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Samarium Diiodide-Mediated Pinacolization of Diketones – II. Synthesis of Polycyclic Frameworks Containing a Cyclobutane-1,2-diol and a Cyclopentane-1,2-diol

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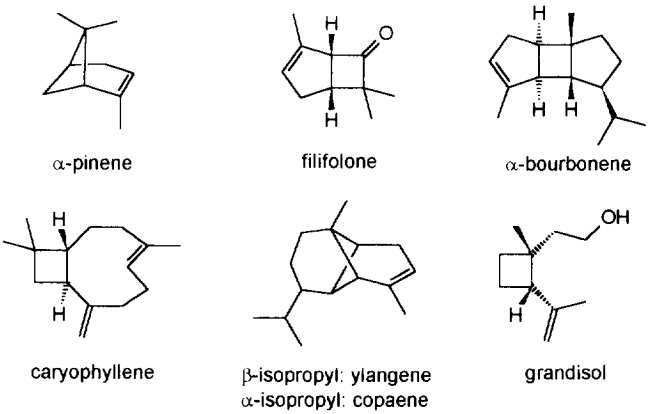
Abstract: The title reaction has been applied to the synthesis of a variety of polycyclic networks. Scope and limitations of the procedure are evaluated. Copyright © 1996 Elsevier Science Ltd

Polycyclic and functionalized cyclobutanes are of interest in natural products synthesis and selected examples are shown in Scheme 1. Similarly, five-membered rings are ubiquitous in polycyclic systems.

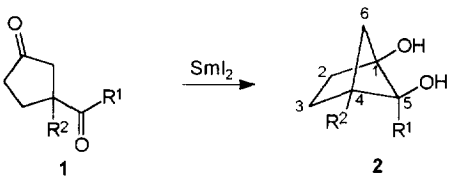


Scheme 1. Naturally Occurring Monoterpenes and Sesquiterpenes

We here describe the synthesis of a variety of polycyclic 1,2-diols by SmI_2-mediated pinacol coupling.[1] As in our earlier work we were interested to probe scope and limitations of this procedure and to find out how much additional strain will be tolerated from starting diketones *en route* to polycyclic 1,2-diols.

Pinacolization of β-acylated cyclopentanones **1a - c** and of β-aroylated cyclopentanones **1d - j** afforded strained norpinane-1,5-diols in moderate yield (ca. 30 - 40%). *o*-Tolyl derivative **1e** as well as *o*-anisyl derivative **1h** did not cyclize, presumably for steric reasons. The carbonyl group of *p*-anisyl ketone **1j** (which can be regarded as a benzenologous ester) is deactivated relative to *m*-anisyl ketone **1i**. Presumably for this reason, the yield of **2j** (15%) was lower than that of **2i** (30%). It is well known that esters are generally inert to reduction by SmI_2.[2] The effect of the pre-angular benzyl group in diketone **1k** (R^2 = benzyl) on the yield of pinacol is spectacular (81%). Simultaneously, the stereochemical requirement of the formation of *cis*-configurated diol is somewhat relaxed: *trans*-1,2-diol was formed as a minor component (*cis* : *trans* = 13 : 1).

Table 1. Synthesis of Norpinane-1,5-diols (Bicyclo[2.1.1]hexane-1,5-diols) **2**.

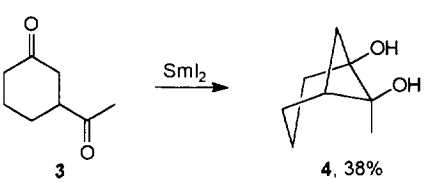


1 **2**

	R^1	R^2	Yield [%]
a	methyl	H	40
b	ethyl	H	37
c	benzyl	H	40
d	phenyl	H	33
e	*o*-tolyl	H	---
f	*m*-tolyl	H	39
g	*p*-tolyl	H	42
h	*o*-anisyl	H	---
i	*m*-anisyl	H	30
j	*p*-anisyl	H	15
k	*p*-tolyl	benzyl	81[a]

[a]Combined yield of *cis*-diol and *trans*-diol (in which R^1 and OH group at carbon C-5 are interchanged) is *cis* : *trans* = 13 : 1.

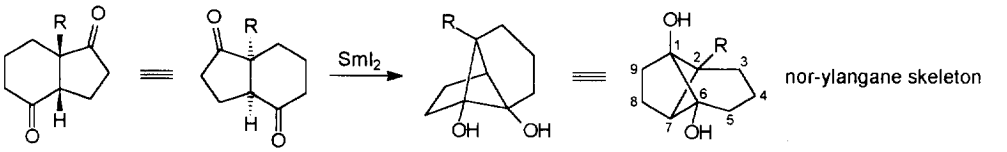
Similar to the preparation of functionalized norpinanes (Table 1) the homologous pinane skeleton is accessible from 3-acetylcyclohexanone (**3** → **4**) (Scheme 2).



3 **4**, 38%

Scheme 2.

The effect of angular methyl group on the yield of cyclization is very marked in bicyclic *cis*-hydrindione **5** and somewhat less, in *cis*-decalin-1,5-dione **7**. Thus, the monomethylated tricyclo[4.3.0.$0^{2,7}$]nonane framework **6b** is formed in 75% yield [*vs.* **6a** (18%)]. For the tricyclo[4.4.0.$0^{2,7}$]decanes prepared, the absolute yield of methylated **8b** is lower (32%), although the increase from **8a** to **8b** (ca. 3.6 fold) is similar. Tricyclic **6** is of the nor-ylangane type. The homologous tricyclo[4.4.0.$0^{2,7}$]decane framework occurs naturally in ylangane and copaene (cf. Scheme 1).

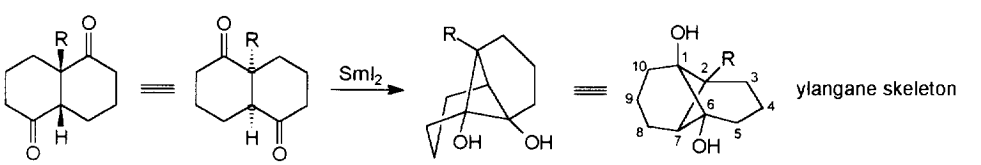


5a: R = H
5b: R = Me

6a, 18%
6b, 75%

Scheme 3.

