172. Functionalized Cycloheptanes from Bicyclo[4.2.1]nonanes

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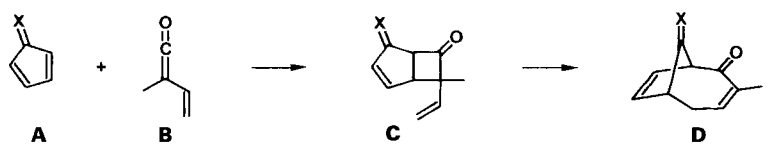
Summary

Several oxidative, reductive and C,C-cleavage reactions were performed starting from the three bicyclo[4.2.1]nona-3,7-diene-2-one derivatives **1**, **5** and **18**. The oxidations were selective and led to the diols **2**, **8** and **9**, and the epoxides **6**, **9**, and **20**. The reductions were selective only in the case of **20**→**21**; otherwise they led to mixtures of the alcohols **10** and **11**, and of the dienes **14** and **15**. The periodate ring cleavages afforded the functionalized cycloheptane derivatives **3**, **12**, **13** and **16**. Configurational assignments were made on the basis of detailed ^{1}H-NMR and X-ray analysis of **20**.

1. Introduction. – Recently, we described the two-step preparation of bicyclo-[4.2.1]nona-3,7-dien-2-one derivatives **D** by the [2 + 2]cycloaddition of vinylketenes **B** to cyclopentadiene and to 6,6-dimethylfulvene **A**, followed by a *Cope* rearrangement of the cycloadducts **C** [1]. We now report on some transformations of the readily available systems **D** to obtain specially functionalized cycloheptane derivatives.

Scheme 1

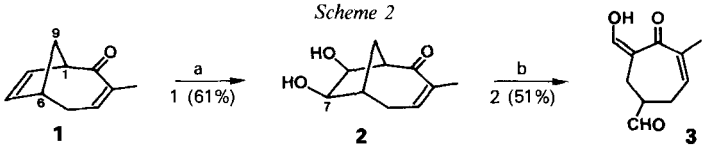


X = H_2 or $C(CH_3)_2$

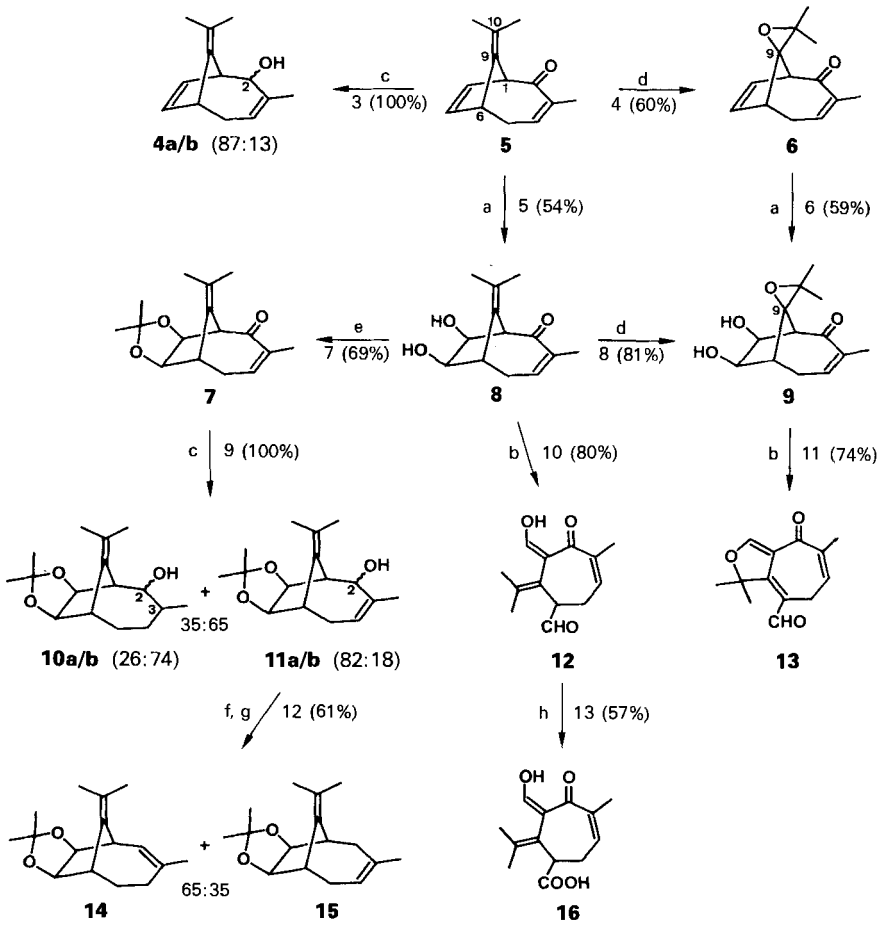
2. Transformations. – Our results are shown in *Schemes 2, 3* and *4*, where the reactions are numbered line by line from left to right. The same number is used for the corresponding experiment in the *Exper. Part.* Next to the reaction number, the yield is given in brackets and the method used is represented by a letter, referring to the legend below *Scheme 4*. Where more than one substance was isolated, the ratio in the crude product is mentioned. Additional comments, if required, are given in *Section 3*.

The starting materials were the bicyclic compounds **1** and **5**, prepared as described in [1] from α-methylbut-2-enoyl chloride and cyclopentadiene or 6,6-dimethylfulvene, respectively. For two exploratory experiments, we used the tricyclic compounds **18**/**19** synthesized by the same approach from 6,6-dimethylfulvene and the acid chloride **17**.

