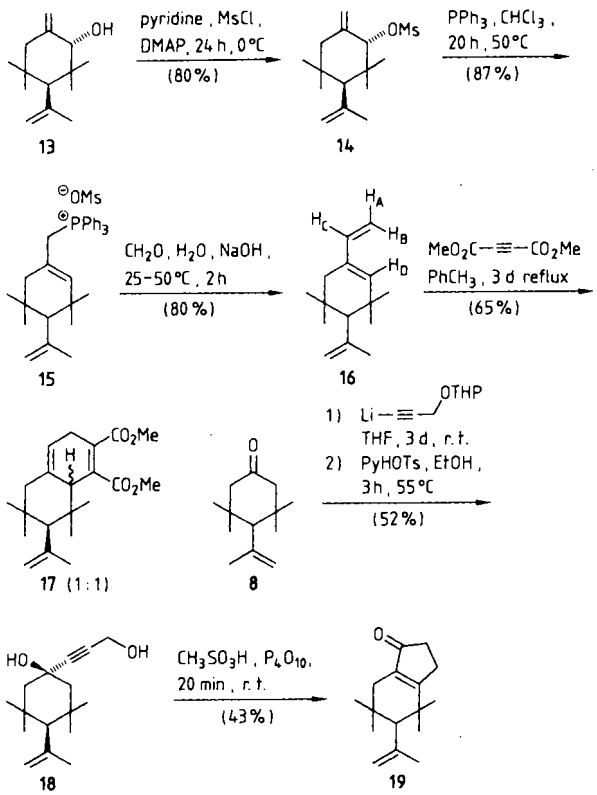


a: 1) 5 eq $LiCH_2CO_2Li$, dioxane, 20 h reflux; 2) HCl, EtOH, 3 h, 50 °C.—*b*: $LiAlH_4$, Et_2O, 5 h, 0 °C.—*c*: MsCl, DABCO, DMAP (cat.), $CHCl_3$, 18 h, r.t.—*d*: DABCO.—*e*: DABCO (ca. E1).

Entry into the *E*-series was reached via spiroepoxide **6-E**, which was opened nucleophilically, using 5 equivalents of the dianion of acetic acid. Addition of hexamethylphosphoric amide to the suspension of the dianion in dioxane did not improve the yield. Reduction of the spirolactone **10-E** afforded diol **9-E** which was converted into **11-E**, using the conditions for the conversion of **9-Z** into **11-Z**. In this

case, formation of the spiroether **11-E** was less efficient. Probably several factors are responsible for the different cyclization behaviour of diol **9-Z** and diol **9-E**. In **9-E** the tertiary hydroxyl group is equatorial and therefore more accessible than the axial hydroxyl group in **9-Z**. Under the reaction conditions, not only the cyclizable monomesylate **12a** is formed, but also bismesylate **12b** which, at the latest on workup suffers elimination to yield the observed olefin **12c**. Furthermore, the spiroether oxygen is axial in **11-Z** and equatorial in **11-E**. Since oxygen is sterically less demanding than a methylene group, it is likely that **11-Z** is also thermodynamically more stable than **11-E** (cf. syntriaxial repulsions discussed in ref.[6]).

Edge-Annulations: The tetramethyllimonene skeleton is crowded and only a few edge-annulations were successful. Allylic alcohol **13**[8] was converted in three steps into the conjugated vinylcyclohexene **16** as outlined.

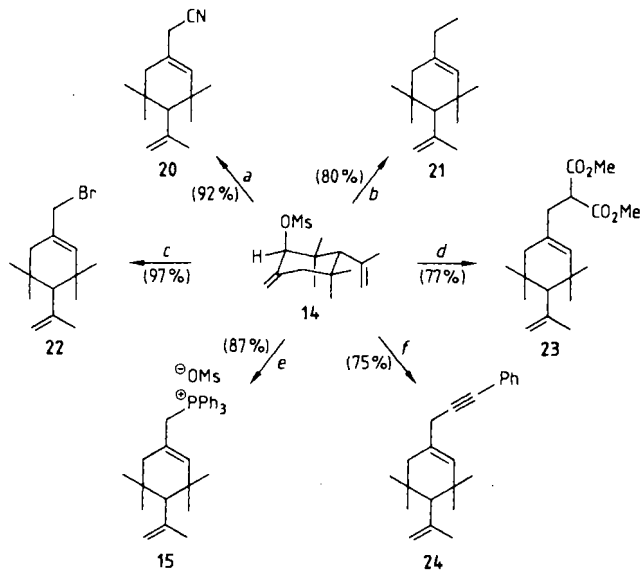


14 was converted into phosphonium salt **15** in an S_N2' reaction. The Wittig reaction with formaldehyde could be performed in an aqueous solution[9]. The Diels-Alder reaction of **16** with dimethyl acetylenedicarboxylate furnished **17** as a 1:1 mixture of diastereoisomers, i.e. without any π-facial selectivity.

The cyclopentenone annulation of **8** was accomplished by a Rupe-Nazarov sequence. As expected by now, addition of the acetylenic anion to **8** was *anti* to the isopropyl group and gave **18**. Cyclization of **18** with methanol/sulfuric acid[10] was not successful. However, the more acidic CH_3SO_3H/P_4O_{10} system[11] gave the desired enone **19** in 43% yield. The success of this annulation can be attributed to the establishment of two new sp^2 centres in the ring, which are probably useful for compensating the steric demand of the existing two quaternary centres. Consistently, TM-isocrypton **8** could be converted into its enol acetate and also enamine (establishment of a further sp^2 centre in the ring), but attempts to α-alkylate ketone **8** and its enamine failed.

S_N2' Reactions: S_N2' Reactions continue to attract mechanistic and synthetic attention[12]. In mesylate **14** the mesyloxy group adopts a quasi-axial position (Scheme 2) and the breaking C–OMs σ bond should be able to overlap with the allylic π bond. Furthermore, the C–OMs carbon is highly hindered towards direct nucleophilic attack, whereas the terminal methylene group is easily accessible. In fact, the secondary allylic mesylate **14** proved to be inherently unstable and had to be kept at −20°C to prevent decomposition. S_N2' Reactions proceeded smoothly between 50–70°C with a *variety of nucleophiles*. At higher temperature **14** decomposed. Since the reagents included a neutral nucleophile such as triphenylphosphane and anions of quite different steric demand and nucleophilicity, a case can be made for a slow ionization of **14** at 50–70°C to a contact ion-pair, followed by rapid nucleophilic attack, as suggested by Bordwell[12b]. Although a *syn*- and an *anti*-facial S_N2' reaction cannot be distinguished in **14**, *syn*-facial attack should be favoured sterically, similar to hydroboration (**4**→**5**).