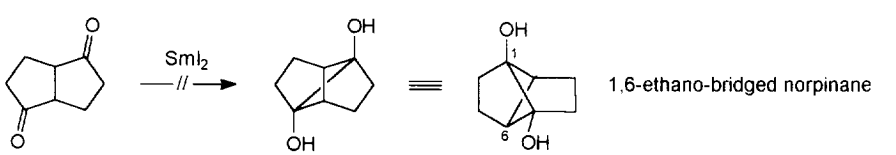
Note that the tricyclic 1,2-diols having the nor-ylangane skeleton **6a, b** and ylangane skeleton **8a, b** are necessarily *trans*-diols with respect to the doubly bracketed 4-membered ring.



7a: R = H
7b: R = Me

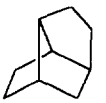
8a, 9%
8b, 32%

ΔE = 61.9 - 19.9 = 42.0 kcal mol^{-1}
64.8 - 23.4 = 41.4 kcal mol^{-1}



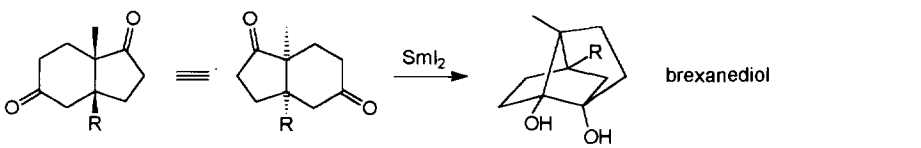
Scheme 4.

Bicyclo[3.3.0]octane-2,6-dione failed to cyclize, the potential cyclobutanediol being too strained (Scheme 4). *cis*-Fused hydrindanediones **9a, b**, which are readily obtainable from steroidal building blocks,[3] are isomeric with bicyclic diketones **5a, b** (Scheme 3) and serve as precursors to brexanes (Scheme 6). The parent brexane is a C_9 tricycle containing a norbornane skeleton with an ethano bridge attached *exo* to norbornane (Scheme 5).[4]



brexane
Tricyclo[4.3.0.0^{3,7}]nonane

Scheme 5.

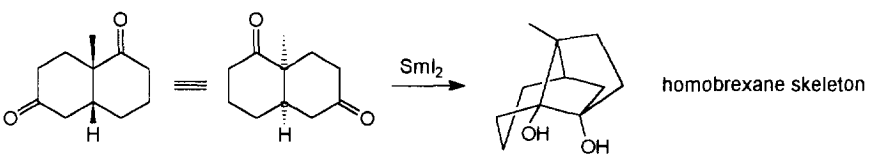


9a: R = H
9b: R = OH

10a, 66% ΔE = 40.0 - 22.2 = 17.8 kcal mol^{-1}
10b, 40% 42.5 - 24.0 = 18.5 kcal mol^{-1}

Scheme 6.

Hydrogenation of the Wieland-Miescher ketone[5] afforded decalindione **11**, a bicyclic 1,5-diketone. Its cyclization complements that of isomeric **7b**, a 1,4-diketone (Scheme 4), and furnished the doubly bridged cyclopentane-1,2-diol **12**. This tricycle is a homobrexanediol. (Scheme 7).

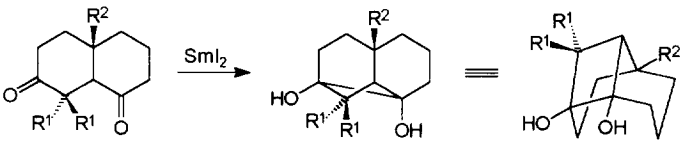


11 **12**, 85%

Scheme 7.

In the cyclization of *cis*-decalindiones **13a - d** both one angular methyl group (cf. **13b**) and a geminal dimethyl group (cf. **13c**) increased the yield of pinacol **14b** and **14c**, respectively, to more than 90% (Table 2). In 1,4-diketone **13d** steric repulsion in the transition state may be responsible for the drop in yield. The formation of monoketo alcohol (42%) supports this assumption (cf. also 2,4,4,5,5,7-hexamethyl-3,6-dione which did not cyclize[1]).

Table 2.

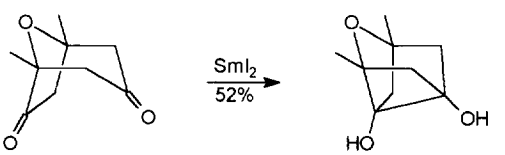


13 **14**

	R^1	R^2	Yield [%]
a	H	H	70
b	H	Me	94[a]
c	Me	H	90[a]
d	Me	Me	37[b]

[a]Pinacolization also in presence of MeOH. [b]Additional monoalcohol (42%); structure unknown.

During the synthesis of the dioxatricyclic core of the marine natural product dictyoxetane we recently prepared 1,5-dimethyl-8-oxabicyclo[3.2.1]octane-3,6-dione (**15**).[6] Pinacolization afforded the 2-oxatricyclo-[3.2.1.$0^{3,6}$]octane framework **16** in 52% yield. HyperChem calculations suggest that the formation of the oxatricycle **16** is accompanied by an energy increase of 40.8 kcal mol^{-1}.



15 **16**

HyperChem 3.0 energy [kcal mol^{-1}] 20.6 61.4 ΔE = 40.8

Scheme 8.

Conclusions. In polycyclic systems it is usually the bridgehead position which is the hardest to functionalize. The pinacol coupling outlined makes it comparatively easy to build up polycycles with alkyl and hydroxy groups at the bridgehead. Thus, the strained norpinane-1,5-diols in Table 1 are all hydroxylated at carbon C(1) and alkylated at carbon C(4). On pinacolization of bicyclic to tricyclic hydrocarbons one obtains four bridgehead carbons altogether. In the nor-ylangane/ylangane systems prepared (Scheme 3, 4) one bridgehead carbon is alkylated and two are hydroxylated. In the brexane and homobrexane series three and even all four bridgehead carbons are substituted, also in **14** and oxatricycle **16**.

In fact, quaternary centres as in **2k** (Table 1) improve the yield of pinacol strongly (81%). Similarly, a suitably placed angular methyl group (e. g. **5a** *vs.* **5b**) facilitates cyclization (18% *vs.* 75%).