Scheme 2



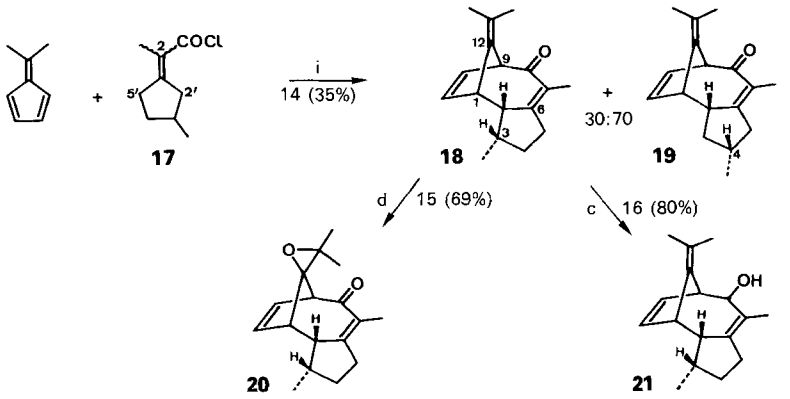
Scheme 3



The latter resulted from a condensation of 3-methylcyclopentanone with the *Wittig-Horner* reagent of α-bromo-propionic ester, followed by saponification and chlorination (see *Exper. Part*).

In addition to affording a number of cycloheptane derivatives containing special functional groups (compounds **3, 12, 13** and **16**) as synthetic intermediates, our results illustrate the following effects evidently characteristic for our bicyclononane systems:

Scheme 4



Methods. a: *N*-Methylmorpholine *N*-oxide, cat. OsO_4, THF/H_2O, r.t., 16 h [2]. b: $NaIO_4$, THF/H_2O or Et_2O/H_2O or H_2O, r.t., 5 min to 1 h. c: $NaBH_4$, EtOH, r.t., 4–8 h. d: *m*-chloroperbenzoic acid, CH_2Cl_2, 0°–r.t., 2–8 h. e: Acetone, TsOH, molecular sieve (3 Å), r.t., 16 h. f: MsCl, Et_3N, Et_2O, −50 to −20°, 16 h. g: $LiAlH_4$, THF, r.t., 2 h. h: Ag_2O (excess), NaOH, r.t., 45 min. i: Et_3N, hexane, reflux, 3 days.

1) The OsO_4 hydroxylation was site-selective at the least substituted, non-conjugated C(7),C(8)-double bond in the five-membered ring of the bicyclic compounds **1, 5** and **6** and stereoselective *(syn)* from the smaller bridge-side to give the diols **2, 8, 9** and hence the 1,3-dioxalane **7**. *2)* The attack of the peracid was site-selective at the most substituted, non-conjugated double bond of the compounds **5, 8** and **18** and stereoselective from the side of the CH=CH bridge to give the epoxides **6, 9** and **20**. *3)* With $NaBH_4$ in EtOH the carbonyl group of **5, 7** and **18** was reduced to allylic alcohols **4, 11** (both stereoisomers) and **21** (one stereoisomer); in the case of **7**, the double bond was first attacked in part of the molecules to give the saturated alcohols **10**. *4)* Mesylation of **11** followed by $LiAlH_4$ reduction led to a mixture of double-bond-isomeric dienes **14** and **15**. *5)* Periodate oxidation of **2, 8** and **9** cleaved the C(O),C(O)-bond to give the dialdehydes **3** and **12** in the absence of the epoxide group, but the formyl-dihydrofurane **13** in its presence.

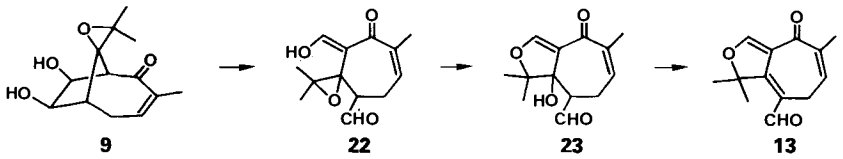
3. Remarks to Transformations. – *To Steps 1, 5 and 6.* The configuration of the two OH-groups in **2, 8** and **9** was deduced from the small ^{1}H-NMR coupling (1 and 1.5–2 Hz, respectively) between the H-pairs at C(7),C(6) and at C(8),C(1), which are in better agreement with known values for *endo*-(0–2 Hz) than for *exo*-(3–4 Hz) H-atoms at such positions in many norbornane systems [3].

To Step 3. Although **4a** and **4b** were separated by chromatography their configuration at C(2) could not be deduced.

To Steps 4 and 8. The configuration at C(9) of **6** and **9** (position of the epoxide O-atom) was assigned on the assumption of a similar stereoselectivity as found in the formation of **20** (see remark to *Step 15*).

To Step 9. Although the four alcohols **10a,b** and **11a,b** were separated by chromatography, the configuration at C(2) in **11** and the ones at C(2) and C(3) in **10** could not be deduced.

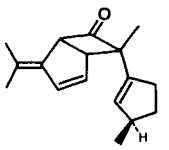
Scheme 5



To Step 11. A plausible mechanism for the conversion of **9** to **13** passes through the intermediates **22** and **23**.

To Step 12. The intermediate mesylate appears to react faster by S_N2' hydride attack (to give **14**) than by S_N2 attack (to give **15**).

To Step 14. The constitutional isomers **18** and **19** are formed from the two ketenes resulting by deprotonation of the acid chloride **17** at C(2') and C(5'), respectively. According to our previous experience [1] the initial adducts of these two ketenes should have been **24** and **25**. Since only **18** and **19** were isolated, it appears likely that the *Cope* rearrangements **24**→**18** and **25**→**19** had already occurred under the reaction conditions employed (3 days at 70°). Besides **18** and **19**, at least one other component, presumably



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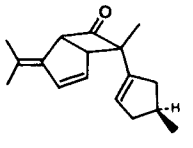

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a stereoisomer of either **18** or **19**, was observed in the GC of the crude reaction product. The constitutions and configurations of **18** and **19** were deduced by their 400-MHz ^{1}H-NMR spectra (see *Exper. Part*) and, in the case of **18**, confirmed by the X-ray analysis of its epoxidation product **20**.

To Step 15. The structure of the epoxide **20**, obtained by an X-ray analysis[1]), is shown in the stereoscopic plot of the *Figure*.