Scheme 2. S_N2' Reactions of the crowded 1-mesyloxy-2-methylenecyclohexane **14**



a: KCN/18-crown-6, CH_3CN, 6 h, 50°C.—*b*: Me_2CuLi, Et_2O, 2 h, −10°C.—*c*: LiBr, DMF, 3.5 h, 50°C.—*d*: $ClMgCH(CO_2Me)_2$, THF, 20 h, 70°C.—*e*: PPh_3, $CHCl_3$, 20 h, 50°C.—*f*: $ClMgC{\equiv}CPh$, THF, 3 h, 60°C.

Conclusions: The stereoselective oxygenation reactions now described complete the known oxygenations of tetramethyllimonene derivatives. Both spiroannulations at C(1) and edge annulations at C(1)–C(2) are feasible, the latter being experimentally more difficult. The success of the Rupe-Nazarov reaction (**18**→**19**) suggests that it is important to retain the C(1)=C(2) bond of the parent tetramethyllimonene (**1**), the formation of which has a fairly high driving

force. In this fashion, nonbonded repulsion originating from the two *gem*-dimethyl groups is minimized.

We thank Dr. *Detlef Pauluth* for the hydroboration experiment and the *Fonds der Chemischen Industrie* for support of this work.

Experimental

Abbreviations: r. t. = room temperature. – DMAP = 4-(Dimethylamino)pyridine. – DABCO = 1,4-Diazabicyclo[2.2.2]-octane.

1-Hydroxymethyl-3,3,5,5-tetramethyl-4-(1-methylethenyl)cyclohexane (*cis*-**5**): A solution (72 ml, 36 mmol) of 9-BBN in hexane was dropped to **4**[3] (7.68 g, 40 mmol) under argon. After 17 h at r. t. and 3 h at 70°C, the solution was cooled to r. t. and ethanol (24 ml), 6 M NaOH (8 ml) and 30% H_2O_2 (16 ml) were successively added with stirring. After 2 h at 50°C, the mixture was cooled to r. t., the aqueous phase was saturated with K_2CO_3 and extracted with light petroleum (3 ×). The combined organic phase was dried (Na_2SO_4) and the solvent was evaporated. Chromatography on silica gel (silica gel:product, 10:1) and elution with light petroleum allowed to separate unreacted **4** and **1**. *cis*-**5** was eluted with ether, and the crude product was distilled (kugelrohr), giving a colourless crop of crystals, which were recrystallized from pentane at –30°C; yield 5.81 g (77%), b.p. 100°C/0.1 Torr, m.p. 44–46. – IR ($CHCl_3$): 3630 and 3460 cm^{-1} (OH), 3100 and 3080 (C–H unsatd.), 2930 (C–H sat.). – ^1H NMR (90 MHz, $CDCl_3$): δ = 0.91 (s, 6H, 2 CH_3), 1.07–1.53 (m, 4H, 2 CH_2), 1.16 (s, 6H, 2 CH_3), 1.46 (s, 1H, OH), 1.78 (br s, 4H, CH_3, *tert*-CH), 1.67–2.04 (m, 1H, $CHCH_2OH$), 3.36–3.60 (m, 2H, $CHCH_2OH$), 4.67 (br s, 2H, olefin CH_2). – MS: *m/z* (%) = 210 (22, M^+), 123 (40), 111 (78), 99 (30), 97 (72), 96 (36), 95 (40), 83 (42), 82 (37), 81 (100).

$C_{14}H_{26}O$ (210.4) Calcd. C 79.94 H 12.46
Found C 79.80 H 12.46

trans-**5**: A 50-ml round-bottomed flask with magnetic stirrer and dropping funnel with drying tube was charged with $LiAlH_4$ (0.39 g, 10.4 mmol) in absol. ether (8 ml). A solution of *trans*-**7** (1.8 g, 8.7 mmol) in absol. ether (2 ml) was dropped into the mixture which was stirred for 3 h at r. t. The excess of $LiAlH_4$ was decomposed with ethyl acetate, and an aqueous solution (15 ml) of NH_4Cl was added. The aqueous phase was washed with ether (3 ×), the combined organic phase was washed with saturated aqueous NaCl, dried (Na_2SO_4), and the solvent was removed to leave a colourless crop of crystals, which were purified by chromatography (silica gel, CH_2Cl_2:MeOH, 250:1); yield 1.4 g (77%), colourless crystals, m.p. 63–64°C. – IR ($CHCl_3$): 3620 cm^{-1} (OH), 2945, 2910, 2860, 1638, 1015. – ^1H NMR (200 MHz, $CDCl_3$): δ = 0.86 (s, 6H, eq CH_3), 0.91 (d, 2H, ax CH_2), 1.08 (s, 6H, ax CH_3), 1.51 (m, 2H, eq CH_2), 1.59 (s, 1H, allyl CH), 1.81 (s, 3H, olefin CH_3), 1.75–1.98 (m, 1H, $CHCH_2OH$), 2.67 (s, 1H, OH), 3.41 (d, 2H, CH_2OH), 4.72 + 5.01 (s, 1H each, olefin H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 23.15 (q, eq CH_3), 30.97 (m, br, allyl CH_3), 33.19 (d, $CHCH_2OH$), 33.50 (q, ax CH_3), 35.23 [s, $(CH_3)_2C$], 46.71 (t, 2 CH_2), 62.04 (m, br, allyl CH), 68.66 (t, CH_2OH), 112.8 (m, br, $H_2C=CCH_3$), 145.2 (s, $H_2C=CCH_3$). – MS: *m/z* (%) = 210 (8, M^+), 195 (3), 123 (36), 111 (65), 97 (46), 95 (30), 81 (100). – Exact mass calcd. for $C_{14}H_{26}O$, 210.1983662; found 210.1984212.

