243. A Further Synthetic Approach to the Adamantane Isomer 2,5-Trimethylenenorbornane (Tricyclo[5.3.0.0^{3,9}]decane, 4-Homotwistbrendane)

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Summary

A further synthetic approach to 2,5-trimethylenenorbornane (**1**; tricyclo-[5.3.0.0^{3,9}]decane, 4-homotwistbrendane), a member of the 'adamantaneland', is described starting from methyl 5-oxo-2*endo*-norbornanecarboxylate (**5**). The required C_2-chain was introduced by a *Wittig-Horner* reaction and the ring closure of the trimethylene bridge achieved by an acyloin condensation.

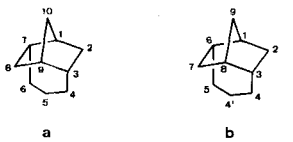
In the course of our studies on isomeric tricyclic hydrocarbons of the 'adamantaneland'[1]), we recently described a first synthesis of the title isomer, 2,5-trimethylenenorbornane (**1**)[2]). Solvolysis of the *p*-toluenesulfonate **2** of protoadamant-4-en-10*endo*-ol yielded among others the allylic alcohols **3** and **4** with the desired C-skeleton [2]. Subsequent conversions of the latters led to **1**.

In view of further investigations on the adamantane rearrangement of **1**, especially with specifically labelled analogues, we report a second synthetic approach to **1** and derivatives thereof, starting from the properly 2,5-difunctionalized norbornane **5**. As the only evaluated synthesis of **5** [3] is an unspecific one, we decided to prepare **5** from the known ester **6** [4] by the following route: epoxidation and lactonization of **6** with trifluoroperacetic acid [5] gave the known [6] hydroxy lactone **7** (94%), which was oxidized to the keto lactone **8** (80%) with

[1]) 'Adamantaneland': a set of 19 isomeric $C_{10}H_{16}$-hydrocarbons [1].

[2]) Compound **1** is also called 2,5-trimethylene-8,9,10-trinorbornane, tricyclo[5.3.0.0^{3,9}]decane (**a**), 4-homotwistbrendane (**b**). In the present communication the numbering of the C-atoms follows the trimethylenenorbornane nomenclature. The correct IUPAC names are added in parentheses in the *Exper. Part.*

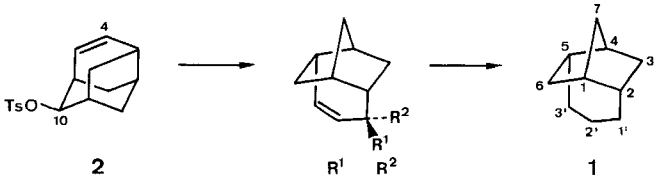
Scheme 1



a **b**

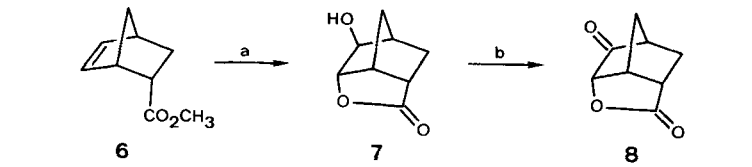
0018-019X/82/8/2453-05$01.00/0

Scheme 2

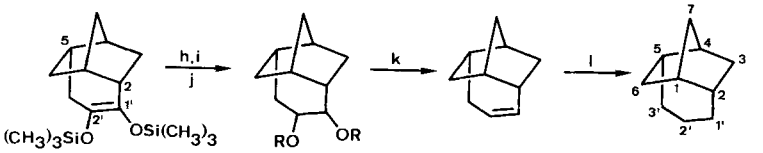


	R^1	R^2
3	OH	H
4	H	OH

Scheme 3



	R^1	R^2
9	CO_2CH_3	H
10	H	CO_2CH_3



13	R = H
14	R = Ms

[a]) 90% H_2O_2-solution, $(CF_3CO)_2O$, $K_2HPO_4 \cdot 3\,H_2O$, CH_2Cl_2, 15 min, 0° [5]. [b]) RuO_2, $NaIO_4$, $CHCl_3$, H_2O [7]. [c]) Zn, AcOH, reflux. [d]) CH_2N_2. [e]) $(CH_3O)_2P(O)CH_2CO_2CH_3$, NaH, benzene, 70°. [f]) H_2, 10% Pd/C, AcOEt. [g]) Na, toluene, $(CH_3)_3SiCl$, reflux. [h]) H_2, 10% Pd/C, CH_3OH. [i]) $LiAlH_4$, Et_2O. [j]) CH_3SO_2Cl, *N,N*-dimethylaminopyridine, pyridine. [k]) Na, anthracene, THF [10]. [l]) H_2, 5% $Pd/CaCO_3$, pentane [2].