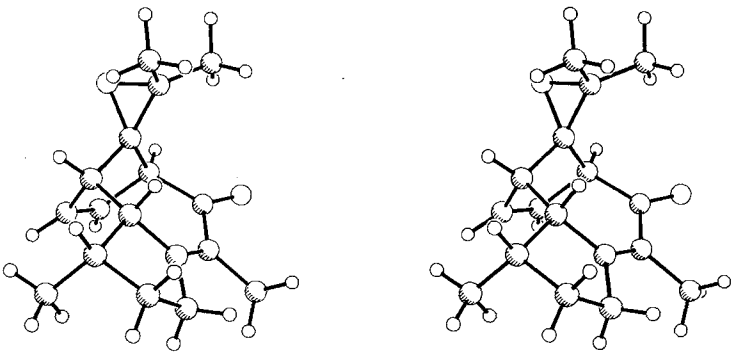

Figure. *Stereoscopic plot of the epoxide* **20**

[1]) This analysis was performed in our X-ray laboratory by Drs. *J.H. Bieri* and *R. Prewo*, who expect to publish details elsewhere.

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Experimental Part

General. See [1]. Selective ^{1}H-NMR decoupling experiments are indicated by a chemical shift value in square brackets behind the value of the coupling which is removed upon irradiation at the chemical shift.

1. *(1R*,6S*,7R*,8S*)-7,8-Dihydroxy-3-methylbicyclo[4.2.1]non-3-en-2-one* (**2**). A solution of 1.6 g (11 mmol) of *3-methylbicyclo[4.2.1]nona-3,7-dien-2-one* (**1**) [1], 1.6 g (12 mmol) *N*-methylmorpholine-*N*-oxide monohydrate and a catalytic amount of OsO_4 (50 mg) in 50 ml of THF/H_2O (9:1) was stirred at r.t. for 16 h [2]. A slurry of 8 g $MgSiO_3$ in 40 ml H_2O and 100 mg of $NaHSO_3$ was added, the mixture stirred for 1 h and filtered. The filtrate was extracted with EtOAc, dried and concentrated to give a solid residue, which was recrystallized from Et_2O/hexane to give 1.2 g (61%) of **2** as a colorless powder, m.p. 77–80°. UV (EtOH): 237 (8000). IR ($CHCl_3$): 3690*w*, 3400 br., 1655*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 6.28 (*m*, 1H, H–C(4)); 4.31 (*dd*, J = 5 [4.04] and 2 [2.97], 1H, H–C(8)); 4.04 (*dd*, J = 5 [4.31] and 1, H–C(7)); 3.0–3.9 (br., 2H, 2 OH); 2.97 (split *d*, J = 8, 1H, H–C(1)); 2.7–2.3 (*m*, 4H, 2H–C(5), H–C(6) and H–C(9)); 1.80 (split *s*, 3H, CH_3–C(3)); 1.74 (*d*, J = 8, 1H, H–C(9) *syn* to C(7)–C(8)). Anal. calc. for $C_{10}H_{14}O_3$ (182.22): C 65.91, H 7.74; found: C 65.15, H 7.59.

2. *6-Hydroxymethylidene-4-methyl-5-oxo-3-cycloheptenecarbaldehyde* (**3**). A solution of 182 mg (1 mmol) **2** and 214 mg (1 mmol) $NaIO_4$ in 5 ml THF/H_2O (1:1) was stirred for 1 h at r.t. and the product extracted with Et_2O. The Et_2O extract was dried, evaporated and the residue distilled at 150–170°/12 Torr, to give 92 mg (51%) of **3** as a yellow oil. UV (EtOH): 312 (5800), 260 (3750). IR ($CHCl_3$): 2730*w*, 1730*s*, 1642*s*, 1620*s*, 1570*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 15.0 (br. *s*, 1H, =O...H–O–); 9.60 (*s*, 1H, H–C=O); 8.17 (*s*, 1H, H–C=C(6)); 6.45 (*tq*, J = 7.5 and 1.5, 1H, H–C(3)); 2.87 (*quint.* J = 7, 1H, H–C(1)); 2.5–2.2 (*m*, 4H, 2H–C(2) and 2H–C(7)); 1.85 (br. *s*, 3H, CH_3–C(4)). MS: 180 (6, M^+), 105 (22), 96 (100), 79 (22), 66 (24). Anal. calc. for $C_{10}H_{12}O_3$ (180.21): C 66.60, H 6.71; found: C 66.36, H 7.00.

3. *(1R*,6S*)-2-Hydroxy-9-isopropylidene-3-methylbicyclo[4.2.1]nona-3,7-diene* (**4**). To an ice-cooled solution of 0.83 g (22 mmol) $NaBH_4$ in 75 ml abs. EtOH was added 2.3 g (12.2 mmol) of *(1R*,6S*)-9-isopropylidene-3-methylbicyclo[4.2.1]nona-3,7-dien-2-one* (**5**) [1] and the mixture stirred for 4 h at r.t. After removing the EtOH, H_2O was added and the mixture extracted with CH_2Cl_2, dried ($MgSO_4$) and concentrated to give 2.3 g (100%, crude) of a 87:13 (GC–A) mixture of the two diastereomers **4a** and **4b**. The components were separated by chromatography (LC–A, hexane/EtOAc 9:1).

Data for **4a** (95% pure, GC–A): m.p. 58–60°. IR ($CHCl_3$): 3590*m*, 3450 br., 1380*m*, 1005*s*, 985*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 5.90 and 5.77 (both *dd*, both J = 6 and 3, each 1H, H–C(7) and H–C(8)); 5.09 (br. *d*, J = 5, 1H, H–C(4)); 3.97 (br. *s*, 1H, H–C(2)); 3.64 (br. *s*, 1H, H–C(1)); 3.46 (br. *s*, 1H, H–C(6)); 2.41 and 2.15 (both br. *d*, both J = 18, each 1H, 2H–C(5)); 1.84 (split *s*, 3H, CH_3–C(3)); 1.80 and 1.75 (both *s*, each 3H, $(CH_3)_2$C=C(9)); 1.58 (br. *s*, 1H, OH). MS: 190 (2, M^+), 107 (65), 106 (100), 91 (43). Anal. calc. for $C_{13}H_{18}O$ (190.29): C 82.06, H 9.54; found: C 81.83, H 9.32.

