95. Preparation of Bicyclo[3.3.0]octane-2,8-dione- and Decalin-1,8-dione-Derivatives[1])

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Summary

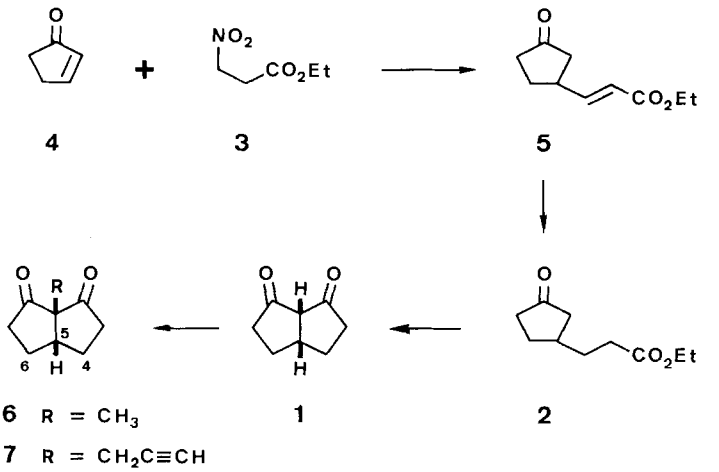
Alkylation of bicyclo[3.3.0]octane-2,8-dione (**1**), which is prepared by a modification of the procedure described in the literature, gives the methyl- and propynyl-derivatives **6** and **7** *(Scheme 1)*. In addition to the method described previously *(Scheme 2)*, 9-methyl-*cis*-decalin-1,8-dione **9** is obtainable stereoselectively either by cyclization of keto-acid **16**, or by aldol cyclization of keto-aldehyde **26** and oxydation of the resulting alcohols **24** and **25** *(Scheme 4)*. The *β*-keto-alcohols **24** and **25** undergo a base-catalyzed isomerization; the *trans*-decalin isomers **27** and **28** are not detected in this equilibrium mixture *(Schemes 4* and *5)*. Monoreduction of *cis*-dione **9** gives the *endo*-alcohol **25**, while **27** is the favored product of the reduction of *trans*-dione **10** *(Scheme 4)*. Optically pure (+)-**25** can be prepared from (9*S*,10*R*)-monoacetal **29** *(Scheme 5)*.

This communication describes the syntheses of the bicyclo[3.3.0]octane-2,8-dione and decalin-1,8-dione derivatives, used as substrates in the previous reports on the preparation of optically active compounds by enantiotopically differentiating reactions [2] [3].

1. Bicyclo[3.3.0]octanes. – Bicyclo[3.3.0]octane-2,8-dione (**1**) was prepared as described by *Stetter* [4a] and *Eaton* [4b] from propionate **2**, which was, however, obtained more conveniently than described in [4]: addition of 3-nitro-propionate **3** to cyclopentenone **4** [5] and hydrogenation of the resulting acrylate **5** gives **2** in 52% overall yield *(Scheme 1)*. Alkylation of the Na-salt of **1** which CH_3I and 3-propynyl bromide, respectively, gave the angularly substituted derivatives **6** and **7** in high yield *(Scheme 1)*. The *cis*-junction of the rings in **6** and **7** follows from comparison of their ^{1}H-NMR spectra with the published spectrum of **1** [4b]: the coupling constants J of H–C(5) with H_{exo} and H_{endo} of C(4) and C(6) are twice 6 Hz for diones **1** and **7**, 5.5 and 7 Hz for **6** (see *Exper. Part*). The alternative highly strained *trans*-junction can be excluded in the case of **6** and **7** by the similarity of these coupling constants with the values of the parent compound **1**.

[1]) These results are comprised in the Ph. D. thesis of *P. M.* [1].

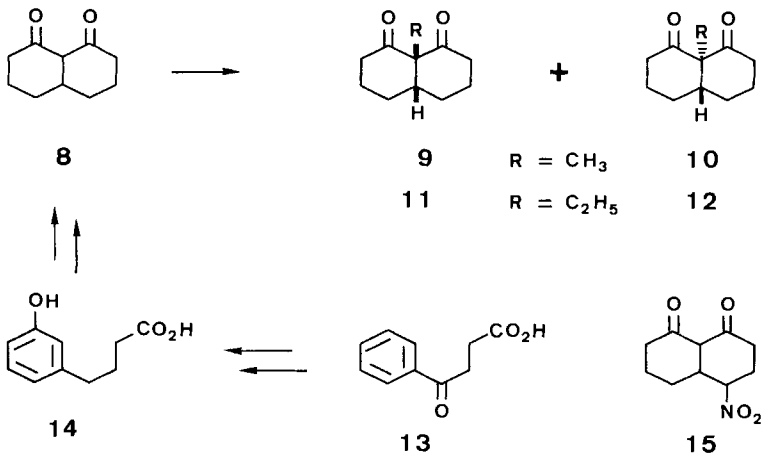
Scheme 1



2. Decalin-1,8-diones. – It has been shown, that alkylation of the Na-salt of decalin-1,8-dione (**8**) with CH_3I gives a mixture of *cis*-dione **9** (54%) and its *trans*-isomer **10** (33%) [2]. The 9-ethyl-derivatives **11** and **12** have been obtained analogously in 58% and 17% yield, respectively [1] *(Scheme 2)*. The assignment of the isomeric structures **9** and **10** is based on low-temperature ^{13}C-NMR experiments and on differences of their reactivity in the base-catalyzed alcoholysis [2].