RuO_4 [7]. Treatment of **8** with Zn/CH_3COOH followed by methylation with diazomethane led to the envisaged keto ester **5** in 60% yield. The missing C_2-side chain at C(5) was introduced by a *Wittig-Horner* reaction to afford a separable 3.3:1 mixture (97%) of the two configurational isomers **9**[3]) and **10**[3]). Hydrogenation of both compounds quantitatively gave the *endo,endo*-disubstituted norbornane derivative **11**[4]). The key step of our synthesis was the ring closure of **11** to a 2,5-trimethylenenorbornane derivative. This could easily be achieved by a modified acyloin condensation [8] yielding the bisilylated acyloin **12** (76%). Its treatment with 10% Pd/C [9] under H_2-atmosphere and subsequent reduction with $LiAlH_4$ gave a mixture of diastereomeric alcohols **13** (87%), which was converted to a mixture of methanesulfonates **14** (88%). Subsequent elimination with sodium anthracene [10] led to the olefine **15** (51%), which very recently we already had prepared by an independent route [2] and had converted by hydrogenation to the title compound 2,5-trimethylenenorbornane (**1**) [2].

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Experimental Part

Spectral data[2]). – *General.* IR. spectra were recorded in CCl_4 on a *Perkin-Elmer-297* spectrophotometer, bands are given in cm^{-1}. ^{1}H-NMR. spectra ($CDCl_3$) were measured on a *Varian HA-100* or *Bruker WM-300* using $CDCl_3$ as solvent. Chemical shifts are given in ppm relative to TMS as internal standard; J = spin-spin coupling constant (Hz), $w_{1/2}$ = half width at half height (Hz). Mass spectra (MS.) were performed on a *Hitachi-Perkin-Elmer-RMU-6M* instrument at 70 eV ionizing electron energy, source temp. 180°, inlet temp. 200°. The most important ions are listed as *m/z* values with relative intensities (% of base peak) in parenthesis.

*Methyl 5-[(E)-methoxycarbonylmethylidene]-8,9,10-trinorbornane-2*endo*-carboxylate* (**9**). – IR.: 3018*w*, 1742*s*, 1716*s*, 1667*m*, 1451*w*, 1436*m*, 1421*w*, 1360*m*, 1307*w*, 1282*w*, 1270*m*, 1254*w*, 1230*w*, 1204*s*, 1167*m*, 1147*m*, 1133*m*, 1114*w*, 1072*w*, 1034*m*, 920*w*, 904*w*. – ^{1}H-NMR. (300 MHz): 1.5–1.6 (*m*, 2 H–C(7)); 1.79 ($d\times d$, $J(gem)$ = 12.5, $J(2exo,3endo)$ = 4.5, H_{endo}–C(3)); 1.96 ($d\times d\times d$, $J(gem)$ = 12.5, $J(2exo,3exo)$ = 11.5, $J(3exo,4)$ = 5, H_{exo}–C(3)); 2.52 (*m*, $w_{1/2}\approx 6$, 2 H–C(6)); 2.78 (*m*, $w_{1/2}\approx 9$, H–C(1)); 2.87 (*m*, $w_{1/2}\approx 9$, H–C(4)); 2.89 (*m*, $w_{1/2}\approx 23$, H_{exo}–C(2)); 3.67 and 3.68 (2 *s*, H_3CO_2C–C(2) and H_3CO_2C–C(1')); 5,78 (*t*, J = 3, H–C(1')). – MS.: 224 (2, M^+, $C_{12}H_{16}O_4$), 193 (30), 192 (53), 165 (17), 164 (32), 138 (100), 133 (18), 132 (13), 123 (15), 107 (23), 106 (95), 105 (67), 104 (22), 91 (28), 87 (28), 79 (53), 78 (46), 77 (44), 67 (15), 66 (14), 65 (18), 59 (33), 55 (38), 41 (19), 39 (34), 27 (20), 15 (30).

*Methyl 5-[(Z)-methoxycarbonylmethylidene]-8,9,10-trinorbornane-2*endo*-carboxylate* (**10**). – IR.: 3020*w*, 1743*s*, 1723*s*, 1666*m*, 1449*w*, 1435*m*, 1364*m*, 1315*w*, 1297*m*, 1280*m*, 1269*w*, 1254*w*, 1213*s*, 1197*m*, 1175*w*, 1166*s*, 1137*s*, 1116*w*, 1029*m*, 950*w*, 939*w*, 915*w*, 907*w*, 853*w*. – ^{1}H-NMR. (300 MHz): 1.45–1.65 (*m*, *AB*-part, 2 H–C(7)); 1.77 ($d\times d\times d$, $J(gem)$ = 13, $J(2exo,3endo)$ = 5, $J(3endo,7^{C(5)})^{5}$ = 2.5,

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[3]) We assign the (*E*)-configuration to the major product **9** and the (*Z*)-configuration to the minor isomer **10** on the basis of their ^{1}H-NMR. data for H–C(4) and 2 H–C(6). Due to the close vicinity of the ester group in **9** the C(6)-methylene group is shifted downfield (2 H–C(6) at 2.52 and H–C(4) at 2.87 ppm), whereas in **10** H–C(4) is strongly deshielded (H–C(4) at 4.04 and 2 H–C(6) at 2.15–2.35 ppm).