Data for **4b** (99% pure, GC–A): m.p. 91–93°. IR ($CHCl_3$): 3600*m*, 3460 br., 1375*m*, 1225 br., 1000*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 6.12 and 5.98 (both *ddd*, both J = 6.5, 3, and 1, each 1H, H–C(7) and H–C(8)); 5.14 (br. *s*, 1H, H–C(4)); 4.24 (br. *s*, 1H, H–C(2)); 3.66 (br. *s*, 1H, H–C(1)); 3.40 (br. *s*, 1H, H–C(6)); 2.37 and 2.14 (both *dm*, both J = 18, each 1H, 2H–C(5)); 1.79 (split *s*, 3H, CH_3–C(3)); 1.72 and 1.68 (both *s*, each 3H, $(CH_3)_2$C=C(9)). MS: 190 (4, M^+), 107 (70), 106 (100), 91 (45). Anal. calc. for $C_{13}H_{18}O$ (190.29): C 82.06, H 9.54; found: C 82.17, H 9.29.

4. *(1R*,6S*,9R*)-3,3',3'-Trimethylspiro[bicyclo[4.2.1]nona-3,7-diene-9,2'-oxirane]-2-one* (**6**). An ice-cooled solution of 24.7 g (143 mmole) *m*-chloroperbenzoic acid in 300 ml dry CH_2Cl_2 was treated in portions with 26.0 g (138 mmol) **5** [1] during 30 min and stirred at r.t. for 8 h. After adding 50 ml 1N NaOH solution, the org. phase was separated, washed with sat. $NaHCO_3$ solution, dried (Na_2SO_4) and concentrated, leaving a solid residue, which was recrystallized from petrol ether to give 17.0 g (60%) of **6** as colorless plates, m.p. 67–69°. UV (EtOH): 236 (4200). IR (CCl_4): 1660*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 6.15 (br. *t*, $J \approx 4$, 1H, H–C(4)); 6.05–5.95 (*m*, 2H, H–C(7), H–C(8)); 3.39 (*d*, J = 2, 1H, H–C(1)); 2.81 (br. *s*, 1H, H–C(6)); 2.90 and 2.49 (both *dm*, both J = 19, each 1H, 2H–C(5)); 1.84 (split *s*, 3H, CH_3–C(3)); 1.39 and 1.25 (both *s*, each 3H, 2CH_3–C(3')). Anal. calc. for $C_{13}H_{16}O_2$ (204.27): C 76.44, H 7.90; found: C 76.09; H 8.23.

5. *(1R*,6S*,7R*,8S*)-7,8-Dihydroxy-9-isopropylidene-3-methylbicyclo[4.2.1]non-3-en-2-one* (**8**). Hydroxylation (as in *Exp. 1)* of 1.9 g (10 mmol) **5** [1] with 1.5 g (11 mmol) *N*-methylmorpholine-*N*-oxide monohydrate and 50 mg OsO_4, gave, after recrystallization from EtOAc, 1.2 g (54%) of **8** as colorless needles, m.p. 158–161°. UV (EtOH): 233 (8000). IR ($CHCl_3$): 3540 br., 3400 br., 1660*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 6.19 (br. *t*, $J \approx 4$, 1H, H–C(4)); 4.43 (*dd*, $J = 5$ [4.05] and 1.5, 1H, H–C(8)); 4.05 (*dd*, $J = 5$ [4.43] and 1 [3.15], 1H H–C(7)); 3.60 (br. *s*, 1H, H–C(1)); 3.40 (br. *s*, 1H, OH); 3.15 (br. *d*, $J = 6$, 1H, H–C(6)); 2.93 (br. *s*, 1H, OH); 2.64 and 2.42 (both *dm*, both $J = 20$, each 1H, 2H–C(5)); 1.81 (split *s*, 3H, CH_3–C(3)); 1.74 and 1.67 (both *s*, each 3H, $(CH_3)_2$C=C(9)). MS: 222 (5, M^+), 122 (47), 105 (22), 91 (45), 77 (37), 41 (100). Anal. calc. for $C_{13}H_{18}O_3$ (222.29): C 70.24, H 8.16; found: C 70.11, H 8.02.

6. *(1R*,6S*,7S*,8R*,9R*)-7,8-Dihydroxy-3,3',3'-trimethylspiro[bicyclo[4.2.1]non-3-ene-9,2'-oxirane]-2-one* (**9**). Hydroxylation (as in *Exp. 1*) of 4.1 g (20 mmol) **6** with 3.0 g (22 mmol) *N*-methylmorpholine-*N*-oxide monohydrate and 100 mg OsO_4 gave, after trituration with Et_2O, 2.8 g (59%) of a solid which was recrystallized from $CHCl_3$ to give **9** as colorless needles, m.p. 119°. UV (EtOH): 238 (7600). IR ($CHCl_3$): 3400 br., 1655*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 6.35 (br. *t*, $J \approx 4$, 1H, H–C(4)); 4.36 (*dd*, $J = 5$ [4.13] and 2 [2.92], 1H, H–C(8)); 4.13 (*dd*, $J = 5$ [4.36] and 1, 1H, H–C(7)); 2.92 (*dd*, $J = 3$ and 3 [4.36], 1H, H–C(1)); 2.75 and 2.40 (both *dm*, both $J = 20$, each 1H, 2H–C(5)); 2.4–2.3 (*m*, 1H, H–C(6)); 1.85 (split *s*, 3H, CH_3–C(3)); 1.35 and 1.23 (both *s*, each 3H, $2CH_3$–C(3')). ^{13}C-NMR ($CDCl_3$): 198.1 (*s*, C(2)); 139.6 (*d*, C(4)); 133.5 (*s*, C(3)); 79.4 and 76.8 (each *d*, C(7), C(8)); 73.0 (*s*, C(3')); 66.0 (*d*, C(1)); 59.0 (*s*, C(9)); 47.7 (*d*, C(6)); 30.9 (*t*, C(5)); 21.7, 21.5 and 21.1 (each *q*, CH_3–C(3), 2 CH_3–C(3')). MS: 220 (6, ($M^+ - H_2O$)), 161 (20), 147 (24), 133 (28), 120 (25), 109 (22), 105 (40), 95 (22), 93 (26), 91 (69). Anal. calc. for $C_{13}H_{18}O_4$ (238.14): C 65.53, H 7.61; found: C 65.51, H 7.34.