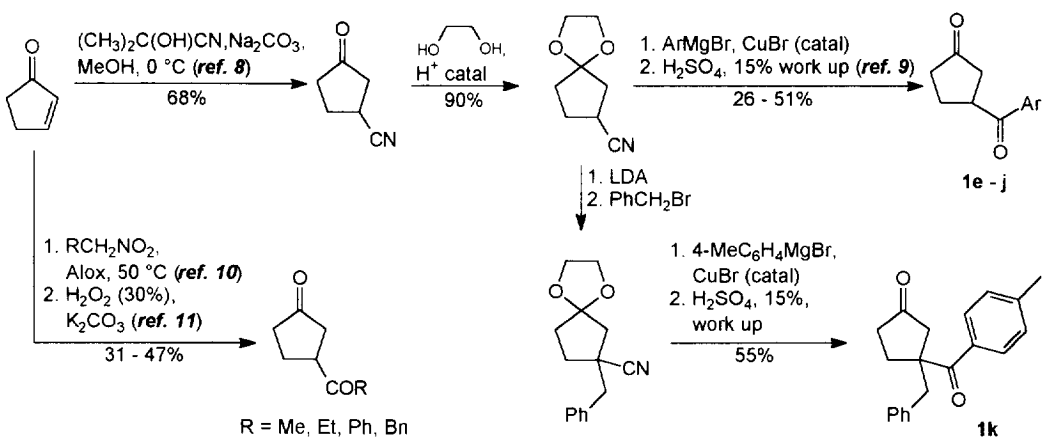
According to HyperChem calculations a strain energy increase of up to ~40 kcal mol^{-1} is accommodated, as in the conversion of diketone **7b** into ylangane **8b**. For comparison, the strain enthalpy of simple cyclobutane

is 27.4 kcal mol^{-1}.[7] Thus, the SmI_2-promoted pinacolization is an attractive route to a variety of multifunctionalized and strained polycycles. An ester group and a *p*-chlorophenyl group are tolerated, as well as an internal hydroxy group (Scheme 6, **10b**) and, of course, a methoxyphenyl group. The polycycles prepared are of general interest and also analogs or precursors of natural products.

EXPERIMENTAL

General Remarks. See Part I.[1]

Synthesis of 1,4-Diketones and 1,5-Diketones. The norpinane precursors **1a - d** as well as pinane precursor **3** were obtained by Michael addition of the primary nitroalkanes to cyclopentanone and cyclohexanone (60 °C, Alox B) followed by Nef reaction with H_2O_2/K_2CO_3. Arylated 1,4-Diketones **1e - j** as well as **1k** were prepared as follows:[12]



General Procedure for the Cyclization with SmI_2. A 50 mL three-necked flask equipped with gas inlet and reflux condenser was charged with SmI_2 (375 mg, 2.50 mmol) and heated under a weak stream of N_2. 1,2-Diiodoethane (592 mg, 2.10 mmol) was added and the mixture cooled to 0 °C. THF (30 mL) was added and the mixture stirred for 10 min (the colour of the solution turns to dark blue). The SmI_2 solution was stirred for 50 min at r.t., then heated to reflux and the diketone (1.00 mmol) in THF (5 mL) was added slowly. *Work up - Method A.* The reaction was quenched with 1 N HCl and the aqueous layer extracted with EtOAc (3 ×). The combined organic layer was extracted with sat. aq. $Na_2S_2O_3$ solution, water and brine and dried ($MgSO_4$). After removal of the solvent the crude product was purified by chromatography. *Method B.* The reaction was quenched with 1 N HCl, the aqueous layer saturated with NaCl and extracted with E for 1 d (Ludwig extractor). The organic layer was dried ($MgSO_4$), evaporated and chromatographed. *Method C.* After complete reaction sat. aq. $NaHCO_3$ solution and brine were added and the aqueous layer was extracted with E. The organic layer was freed from iodine by treatment with sat. aq. $Na_2S_2O_3$ solution. After drying ($MgSO_4$) and removal of the solvent the crude product was chromatographed. *Method D.* The reaction was quenched with 1 N HCl, E was added and the organic layer was washed with sat. aq. $Na_2S_2O_3$ solution (2 ×). The aqueous

layer was reextracted with E, the combined organic layer washed with brine and dried ($MgSO_4$). The solvent was removed and the crude product purified by chromatography.

5-Methyl-bicyclo[2.1.1]hexan-1,5-diol (**2a**). Diketone **1a** (126 mg, 1.00 mmol) was allowed to react for 3 h according to the general procedure (work up: method A) to afford **2a**, 51 mg (40%), yellowish oil. IR ($CHCl_3$) ν 3588, 3400, 2968, 1456, 1404, 1264, 1232, 1172 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.01 (s, 3 H, CH_3), 1.13 - 1.22 (m, 1 H), 1.35 - 1.47 (m, 4 H), 1.74 - 1.82 (m, 1 H), 2.23 - 2.33 (m, 1 H), 4.44 (s, 1 H, C(1)OH), 5.26 (s, 1 H, C(2)OH); ^{13}C NMR δ 24.55 (+, C-4), 27.36 (+, C-3), 38.80 (–, C-5), 40.82 (+, C-6), 48.51 (–, C-7), 80.33 (+, C-2), 83.45 (+, C-1); MS *m/z* 129 (M^++1, 1) , 128(M^+, 4), 110 (4), 95 (19), 87 (58), 71 (100).

5-Ethyl-bicyclo[2.1.1]hexane-1,5-diol (**2b**). Diketone **1b** (140 mg, 1.00 mmol) was allowed to react for 3 h according to the general procedure (work up: method B) to afford **2b**, 53 mg (37%), yellowish oil. IR ($CHCl_3$) ν 3338, 2965, 2880, 1463, 1304, 1230, 1173, 997 cm^{-1}; ^1H NMR (DMSO-d_6) δ 0.82 (t, $^3J_{7,8}$ = 7.5 Hz, CH_3), 1.10 - 1.19 (m, 1 H), 1.30 - 1.51 (m, 6 H), 1.77 - 1.86 (m, 1 H), 2.19 - 2.30 (m, 1 H), 4.25 (s, 1 H, C(1)OH), 5.26 (s, 1 H, C(2)OH), ^{13}C NMR δ 7.67 (+, C-7), 24.50 (+, C-4), 27.40 (+, C-3), 37.45 (–, C-5), 40.54 (+, C-6), 80.93 (+, C-2), 86.01 (+, C-1); MS *m/z* 143 (M^++1, 2), 142 (M^+, 7), 113 (15), 101 (45), 85 (100); HRMS calcd. for $C_8H_{14}O_2$: 142.0994, found 142.0997.