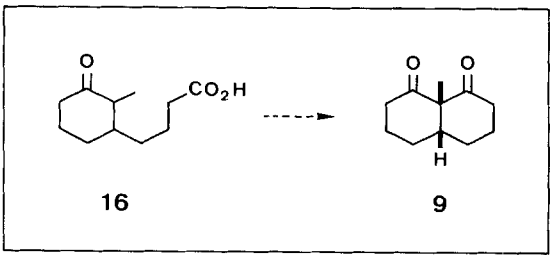
Since the reported synthesis of **8**, proceeding *via* succinoylated benzene **13** and 4-(3'-hydroxyphenyl)butyric acid **14** [6] *(Scheme 2)*, is rather laborious, a more efficient preparation giving better yields was sought for[2]). It was furthermore desirable to

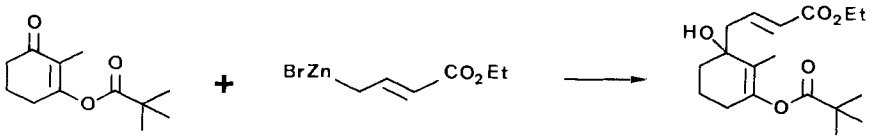
Scheme 2



[2]) An access *via* the nitro-derivative **15** *(Scheme 2)*, obtainable from cyclohexenone and 4-nitro-butyrate in two steps [7], was rejected, because of the low overall yield of this sequence (20%).

Scheme 3





develop a method affording selectively the *cis*-decalin **9**[3]), a compound which gave especially rewarding results in enantiotopically differentiating transformations [2] [3]. Since non-enolizable β-diketones are accessible by cyclocondensation of keto-acids in strongly acidic media [8], butyric acid **16** was chosen as a possible precursor of **9** *(Scheme 3)*. The selective formation of *cis*-decalin **9** could be anticipated by the known preference of the *cis*-decalin-formation in kinetically controlled cyclizations of substituted cyclohexanones [9] [10][4]).

The synthesis of acid **16** was first approached by the addition of the *Reformatzky* reagent **17**, derived from 4-bromo-crotonate, to the enol-pivalate **18** *(Scheme 3)*[5]). This reaction was, however, found to be rather sluggish, giving the adduct **19** in yields of 7–27% together with *ca.* 60% of starting material **18** *(Scheme 3)* [14][6]).

As a consequence, this approach was abandoned in favor of a variant involving the known keto-alcohol **20** [9], which could by oxidized in good yield with $RuO_4/NaIO_4$ [17] to acid **16** *(Scheme 4)*. Alcohol **20** was prepared in 57% overall yield by the addition of the *Grignard* reagent **21**, derived from 4-benzyloxybutyl bromide [18], to 3-ethoxy-2-methy-2-cyclohexene-1-one (**22**) [13a], followed by catalytic hydrogenation

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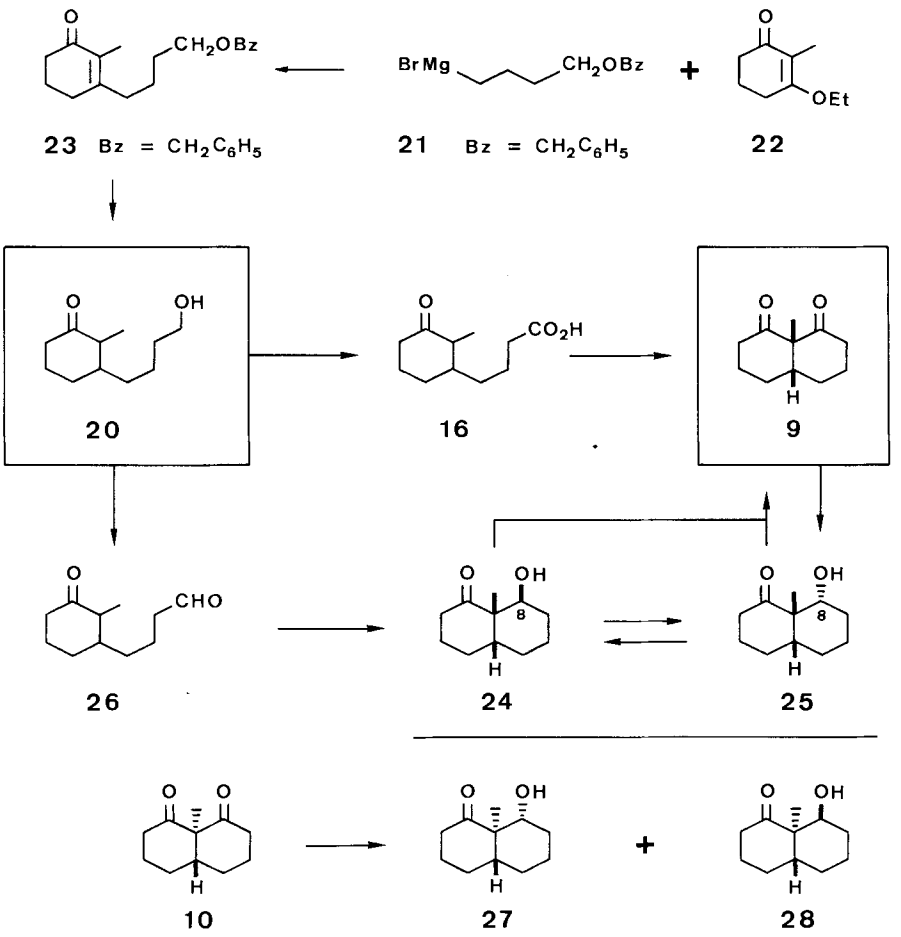
[3]) The ratio of **9** and **10**, obtained by alkylation of **8** *(Scheme 2)*, could not be altered further in favor of **9** [1].

[4]) It has, however, to be noted, that, while *cis*-bicyclo[4.3.0]undecanes are still formed selectively [11], mixtures of *cis*- and *trans*-isomers have been obtained in the case of a bicyclo[5.3.0]decane derivative [12].

[5]) Enolester **18** was obtained in 93% yield from 2-methylcyclohexane-1,3-dione [13] by treatment with pivalic anhydride in pyridine containing catalytic amounts of 4-(dimethylamino)pyridine [14].

[6]) Zn activated with H_2SO_4 or Zn/Cu-couple [15] was used in these experiments. The major problem of this reaction, which was not affected significantly by sonication, seems to be desactivation of the metal surface. An improvement by the continuous-flow method developped by *Ruppert & White* [16] is therefore probable.