7. *(1R*,6S*,7R*,8S*)-7,8-*O*-Isopropylidene-9-isopropylidene-3-methylbicyclo[4.2.1]non-3-en-2-one* (**7**). To a solution of 1.1 g (4.95 mmol) of **8** in 60 ml acetone was added 250 mg TsOH and 5 g active molecular sieve (3Å). After stirring the reaction mixture for 16 h at r.t., 300 mg NaOAc was added and the mixture stirred for 30 min, filtered and concentrated to give 1.2 g (92%) of a viscous oil which, after distillation at 150°/0.03 Torr, yielded 900 mg (69%) of **7** as a colorless oil. IR (film): 1665*s*, 1385*s*, 1375*s*, 1215*s*, 1053*s*. UV (EtOH): 234 (7400). ^{1}H-NMR (200 MHz, $CDCl_3$): 6.17 (br. *t*, $J \approx 4$, 1H, H–C(4)); 4.64 and 4.46 (both *d*, both $J = 5.5$, each 1H, H–C(7) and H–C(8)); 3.72 (br. *s*, 1H, H–C(1)); 3.18 (br. *t*, $J \approx 3$, 1H, H–C(6)); 2.6–2.3 (*m*, 2H, 2H–C(5)); 1.83 (split *s*, 3H, CH_3–C(3)); 1.77 and 1.71 (both *s*, each 3H, $(CH_3)_2$C=C(9)); 1.37 and 1.28 (both *s*, each 3H, $2CH_3$–C(O,O)). MS: 262 (56, M^+), 166 (79), 160 (34), 141 (49), 131 (41), 107 (100), 90 (43), 68 (61), 55 (35). Anal. calc. for $C_{16}H_{22}O_3$ (262.35): C 73.25, H 8.45; found: C 72.98, H 8.70.

8. *Preparation of* **9** *from* **8**. Epoxidation (as in *Exp. 4*) of **8** (40 mg) with 1.1 mol-equiv. *m*-chloroperbenzoic acid at r.t. for 2 h gave 35 mg (81%) **9** (by ^{1}H-NMR).

9. *(1R*,6R*,7S*,8R*)-7,8-*O*-Isopropylidene-9-isopropylidene-3-methylbicyclo[4.2.1]nonan-2-ol* (**10**) *and (1R*,6R*,7S*,8R*)-7,8-*O*-Isopropylidene-9-isopropylidene-3-methylbicyclo[4.2.1]non-3-en-2-ol* (**11**). An ice-cooled suspension of 184 mg (4.9 mmol) $NaBH_4$ in 20 ml abs. EtOH containing 636 mg (2.4 mmol) of **7** was stirred at r.t. for 4 h, concentrated, poured into 50 ml H_2O and extracted three times with CH_2Cl_2. After drying ($MgSO_4$) and evaporating the solvent, 640 mg (100%) of a viscous oil containing **10a, 11a, 10b** and **11b** in a ratio of 9:53:26:12 (GC-A, order of elution) was obtained. Trituration of the oil with hexane yielded **11a** as colorless crystals, m.p. 92–93°. Multiple chromatography of the mother liquor material (LC-A and GC-B) gave **10a, 10b** and **11b** in small quantities as oils.

Data for **10a** (75% pure, GC–A): IR ($CDCl_3$): 3620*w*, 3570*m*, 1210*s*, 1043*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 4.35 and 4.27 (both *d*, both $J = 6$, each 1H, H–C(7) and H–C(8)); 3.61 (*m*, 1H, H–C(2)); 3.24 (br. *d*, $J = 4$, 1H, H–C(1)); 2.95 (br. *d*, $J = 10$, 1H, H–C(6)); 1.9–1.8 (*m*, 1H, H–C(3)); 1.76 and 1.64 (both *s*, each 3H, $(CH_3)_2$C=C(9)); 1.6–1.2 (*m*, 5H, 2H–C(4), 2H–C(5) and OH); 1.33 and 1.26 (both *s*, each 3H, $2CH_3$–C(O,O)); 0.93 (*d*, $J = 7$, CH_3–C(3)).

Data for **11a** (93% pure, GC–A): IR ($CDCl_3$): 3680*w*, 3570*m*, 1373*s*, 1211*s*, 1045*s*, 991*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 5.33 (br. *s*, 1H, H–C(4)): 4.26 and 4.20 (both *d*, both $J = 6$, each 1H, H–C(7) and H–C(8)); 4.01 (*dd*, $J = 11$ and 5.5, 1H, H–C(2)); 3.27 (br. *d*, $J = 5.5$, 1H, H–C(1)); 3.05 (br. *t*, $J \approx 3$, 1H, H–C(6)); 2.4–2.1 (*m*, 2H, 2H–C(5)); 1.86 (split *s*, 3H, CH_3–C(3)); 1.82 and 1.79 (both *s*, each 3H, $(CH_3)_2$C=C(9)); 1.51 (*d*, $J = 11$, 1H, OH); 1.37 and 1.26 (both *s*, each 3H, $2CH_3$–C(O,O)). MS: 264 (15, M^+), 206 (23), 122 (100). Anal. calc. for $C_{16}H_{24}O_3$ (264.37): C 72.69, H 9.15; found: C 72.63, H 9.29.

Data for **10b** (100% pure, GC–A): IR ($CDCl_3$): 3680*w*, 3620*m*, 1217*s*, 1044*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 5.08 and 4.27 (both *d*, both $J = 6$, each 1H, H–C(7) and H–C(8)); 3.96 (*dd*, $J = 9$ and 4, 1H, H–C(2)); 3.2–3.0 (*m*, 2H, H–C(1) and H–C(6)); 1.69 and 1.65 (both *s*, each 3H, $(CH_3)_2$C=C(9)); 1.37 and 1.29 (both *s*,

each 3H, $2CH_3$–C(O,O)); 1.5–1.1 (*m*, 6H, H–C(3), 2H–C(4), 2H–C(5) and OH); 0.92 (*d*, $J = 7$, 3H, CH_3–C(3)).