$C_{14}H_{26}O$ (210.4) Calcd. C 79.94 H 12.46
Found C 79.69 H 11.89

3,3,5,5-Tetramethyl-4-(1-methylethenyl)-1-cyclohexanecarbaldehyde (*cis*-**7**): Dry, finely powdered CrO_3 (0.6 g, 6 mmol) was stirred into a solution of absol. pyridine (0.95 g, 12 mmol) in absol. CH_2Cl_2 (15 ml) and the mixture was stirred for 15 min with exclusion of moisture. *cis*-TM-shisool (0.21 g, 1 mmol) in CH_2Cl_2 (1 ml) was added, and the mixture was stirred for further 15 min. After addition of water (1 ml), the resulting mixture was filtered through filter paper and then rapidly through alumina (5 g, neutral, activity IV, CH_2Cl_2). The filtrate was washed with ice-cold 1 N HCl, aqueous $NaHCO_3$, aqueous NaCl, and dried (Na_2SO_4). After removal of the solvent in vacuo, a colourless oil containing **8** (5–10%) was obtained. Attempted chromatography caused partial epimerization of *cis*-**7** into *trans*-**7**; yield of *cis*-**7**: 0.15 g (72%). – IR ($CHCl_3$): 2980 cm^{-1} vs, 1718 vs. – ^1H NMR (200 MHz, $CDCl_3$) (because of hindered rotation of the isopropenyl group some of the signals are split and strongly broadened): δ = 0.93 + 0.96 (s, 6H, CH_3), 1.15 (s, 6H, CH_3), 1.33–1.71 (m, 4H, CH_2), 1.8 + 1.82 (s, 4H, allyl CH_3 + CH), 2.44–2.88 (m, 1H, CH–CHO). 4.55–5.19 (m, 2H, olefin H) 9.65–9.8 (m, 1H, CHO). – MS: *m/z* (%) = 208 (4, M^+), 123 (40), 113 (71), 97 (68), 96 (100). – Exact mass calcd. for $C_{14}H_{24}O$, 208.182706; found 208.182766.

trans-**7**: A solution of *cis*-**7** (3.9 g, 18.8 mmol) and DBU (0.65 g, 4.3 mmol) in methanol (100 ml) was refluxed for 18 h under N_2. The solvent was evaporated to leave an oil which was taken up in ether (50 ml) and extracted with 5% HCl (20 ml), aqueous $NaHCO_3$ (20 ml) and aqueous NaCl (20 ml). The organic phase was dried (Na_2SO_4), and the solvent was removed giving a yellow oil which was chromatographed (ether:light petroleum, 1:12); yield 1.92 g (55%), colourless oil. – IR ($CHCl_3$): 2945 cm^{-1} vs, 1718 vs. – ^1H NMR (200 MHz, $CDCl_3$): δ = 0.92 (s, 6H, eq CH_3), 1.1 (s, 6H, ax CH_3), 1.2 (d, *J* = 13 Hz, 2H, ax CH_2), 1.61 (s, 1H, allyl CH), 1.72 (m, 2H, eq CH_2), 1.83 (s, 3H, allyl CH_3), 2.5–2.69 (m, 1H, CHCHO), 4.75 + 5.05 (each s, 2H, 2 olefin H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.7 (q, eq CH_3), 31.28 (m, br, allyl CH_3), 33.19 (q, ax CH_3), 35.12 (s, $(CH_3)_2C$), 42.64 (t, CH_2), 44.23 (d, CHCHO), 61.51 (m, br, allyl CH), 113.3 (s, br, $CH_3C=CH_2$), 144.7 (s, $CH_3C=CH_2$), 204.5 (d, CHO). – MS: *m/z* (%) = 208 (4, M^+), 152 (27), 111 (100), 97 (32). – Exact mass calcd. for $C_{13}H_{21}O$ (M^+ – 15), 193.1592409; found 193.1592441.

1-(3-Hydroxypropyl)-3,3,5,5-tetramethyl-4-(1-methylethenyl)-1-cyclohexanol (**9-Z**): A flame-dried 25-ml two-necked flask with septum and reflux condenser with nitrogen inlet was charged with a suspension of powdered lithium (66 mg, 9.5 mmol) in light petroleum. The solvent was removed in vacuo and the apparatus was filled with N_2. After addition of ether (3 ml) the apparatus was immersed into an ultrasonic bath filled with water. The reaction was started by adding 2 drops of 1-bromo-4,6-dioxa-5-methyloctane at r. t. and then cooled to 0°C, while a solution of TM-isocrypton **8** (0.58 g, 3 mmol) and bromoacetal (0.95 g, 4.5 mmol) in absol. ether (4 ml) was dropped in. After 4 h at 0°C, the mixture was stirred into an ice-cold solution of half-saturated NH_4Cl (10 ml). The aqueous phase was separated and extracted with ether (10 ml, 2 ×). The combined organic phase was dried (Na_2SO_4), and the solvent was evaporated. The resulting acetal was cleaved with pyridinium tosylate (76 mg, 0.3 mmol) in ethanol (25 ml) at 55°C for 3 h. After evaporation of ethanol the residue was filtered through basic alumina (10 g, activity II–III) with ether-ethanol (6:1) to give colourless crystals which were recrystallized from CH_2Cl_2; yield 0.34 g (44%), m.p. 142–143°C. – IR (KBr): 3330 cm^{-1} br, s, 2970 s, 1228 m, 1065 m. – ^1H NMR (200 MHz, $CDCl_3$): δ = 0.88 (s, 6H, eq CH_3), 1.26 (m, 8H, ax CH_3 + ax CH_2), 1.48 (d, 2H, eq CH_2), 1.54–1.8 (m, 7H, CH + CH_2 + 2OH), 3.77 (t, 2H, CH_2OH), 4.8 + 5.06 (s, br. 1H, each, 2 olefin H). – MS (60°C): *m/z* (%) = 254 (2, M^+), 195 (48), 139 (58), 97 (70), 96 (100). – Exact mass calcd. for $C_{16}H_{28}O$ (M^+ – 18), 236.214016; found 236.214005.

9-E: A 25-ml round-bottomed flask was charged with $LiAlH_4$ (38 mg, 1 mmol) in absol. ether (1 ml) and lactone **10-E** (0.25 g, 1 mmol) in absol. ether (12 ml) was stirred in. The mixture was stirred for 5 h at 0 °C with exclusion of moisture. The excess $LiAlH_4$ was destroyed by dropping in 2 ml of ice-cold water and subsequent acidification with 10% H_2SO_4 (4 ml). The product was separated and the organic phase was washed with aqueous $NaHCO_3$ (5 ml), aqueous NaCl (5 ml), and dried (Na_2SO_4). After removal of the solvent the product was recrystallized from CH_2Cl_2, giving colourless crystals; yield 0.22 g (87%), m.p. 119–121 °C. – IR (KBr): 3360 cm^{-1} s, br, 3290 s, br, 2965 vs, 2950 vs, 1643 m, 1240 m, 1065 m. – ^1H NMR (200 MHz, $CDCl_3$): δ = 0.98 + 1.05 (s, each 6H, $4CH_3$), 1.33 (d, J = 14 Hz, 2H, ax CH_2), 1.4–1.62 (m, 6H, eq CH_2 + $2CH_2$), 1.77 (s, 3H, allyl CH_3), 1.88 (s, br, allyl CH), 3.37 (t, 2H, CH_2OH), 3.78 + 4.32 (s, br, each 1H, 2OH), 4.64 + 4.89 (s, each 1H, 2 olefin H). – ^{13}C NMR (50 MHz, [D$_6$]DMSO): δ = 26.68 [t, $CH_2(CH_2)_2OH$ + $CH_2CH_2CH_2OH$]. 27.0 (m, br, allyl CH_3), 34.12 (q, $4CH_3$), 50.06 [m, br, $2(CH_3)_2CCCH_2$], 60.42 (m, br, CH), 61.65 (t, CH_2OH), 70.64 [s, $(CH_2)_3COH$], 113 (m, br, $CH_3C=CH_2$), 146.0 (s, $CH_3C=CH_2$). – MS: m/z (%) = 254 (0, M^+), 236 (2), 195 (9), 125 (20), 97 (47), 96 (100). – Exact mass calcd. for $C_{16}H_{28}O$ (M^+ – 18), 236.21414163; found 236.214005.