Scheme 4



of cyclohexene **23** *(Scheme 4)*[7]). Cyclization of acid **16** in 10% P_2O_5/CH_3SO_3H[8]) finally afforded *cis*-decaline **9** containing no detectable amounts of *trans*-isomer **10** in 48% yield from alcohol **20**.

In addition to the acid-mediated cyclization of **16**, *cis*-dione **9** can be obtained from alcohol **20** in 61% overall yield by oxidation of the aldols **24** and **25** with pyridinium chlorochromate on alumina [22] *(Scheme 4)*[9]). Oxidation of **20** with pyridinium

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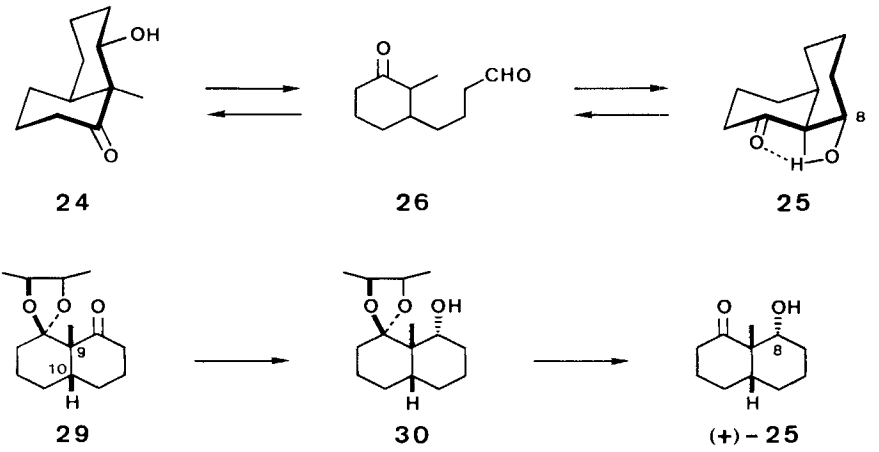
[7]) Reagent **21** was chosen from a variety of analogous reagents [9] [10d] [19], because of the ease of preparation and its stability. Still another possibility for the preparation of **16**, avoiding the oxidation of alcohol **20**, would be the use of 4-bromobutyric acid protected as an ortho-ester with 2,4,10-trioxaadamantane structure [20].

[8]) This reagent has been introduced as a substitute for the capricious polyphosphoric acid [21].

[9]) The oxidation of more sensitive β-hydroxy-ketones has been achieved with DMSO/oxalyl chloride [23] or *Collins* reagent [12] [23].

Scheme 5



chlorochromate [24] affords aldehyde **26**, which, upon treatment with K_2CO_3/CH_3OH, cyclizes to the *exo*-alcohol **24** (67%) and *endo*-isomer **25** (20%) with no detectable amounts of *trans*-decalones **27** and **28** *(Scheme 4)*[4])[10]). The alcohols **24** and **25** can be equilibrated in good yield *via* aldehyde **26** by base catalysis *(Scheme 5)*. In CH_3OH/K_2CO_3 the *exo*-isomer **24** is favored with a 71:29 ratio of **24**/**25** starting from either pure **24** or **25**. In toluene this preference is reversed[11]). Treatment of pure **24** with *t*-BuOK/toluene affords a 69:31 mixture of **25** and **24**, while **25** and **24** are isolated in a 80:20 ratio starting from pure **25**. It seems, that **24** with greater separation of the keto and alcohol function is more stable in H-bonding solvents, while the H-bridge of **25** makes this isomer more favorable in non-polar solvents.

Monoreduction of the diones **9** and **10** is best achieved with $Li[HAl(t\text{-}BuO)_3]$ at low temperature. The *endo*-alcohol **25** is the favored product of *cis*-dione **9**, while **24** is detected only in trace amounts. As expected alcohol **27** with equatorial OH-substituent is isolated in excess (78%) together with *ca.* 5% of isomer **28** from the reduction of *trans*-isomer **10** *(Scheme 4)*[12]). Finally, optically pure (+)-**25** is obtainable by hydride-

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[10]) The relative configuration of C(8) in **24** and **25** was deduceable from IR and NMR data. A characteristic difference between the isomers **24** and **25**, the favored conformations of which are depicted in *Scheme 5*, is the possibility of H-bonding, existing only for the *endo*-isomer **25**. This is reflected in $CHCl_3$-solutions of **25** by a concentration-independent IR band at 3450 cm^{-1} [1], and by a coupling constant of 11.5 Hz between HO–C(8) and H–C(8), observed in the ^{1}H-NMR-spectrum of **25** only. Couplings to alcoholic H-atoms can be observed under conditions of slow chemical exchange. The rates of intermolecular H-exchange are diminished by intramolecular H-bonding. An affirmation of this assignment is given by a shift difference of 8.5 ppm between the ^{13}C-resonances of the CH_3-substituents. The high-field shift in the case of *exo*-isomer **24**, with equatorial CH_3-group in the cyclohexanone ring, is due to a stereoelectronic effect of the adjacent carbonyl group [25]. Comparison of the ^{13}C-NMR spectra of the decalin-1,8-diones **9** and **10** [2] with the values of 9-methyl-*cis*- and 9-methyl-*trans*-decalin [26] leads to the conclusion, that this 'shielding'-effect of the carbonyl-group affects only the equatorial CH_3-groups.

[11]) For an experimental description of the isomerizations starting from the favored isomers, **24** in CH_3OH, **25** in toluene, see [1].

[12]) The structural assignment of **27** and **28** by their ^{1}H-NMR spectra is straightforward (see *Exper. Part*).

reduction of monoacetal **29** with (9*S*,10*R*)-configuration [2], followed by deprotection of the resulting alcohol **30** with wet silica gel [27] (*Scheme 5*)[13]).

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Experimental Part

General Remarks. See [2] and [3a].