[4]) According to GC. analysis only < 2% of an 5*exo*-epimer was formed.

[5]) The right superscripts C(5) and C(2) mean that the H-atom at C(7) is, with respect to the bridge, on the same side as C(5) and C(2), respectively.

H_{endo}–C(3)); 2.02 ($d\times d\times d$, $J(gem)=13$, $J(2exo,3exo)=12$, $J(3exo,4)=4.5$, H_{exo}–C(3)); 2.15–2.35 (*m*, *AB*-part, 2 H–C(6)); 2.70 (*m*, $w_{1/2}\approx 8$, H–C(1)); 2.90 ($d\times d\times d\times d$, $J(2exo,3exo)=12$, $J(2exo,3endo)=5$, $J(1,2exo)=4.5$, $J=1$, H_{exo}–C(2)); 3.68 and 3.70 (2 *s*, H_3CO_2C–C(2) and H_3CO_2C–C(1')); 4.04 ($d\times m$, $J(3exo,4)=4.5$, $w_{1/2}\approx 8$, H–C(4)); 5.58 (*m*, $w_{1/2}\approx 5$, H–C(1')). – MS.: 224 (2, M^+, $C_{12}H_{16}O_4$), 193 (28), 192 (44), 165 (15), 164 (30), 138 (100), 133 (20), 132 (14), 123 (14), 107 (21), 106 (75), 105 (63), 104 (21), 91 (27), 87 (28), 79 (49), 78 (43), 77 (41), 67 (14), 66 (13), 65 (17), 59 (32), 55 (36), 41 (22), 39 (35), 29 (10), 27 (21), 15 (33).

Methyl 5endo-*methoxycarbonyl-8,9,10-trinorbornane-2*endo-*acetate* (**11**). – IR.: 1742–1737*s*, 1458*w*, 1452*w*, 1435*m*, 1378*w*, 1348*w*, 1308*w*, 1301*w*, 1290*w*, 1240*m*, 1197*s*, 1178*s*, 1122*w*, 1047*w*, 1023*w*, 1003*w*, 912*w*. – ^{1}H-NMR. (300 MHz): 0.79 ($d\times d\times d$, $J(gem)=13.5$, $J(2exo,3endo)=5$, $J(3endo,7^{C(5)})^5=2$, H_{endo}–C(3)); 1.45–1.55 (*m*, 2 H–C(7)); 1.55 ($d\times d\times d\times d$, $J(gem)=13.5$, $J(5exo,6exo)=11.5$, $J(1,6exo)=4.5$, $J(2exo,6exo)=2$, H_{exo}–C(6)); 1.76 ($d\times d\times d\times d$, $J(gem)=13.5$, $J(2exo,3exo)=11.5$, $J(3exo,4)=5$, $J(3exo,5exo)=2$, H_{exo}–C(3)); 1.96 ($d\times d\times d$, $J(gem)=13.5$, $J(5exo,6endo)=5$, $J(6endo,7^{C(2)})^5=2.5$, H_{endo}–C(6)); 2.24 ($d\times m$, $J(1,6exo)=4.5$, $w_{1/2}\approx 10$, H–C(1)); 2.27 (*m*, $w_{1/2}\approx 25$, H_{exo}–C(2)); 2.45–2.55 (*m*, H–C(4) and $H_3CO_2CCH_2$–C(2)); 2.78 ($d\times d\times d\times d$, $J(5exo,6exo)=11.5$, $J(5exo,6endo)=5$, $J(4,5exo)=4.5$, $J(3exo,5exo)=2$, H_{exo}–C(5)); 3.66 and 3.69 (2 *s*, H_3CO_2C–C(5) and $H_3CO_2CH_2C$–C(2)). – MS.: 226 (3, M^+, $C_{12}H_{18}O_4$), 195 (59), 194 (97), 167 (30), 166 (76), 162 (40), 153 (21), 152 (36), 138 (24), 135 (25), 134 (40), 121 (22), 120 (14), 117 (14), 108 (19), 107 (64), 106 (37), 105 (17), 100 (12), 99 (24), 93 (71), 92 (42), 91 (49), 87 (70), 81 (22), 80 (100), 79 (97), 78 (25), 77 (44), 74 (34), 67 (63), 66 (76), 65 (27), 59 (63), 55 (43), 54 (16), 53 (27), 43 (16), 41 (60), 39 (45), 29 (13), 27 (23), 15 (42).