Data for **11b** (100% pure, GC–A): IR ($CDCl_3$): 3690*m*, 3600*m*, 1375*m*, 1216*s*, 1043*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 5.25 (br. *s*, 1H, H–C(4)); 4.52 and 4.18 (both *d*, both $J = 6$, each 1H, H–C(7) and H–C(8)); 4.03 (br. *s*, 1H, H–C(2)); 3.05 (br. *d*, $J = 4$, 1H, H–C(1)); 2.97 (br. *t*, $J \approx 3$, 1H, H–C(6)); 2.3–2.0 (*m*, 2H, 2H–C(5)); 1.79 (split *s*, 3H, CH_3–C(3)); 1.73 and 1.69 (both *s*, each 3H, $(CH_3)_2$C=C(9)); 1.36 and 1.26 (both *s*, each 3H, $2CH_3$–C(O,O)).

10. *6-Hydroxymethylidene-7-isopropylidene-4-methyl-5-oxo-3-cycloheptenecarbaldehyde* (**12**). From 110 mg (0.5 mmol) **8** and 106 mg (0.5 mmol) $NaIO_4$ (as in *Exp. 2*) was obtained, after distillation at 140°/0.2 Torr, 88 mg (80%) of **12** as a yellow oil. UV (EtOH): 316 (4100), 259 (4200). IR ($CHCl_3$): 1727*s*, 1644*s*, 1618*s*, 1565*m*. ^{1}H-NMR (90 MHz, $CDCl_3$): 15.3 (br., 1H, =O...H–O–); 9.52 (*d*, $J = 1.5$, 1H, H–C=O); 8.20 (br. *s*, 1H, H–C=C(6)); 6.18 (*tq*, $J = 7.5$ and 1.5, 1H, H–C(3)); 3.90 (br. *dd*, $J = 10.5$ and 5, 1H, H–C(1)); 2.8–2.1 (*m*, 2H, 2H–C(2)); 1.92 (split *s*, 3H, CH_3–C(4)); 1.80 and 1.85 (both *s*, each 3H, $(CH_3)_2$C=C(7)). MS: 220 (30, M^+), 205 (100), 191 (84), 173 (30), 145 (59), 131 (42), 121 (45), 105 (57), 91 (79), 77 (54). Anal. calc. for $C_{13}H_{16}O_3$ (220.27): C 70.89, H 7.32; found: C 71.08, H 7.38.

11. *5,10,10-Trimethyl-6-oxo-9-oxabicyclo[5.3.0]deca-1,4,7-triene-2-carbaldehyde* (**13**). From 76 mg (0.3 mmol) **9** and 70 mg (0.3 mmol) $NaIO_4$ (as in *Exp. 2*) was obtained, after recrystallization from Et_2O/hexane, 52 mg (74%) of **13** as yellow powder, m.p. 130–132°. UV (EtOH): 333 (11300), 245 (8300). IR ($CHCl_3$): 1660 *m*, 1647*s*, 1630*s*, 1610*s*, 1550*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 9.86 (*s*, 1H, H–C=O); 8.04 (*s*, 1H, H–C(8)); 6.37 (*tq*, $J = 6.5$ and 2, 1H, H–C(4)); 3.30 (*dd*, $J = 6.5$ and 2, 2H, 2H–C(3)); 1.92 (split *s*, 3H, CH_3–C(5)); 1.78 (*s*, 6H $2CH_3$–C(10)). ^{13}C-NMR ($CDCl_3$): 189.2 (*s*, C(6)); 186.5 (*d*, CH=O); 168.2 (*d*, C(8)); 160.9 (*s*, C(1)); 139.8 (*d*, C(4)); 135.8, 122.7 and 121.6 (each *s*, C(2), C(7), C(5)); 96.1 (*s*, C(10)); 29.6 (*q*, CH_3–C(5)); 24.3 (*t*, (C(3)); 19.2 (*q*, 2 CH_3–C(10)). MS: 218 (18, M^+), 190 (100), 174 (31), 161 (41) 148 (38), 146 (20), 128 (20), 120 (21), 105 (23), 91 (32), 77 (22), 65 (13). Anal. calc. for $C_{13}H_{14}O_3$ (218.25): C 71.54, H 6.47; found: C 71.64, H 6.22.

12. *(1R*,6S*,7R*,8S*)-7,8-O-Isopropylidene-9-isopropylidene-3-methylbicyclo[4.2.1]non-2-ene* (**14**) *and -3-ene* (**15**). To a solution of 264 mg (1 mmol) of **11a** in 20 ml dry Et_2O at –50° was added 0.15 g (1.5 mmol) Et_3N and 171 mg (1.5 mmol) CH_3SO_2Cl and the mixture was allowed to stand at –20° for 18 h. The mixture was washed twice with cold 5% HCl, once with sat. Na_2CO_3 solution and once with brine. The org. phase was dried ($MgSO_4$) and concentrated to give 235 mg (70%) of the crude mesylate. A solution of the latter in 10 ml dry THF was treated with 43 mg (1.1 mmol) $LiAlH_4$ at 0° and the mixture stirred at r.t. for 2 h. After cautiously adding a sat. solution of sodium potassium tartarate, the mixture was extracted with Et_2O, dried ($MgSO_4$) and concentrated to give 150 mg (61%) of 65:35 mixture of **14/15** (GC-A and ^{1}H-NMR) as an oil, which was separated by GC-B.

Data for **14** (95% pure, GC–A): IR ($CDCl_3$): 2930*s*, 1265*s*, 1215*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 5.64 (br. *d*, $J = 9$, 1H, H–C(2)); 4.45 and 4.41 (both *d*, both $J = 6$, each 1H, H–C(7), H–C(8)); 3.1–3.0 (*m*, 2H, H–C(1), H–C(6)); 2.0–1.9 (*m*, 2H, 2H–C(4)); 1.66 (*s*, 9H, CH_3–C(3), $(CH_3)_2$C=C(9)); 1.8–1.6 (*m*, 2H, 2H–C(5)); 1.35 and 1.27 (both *s*, each 3H, $2CH_3$–C(O,O)).