1. Bicyclo[3.3.0]octane Derivatives. – *Ethyl 3-(3'-Oxocyclopentyl)acrylate* (**5**) [5]. To a solution of nitropropionate **3** (4.163 g, 28.3 mmol) in dry THF (50 ml) 23.6 ml of 1.2N *t*-BuOK/THF (*ca.* 28.3 mmol) were added at −20° within 45 min (Ar). After stirring for 15 min, freshly distilled cyclopentenone **4** (2.322 g, 28.3 mmol) was added in 30 min at −20°. The mixture was then allowed to warm up to r.t. in 3 h, CH_3OH (5 ml) was added, and stirring at r.t. was continued for 3.5 days. The reaction was quenched with 2N HCl (100 ml) and worked up with Et_2O. Flash chromatography (silica gel, hexane/Et_2O 1:1) gave 3.03 g (58%) of **5**. IR ($CHCl_3$): 2970*m*, 2935*w*, 2900*w*, 1734*s*, 1706*s*, 1652*m*, 1454*w*, 1443*w*, 1401*w*, 1368*m*, 1304*m*, 1271*m*, 1180*m*, 1149*m*, 1086*w*, 1036*m*, 980*m*, 861*w*. ^{1}H-NMR (100 MHz, $CDCl_3$): 1.28 (*t*, *J* = 7, CH_3CH_2O); 1.60–2.64 (*m*, 6H); 2.75–3.25 (*m*, H–C(1')); 4.19 (*q*, *J* = 7, CH_3CH_2O); 5.86 (*dd*, *J* = 16 and 1.5, H–C(2)); 6.95 (*dd*, *J* = 16 and 7, H–C(3)). MS: 182 (58, M^+), 154 (19), 153 (61), 138 (9), 137 (68), 136 (22), 127 (23), 126 (12), 125 (15), 123 (8), 113 (5), 112 (7), 111 (10), 110 (11), 109 (76), 108 (34), 107 (8), 99 (23), 98 (22), 97 (20), 95 (20), 82 (18), *81* (100), 80 (24), 79 (22), 67 (46), 55 (24), 53 (37), 43 (20), 42 (22), 40 (19), 29 (28).

Ethyl 3-(3'-Oxocyclopentyl)propionate (**2**). Acrylate **5** (6.955 g, 37.8 mmol) was hydrogenated in 2 portions (1.218 g and 5.373 g) in EtOH (30 ml and 150 ml) at normal pressure (5 h), using 5% Pd/C (0.8 g and 3.5 g) as catalyst. Bulb-to-bulb distillation (120°/0.5 mm) of the crude product, obtained by filtration (*Celite*) and evaporation of the solvent, gave 5.808 g (83%) of **2**. Chromatography (silica gel, hexane/Et_2O 1:1) of the residue of the distillation gave another 0.472 g (7%) of **2**. IR (CCl_4): 2980*m*, 2960*m*, 2930*m*, 2880*w*, 1737*s*, 1477*w*, 1459*w*, 1451*w*, 1445*w*, 1406*m*, 1372*m*, 1349*m*, 1321*w*, 1303*m*, 1256*m*, 1238*m*, 1180*s*, 1156*s*, 1133*m*, 1092*m*, 1033*m*, 938*w*, 893*w*, 867*w*. ^{1}H-NMR (100 MHz, $CDCl_3$): 1.26 (*t*, *J* = 7, CH_3CH_2O); 1.50–1.98 (*m*, 4H); 2.04–2.60 (*m*, 7H); 4.13 (*q*, *J* = 7, CH_3CH_2O). MS: 184 (4, M^+), 166 (6), 156 (1), 155 (1), 139 (45), 128 (3), 121 (5), 111 (8), 110 (8), 109 (5), 101 (7), 97 (10), 96 (88), 95 (8), 93 (8), 89 (8), 88 (27), 84 (8), *83* (100), 82 (19), 73 (10), 70 (14), 69 (13), 67 (10), 61 (23), 60 (20), 56 (12), 55 (52), 43 (11), 41 (26), 39 (16), 29 (32).

Bicyclo[3.3.0]octane-2,8-dione (**1**). Dione **1** (2.891 g, 84%) was obtained from ester **2** (4.575 g, 24.85 mmol) according to [4b].

1-Methylbicyclo[3.3.0]octane-2,8-dione (**6**). To a suspension of NaH (83 mg, 55–60% suspension in nujol, 1.9–2.1 mmol) in THF (1 ml) dione **1** (278 mg, 2.014 mmol), dissolved in THF (9 ml), was added in 5 min (Ar). After stirring for 30 min, CH_3I (0.25 ml, *ca.* 4 mmol) was added and stirring at r.t. was continued for 2 h. The mixture was then poured to 10% aq. KH_2PO_4 (50 ml) and worked up with Et_2O. Chromatography (silica gel, hexane/Et_2O 1:1) afforded 269 mg (87%) of **6**. M.p. 52° (Et_2O/hexane). IR (CCl_4): 2960*m*, 2880*m*, 1761*s*, 1722*s*, 1458*m*, 1449*m*, 1409*m*, 1368*w*, 1328*w*, 1313*w*, 1276*w*, 1254*w*, 1212*m*, 1198*m*, 1155*m*, 1140*m*, 1085*m*, 1056*m*, 1033*m*, 1023*m*, 973*w*, 943*w*, 913*w*, 849*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.23 (*s*, CH_3–C(1)); 1.79 (*dddd*, *J* = 13, 8.5, 7, and 5.5) and 2.22 (*tdd*, *J* = 7.5, 13, and 7) (2H–C(4), 2H–C(6)); 2.28–2.49 (*m*, 2H–C(3), 2H–C(7)); 2.74 (*tt*, *J* = 5.5 and 7, H–C(5)). MS: *152* (100, M^+), 134 (12), 125 (8), 124 (76), 123 (28), 110 (18), 109 (52), 108 (27), 106 (9), 97 (26), 96 (33), 95 (32), 82 (55), 81 (32), 80 (13), 79 (15), 69 (18), 68 (49), 67 (76), 56 (18), 55 (35), 54 (16), 53 (26), 41 (41), 40 (12), 39 (30). Anal. calc. for $C_9H_{12}O_2$ (152.19): C 71.03, H 7.95; found: C 71.23, H 7.75.