$C_{16}H_{30}O_2$ (254.2) Calcd. C 75.54 H 11.89
Found C 75.21 H 11.79

7,7,9,9-Tetramethyl-8-(1-methylethenyl)-1-oxaspiro[4.5]decan-2-one (**10-Z**): Dry, finely powdered CrO_3 (1.2 g, 12 mmol) was stirred into a solution of absol. pyridine (1.9 g, 24 mmol) in absol. CH_2Cl_2 (30 ml) and stirred for 15 min under exclusion of moisture. Diol **9-Z** (0.25 g, 1 mmol) in absol. CH_2Cl_2 (2 ml) was added, and the solution was stirred for further 15 min at r. t. The reaction was stopped by adding water (0.3 ml), and the resulting solution was taken up in ether and filtered through filter paper and then through basic alumina (activity II–III). The filtrate was washed with 5% ice-cold HCl (10 ml) and dried (Na_2SO_4). After removal of the solvent a colourless solid was obtained which was crystallized from ether/light petroleum (1:1), giving colourless needles; yield 0.19 g (76%), m.p. 180–181 °C. – IR (KBr): 2955 cm^{-1} s, 1760 vs, 1218 s, 1172 s. – ^1H NMR (200 MHz, $CDCl_3$): δ = 0.89 (s, 6H, eq CH_3), 1.24 (s, 6H, ax CH_3), 1.41 (d, J = 14 Hz, 2H, CH_2), 1.69 (m, 1H, allyl CH), 1.84 (s, br, allyl CH_3), 1.94 (t, J = 8.5 Hz, 2H, CH_2C-O), 2.53 (t, J = 8.5 Hz, 2H, $CH_2C=O$), 4.82 + 5.08 (s, br, 1H each, 2 olefin H). – MS: m/z (%) = 250 (8, M^+), 139 (100), 97 (38), 96 (77). – Exact mass calcd. for $C_{16}H_{26}O_2$, 250.193281; found 250.196487.

$C_{16}H_{26}O_2$ (250.4) Calcd. C 76.81 H 10.40
Found C 76.24 H 10.35

10-E: A flame-dried 100-ml two-necked flask with septum, reflux condenser with nitrogen inlet and magnetic stirrer was charged with diisopropylamine (1.01 g, 10 mmol) in ether (5 ml), and 1.5 M *n*-butyllithium (6.7 ml, 10 mmol) in hexane was slowly syringed in. The solution was stirred for 10 min at –10 °C, the solvent was evaporated in vacuo and replaced by absol. dioxane (15 ml). A solution of glacial acetic acid (0.3 g, 5 mmol) in absol. dioxane (2 ml) was vigorously stirred in at room temperature, and the mixture was warmed to 30–35 °C for 30 min. Spiroepoxide **6-E** (0.21 g, 1 mmol) in dioxane (5 ml) was added, the mixture was refluxed for 20 h, cooled to 0 °C, and ice/water (25 ml) was added slowly. The organic phase was separated and twice extracted with water (10 ml each). The combined aqueous phase was washed with ether and, after addition of ethanol (10 ml), warmed to 50 °C. The mixture was acidified with 6 N HCl against congo red, maintained for 3 h at 50 °C, cooled and extracted with $CHCl_3$ (3 × 10 ml). The combined organic phase was washed with 2 N NaOH (2 × 5 ml), aqueous NaCl (10 ml), and dried ($MgSO_4$). After removal of the solvent the residue was recrystallized from ether/light petroleum (1:1), giving a colourless solid; yield 0.1 g (40%), m.p. 132 to 134 °C. – IR (KBr): 2945 cm^{-1} s, 1778 vs, 1763 vs, 1185 s. – The two carbonyl bands indicated the presence of two rotamers in the solid. In $CHCl_3$ one carbonyl band was visible. – ^1H NMR (200 MHz, $CDCl_3$): δ = 0.98 (s, br, 3H, eq CH_3), 1.14 (s, 3H, ax CH_3), 1.75 (d, J = 0.5 Hz, 4H, $2CH_2$), 1.85 (s, 4H, allyl CH_3 and allyl CH), 2.17–2.4 (m, br, 2H, CH_2C-O), 2.62 (t, 2H, $CH_2-C=O$), 4.72 + 5.08 (s, br, 1H each, 2 olefin H). – ^{13}C NMR (20 MHz, $CDCl_3$): δ = 24.94 (m, br, allyl CH_3), 29.0 (t, $CH_2C=O$), 31.27 (m, br), 34.05 (q, $4CH_3$), 35.67 [s, br, 2 $(CH_2)_3C$], 50.74 [t, 2 $(CH_3)_2CCH_2$], 60.28 (m, br, CH), 87.18 [s, $(CH_3)_2C-O$], 113.1 (m, br, $C=CH_2$), 144.4 (s, $C=CH_2$), 176.0 (s, C=O). – MS (80 °C): m/z (%) = 250 (3, M^+), 139 (100), 97 (23), 96 (62). – Exact mass calcd. for $C_{16}H_{26}O_2$, 250.193281; found 250.193328.