5-Benzyl-bicyclo[2.1.1]hexane-1,5-diol (**2c**). Diketone **1c** (202 mg, 1.00 mmol) was allowed to react for 30 min according to the general procedure (work up: method B) to afford **2c**, 82 mg (40%), yellowish oil. IR ($CHCl_3$) ν 3580, 3000, 2968, 1600, 1452, 1296, 1264, 1232, 1152 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.12 - 1.25 (m, 1 H), 1.41 - 1.82 (m, 5 H), 2.25 (m, 1 H), 2.60, 2.81 (d, $^2J_{7,7}$ = 14 Hz, PhCH_2), 4.37 (s, 1 H, OH), 5.40 (s, 1 H, OH), 7.20 - 7.40 (m, 5 H, arom. H); ^{13}C NMR δ 24.73 (+, C-4), 27.19 (+, C-3), 35.58 (+, C-7), 38.39 (–, C-5), 40.53 (+, C-6), 81.07 (+, C-2), 84.90 (+, C-1), 126.44 (–, CCHCHCH), 128.50 (–, CCHCH), 129.80 (–, CCH), 137.40 (+, CCH); MS *m/z* 205 (M^++1, 2), 204 (M^+, 4), 186 (2), 147 (10), 129 (31), 113 (39), 91 (100); HRMS calcd. for $C_{13}H_{16}O_2$: 204.1150, found 204.1143.

5-Phenyl-bicyclo[2.1.1]hexane-1,5-diol (**2d**). Diketone **1d** (188 mg, 1.00 mmol) was allowed to react for 16 h according to the general procedure (work up: method A) to afford **2d**, 63 mg (33%), yellowish liquid. IR (film) ν 3369, 2966, 2939, 1485, 1463, 1378, 1304, 1172 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.10 - 1.27 (m, 2 H), 1.27 - 1.38 (m, 1 H), 1.38 - 1.53 (m, 2 H), 2.36 (m, 1 H), 2.44 (m, 1 H), 5.05 (s, 1 H, OH), 5.85 (s, 1 H, OH), 7.26 (m, 5 H, arom. H); ^{13}C NMR δ 24.35 (+, C-3), 27.06 (+, C-4), 37.76 (–, C-5), 40.39 (+, C-6), 81.68 (+, C-2), 86.33 (+, C-1), 126.85 (–,CCH), 127.5 (–,CCHCHCH), 128.44 (–,CCHCH), 141.01 (+,CCH); MS *m/z* 190 (M^+, 11),172 (12), 133 (100), 120 (81), 105 (94), 77 (89); HRMS calcd. for $C_{12}H_{14}O_2$: 190.0994, found 190.0997.

5-m-Tolyl-bicyclo[2.1.1]hexane-1,5-diol (**2f**). Diketone **1f** (202 mg, 1.00 mmol) was allowed to react for 2 h according to the general procedure (work up: method A) to afford **2f**, 80 mg (39%), colourless solid, m.p. 102 - 103 °C. IR ($CHCl_3$) ν 3596, 3424, 2976, 1300, 1228, 1156, 1064, 1048, 1024 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.12 - 1.24 (m, 2 H), 1.30 - 1.37 (m, 1 H), 1.37 - 1.46 (m, 2 H), 2.29 (s, 3 H, CH_3), 2.31 - 2.37 (m, 1 H), 2.39 - 2.48 (m, 1 H), 5.00 (br. s, 1 H, OH), 5.80 (br. s, 1 H, OH), 6.97 - 7.27 (m, 4 H, arom. H); ^{13}C NMR δ 21.39 (–, CH_3), 24.41 (+, C-3), 26.86 (+, C-4), 37.72 (–, C-5), 40.28 (+, C-6), 81.59 (+, C-2), 86.49 (+, C-1), 123.76, 127.31, 128.44 (–, arom. C), 138.14 (+, CCH_3), 140.58 (+, arom. C); MS *m/z* 204 (M^+, 15), 186 (13), 163 (25), 147 (97), 134 (88), 119 (100), 92 (79); HRMS Calcd. for $C_{13}H_{16}O_2$: 204.1150, found 204.1146.

5-p-Tolyl-bicyclo[2.1.1]hexane-1,5-diol (**2g**). Diketone **1g** (202 mg, 1.00 mmol) was allowed to react for 2.5 h according to the general procedure (work up: method A) to afford **2g**, 86 mg (42%), yellowish liquid. IR ($CHCl_3$) ν 3596, 3448, 2972, 2932, 1604, 1512, 1296, 1156, 1048, 820 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.09 - 1.22 (m, 2 H), 1.29 - 1.48 (m, 3 H), 2.28 (s, 3 H, CH_3), 2.38 - 2.47 (m, 1 H), 4.94 (s, 1 H, OH), 5.80 (s, 1 H, OH), 7.11 (d, ^3J = 8 Hz, 2 H, arom. H), 7.20 (d, ^3J = 8 Hz, 2 H, arom. H); ^{13}C NMR δ 21.24 (–, CH_3), 24.53 (+, C-3), 26.99 (+, C-4), 37.84 (+, C-5), 40.46 (+, C-6), 81.74 (+, C-2), 86.31 (+, C-1), 126.72, 129.25 (–, arom. C), 137.35, 137.98 (+, arom. C); MS *m/z* 204 (M^+, 4), 187 (8), 186 (5), 147 (60), 134 (54), 129 (11), 119 (100), 105 (57).

5-m-Anisyl-bicyclo[2.1.1]hexane-1,5-diol (**2i**). Diketone **1i** (218 mg, 1.00 mmol) was allowed to react for 2.5 h according to the general procedure (work up: method A) to afford **2i**, 66 mg (30%), yellowish oil. IR ($CHCl_3$) ν 3592, 3444, 2976, 1580, 1484, 1288, 1156, 1044 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.11 - 1.54 (m, 5 H), 2.26 - 2.38 (m, 1 H), 2.38 - 2.47 (m, 1 H), 3.73 (s, 3 H, OMe), 5.05 (s, 1 H, OH), 5.95 (s, 1 H, OH), 6.72 - 6.95 (m, 3 H, arom. H), 7.24 (t, ^3J =8 Hz, MeOCCHC*H*); ^{13}C NMR δ 24.51 (+, C-4), 26.94 (+, C-3), 37.87 (–, C-5), 40.33 (+, C-6), 55.19 (–, C-13), 81.69 (+, C-2), 86.39 (+, C-1), 112.40, 113.17 (–, MeOC*C*H), 119.09 (–, MeOC(CH)$_2$*C*H), 129.71 (–,MeOCCH*C*H), 142.22 (+, MeOCCH*C*), 159.64 (+, MeO*C*); MS *m/z* 221 (M^++1, 2), 220 (M^+, 12), 202 (13), 163 (71), 150 (81), 135 (100), 110 (53); HRMS calcd. for $C_{13}H_{16}O_3$: 220.10995, found 220.1090.