1-(2'-Propynyl)bicyclo[3.3.0]octane-2,8-dione (**7**). To a suspension of NaH (66 mg, 55–60% suspension in nujol, 1.5–1.65 mmol) in THF (1 ml) a solution of **1** (233 mg, 1.688 mmol) in THF (5 ml) was added. After stirring for 30 min, propynyl bromide (0.23 ml, *ca.* 3 mmol) was added, and stirring at r.t. was continued for 20 h. Workup as above and chromatography (silica gel, hexane/Et_2O 1:1) gave 249 mg (83%) of **7**. M.p. 93–94°

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[13]) Attempts to effect an enantiotopically differentiating mono-reduction of **9** were not met with success [1].

(Et_2O/pentane). IR ($CHCl_3$): 3305*s*, 2960*m*, 2950*m*, 2880*m*, 2120*w*, 1758*s*, 1718*s*, 1458*m*, 1419*w*, 1405*m*, 1332*w*, 1301*m*, 1274*w*, 1260*w*, 1191*w*, 1140*s*, 1110*m*, 1083*m*, 1060*w*, 1032*m*, 985*w*, 943*w*, 880*w*, 835*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.74–1.88 (*m*, 2H); 1.97 (*t*, J = 2.6, H–C(3')); 2.24–2.53 (*m*, 6H); 2.59 (*d*, J = 2.6, 2H–C(1')); 3.15 (*quint.*, $J \approx 6$, H–C(5)). MS (*di.*): 176 (26, M^+), 161 (5), 148 (47), 147 (13), 134 (15), 133 (31), 121 (12), 120 (59), 119 (19), 106 (18), 105 (33), 104 (14), 92 (30), *91* (100), 79 (22), 78 (42), 77 (23), 65 (24), 63 (13), 55 (25), 53 (15), 52 (12), 51 (20), 43 (22), 41 (22), 39 (31). Anal. calc. for $C_{11}H_{12}O_2$ (176.21): C 74.97, H 6.86; found: C 74.97, H 6.67.

2. Decalin-1,8-dione Derivatives. – *3-(4'-Benzyloxybutyl)-2-methyl-2-cyclohexene-1-one* (**23**). 4-Benzyloxybutyl bromide [18] (2.584 g, 10.63 mmol) dissolved in THF (10 ml) was added in 3 h to a suspension of Mg (272 mg, 11.2 mgAt) in THF (10 ml), boiling under reflux (Ar). After heating for 2 h under reflux, the mixture was cooled with ice, and a solution of *3-ethoxy-2-methyl-2-cyclohexene-1-one* (**22**) [13a] (1.48 g, 9.60 mmol) in THF (10 ml) was added in one batch. After stirring at 0° (1 h) and at r.t. (2 h), the reaction was quenched by the addition of 10% H_2SO_4 (50 ml) under ice-cooling. The mixture was stirred for 5 min, worked up with Et_2O, and the crude product was purified by flash-chromatography (silica gel, hexane/Et_2O 1:1) giving 1.62 g (62%) of **23**. IR ($CHCl_3$): 3000*w*, 2940*m*, 2865*m*, 1650*s*, 1622*m*, 1492*w*, 1452*m*, 1430*w*, 1380*m*, 1357*m*, 1328*m*, 1304*w*, 1097*m*, 1024*w*, 907*w*, 873*w*. ^{1}H-NMR (100 MHz, $CDCl_3$): 1.74 (*t*, J = 2, CH_3–C(2)); 1.40–2.05 (*m*, 6H); 2.10–2.46 (*m*, 6H); 3.46 (*t*, J = 6, 2H–C(4')); 4.47 (*s*, $C_6H_5CH_2O$); 7.1–7.4 (*m*, $C_6H_5CH_2O$). MS: 272 (3, M^+), 236 (1), 218 (2), 203 (2), 181 (12), 163 (8), 145 (5), 137 (8), 124 (11), 121 (12), 108 (23), 107 (22), 105 (6), *91* (100), 79 (40), 77 (24), 67 (10), 65 (12), 55 (15), 53 (8), 51 (10), 43 (10), 41 (13), 39 (10). Anal. calc. for $C_{18}H_{24}O_2$ (272.37): C 79.37, H 8.88; found: C 79.27, H 8.91.

3-(4'-Hydroxybutyl)-2-methyl-1-cyclohexanone (**20**) [9]. To a suspension of 10% Pd/C (85 mg) in 95% EtOH (25 ml) **23** (926 mg, 3.4 mmol) was added. After stirring for 5 h under H_2 at normal pressure (r.t.), the catalyst was removed by filtration (*Celite*). Flash-chromatography (silica gel, hexane/Et_2O 1:3) of the residue of the filtrate gave 574 mg (92%) of **20**, mixture of 1,2-epimers, *trans/cis ca.* 1:1, according to ^{1}H-NMR. IR ($CHCl_3$): 3615*m*, 3720–3240*w*, 2935*s*, 2860*s*, 1700*s*, 1455*m*, 1425*w*, 1377*m*, 1353*w*, 1343*w*, 1310*m*, 1147*w*, 1067*m*, 1045*m*, 1022*m*, 962*w*. ^{1}H-NMR (100 MHz, $CDCl_3$): 0.99 (*d*, J = 7) and 1.03 (*d*, J = 6) (CH_3–C(2)); 1.66 (*br.s*, *exchangeable with D_2O*, OH); 0.80–2.76 (*m*, 14H); 3.38–3.80 (*m*, *3 main peaks*, 2H–C(4')). MS: 184 (5, M^+), 169 (1), 166 (2), 141 (5), 137 (7), *111* (100), 97 (15), 95 (25), 83 (16), 81 (18), 79 (11), 69 (17), 67 (25), 55 (58), 43 (12), 41 (41), 31 (12). Anal. calc. for $C_{11}H_{20}O_2$ (184.27): C 71.70, H 10.94; found: C 71.75, H 10.86.