Data for **15** (96% pure, GC–A): IR ($CDCl_3$): 2930*s*, 1260*s*, 1220*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 5.22 (br. *s*, 1H, H–C(4)); 4.20 and 4.16 (both *d*, both $J = 6$, each 1H, H–C(7), H–C(8)); 2.95 (br. *s*, 2H, H–C(1), H–C(6)); 2.2–2.0 (*m*, 4H, 2H–C(2), 2H–C(5)); 1.70 (*s*, 9H, CH_3–C(3), $(CH_3)_2$C=C(9)); 1.37 and 1.25 (both *s*, each 3H, $2CH_3$–C(O,O)).

13. *6-Hydroxymethylidene-7-isopropylidene-4-methyl-5-oxo-3-cycloheptenecarboxylic Acid* (**16**). To a suspension of 1.0 g (6.5 mmol) $AgNO_3$ in 25 ml of 1N NaOH, 75 ml H_2O and 100 ml EtOH was added 440 mg (2.0 mmol) of **12** in 5 ml EtOH. After stirring at r.t. for 3 h, the mixture was filtered, the EtOH removed and the H_2O-solution washed with Et_2O, acidified with 10% HCl and extracted with Et_2O. Drying and evaporating the extract left a solid residue, which was triturated with pentane to yield 270 mg (57%) **16** as a colorless solid, m.p. 136–139°. IR ($CHCl_3$): 3600–2400 br., 1705*s*, 1650*m*, 1620*s*, 1570*s*. ^{1}H-NMR (90 MHz, $CDCl_3$): 8.15 (*s*, 1H, H–C=C(6)); 6.05 (split *t*, $J = 7.5$, 1H, H–C(3)); 3.85 (*dd*, $J = 9$ and 7, 1H, H–C(1)); 2.7–2.2 (*m*, 2H, 2H–C(2)); 1.85 (*s*, 3H, CH_3–C(4)); 1.80 and 1.70 (both *s*, each 3H, $(CH_3)_2$C=C(7)).

14a. *2-(3'-Methylcyclopentylidene)propionyl Chloride* (**17**). A suspension of 4.75 g (109 mmol) NaH (55% dispension in mineral oil) in 30 ml dry dimethoxyethane, to which had been added 23.8 g (100 mmol) triethyl 2-phosphonopropionate, was stirred for 1 h at r.t., treated with 10.7 g (109 mmol) 3-methylcyclopentanone at once and then refluxed for 4 h. After cooling and adding 30 ml H_2O, the mixture was extracted with Et_2O, the extract dried (Na_2SO_4) and concentrated. A solution of the residual ester and 8.0 g (200 mmol) NaOH in 70 ml

3:4 EtOH/H_2O was heated for 8 h, concentrated, washed with Et_2O, acidified with 10% HCl and extracted with Et_2O. The Et_2O-extracts were dried (Na_2SO_4) and concentrated, leaving a residue which was recrystallized from petrol ether to give 11.5 g (75%) of 2-(3'-methylcyclopentylidene)propionic acid as colorless needles, m.p. 87–89°. IR ($CHCl_3$): 3400 br., 1680*s*, 1630*m*. Anal. calc. for $C_9H_{14}O_2$ (154.21): C 70.10, H 9.15; found: C 70.56, H 9.52. To 6.6 g (43 mmol) of this acid was added dropwise 7.3 ml (85 mmol) oxalyl chloride at 0° and the mixture stirred for 16 h at r.t. Distillation of the residue, after the removal of excess oxalyl chloride, gave 6.0 g (81%) of **17** as colorless liquid, b.p. 70–90/0.5 Torr, consisting (^{1}H-NMR) of a 1:1 mixture of the (*E*)- and (*Z*)-isomer. IR (CCl_4): 1783*s*, 1756*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 3.1–2.8 (*m*, 6H, 2H–C(2'), 2H–C(4') and 2H–C(5')); 2.04 (split *s*, 3H, CH_3–C(2)); 1.5–1.2 (*m*, 1H, H–C(3')); 1.05 and 1.07 (both *d*, both J = 6.5, intensity ratio 1:1, together 3H, CH_3–C(3')).

14b. *(1R*,2S*,3R*,9R*)-12-Isopropylidene-3,7-dimethyl-* (**18**) *and (1R*,2S*,4S*,9R*)-12-Isopropylidene-4,7-dimethyltricyclo[7.2.1.0^{2,6}]dodeca-6,10-dien-8-one* (**19**). To a refluxing solution of 2.7 g (25 mmol) 6,6-dimethylfulvene and 2.0 g (20 mmol) Et_3N in 20 ml dry hexane was added a solution of 3.3 g (19 mmol) **17** in 5 ml hexane. After refluxing for 3 days, the mixture was washed with H_2O dried ($MgSO_4$) and concentrated. Chromatography (LC-B, hexane/Et_2O 49:1) of the oily residue gave two fractions. Fraction 1 (0.87 g, 19%) consisted of a 44:56 mixture (GC-A) of an unidentified component **X** and **19**; fraction 2 (1.38 g, 30%) consisted of a 18:46:36 mixture (GC-A) of **X**, **19** and **18**. Two crystallizations of fraction 1 from hexane yielded pure **19**, m.p. 118–120°, and the same of fraction 2 afforded pure **18**, m.p. 154–156°.