7,7,9,9-Tetramethyl-8-(1-methylethenyl)-1-oxaspiro[4.5]decane (**11-Z**): A 25-ml flask with septum, magnetic stirrer and drying tube was charged with diol **9-Z** (0.53 g, 2 mmol), DMAP (12 mg, 0.1 mmol), and DABCO (0.34 g, 6 mmol) in absol. $CHCl_3$ (10 ml). Methanesulfonyl chloride (0.28 g, 2.4 mmol) in $CHCl_3$ (2 ml) was stirred in at 0 °C. The reaction mixture was stirred overnight, taken up in ether (50 ml), washed with water (3 × 10 ml each), and dried (Na_2SO_4). After removal of the solvent the residue was filtered through silica gel (10 g) with ether-light petroleum (1:10). The solid so obtained was recrystallized from light petroleum at –20 °C; yield 0.34 g (72%), m.p. 35–36 °C. – IR ($CHCl_3$): 2950 cm^{-1} vs, 1060 s, 1038 s. – ^1H NMR (90 MHz, $CDCl_3$): δ = 0.84 (s, 6H, eq CH_3), 1.26 (s, 6H, ax CH_3), 1.29 (d, 2H, ax CH_2), 1.51–1.7 [m, 6H eq CH_2, CH_2CH_2O, $CH_2(CH_2)_2O$], 1.94 (s, 4H, allyl CH_3 + allyl CH), 3.83 (t, J = 6.5 Hz, 2H, CH_2O), 4.78 + 5.0 (s, br, 1H each, 2 olefin H). – MS: m/z (%) = 236 (8, M^+), 125 (100), 97 (33), 96 (99). – Exact mass calcd. for $C_{16}H_{28}O$, 236.214016; found 236.214005.

$C_{16}H_{28}O$ (236.4) Calcd. C 81.29 H 11.94
Found C 80.74 H 11.74

11-E: The compound was prepared as described for **11-Z**: Diol **9-E** (0.42 g, 1.7 mmol), DMAP (15 mg, 0.12 mmol), DABCO (0.88 g, 6 mmol) in 8 ml of absol. $CHCl_3$, methanesulfonyl chloride (0.28 g, 2.4 mmol) in 2 ml of absol. $CHCl_3$. The resulting product mixture was chromatographed (silica gel, 20 g, ether/light petroleum, 1:10) giving a colourless solid; yield 0.18 g (45%), m.p. 33–35 °C. – IR ($CHCl_3$): 3000 cm^{-1} s, 2955 s, 1050 m. – ^1H NMR (90 MHz, $CDCl_3$): δ = 0.93 (s, 6H, eq CH_3), 1.1 (s, 6H, ax CH_3), 1.26 (s, 1H, allyl CH), 1.42 (d, J = 3.5 Hz, 4H, $2CH_2$), 1.5–2.1 [m, 4H, CH_2CH_2O, $CH_2(CH_2)_2O$], 1.82 (s, 3H, allyl CH_3), 3.72 (t, 2H, CH_2O), 4.69 + 5.0 (s, br, 1H each, 2 olefin H). – MS: m/z (%) = 236 (5, M^+), 125 (93), 97 (30), 96 (100). – Exact mass calcd. for $C_{16}H_{28}O$, 236.214016; found 236.214005.

3,3,5,5-Tetramethyl-1-methylene-4-(1-methylethenyl)-2-methylsulfonylcyclohexane (**14**): In a 100-ml round-bottomed flask with dropping funnel, drying tube, and magnetic stirrer allylic alcohol **13** (2.08 g, 10 mmol) and DMAP (80 mg, 0.7 mmol) were dissolved in absol. pyridine (20 ml). A solution of methanesulfonyl chloride (1.75 g, 11 mmol) in absol. pyridine (8 ml) was stirred in at –5 °C and the mixture was stirred for further 24 h at 0 °C. After addition of ice/water (20 ml) the resulting mixture was added to ether (50 ml), the aqueous phase was separated and extracted with ether (2 × 20 ml). For the removal of pyridine the combined organic phase was washed with several portions (20 ml each) of ice-cold 10% HCl until the aqueous phase was acidic. The organic phase was washed with 10 ml of aqueous $NaHCO_3$ and NaCl, and then dried (Na_2SO_4). The solvent was evaporated at 0 °C to leave yellow

crystals, which were dissolved at r. t. in the minimum amount of ether-light petroleum (1:1) and allowed to crystallize at −40°C. Recrystallization was repeated until the crystals were colourless. The resulting secondary allylic mesylate was very sensitive and had to be stored at −20°C. Fast workup was desirable; yield 2.3 g (80%), m.p. 71°C. – IR (KBr): 2975 cm^{-1} s, 1352 s, 1172 vs. – ^1H NMR (90 MHz, $CDCl_3$): δ = 0.97 + 1.02 + 1.04 + 1.08 (s, 3H each, $4CH_3$), 1.84 (s, 3H, allyl CH_3), 1.96–2.4 [m, 3H, allyl CH_2, $(CH_3)_2CH$], 2.96 (s, 3H, CH_3SO_3), 4.61 (s, 1H, $CHOSO_2Me$), 4.77 (s, 1H, $CH_3C=CH_2$), 5.0 + 5.17 (m, 3H, 2 methylene-H + $CH_3C=CH_2$). – MS: *m/z* (%) = 286 (0.5, M^+), 207 (12), 190 (38), 175 (57), 164 (32), 149 (35), 147 (43), 135 (51), 133 (37), 121 (46), 119 (61), 111 (27), 107 (48), 105 (43), 97 (100), 96 (98). – Exact mass calcd. for $C_{14}H_{23}O$ (M^+ – 79), 207.174891; found 207.174836.

⟨[3,3,5,5-Tetramethyl-4-(1-methylethenyl)-cyclohexenyl]methyl⟩-triphenylphosphonium Methanesulfonate (**15**): A solution of mesylate **14** (1.72 g, 6 mmol) and PPh_3 (1.73 g, 6.6 mmol) in $CHCl_3$ (15 ml) was warmed at 50°C for 20 h. The solution was transferred into a 250-ml flask and the solvent was removed in vacuo, leaving a voluminous and viscous mass. After addition of ether (50 ml) and stirring for 30 min, a colourless powder resulted, which was suction-filtered, washed with plenty of ether, and dried in vacuo; yield 2.85 g (87%), m.p. 132–136°C. – IR (KBr): 2965 cm^{-1} m, 1435 s, 1200 vs, 1112 s. – ^1H NMR (200 MHz, $CDCl_3$): δ = 0.75 + 0.76 + 0.9 + 0.92 (s, 12H, $4CH_3$), 1.55–1.67 (m, 3H, allyl CH_2), 1.76 (s, 4H, allyl CH_3 + CH), 2.71 (s, 3H, SO_2CH_3), 4.36 (d, J_{gem} = 7.5 Hz, 2H, CH_2PPh_3), 4.65 + 4.94 (s, 1H each, $CH_3C=CH_2$), 5.24 [m, 1H, $(CH_3)_2CCH=C$], 7.63–7.89 (m, 15H, 3 phenyl). – MS: (280°C): *m/z* (%) = 453 (27, M^+ of cation), 437 (57), 356 (32), 341 (30), 262 (100), 183 (70), 108 (33). – Exact mass calcd. for $C_{32}H_{38}P$ (M^+ of cation), 453.2711155; found 453.2782061.