4-(2'-Methyl-3'-oxocyclohexyl)butyric Acid (**16**). To a mixture of $NaIO_4$ (1.926 g, 9.0 mmol) and RuO_2 (7 mg) in 18 ml of H_2O/acctone 2:1 (*v/v*) cooled to 10° in an ice-bath **20** (553 mg, 3.0 mmol) in acetone (10 ml) was added at such a rate, that the temperature did not exceed 25°. After stirring at r.t. for 5 h, the white precipitate of $NaIO_3$ was separated by filtration (*Celite*) and part of the solvent was evaporated at reduced pressure. Workup with Et_2O gave 608 mg of crude acid **16**.

4-(2'-Methyl-3'-oxocyclohexyl)butanal (**26**). Alcohol **20** (503 mg, 2.735 mmol) dissolved in CH_2Cl_2 (10 ml) was added to a stirred suspension of pyridinium chlorochromate [24] (1.18 g, 5.47 mmol) in CH_2Cl_2 (10 ml). Stirring at r.t. was continued for 3 h. After the addition of Et_2O (50 ml), the mixture was filtered (*Celite*), the solvent of the filtrate evaporated at reduced pressure, and the residue, dissolved in Et_2O, filtered through a fritted funnel charged with silica gel. Evaporation gave 483 mg (97%) of **26**. Re-chromatography (silica gel, hexane/Et_2O 1:1) of **26** from a different experiment gave an analytical sample (58% recovery), mixture of 1',2'-epimers, *trans/cis ca.* 1:1, according to ^{1}H-NMR. IR (CCl_4): 2965*m*, 2930*s*, 2860*m*, 2815*m*, 2760*m*, 1725*s*, 1709*s*, 1450*m*, 1445*m*, 1425*m*, 1407*w*, 1385*w*, 1377*m*, 1309*w*, 1213*m*, 1200*m*, 1190*m*, 1179*m*, 1140*w*, 960*w*. ^{1}H-NMR (80 MHz, $CDCl_3$): 1.00 and 1.05 (2*d*, J = 7, CH_3–C(2')); 0.85–2.90 (*m*, 14H); 9.73 (*m*, $w_{1/2} \approx 4$, H–C(1)). MS: 182 (8, M^+), 167 (1), 165 (0.5), 153 (3), 139 (3), 124 (5). *111* (100), 97 (22), 95 (10), 93 (10), 83 (22), 82 (21), 81 (20), 79 (16), 70 (11), 69 (15), 68 (12), 67 (30), 55 (59), 43 (13), 41 (39), 39 (16).

Cyclization of Aldehyde **26**. Crude **26** (483 mg) was dissolved in 10 ml of sat. K_2CO_3/CH_3OH (*ca.* 4%, *w/v*). After standing for 16 h at r.t., the mixture was worked up with Et_2O affording 470 mg (97%) of a mixture of **24** and **25**. Chromatography (silica gel, hexane/Et_2O 1:1) of a sample obtained analogously from 34 mg (0.186 mmol) of **26** gave 7 mg (20%) of **25** and 23 mg (67%) of **24**.

(8S,9S*,10R*)-8-Hydroxy-9-methyl-1-decalone* (**24**). IR(CCl_4): 3640*w*, 3600–3100*m*, 2940*s*, 2870*s*, 1702*s*, 1468*m*, 1447*m*, 1425*m*, 1380*m*, 1363*w*, 1342*w*, 1314*m*, 1270*m*, 1242*w*, 1200*m*, 1138*m*, 1117*m*, 1104*m*, 1090*m*, 1065*m*, 1049*m*, 1012*m*, 990*m*, 965*m*, 943*w*, 927*w*, 912*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.21 (*s*, CH_3–C(9)); 1.30–1.47 (*m*, 1H); 1.48–1.91 (*m*, 8H); *ca.* 1.57 (*m*, $w_{1/2} \approx 9$, *exchangeable with D_2O*, OH); 1.94–2.08 (*m*, 2H); 2.44–2.52 (*m*, *3 main peaks*, 2H–C(2)); 4.17 (*br.s*, $w_{1/2} \approx 16$, *after exchange with D_2O 4 main peaks*, H–C(8)). ^{13}C-NMR (75.5 MHz, $CDCl_3$): 16.5 (CH_3–C(9)); 20.1 and 24.3 (C(3), C(6)); 26.3 and 27.0 (C(4), C(5)); 30.2

(C(7)); 37.9 (C(2)); 43.1 (C(10)); 54.3 (C(9)); 69.6 (C(8)); 216.2 (C(1)): MS: 182 (13, M^+), 167 (19), 164 (13), *111* (100), 108 (12), 95 (7), 93 (12), 81 (5), 79 (6), 69 (5), 67 (8), 55 (13), 43 (14), 41 (12), 39 (7).

*(8*R*,*9*S*,*10*R*)*-8-Hydroxy-9-methyl-1-decalone* (**25**). M.p. 60° (Et_2O/pentane). IR (CCl_4): 3540*m*, 2990*w*, 2970*m*, 2945*s*, 2885*m*, 2870*m*, 1693*s*, 1467*m*, 1458*m*, 1447*m*, 1421*m*, 1410*m*, 1375*m*, 1364*w*, 1347*w*, 1337*w*, 1314*m*, 1302*w*, 1288*w*, 1252*w*, 1239*w*, 1208*m*, 1179*w*, 1159*m*, 1148*m*, 1130*m*, 1100*m*, 1087*s*, 1056*s*, 1025*m*, 1010*w*, 984*m*, 942*w*, 910*w*, 902*w*, 857*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.24–1.43 (*m*, 3H); 1.50 (*s*, CH_3–C(9)); 1.48–1.84 (*m*, 4H); 1.85–2.04 (*m*, 3H); 2.13–2.29 (*m*, 2H); 2.50–2.66 (*m*, H–C(2)); 3.08 (*ddd*, J = 11.5, 11.5, and 4.5, *after exchanging with* D_2O, *dd*, J = 11.5 and 4.5, H–C(8)); 3.56 (*d*, J = 11.5, *exchangeable with* D_2O, OH): ^{13}C-NMR (75.5 MHz, $CDCl_3$): 21.7 and 24.1 (C(3), C(6)); 23.3 (CH_3–C(9)); 25.7 and 28.7 (C(4), C(5)); 32,3 (C(7)); 38.7 (C(2)); 45.6 (C(10)); 53.5 (C(9)); 78.4 (C(8)); 219.6 (C(1)). MS: 182 (18, M^+), 167 (2), 164 (4), 137 (2), 124 (3), *111* (100), 95 (10), 93 (9), 81 (6), 79 (4), 77 (3), 67 (10), 55 (10), 43 (10), 41 (11), 39 (5). Anal. calc. for $C_{11}H_{18}O_2$ (182.25): C 72.49, H 9.96; found: C 72.35, H 9.82.