Data for **18**. IR ($CHCl_3$): 1643*s*, 1602*m*. ^{1}H-NMR (400 MHz, C_6D_6): 5.90 and 5.80 (both *ddd*, both J = 6, 2.8 and 0.8, each 1H, H–C(10), H–C(11)); 4.25 (*dd*, J = 2.8 and 0.8, 1H, H–C(9)); 3.47 (*ddd*, J = 2.8, 2.5 and 0.8, 1H, H–C(1)); 2.76 (*ddddq*, J = 6, 2.5, 2.5 and 2.5, 1H, H–C(2)); 2.12 (*ddddq*, J = 18.5, 11.5, 8, 2.5 and 1.5, 1H, H–C(5)); 2.06 (*qdd*, J = 7, 6.3 and 6, 1H, H–C(3)); 2.01 (*ddq*, J = 18.5, 9 and 1.5, 1H, H–C(5)); 1.88 (*ddd*, J = 2.5, 1.5 and 1.5, 3H, CH_3–C(7)); 1.63 and 1.53 (both *s*, each 3H, $(CH_3)_2C$=C(12)); 1.36 (*dddd*, J = 12.5, 11.5, 9 and 6.3, 1H, H–C(4)); 1.14 (*dd*, J = 12.5 and 8, 1H, H–C(4)); 0.63 (*d*, J = 7, 3H, CH_3–C(3)). MS: 242 (2, M^+), 136 (84), 121 (100), 91 (22).

Data for **19**. UV (EtOH): 263 (5510). IR ($CHCl_3$): 1644*s*, 1602*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 6.07 (*dd*, J = 6 and 2.5, 1H, H–C(10)); 6.04 (*ddd*, J = 6, 2.5 [3.63] and 0.8, 1H, H–C(11)); 4.04 (br. *d*, J = 2.5, 1H, H–C(9)); 3.63 (*dd*, J = 2.5 and 2.5 [2.87], 1H, H–C(1)); 2.87 (*dm*, J = 13 [1.11], 1H, H–C(2)); 2.61 (br. *dd*, J = 18 and 6.5, 1H, H–C(5)); 2.0–1.9 (*m*, 2H, H–C(3), H–C(4)); 1.87 (split *dd*, J = 18 and 9.5, 1H, H–C(5)); 1.74 and 1.65 (both *s*, each 3H, $(CH_3)_2C$=C(12)); 1.70 (*ddd*, J = 2.5 [2.87], 1.5 [2.61] and 1.5, 3H, CH_3–C(7)); 1.11 (*ddd*, J = 13, 13 and 13 [2.87], 1H, H–C(3)); 1.05 (*d*, J = 7, 3H, CH_3–C(4)). ^{1}H-NMR (400 MHz, C_6D_6): 5.96 and 5.83 (both *ddd*, both J = 6, 2.8 and 0.8, each 1H, H–C(10), H–C(11)); 4.29 (br. *d*, J = 2.5, 1H, H–C(9)); 3.43 (br. *t*, J = 3, 1H, H–C(1)); 2.66 (br. *d*, $J \approx 13$, 1H, H–C(2)); 2.25 (br. *dd*, $J \approx 18$ and 6, 1H, H–C(5)); 1.86 (split *s*, 3H, CH_3–C(7)); 1.66 and 1.54 (both *s*, each 3H, $(CH_3)_2C$=C(12)); 1.64–1.46 (*m*, 3H, H–C(3), H–C(4) and H–C(5)); 0.84 (*ddd*, J = 13, 13 and 11, 1H, H–C(3)); 0.83 (*d*, J = 6.5, 3H, CH_3–C(4)). MS: 242 (2, M^+), 136 (100), 93 (24).

15. *(1R*,2S*,3R*,9R*,12R*)-3,7,3',3'-Tetramethylspiro[tricyclo[7.2.1.0^{2,6}]dodeca-6,10-diene-12,2'-oxirane]-8-one* (**20**). Epoxidation (as in *Exp. 4*) of 304 mg (1.3 mmol) **18** with 229 mg (1.3 mmol) *m*-chloroperbenzoic acid gave 334 mg of a crude, solid material which was recrystallized from hexane/EtOAc to give 224 mg (69%) **20** as colorless crystals, m.p. 138–139°. A crystal suitable for X-ray analysis was obtained by slow crystallization from $(i\text{-Pr})_2O$. IR ($CHCl_3$): 1645*s*, 1610*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 6.15–6.05 (*m*, 2H, H–C(10) and H–C(11)); 3.25 (*d*, J = 2.5, 1H, H–C(9)); 3.1–3.0 (*m*, 1H, H–C(2)); 2.95 (*t*, J = 2.5, 1H, H–C(1)); 2.6–2.3 (*m*, 3H, H–C(3) and 2H–C(5)); 1.78 (split *s*, 3H, CH_3–C(7)); 1.9–1.6 (*m*, 2H, 2H–C(4)); 1.40 and 1.30 (both *s*, each 3H, $2CH_3$–C(3')); 0.90 (*d*, J = 7, 3H, CH_3–C(3)). MS: 258 (3, M^+), 216 (28), 188 (63), 174 (23), 173 (100), 157 (23), 136 (24), 129 (28), 121 (63), 115 (26), 91 (51), 77 (40). Anal. calc. for $C_{17}H_{22}O_2$ (258.36): C 79.03, H 8.58; found: C 79.00, H 8.54.

16. *(1R*,2S*,3R*,9R*)-12-Isopropylidene-3,7-dimethyltricyclo[7.2.1.0^{2,6}]dodeca-6,10-dien-8-ol* (**21**). From 154 mg (0.64 mmol) **18** and 48 mg (1.3 mmol) $NaBH_4$ (as in *Exp. 3*) after 8 h at r.t., was obtained 124 mg (80%) **21** as a gum. IR ($CHCl_3$): 3580*m*, 3470 br., 1377*s*, 992*s*, 980*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 5.95 and 5.85 (both *ddd*, both J = 6, 2.5 and 0.5, each 1H, H–C(10), H–C(11)); 4.04 (*d*, $J \approx 4$, 1H, H–C(8)); 3.57 (*dd*, J = 4 and 2.5, 1H, H–C(9)); 3.51 (*dd*, J = 3.5 and 2.5, 1H, H–C(1)); 2.78 (br. *s*, 1H, H–C(2)); 2.4–0.9 (*m*, 6H, H–C(3), 2H–C(4), 2H–C(5), OH); 1.75 (br. *s*, 9H, CH_3–C(7), $(CH_3)_2C$=C(12)); 0.84 (*d*, J = 7, 3H, CH_3–C(3)). MS: 242 (2, M^+), 138 (57), 123 (84), 107 (100), 91 (55).

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