1-Ethenyl-3,3,5,5-tetramethyl-4-(1-methylethenyl)cyclohexene (**16**): Aqueous NaOH (50%, ca. 2.2 ml) was stirred into a solution of phosphonium salt **15** (1.4 g, 2.6 mmol) in aqueous HCHO (11.7 ml) until the temperature inside the flask had reached 50°C. A further portion (0.2 ml) of sodium hydroxide was added and the mixture was stirred for 2 h and extracted with ether (3 × 10 ml). The combined ether phase was dried (Na_2SO_4) and the bulk of the solvent was removed at normal pressure. The crude product was filtered through silica gel (5 g) with pentane and the pentane was taken off at normal pressure (the product is volatile in vacuo) to give a colourless liquid; yield 0.34 g (64%). – IR ($CHCl_3$): 2970 cm^{-1} s, 1640 m, 1603 m. – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.01 + 1.02 + 1.06 (s, 12H, $4CH_3$), 1.84 (m, 3H, allyl CH_3), 1.93 (s, br, 1H, allyl CH), 1.96 + 2.04 (d, J_{gem} = 10 Hz, 1H each, allyl CH_2), 4.73 + 4.97 (s, 1H each, $CH_3C=CH_2$), 4.92 (d, J_{cis} = 11 Hz, 1H, H_A), 5.07 (d, J_{trans} = 17.5 Hz, 1H, H_B), 5.45 (m, 1H, H_D), 6.37 (dd, J_{cis} = 11 Hz, J_{trans} = 17.5 Hz, 1H, H_C). – MS: *m/z* (%) = 204 (14, M^+), 189 (18), 133 (25), 96 (100), 93 (75). – Exact mass calcd. for $C_{15}H_{24}$, 204.1878014; found 204. 1877841.

Dimethyl 3,5,6,7,8,8a-Hexahydro-6,6,8,8-tetramethyl-7-(1-methylethenyl)naphthaline-1,2-dicarboxylate (**17**): Diene **16** (1.1 g, 5.6 mmol) and dimethyl acetylenedicarboxylate (1.59 g, 11.3 mmol) in absol. toluene (30 ml) were refluxed for 3 d under N_2. The solvent was removed in vacuo, and the product was chromatographed (silica gel, 100 g, ether/light petroleum, 1:3), affording a colourless solid which contained the two diastereoisomers in a ratio of 1:1. Slow crystallization from light petroleum gave one compound in 90% isomeric purity, albeit with considerable losses; yield 1.26 g (65%) mixture, m.p. 87–92°C. – IR ($CHCl_3$): 2970 cm^{-1} m, 1730 vs, 1442 s, 1275 vs. – ^1H NMR (200 MHz, $CDCl_3$, 90% isomeric purity): δ = 0.85 (s, 3H) + 0.92 (s, 6H) + 0.98 (s, 3H) ($4CH_3$), 1.81 (s, 3H, allyl CH_3), 1.93 (s, 1H, $[(CH_3)_2C]_2CH$), 1.98 [s, 2H, $(CH_3)_2CCH_2$], 2.87 (m, 1H, diallyl CH), 3.01–3.17 (m, 2H, diallyl CH_2), 3.73 (s, 3H) + 3.76 (s, 3H) ($2CO_2CH_3$), 4.75 + 5.04 (s, 1H each, $CH_3C=CH_2$), 5.48 (m, 1H, olefin CH). – MS: *m/z* (%) = 346 (4, M^+), 250 (29), 176 (23), 149 (27), 97 (100). – Exact mass calcd. for $C_{21}H_{30}O_4$, 346.2144108; found 346.2142454.

(Z)-1-(3-Hydroxy-1-propynyl)-3,3,5,5-tetramethyl-4-(1-methylethenyl)-1-cyclohexanol (**18**): A 10-ml two-necked flask with septum, magnetic stirrer and nitrogen inlet was filled with N_2 and charged with THF (2 ml) and 1.6 ml (2.5 mmol) of a 1.5 M solution of *n*-butyllithium in hexane. The mixture was cooled to −30°C and 3-(tetrahydropyran-2-yloxy)propyne (0.35 g, 2.5 mmol) in absol. THF (0.5 ml) was dropped in. After 10 min a solution of TM-isocrypton (**8**) (0.195 g, 1 mmol) in absol. THF (0.5 ml) was dropped in and the mixture was allowed to reach room temperature. After being stirred for 3 d, the mixture was quenched with 2 ml of half-concentrated aqueous NH_4Cl, and the aqueous phase was extracted with ether (3 × 15 ml). The combined organic phase was dried (Na_2SO_4), the solvent was evaporated, and the THF ether was cleaved with pyridinium tosylate as described for **9-Z**. After recrystallization from $Et_2O/CHCl_3$ (10:1) a light yellow powder was obtained; yield 0.13 g (52%), m.p. 175–179°C. – IR (KBr): 3320 cm^{-1} s, br, 2955 s, 2865 m, 1188 m, 1022 s. – ^1H NMR (200 MHz, [D_6]DMSO): δ = 0.8 (s, 6H, eq CH_3), 1.18 (s, 6H, ax CH_3), 1.37 (d, J_{gem} = 13 Hz, 2H, ax CH_2), 1.58 (s, br, 1H, allyl CH), 1.70 (s, 3H, allyl CH_3), 1.74 (d, 2H, eq CH_2), 4.06 (d, *J* = 5 Hz, 2H, CH_2OH), 4.72 (s, 1H, olefin H), 5.0 + 5.05 (m, 2H, olefin H + OH), 7.0–7.7 (s, br, OH). – MS (200°C): *m/z* (%) = 250 (0, M^+), 232 (2), 139 (65), 97 (23), 96 (100). – Exact mass calcd. for $C_{16}H_{24}O$ (M^+ – 18), 232.1827161; found 232.1826126.