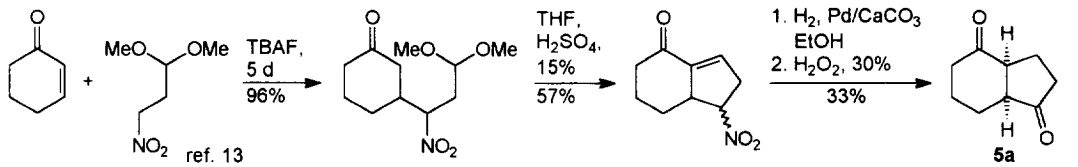
5-p-Anisyl-bicyclo[2.1.1]hexane-1,5-diol (**2j**). Diketone **1j** (218 mg, 1.00 mmol) was allowed to react for 2.5 h according to the general procedure (work up: method A) to afford **2j**, 33 mg (15 %), yellowish oil. IR ($CHCl_3$) ν 3596, 3416, 2968, 1608, 1512, 1296, 1248, 1176, 1036, 836 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.09 - 1.23 (m, 2 H), 1.30 - 1.36 (m, 1 H), 1.36 - 1.45 (m, 2 H), 2.27 - 2.35 (m, 1 H), 2.39 - 2.48 (m, 1 H), 3.74 (s, 3 H, OMe), 4.90 (s, 1 H, OH), 5.78 (s, 1 H, OH), 6.86 (m, ^3J =9 Hz, 2 H, arom. H), 7.22 (m, ^3J =9 Hz, 2 H, arom. H), ^{13}C NMR δ 24.57 (+, C-3), 26.93 (+, C-4), 37.96 (–, C-5), 40.52 (+, C-6), 55.23 (–, OMe), 81.8 (+, C-2), 86.11 (+, C-1), 114.01 (–, MeOC*C*H), 129.06 (–, MeOCCH*C*H), 133.16 (+, MeOC(CH)$_2$*C*), 159.05 (+, MeO*C*); MS *m/z* 220 (M^+, 3), 202 (3), 163 (34), 135 (40), 85 (100), 83 (100); HRMS calcd. for $C_{13}H_{16}O_3$: 220.10995, found 220.1091.

4-Benzyl-5-p-tolyl-bicyclo[2.1.1]hexane-1,5-diol (**2k**). Diketone **1k** (292 mg, 1.00 mmol) was allowed to react for 2 h according to the general procedure (work up: method A) to afford **2k**, 239 mg (81%), colourless needles, m.p. 179 - 180 °C, *cis/trans* = 13 : 1. IR ($CHCl_3$) ν 3596, 2928, 1600, 1512, 1496, 1296, 1228, 1084 cm^{-1}; ^1H NMR (DMSO-d_6) δ 0.92 - 1.10 (m, 2 H), 1.26 - 1.44 (m, 1 H), 1.49 - 1.73 (m, 2 H), 1.82 - 2.02 (m, 1 H), 2.30 (s, 3 H, CH_3), 2.39, 2.68 (d, ^2J = 13 Hz, PhCH_2), 5.12 (s, 1 H, OH_{trans}), 5.28 (s, 1 H, OH_{cis}), 5.62 (s, 1 H, OH_{cis}), 5.71 (s, 1 H, OH_{trans}), 6.92 (m, 2 H, arom. H), 7.16 - 7.28 (m, 5 H, arom. H), 7.87 (d, ^3J = 8 Hz, 2 H, arom. H); ^{13}C NMR δ 20.68 Å (–, CH_3), 26.64 (+), 30.53 (+), 36.19 (+), 48.13 (+), 78.69 (+, C-OH_{trans}), 80.63 (+, C-OH_{cis}), 80.86 (+, C-OH_{cis}), 83.50 (+, C-OH_{trans}), 125.43, 127.61, 127.84, 129.01, 129.64 (–, arom. C), 134.94, 138.91, 138.95 (+, arom. C), one C atom is hidden under the DMSO signal; MS *m/z* 295(M^++1, 1), 294 (M^+, 3), 276 (7), 203 (11), 119 (100), 92 (95). HRMS calcd. for $C_{20}H_{22}O_2$: 294.1620, found 294.1616.

6-Methyl-bicyclo[3.1.1]heptane-cis-*1,6-diol* (**4**). Diketone **3** (140 mg, 1.00 mmol) was allowed to react for 30 min according to the general procedure (work up: method C) to afford **4**, 54 mg (38%), colourless solid. IR ($CHCl_3$) ν 3564, 3428, 2992, 2956, 2872, 1444, 1376, 1340, 1312, 1120, 1052, 932 cm^{-1}; ^1H NMR δ 1.17 (s,

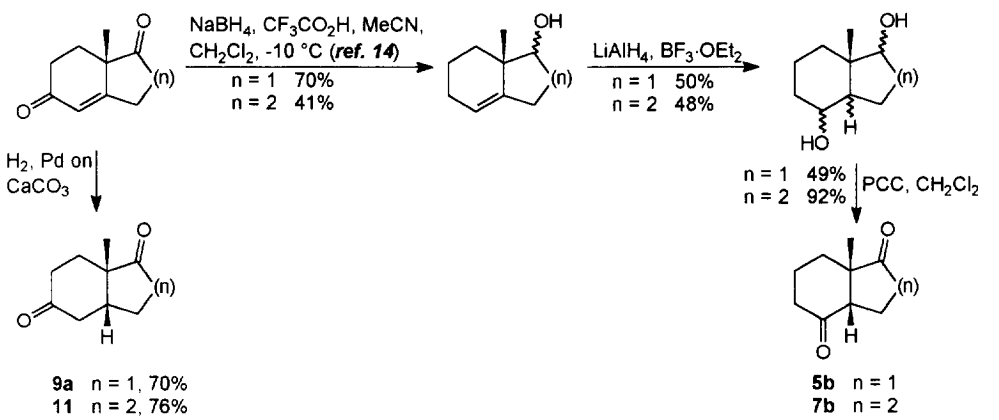
3 H, CH_3), 1.52 - 1.93 (m, 6 H), 1.80 (d, J = 9 Hz, 1 H, C*H*H), 2.00 - 2.07 (m, 1 H, CH*H*), 2.30 (br. t, 1 H, CH), 3.48 (br. s, 1 H, OH), 3.92 (br. s, 1 H, OH); ^{1}H NMR (DMSO-d_6) δ 0.99 (s, 3 H, CH_3), 1.44 - 1.73 (m, 6 H), 1.78 - 1.87 (m, 1 H, C*H*H), 1.62 (d, J = 10 Hz, 1 H, CH*H*), 2.17 (br. t, 1 H, CH), 4.37 (s, 1 H, OH), 4.49 (s, 1 H, OH); ^{13}C NMR δ 15.34, 24.81, 31.94, 35.15 (+, CH_2), 17.27 (–, CH_3), 37.58 (–, CH), 75.85, 81.96 (+, C-OH); MS *m/z* 142 (M^+, 6), 124 (5), 109 (8), 99 (14), 87 (64), 84 (100), 81 (30), 71 (47), 69 (64). Anal. Calcd. for $C_8H_{14}O_2$: C, 67.56; H, 9.93. Found: C, 67.67; H, 9.83.