Isomerization of Aldols **24** and **25**. – a) *In CH_3OH/K_2CO_3.* A solution of **25** (73 mg, 0.401 mmol) in 5 ml of sat. K_2CO_3/CH_3OH (*ca.* 4%, *w/v*) was stirred at r.t. for 28 h. Workup with Et_2O gave a mixture of **24** and **25**. GC (*UCON*, 160°, 0.35 kg/cm^2): t_R = 2.16 min (29%, **25**), t_R = 3.87 min (71%, **24**). Chromatography (silica gel, hexane/Et_2O 1:1) gave 18 mg (24%) of **25** and 52 mg (71%) of **24**.

b) *In Toluene/*t*-BuOK.* To a solution of aldol **24** (19 mg, 0.104 mmol) in dry toluene (2 ml) 0.15 ml of *ca.* 0.1N *t*-BuOK/toluene (0.015 mmol) were added. After stirring at r.t. for 4 days, the mixture was worked up with Et_2O. Filtration (1 g of silica gel, hexane/Et_2O 1:1) gave 18 mg (94%) of a mixture of **24** (31%) and **25** (69%), according to GC (see *above*).

*9-Methyl-*cis*-decalin-1,8-dione* (**9**). – a) *From Decalin-1,8-dione* (**8**). See [2].

b) *From Acid* **16**. To 533 mg of crude **16** 5 ml of freshly prepared 10% P_2O_5/CH_3SO_3H (*w/v*) were added. After stirring at r.t. for 5 h (Ar), the mixture was poured to ice/H_2O and worked up with Et_2O. Chromatography (silica gel, hexane/Et_2O 2:1) gave 231 mg (48% based on alcohol **20**) of *cis*-dione **9**. Analytical data: see [2].

c) *From Aldols* **24**/**25**. To a solution of crude **24**/**25** (470 mg) in benzene (20 ml) 5.5 g (*ca.* 5.5 mmol) of pyridinium chlorochromate on alumina [22] were added. After stirring at r.t. for 4 h, the mixture was filtered, and the reagent was flushed well with Et_2O. Chromatography (silica gel, hexane/Et_2O 2:1) of the residue of the filtrate afforded 302 mg (61% based on alcohol **20**) of dione **9**. Analytical data: see [2].

Monoreduction of cis*-Dione* **9**. To a suspension of Li[HAl(*t*-BuO)$_3$] (239 mg, 90%, *ca.* 0.85 mmol) in THF (2 ml), cooled to −18°, dione **9** (160 mg, 0.889 mmol), dissolved in THF (3 ml), was added in 5 min. After stirring at −18° for 4 h, 2 ml of 2N HCl were added, and the mixture was worked up with Et_2O. According to GC (see *above*) the crude product (169 mg) contained the epimeric alcohols **24** and **25** in a 1:37 ratio. Chromatography (silica gel, toluene/Et_2O 4:1) yielded 23 mg (14%) of starting material **9** and 129 mg (79%) of **25**.

Monoreduction of trans*-Dione* **10**. Dione **10** [2] (184 mg, 1.022 mmol) was reduced with Li[HAl(*t*-BuO)$_3$] (281 mg, 90%, *ca.* 0.995 mmol) in THF at −20° for 3 h as described above for **9**. Chromatography (silica gel, hexane/Et_2O 2:1) of the crude material (182 mg) gave 10 mg (5%) of **28**, 146 mg (78%) of **27**, and 9 mg (4%) of starting material **10**.

*(8*R*,*9*R*,*10*R*)*-8-Hydroxy-9-methyl-1-decalone* (**27**). M.p. 36° (bulb-to-bulb dist., 100°/12 mm). IR (CCl_4): 3560*m*, 3600–3100*w*, 2990*w*, 2940*s*, 2870*m*, 1695*s*, 1469*w*, 1451*m*, 1427*w*, 1395*w*, 1360*w*, 1338*m*, 1328*m*, 1315*w*, 1300*w*, 1280*m*, 1253*w*, 1240*w*, 1179*w*, 1170*w*, 1130*m*, 1105*m*, 1077*m*, 1051*m*, 1027*w*, 990*w*, 971*w*, 940*w*, 907*w*, 870*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.17 (*s*, CH_3–C(9)); 1.24–1.82 (*m*, 10H); 1.94–2.12 (*m*, H–C(10)); 2.23 (*d*, $J \approx 14.5$, *further splitted by small couplings*, H_{eq}–C(2)); 2.62 (*ddd*, J = 14.5, 13.5, and 7, H_{ax}–C(2)); 3.55 (*d*, J = 2, *exchangeable with* D_2O, OH); 3.88 (*ddd*, J = 11.5, 4.5, and 2, *after exchanging with* D_2O, *dd*, J = 11.5 and 4.5, H–C(8)). ^{13}C-NMR (75.5 MHz, $CDCl_3$): 10.2 (CH_3–C(9)); 23.7 (C(3)); 26.0, 26.6, and 27.0 (C(4), C(5), C(6)); 28.2 (C(7)); 37.6 (C(2)); 44.7 (C(10)); 53.5 (C(9)); 72.8 (C(8)); 219.3 (C(1)). MS: 182 (26, M^+); 167 (10), 164 (6), 137 (3), 124 (4), 112 (13), *111* (100), 108 (8), 97 (4), 95 (5), 93 (9), 82 (5), 81 (5), 79 (4), 67 (8), 55 (11), 43 (11), 41 (10), 39 (5). Anal. calc. for $C_{11}H_{18}O_2$ (182.25): C 72.49, H 9.96; found: C 72.32, H 9.85.