2,3,4,5,6,7-Hexahydro-4,4,6,6-tetramethyl-5-(1-methylethenyl)-1H-inden-1-one (**19**): A 10-ml round-bottomed flask with nitrogen inlet and magnetic stirrer was charged with P_4O_{10} (0.34 g, 1.2 mmol) and freshly distilled methanesulfonic acid (3.56 g, 37 mmol). The mixture was stirred at 80°C until the P_4O_{10} had dissolved, it was then cooled to −10 to −15°C, and diol **18** (0.25 g, 1 mmol) was added in portions. The mixture was stirred for 20 min at r. t., poured into ice/water (10 ml) and extracted with ether (5 × 10 ml). The combined organic phase was washed with aqueous $NaHCO_3$ (10 ml), dried ($MgSO_4$), and the solvent was evaporated to leave a yellow oil which was chromatographed on silica gel (20 g, ether/light petroleum, 1:1), giving a light yellow solid; yield 0.19 g (43%), m.p. 40–43°C. – IR ($CHCl_3$): 2965 cm^{-1} s, 2930 s, 1685 vs, 1635 vs. – ^1H NMR (200 MHz, $CDCl_3$): δ = 0.99 + 1.02 + 1.19 + 1.21 (s, 3H each, $4CH_3$), 1.83 (s, 3H, $CH_3C=CH_2$), 1.92 (m, 1H, allyl CH), 2.01–2.12 [m, 2H, $(CH_3)_2CCH_2$], 2.39–2.47 (m, 2H, $O=CCH_2CH_2$), 2.54–2.63 (m, 2H, $O=CCH_2$), 4.74 + 5.03 (s, 1H each, olefin H). – MS: *m/z* (%) = 232 (34, M^+), 217 (17), 135 (25), 119 (24), 96 (100). – Exact mass calcd. for $C_{16}H_{24}O$, 232.1827161; found 232.1826126.

3,3,5,5-Tetramethyl-4-(1-methylethenyl)-1-cyclohexenyl]acetonitrile (**20**): A suspension of KCN (92 mg, 1.4 mmol), 18-crown-6 (14 mg, 0.05 mmol), and mesylate **14** (0.2 g, 0.7 mmol) in absol. MeCN (2 ml) was stirred for 6 h at 50°C under exclusion of moisture (it is important to maintain the temperature exactly as described). After addition of water (5 ml) the mixture was extracted with CH_2Cl_2 (3 × 30 ml) and dried (Na_2SO_4). The solvent was removed to give a yellow oil; yield 0.14 g (92%). – IR (capillary film): 2970 cm^{-1} s, 2905 s, 2255 w, 1645 m, 1635 m. – ^1H NMR (200 MHz, $CDCl_3$): δ = 0.98 + 1.01 + 1.05 + 1.07 (s, 12H, $4CH_3$), 1.83 (m, 4H, allyl CH_3 + allyl-CH), 1.89–2.03 (m, 2H, CH_2), 2.99 (s, br, CH_2CN), 4.74 + 4.98 (s, br, 1H each, $CH_3C=CH_2$), 5.47 (m,

br, cyclohexenyl H). – MS: *m/z* (%) = 217 (3, M^+), 202 (2), 96 (100), 81 (39). – Exact mass calcd. for $C_{15}H_{23}N$, 217.1830503; found 217.1830058.

1-Ethyl-3,3,5,5-tetramethyl-4-(1-methylethenyl)cyclohexene (**21**): A 25-ml two-necked flask with septum, nitrogen inlet and magnetic stirrer was charged with CuI (0.29 g, 1.5 mmol) in absol. ether (3 ml). The mixture was cooled to −10°C, and 1.9 ml (3 mmol) of a 1.6 M solution of methyllithium in ether was stirred in, resulting in a light yellow solution. Mesylate **14** (0.29 g, 1 mmol) in absol. ether (6 ml) was added dropwise, and the mixture was stirred for 2 h at −10°C. The mixture was poured into saturated aqueous NH_4Cl (10 ml) and stirred for 10 min. The resulting dark-blue solution was extracted with ether (3 × 10 ml) and the combined organic phase was washed with water (3 × 5 ml), dried ($MgSO_4$) and the solvent was removed to leave a colourless liquid; yield 0.16 g (80%). – IR (capillary film): 2970 cm^{-1} s, 2885 m, 1645 w, 1630 w. – ^1H NMR (90 MHz, $CDCl_3$): δ = 0.94 + 0.97 + 1.0 + 1.03 (s, 15H, 5 CH_3), 1.82 (s, 3H, allyl CH_3), 1.70–1.96 (m, 5H, 2 CH_2 + CH), 4.7–4.93 (s, 1H each, $CH_3C{=}CH_2$), 5.06 (s, 1H, cyclohexenyl H). – MS: *m/z* (%) = 206 (5, M^+), 191 (7), 110 (73), 97 (100), 96 (85), 82 (40). – Exact mass calcd. for $C_{15}H_{26}$, 206.2034515; found 206.2033938.

1-Bromomethyl-3,3,5,5-tetramethyl-4-(1-methylethenyl)cyclohexene (**22**): Mesylate **14** (1.49 g, 5.2 mmol) and anhydrous LiBr (0.9 g, 10.4 mmol) in absol. DMF (20 ml) were heated under exclusion of moisture at 50°C for 3.5 h (it is important to maintain the temperature exactly as described, see above). The mixture was poured into water (80 ml) and extracted with light petroleum (4 × 30 ml). The organic phase was washed with aqueous NaCl, dried (Na_2SO_4), and the solvent was removed at r. t. The residue was filtered rapidly through silica gel (10 g) with light petroleum, giving a colourless oil, which was stored at −20°C; yield 1.37 g (97%). – IR ($CHCl_3$): 2960 cm^{-1} vs, 2875 s, 1662 w, 1640 w, 1625 w. – ^1H NMR (200 MHz, $CDCl_3$): δ = 0.99 + 1.0 + 1.01 + 1.05 (s, 12H, 4 CH_3), 1.82 (m, 3H, allyl CH_3), 1.93–1.97 (m, 3H, allyl CH_2 + allyl CH), 3.91 + 3.97 (dd, *J* = 9 Hz, 2H, CH_2Br), 4.73 + 4.98 (s, 1H each, $CH_3C{=}CH_2$), 5.55 (m, 1H, cyclohexenyl H). – MS: *m/z* (%) = 272/270 (1, M^+), 191 (16), 135 (15), 96 (100). – Exact mass calcd. for $C_{14}H_{23}Br$, 270.0983083; found 270.0981942.