Synthesis of 1,4-Diketone **5a**.[12]



Tricyclo[4.3.0.0^{2,7}]nonane-1,6-diol (**6a**). Diketone **5a** (152 mg, 1.00 mmol) was allowed to react for 1.5 h according to the general procedure (work up: method A) to afford **6a**, 28 mg (18%), yellowish liquid. IR ($CHCl_3$) ν 3600, 3528, 2940, 1636, 1338, 1380, 1228, 1124, 1096 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.08 - 1.94 (m, 10 H), 1.97 (s, 2 H), 4.41 (s, 1 H, OH), 5.10 (s, 1 H, OH); ^{13}C NMR δ decomposition during NMR scan, but signals at 77.55 (+) and 81.45 (+) are typical for tertiary C-OH; MS *m/z* 154 (M^+, 2), 136 (9), 105 (9), 73 (100).

1,4-Diketones **5b** and **7b** were prepared by 1,2-carbonyl transpositions of the Robinson annulation products, which were also converted into **9a** and **11** by hydrogenation.



2-Methyl-tricyclo[4.3.0.0^{2,7}]nonane-1,6-diol (**6b**). Diketone **5b** (166 mg, 1.00 mmol) was allowed to react for 4 h according to the general procedure (work up: method D) to afford **6b**, 126 mg (75%), colourless solid, m.p. 115 °C. IR (KBr) ν 3327, 2937, 1357, 1304, 1252, 1161, 1073, 1055 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 0.72 (s, 3 H, CH_3), 1.11 - 1.66 (m, 10 H), 1.85 (s, 1 H, CH), 4.34 (s, 1 H, OH), 4.96 (s, 1 H, OH); ^{13}C NMR δ 15.52 (–, CH_3), 18.20, 20.30, 25.61, 27.62, 27.65 (+, CH_2), 41.61 (–, CH), 42.61 (+, CCH_3), 77.02, 82.06 (+, C-OH); MS (50 °C) *m/z* 168 (M^+, 7), 150 (17), 122 (16), 108 (100).

1,4-Diketone **7a** was obtained by hydrogenation of naphthalene-1,5-diol.

Tricyclo[4.4.0.0^{2,7}]decane-1,2-diol (**8a**). Diketone **7a** (270 mg, 1.60 mmol) was allowed to react for 8 h according to the general procedure (work up: method D) to give **8a**, 10 mg (9%), yellow solid. IR ($CHCl_3$) ν 3900, 3420, 2928, 2864, 1704, 1448, 1192 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.09 - 1.86 (m, 10 H), 1.92 - 2.23 (m, 4 H), 3.14 - 3.43 (br. s, 1 H, OH), 4.28 - 4.46 (br. s, 1 H, OH); MS (80 °C) *m/z* 168 (M^+, 2), 150 (63), 122 (21), 94 (34), 84 (100), 67 (31), 55 (19).

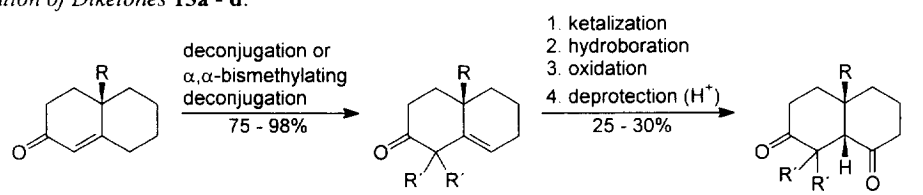
6-Methyl-tricyclo[4.4.0.0^{2,7}]decane-1,2-diol (**8b**). Diketone **7b** (146 mg, 0.810 mmol) was allowed to react for 10 h according to the general procedure (work up: method D) to give **8b**, 21 mg (32%), yellowish solid. IR ($CHCl_3$) ν 3596, 3428, 2948, 2928, 2868, 1704, 1124, 1104, 1076, 1016 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 0.80 (s, 3 H, CH_3), 1.03 - 1.92 (m, 12 H), 1.93 - 2.09 (m, 1 H), 4.23 (br. s, 1 H, OH), 4.32 (br. s, 1 H, OH); MS (80 °C) *m/z* 182 (M^+, 4), 164 /37), 146 (28), 121 (40), 108 (81), 98 (100), 79 (39), 67 (44), 55 (34).

7-Methyl-tricyclo[4.3.0.0^{3,7}]nonane-1,6-diol (**10a**). Diketone **9a** (166 mg, 1.00 mmol) was allowed to react for 2.5 h according to the general procedure (work up: method D) to give **10a**, 111 mg (66%), colourless solid, m.p. 183 - 184 °C. IR (KBr) ν 3402, 2927, 2872, 1476, 1377, 1318, 1138 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 0.82 (s, 3 H, CH_3), 0.97 - 1.60 (m, 8 H), 1.66 - 1.94 (m, 3 H), 4.29 (s, 1 H, OH), 4.38 (s, 1 H, OH); ^{13}C NMR δ 15.12 (–, CH_3), 25.04, 28.42, 30.52, 35.29, 40.36 (+, CH_2), 41.98 (CH), 48.23 (+, *C*CH_3), 81.89, 86.18 (+, C-OH); MS *m/z* 168 (M^+, 79), 150 (33), 135 (85), 97 (100). HRMS calcd. for $C_{10}H_{16}O_2$: 168.1150, found 168.1150.