*(8*S*,*9*R*,*10*R*)*-8-Hydroxy-9-methyl-1-decalone* (**28**). IR (CCl_4): 3580*m*, 3600–3100*w*, 2940*s*, 2870*s*, 1696*s*, 1463*m*, 1451*m*, 1440*m*, 1429*m*, 1386*m*, 1378*m*, 1350*m*, 1340*w*, 1332*w*, 1315*w*, 1300*w*, 1274*m*, 1254*m*, 1240*w*, 1227*m*, 1171*m*, 1155*w*, 1145*m*, 1125*m*, 1103*m*, 1078*m*, 1042*m*, 1004*m*, 968*m*, 940*m*, 927*w*, 880*w*, 855*w*, 840*w*. ^{1}H-NMR (100 MHz, $CDCl_3$): 1.08 (*s*, CH_3–C(9)); 1.16–2.36 (*m*, 12H); 2.38–2.86 (*m*, H_{ax}–C(2)); 2.9–3.35 (*br.*, *exchangeable with* D_2O, OH); 4.02 (*m*, $w_{1/2} \approx 6$, H–C(8)). MS: 182 (21, M^+), 167 (1), 164 (1), 137 (2), 124 (4), 112 (10), *111* (100), 95 (4), 93 (6), 82 (4), 81 (4), 79 (4), 67 (5), 55 (7), 43 (7), 41 (7), 39 (4).

[(8R,9S,10R)-8-Hydroxy-9-methyldecalin]-1-spiro-2'-[(4'R,5'R)-4',5'dimethyl-1',3'-dioxolane] (**30**). Monoacetal **29** [2] (194 mg, 0.77 mmol) in THF (3 ml) was added in 5 min to an ice-cooled mixture of $Li[HAl(t\text{-}BuO)_3]$ (246 mg, 90%, *ca.* 0.87 mmol) in THF (2 ml). After stirring at 0° for 16 h (Ar), the reaction was quenched with sat. $NaHCO_3$-solution (2 ml) and worked up with Et_2O. Chromatography (silica gel, pentane/CH_2Cl_2/Et_2O 20:20:3) gave 192 mg (98%) of **30**. M.p. 115° (pentane). $[\alpha]_D = -36.1°$ ($c = 1.80$, $CHCl_3$). IR (CCl_4): 3620*w*, 3520*w*, 2975*s*, 2930*s*, 2865*s*, 1447*m*, 1405*w*, 1375*m*, 1345*w*, 1332*w*, 1308*w*, 1288*w*, 1282*w*, 1275*w*, 1245*m*, 1220*w*, 1190*m*, 1182*m*, 1167*m*, 1143*m*, 1093*s*, 1052*m*, 1033*s*, 1012*w*, 1001*w*, 975*m*, 948*m*, 921*m*, 897*w*, 880*w*, 856*w*, 842*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.24 and 1.33 (2*d*, $J = 6$, CH_3–C(4'), CH_3–C(5')); 1.25 (*s*, CH_3–C(9)); 1.1–1.9 (*m*, 12H); 1.60 (*br.s*, $w_{1/2} \approx 5$, *exchangeable with* D_2O, OH); 1.96–2.20 (*m*, H–C(10)); 3.50 (*m*, $w_{1/4} \approx 20$, H–C(8)); 3.59 and 3.84 (2*dq*, $J = 8.5$ and 6, H–C(4'), H–C(5')). ^{13}C-NMR (75.5 MHz, $CDCl_3$, −60°): *ca. 5:1-mixture of conformers*, a) *major conformer:* 17.0, 19.2, and 19.3 (CH_3–C(9), CH_3–C(4'), CH_3–C(5')); 23.8, 24.1, 26.4, and 27.1 (C(3), C(4), C(5), C(6)); 31.8 and 32.1 (C(2), C(7)); 42.5 (C(9)); 43.4 (C(10)); 76.4, 78.1, and 81.4 (C(8), C(4'), C(5')); 114.9 (C(1)); b) *minor conformer:* 15.2, 16.2, and 18.0 (CH_3–C(9), CH_3–C(4'), CH_3–C(5')); 19.0, 22.3, 27.4, and 27.8 (C(3), C(4), C(5), C(6)); 30.8 (C(7)); 36.1 (C(2)); 38.6 (C(10)); 44.5 (C(9)); 70.5 and 78.7 (*one signal is hidden by overlapping solvent-peaks*, C(8), C(4'), C(5')); 111.6 (C(1)). MS (*di.*): 254 (9, M^+), 237 (8), 211 (50), 195 (3), 181 (4), 164 (7), 157 (25), 147 (5), 141 (7), *127* (100), 121 (7), 114 (36), 111 (18), 95 (9), 93 (10), 91 (7), 85 (10), 81 (10), 79 (12), 67 (12), 55 (40), 53 (7), 43 (19), 41 (23), 39 (7). Anal. calc. for $C_{15}H_{26}O_3$ (254.36): C 70.83, H 10.30; found: C 70.80, H 10.30.

(8R,9S,10R)-8-Hydroxy-9-methyl-1-decalone ((+)-**25**). To a suspension of silica gel (1 g) in 2 ml of CH_2Cl_2 0.1 ml of 10% aq. oxalic acid was added, followed, after stirring for 10 min, by acetal **30** (93 mg, 0.366 mmol) in CH_2Cl_2 (2 ml). Stirring was continued for 20 h, the reagent was removed by filtration, and the product was isolated by flushing with Et_2O. Chromatography (silica gel, hexane/Et_2O 1:1) of the residue of the filtrate gave 63 mg (94%) of (+)-**25**. M.p. 55° (pentane). $[\alpha]_D = +128.3°$ ($c = 2.09$, $CHCl_3$). Spectral data: see *above*.

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