Dimethyl 2-{[3,3,5,5-Tetramethyl-4-(1-methylethenyl)-1-cyclohexenyl]methyl}malonate (**23**): A flame-dried 25-ml two-necked flask with septum, reflux condenser with nitrogen inlet and magnetic stirrer was filled with N_2 and charged with a solution of freshly distilled dimethyl malonate (1.32 g, 10 mmol) in absol. THF (5 ml). A solution (5.6 ml, 10 mmol) of 1.8 M isopropylmagnesium chloride in THF was stirred in at 0°C. The mixture was allowed to reach r. t., a solution of mesylate **14** (1.1 g, 3.9 mmol) in absol. THF (5 ml) was dropped in and heated together at 70°C for 20 h. The mixture was poured on ice, diluted with ether (50 ml), and shaken with saturated aqueous NH_4Cl (20 ml). The aqueous phase was extracted with ether (3 × 20 ml), the combined organic phase was washed with aqueous $NaHCO_3$ and dried (Na_2SO_4). The solvent was removed and the residue was distilled (kugelrohr) to give a colourless oil; yield 0.95 g (77%), b.p. 185°C/0.05 Torr. – IR (capillary film): 2970 cm^{-1} vs, 2885 s, 1767 vs, 1748 vs, 1240 s, 1158 s. – ^1H NMR (90 MHz, $CDCl_3$): δ = 0.93 + 0.98 + 1.01 (s, 12H, 4 CH_3), 1.74 [m, 2H, $(CH_3)_2CCH_2$], 1.81 (s, 3H, allyl CH_3), 1.91 (s, 1H, allyl CH), 2.52 [d, *J* = 8 Hz, 2H, $CH_2CH(CO_2Me)_2$], 3.72 (s, 6H, 2 CO_2CH_3), 4.69 + 4.94 (s, br, 1H each, $CH_3C{=}CH_2$), 5.16 (s, br, 1H, cyclohexenyl H). – MS: *m/z* (%) = 322 (19, M^+), 307 (7), 226 (27), 194 (51), 162 (39), 107 (47), 96 (100). – Exact mass calcd. for $C_{19}H_{30}O_4$, 322.2144108; found 322.2143527.

3,3,5,5-Tetramethyl-4-(1-methylethenyl)-1-(3-phenyl-2-propynyl)-1-cyclohexene (**24**): A 10-ml two-necked flask with septum, reflux condenser, and magnetic stirrer was charged with 1.1 ml (2 mmol) of a 1.8 M solution of isopropylmagnesium chloride in THF under N_2. Phenylacetylene (0.2 g, 2 mmol) was slowly dropped in at r. t. and the mixture was warmed to 60°C for 45 min. After cooling to r. t. CuI (0.038 g, 0.2 mmol) was added in a counter-current of N_2. The mixture was stirred for 15 min at r. t., a solution of mesylate **14** (0.29 g, 1 mmol) in absol. THF (1 ml) was dropped in, and the mixture was warmed for 3 h to 60°C. The reaction mixture was transferred into a separating funnel containing ice-cold aqueous NH_4Cl (5 ml) and a trace of KCN, shaken well, and the aqueous phase was separated and extracted with ether (3 × 30 ml). The combined organic phase was washed with water (5 ml), dried (Na_2SO_4), and the solvent was removed at 0°C with a rotary evaporator to give a yellow oil (90% pure), which could be stored for only a short time, even in solution at −20°C; yield 0.22 g (75%). – IR ($CHCl_3$): 2964 cm^{-1} s, 2875 s, 1641 w, 1639 w. – ^1H NMR (90 MHz, $CDCl_3$): δ = 0.97 + 1.0 + 1.03 + 1.08 (s, 12H, 4 CH_3), 1.83 (m, 3H, allyl CH_3), 1.78–1.93 (m, 2H, allyl CH_2), 2.0 (s, 1H, allyl CH), 4.72 + 4.96 (m, 1H each, $CH_3C{=}CH_2$), 5.41 (m, 1H, $(CH_3)_2CCH{=}C$), 7.12–7.58 (m, 5H, phenyl H).

CAS Registry Numbers

1: 68930-33-6 / **4**: 83379-10-6 / *cis*-**5**: 113831-05-3 / *trans*-**5**: 113831-04-2 / **6-E**: 96043-23-1 / *cis*-**7**: 99474-99-4 / *trans*-**7**: 99510-30-2 / **8**: 83379-16-2 / **9-Z**: 113831-10-0 / **9-E**: 113831-11-1 / **9-Z** [CH(Me)-OEt]: 113831-12-2 / **10-Z**: 113831-13-3 / **10-E**: 113831-14-4 / **11-Z**: 113831-15-5 / **11-E**: 113831-16-6 / **12a**: 113831-17-7 / **12b**: 113831-18-8 / **12c**: 113831-19-9 / **13**: 81517-76-2 / **14**: 113831-20-2 / **15**: 113831-22-4 / **16**: 113831-23-5 / *cis*-**17**: 113857-70-8 / *trans*-**17**: 113831-24-6 / **18**: 113831-25-7 / **19**: 113831-26-8 / **20**: 113831-27-9 / **21**: 113831-28-0 / **22**: 113831-29-1 / **23**: 113831-30-4 / **24**: 113831-31-5 / 1-bromo-4,6-dioxa-5-methyloctane: 34399-67-2 / dimethyl acetylenedicarboxylate: 762-42-5 / 3-(tetrahydropyran-2-yloxy)-propyne: 6089-04-9 / dimethyl malonate: 108-59-8 / phenylacetylene: 536-74-3

[1] H. M. R. Hoffmann, H. Vathke-Ernst, *Chem. Ber.* **114** (1981) 1464.

[2] [2a] H. M. R. Hoffmann, *Progress Essential Oil Research*, (E.-J. Brunke, Ed.), p. 329, deGruyter, Berlin 1986. – [2b] W. R. Abraham, B. Stumpf, K. Kieslich, S. Reif, H. M. R. Hoffmann, *Appl. Microbiol. Biotechnol.* **24** (1986) 21.

[3] H. M. R. Hoffmann, D. Pauluth, *Liebigs Ann. Chem.* **1985**, 396.

[4] E. V. Dehmlow, M. Lissel, *Synthesis* **1979**, 372.

[5] G. Ohloff, C. Vial, E. Demole, P. Enggist, W. Giersch, E. Jégou, A. J. Caruso, J. Polonsky, E. Lederer, *Helv. Chim. Acta* **69** (1986) 163.

[6] W. Hasel, M. Schnick, M. Jansen, H. M. R. Hoffmann, *Chem. Ber.* **121** (1988) 1469; following paper.

[7] P. E. Eaton, G. F. Cooper, R. C. Johnson, R. H. Mueller, *J. Org. Chem.* **37** (1972) 1947.

[8] R. J. Giguere, G. von Ilsemann, H. M. R. Hoffmann, *J. Org. Chem.* **47** (1982) 4948.

[9] Cf. R. Broos, M. Anteunis, *Synth. Commun.* **6** (1976) 53.

[10] Cf. M. Ramaiah, *Synthesis* **1984**, 529.

[11] G. A. MacAlpine, R. A. Raphael, A. Shaw, A. W. Taylor, H. J. Wild, *J. Chem. Soc., Perkin Trans. 1*, **1976**, 410.

[12] [12a] *Review*: R. M. Magid, *Tetrahedron* **36** (1980) 1901. – [12b] F. G. Bordwell, *Acc. Chem. Res.* **3** (1970) 281.

[17/88]