7-Methyl-tricyclo[4.3.0.0^{3,7}]nonane-1,3,6-triol (**10b**). Diketone **9b** (182 mg, 1.00 mmol) was allowed to react for 16 h according to the general procedure (work up: method D) to give **10b**, 73 mg (40%), yellowish solid. IR (KBr) ν 3387, 2927, 1464, 1378, 1303, 1259, 1124, 1055 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 0.73 (s, 3 H, CH_3), 1.04 - 1.30 (m, 4 H), 1.35 (s, 2 H, H-2), 1.51 - 0.89 (m, 4 H), 4.32 (s, 1 H, OH), 4.42 (s, 1 H, OH), 4.50 (s, 1 H, OH); ^{13}C NMR δ 12.08 (–, CH_3), 24.45, 25.50, 35.53, 35.99, 48.57, 49.65 (+, CH_2, *C*CH_3), 79.94, 80.02, 82.69 (+, C-OH); MS (70 °C) *m/z* 184 (M^+, 3), 166 (44), 151 (9), 123 (100); HRMS calcd. for $C_{10}H_{16}O_3$: 184.1099, found 184.1100.

1-Methyl-tricyclo[4.4.0.0^{2,8}]decane-2,8-diol (**12**). Diketone **11** (73 mg, 0.41 mmol) was allowed to react for 8 h according to the general procedure (work up: method C) to give **12**, 63 mg (85%), colourless solid. IR ($CHCl_3$) ν 3600, 3444, 2928, 2868, 1464, 1308, 1132, 1106, 1088 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 0.80 (s, 3 H, CH_3), 1.02 - 1.28 (m, 3 H), 1.31 - 1.68 (m, 9 H), 1.73 - 1.91 (m, 1 H), 3.88 (s, 1 H, OH), 4.40 (s, 1 H, OH); ^{13}C NMR δ 14.19 (q, CH_3), 17.98, 24.73, 27.65, 33.71, 35.69, 35.89 (t, CH_2), 40.47 (d, CH), 43.62 (s, *C*CH_3), 81.35, 82.95, (s, C-OH); MS *m/z* 182 (M^+, 24), 164 (100), 149 (50), 131 (28), 121 (34), 111 (78), 95 (50), 81 (38), 67 (36), 55 (44).

Preparation of Diketones **13a - d**.[15]



R = H, Me **13 a - d**

Tricyclo[5.4.0.0^{4,8}]decane-4,8-diol (**14a**). Diketone **13a** (166 mg, 1.00 mmol) was allowed to react for 1 h at 36 - 36 °C according to the general procedure (work up: method C) to give **14a**, 118 mg (70%), colourless solid, m.p. 176 °C. IR ($CHCl_3$) ν 3604, 3564, 3444, 3000, 2940, 2876, 1464, 1336, 1236, 1160, 1124, 1072,

1040, 1016, 960, 924 cm^{-1}; ^1H NMR δ 1.29 - 1.68 (m, 6 H), 1.86 - 2.05 (m, 6 H), 2.18 - 2.30 (m, 2 H, CH), 3.22 (br. s, 1 H, OH), 3.80 (br. s, 1 H, OH); ^1H NMR (DMSO-d_6) δ 1.17 - 1.58 (m, 6 H), 1.63 - 2.01 (m, 6 H), 2.05 - 2.18 (m, 2 H, CH), 4.37 (s, 1 H, OH), 4.50 (s, 1 H, OH); ^{13}C NMR δ 19.85, 23.09, 29.50, 29.99, 33.16, 35.54 (+, CH_2), 33.35, 38.84 (–, CH), 77.29, 79.95 (+, C-OH); MS *m/z* 168 (M^+, 2), 149 (13), 135 (9), 121 (11), 110 (100), 97 (87), 79 (63), 67 (39). Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.38; H, 9.59. Found: C, 71.15; H, 9.47.

1-Methyl-tricyclo[5.4.0.0^{4,8}]decane-4,8-diol (**14b**). Diketone **13b** (180 mg, 1.00 mmol) was allowed to react for 30 min according to the general procedure (work up: method C) to give **14b**, 171 mg (94%), colourless solid, m.p. 124 °C. IR (KBr) ν 3377, 2943, 2922, 2872, 2844, 1456, 1329, 1245, 1231, 1159, 1116, 1074, 1025, 958, 902 cm^{-1}; ^1H NMR δ 0.88 (s, 3 H, CH_3), 1.07 - 1.47 (m, 4 H), 1.53 - 1.75 (m, 4 H), 1.83 - 2.01 (m, 4 H), 2.20 (br. t, 1 H, CH), 3.30 (br. s, 1 H, OH), 3.86 (br. s, 1 H, OH); ^1H NMR (DMSO-d_6) δ 0.82 (s, 3 H, CH_3), 1.03 - 1.39 (m, 4 H), 1.47 - 1.82 (m, 8 H), 2.07 (br. t, 1 H, CH), 4.41 (br. s, 1 H, OH), 4.52 (br. s, 1 H, OH); ^{13}C NMR δ 21.11, 29.27, 30.95, 31.87, 34.21, 35.25 (+, CH_2), 29.24 (–, CH_3), 37.57 (+, CCH_3), 45.13 (–, CH), 77.30, 80.37 (+, C-OH); MS *m/z* 182 (M^+, 1), 164 (6), 149 (6), 136 (5), 121 (8), 111 (100), 93 (19), 79 (14), 67 (14). Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.48; H, 9.96. Found: C, 71.80; H, 9.82.