1',2'-Bis (trimethylsilyloxy)-2,5-trimethylene-8,9,10-trinorborn-1'-ene (4,5-Bis (trimethylsilyloxy)tricyclo[5.3.0.0^{3,9}]dec-4-ene; **12**). – IR.: 1671*m*, 1463*w*, 1350*w*, 1330*m*, 1309*w*, 1295*w*, 1278*w*, 1250*s*, 1235*m*, 1203*s*, 1189*m*, 1164*w*, 1148*w*, 1120*m*, 1067*m*, 1017*w*, 1005*w*, 972*w*, 959*m*, 953*m*, 931*w*, 909*m*, 899*m*, 878*s*, 868*s*, 846*s*. – ^{1}H-NMR. (100 MHz, internal standard: $CHCl_3$): 0.13 and 0.15 (2 *s*, each $(CH_3)_3Si$); 1.2–1.9 (*m*, 2 H–C(3), 2 H–C(6) and 2 H–C(7)); 1.9–2.6 (*m*, H–C(1), H–C(2), H–C(4), H–C(5) and 2 H–C(3')). – MS.: 312 (9), 311 (22), 310 (80, M^+, $C_{16}H_{30}O_2Si_2$), 295 (9), 268 (21), 220 (5), 205 (5), 181 (10), 167 (6), 155 (34), 147 (35), 75 (18), 73 (100), 45 (16).

Mixture of 2,5-trimethylene-8,9,10-trinorbornane-1',2'-diols (tricyclo[5.3.0.0^{3,9}]decane-4,5-diols; **13**). – IR.: 3630*w*, 3380*s* br., 1474*m*, 1442*w*, 1402*m*, 1308*m*, 1246*w*, 1203*w*, 1160*w*, 1135*w*, 1114*w*, 1058*s*, 1029*s*, 1012*m*, 991*w*, 973*m*, 943*m*, 924*w*, 896*w*, 850*w*. – ^{1}H-NMR. (100 MHz): 1.0–1.6 (*m*, 5 H); 1.6–2.6 (*m*, 7 H); 2.74 and 2.98 (2 *m*, $w_{1/2}$ each ≈ 8, HO–C(1') and HO–C(2')); 4.1–4.45 (*m*, $w_{1/2}\approx 10$, H–C(1') and H–C(2')). – MS.: 168 (3, M^+, $C_{10}H_{16}O_2$), 150 (47), 135 (13), 132 (17), 122 (14), 121 (28), 120 (15), 119 (25), 117 (27), 109 (41), 108 (45), 107 (22), 106 (38), 105 (14), 104 (22), 97 (10), 96 (61), 95 (42), 94 (32), 93 (59), 92 (85), 91 (60), 84 (10), 83 (26), 82 (13), 81 (69), 80 (86), 79 (97), 78 (27), 77 (36), 70 (54), 69 (15), 68 (17), 67 (100), 66 (84), 65 (14), 57 (22), 55 (23), 54 (11), 53 (17), 43 (10), 41 (42), 39 (25), 29 (11), 27 (15).

Mixture of 2,5-trimethylene-8,9,10-trinorbornane-1',2'-diyl dimethanesulfonates (tricyclo[5.3.0.0^{3,9}]decane-4,5-diyl dimethanesulfonates; **14**). – IR. ($CHCl_3$): 1479*w*, 1447*w*, 1413*w*, 1364*s*, 1337*s*, 1306*w*, 1273*w*, 1173*s*, 1150*w*, 1066*w*, 1038*w*, 1019*m*, 1008*w*, 990*w*, 975*s*, 965*s*, 942*m*, 922*w*, 903*s*, 867*s*. – ^{1}H-NMR. (100 MHz): 1.0–1.8 (*m*, 6 H); 1.8–2.8 (*m*, 6 H); 3.03 and 3.05 (2 *s*, each CH_3SO_3); 5.2–5.5 (*m*, H–C(1') and H–C(2')). – MS.: 324 (M^+ ($C_{12}H_{20}O_6S_2$) not observed), 245 (10), 228 (15), 186 (11), 150 (12), 149 (88), 133 (38), 132 (78), 131 (41), 121 (52), 119 (13), 117 (52), 107 (16), 105 (39), 104 (25), 93 (44), 92 (24), 91 (100), 81 (19), 80 (18), 79 (78), 78 (30), 77 (22), 67 (51), 66 (22), 57 (14), 55 (19), 54 (12), 53 (11), 41 (29), 39 (11).

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