5,5-Dimethyl-tricyclo[5.4.0.0^{4,8}]decane-4,8-diol (**14c**). Diketone **13c** (194 mg, 1.00 mmol) was allowed to react for 3 h according to the general procedure (work up: method C) to give **14c**, 176 mg (90%), colourless solid, m.p. 127 °C. IR ($CHCl_3$) ν 3576, 3000, 2944, 2872, 1464, 1372, 1316, 1180, 1160, 1132, 1048, 1016, 964, 912 cm^{-1}; ^1H NMR δ 1.03 (s, 3 H, CH_3), 1.19 - 1.34 (m, 2 H), 1.42 (s, 3 H, CH_3), 1.46 - 1.73 (m, 4 H), 1.62 (d, J = 4 Hz, 1 H, CH), 1.92 - 2.16 (m, 4 H), 2.84 (br. s, 2 H, OH); ^1H NMR (DMSO-d_6) δ 0.90 (s, 3 H, CH_3), 1.14 - 1.26 (m, 2 H), 1.33 (s, 3 H, CH_3), 1.40 (d, J = 4 Hz, 1 H, CH), 1.44 - 1.61 (m, 4 H), 1.73 - 1.82 (m, 2 H), 1.84 - 2.03 (m, 2 H), 2.07 - 2.18 (m, 1 H, CH), 4.14 (s, 1 H, OH), 4.41 (s, 1 H, OH); ^{13}C NMR δ 17.64, 26.11, 30.19, 30.71, 31.07 (+, CH_2), 20.47, 24.27 (–, CH_3), 31.30 (–, $CHCH_2$), 43.18 (+, CCH_3), 47.20 (–, $CHCHCH_2$), 77.68, 80.99 (+, C-OH); MS *m/z* 196 (M^+, 5), 178 (17), 163 (8), 153 (18), 135 (22), 122 (20), 110 (100), 97 (69), 79 (23), 67 (32). Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.42; H, 10.28. Found: C, 73.22; H, 10.13.

1,5,5-Trimethyl-tricyclo[5.4.0.0^{4,8}]decane-4,8-diol (**14d**). Diketone **13d** (208 mg, 1.00 mmol) was allowed to react for 2 h according to the general procedure (work up: method C) to give **14d**, 78 mg (37%), colourless solid, m.p. 134 °C. IR ($CHCl_3$) ν 3608, 2946, 2871, 1692, 1593, 1460, 1383, 1336, 1299, 1125, 1093, 1040, 1015, 980, 891 cm^{-1}; ^1H NMR δ 1.02 (s, 3 H, CH_3), 1.18 (s, 3 H, CH_3), 1.21 - 1.32 (m, 4 H), 1.44 (s, 3 H, CH_3), 1.46 (s, 1 H, CH), 1.58 - 1.94 (m, 5 H), 1.99 - 2.08 (m, 2 H), 2.87 (br. s, 2 H, OH); ^1H NMR (DMSO-d_6) δ 0.95 (s, 3 H, CH_3), 1.06 (s, 3 H, CH_3), 1.11 - 1.33 (m, 4 H), 1.38 (s, 3 H, CH_3), 1.43 - 1.88 (m, 6 H), 1.71 (s, 1 H, CH), 4.13 (s, 1 H, OH), 4.27 (s, 1 H, OH); ^{13}C NMR δ 19.95, 30.86, 31.01, 31.11, 37.91 (+, CH_2), 22.52, 26.06, 30.45 (–, CH_3), 39.82, 44.92 (+, CCH_3), 55.41 (–, CH), 77.76, 80.23 (+, C-OH); MS *m/z* 210 (M^+, 5), 192 (17), 177 (15), 164 (20), 149 (39), 136 (32), 121 (60), 111 (100), 93 (42), 81 (43), 67 (40). Anal. Calcd. for $C_{13}H_{22}O_2$: C, 74.23; H, 10.55. Found: C, 73.35; H, 10.38.

1,5-Dimethyl-8-oxabicyclo[3.2.1]octane-3,6-dione (**15**). A flame-dried flask was charged with 1,5-dimethyl-8-oxabicyclo[3.2.1]octan-3-one[6] (0.5 g, 3.3 mmol) in abs. THF (18 mL) under N_2 and a solution of BH_3·THF (15 mL, 0.35 M solution in THF) was added at 0 °C. The mixture was stirred for 40 min at 0 °C and for 18 h at r.t., then water (0.8 mL) was added. The solvent was removed, the residue diluted with E (36 mL) and treated

with $K_2Cr_2O_7$ (1.5 g), conc. H_2SO_4 (1.14 mL) and water (4 mL). The mixture was heated to reflux for 6 h and then extracted with E. After drying (Na_2SO_4) and removal of the solvent the crude product was purified by chromatography to afford 1,5-dimethyl-6-hydroxy-8-oxabicyclo[3.2.1]octan-3-one (268 mg, 48%). PCC (220 mg, 1.02 mmol) was mixed with silica gel (500 mg). To this mixture CH_2Cl_2 (5 mL) was added followed by a solution of hydroxyketone (260 mg, 1.53 mmol) in CH_2Cl_2 (10 mL). After 5 h a further portion of PCC (0.5 mmol) was added and stirring was continued for 24 h. Silica gel (1.5 g) was added and the solvent evaporated. Chromatography gave dione **15** (180 mg, 70%). IR ($CHCl_3$) ν 3040, 2984, 1764, 1720, 1336, 1228 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.42 (s, 3 H, CH_3), 1.61 (s,3 H, CH_3), 2.49 (m, 6 H, CH_2); MS *m/z* 169 (M^+ + 1, 2), 168 (M^+, 16), 140 (92), 125 (15), 97 (7), 96 (1), 85 (96), 82 (100), 55 (32).

1,3-Dimethyl-2-oxatricyclo[3.2.1.0^{3,6}]octane-5,6-diol (**16**). Diketone **15** (150 mg, 0.89 mmol) was allowed to react according to the general procedure (work up: method B) to give after chromatography (E) **16**, 79 mg (52%), colourless crystals, m.p. 117 - 118 °C. IR (KBr) ν 3340, 3216, 2960, 2932, 2864, 1440, 1271, 1156, 860 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.01 (s, 3 H, CH_3), 1.24 (s, 3 H, CH_3), 1.33 (dd, *J* = 2, 10 Hz, 1 H, H-7), 1.65 (d, *J* = 10 Hz, 1 H, H-7), 1.69 (m, 2 H, H-4), 1.79 (d, *J* = 10 Hz, 1 H, H-8), 2.13 (dd, *J* = 2, 10 Hz, 1 H, H-8), 5.01 (s, 1 H, OH), 5.46 (s, 1 H, OH); ^{13}C NMR (DMSO-d_6) δ 17.89 (–, CH_3), 19.68 (–, CH_3), 44.60 (+, C-4), 48.10 (+, C-8), 50.77 (+, C-7), 72.40 (+, CCH_3), 75.82 (+, COH), 78.04 (+, CCH_3), 88.58 (+, COH); MS *m z* 171 (M^+ + 1, 1), 170 (M^+, 8), 152 (8), 134 (2), 127 (16), 112 (100), 96 (4), 95 (34), 83 (19), 69 (14); HRMS calcd. for $C_9H_{14}O_3$: 170.0943, found 170.0944.

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