262. Planarisation of Tetracoordinate Carbon Atom. A Further Route to (all-*cis*)-[5.5.5.5]Fenestrane

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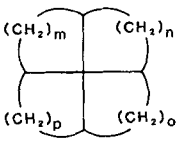
Summary

The synthesis of (all-*cis*)-[5.5.5.5]fenestrane (**3**) from dicyclopentadiene is reported. Key step is the Pd-catalyzed reductive deoxygenation of an appropriately substituted cyclooctanone, which leads to transannular C,C-bond formation.

Introduction. – The increasing interest in fenestrane-type structures **1** (*m,n,o,p* = 1 or 2) is due to the type and extent of strain to be expected for such compounds [1]. The special bonding situation of the central C-atoms in structures of type **1** leads to planoid deformations, which are essentially caused by opening of opposite bond angles (see **2a**) rather than rotation (see **2b**) [2]. We have recently communicated the first preparation of (all-*cis*)-[5.5.5.5]fenestrane (**3**) [3][1]). We report here a further synthesis of this saturated hydrocarbon.



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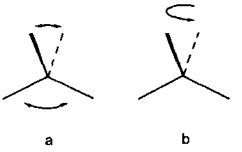


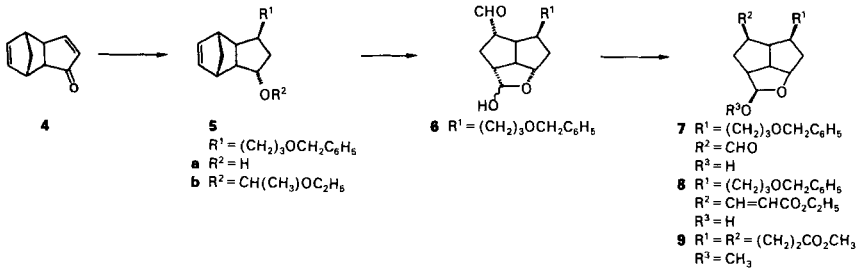
2

Results. – The starting enone **4** readily available from dicyclopentadiene gave *via* CuI-catalyzed 1,4-addition of benzyloxypropyllithium a tricyclic ketone with the side chain in *'exo'*-configuration [5]. Reduction with $NaBH_4$ lead exclusively to the *'endo'*-alcohol **5a**, which subsequently was protected by acid-catalyzed reaction with ethyl vinyl ether (→**5b**). Oxidation of **5b** with $KMnO_4$ according to [6] lead to the tricyclic compound **6** [1b]. The formyl group in **6** could be equilibrated under phase-transfer conditions leading to a 1:9 mixture of **6***('endo')* and **7***('exo')*. Chain-extension in **7** with ethyl (diethoxyphosphoryl)acetate gave the intermediate **8**, which subsequently was transformed into the tricyclic acetal-diester **9** by hydrogenation, followed by aceta-

[1]) For syntheses of other fenestranes, see [4a] [7] ([5.5.5.5]-fenestrane), [4b] ([4.5.5.5]- and [4.4.5.5]fenestrane), and [4c] ([4.4.4.5]fenestrane).

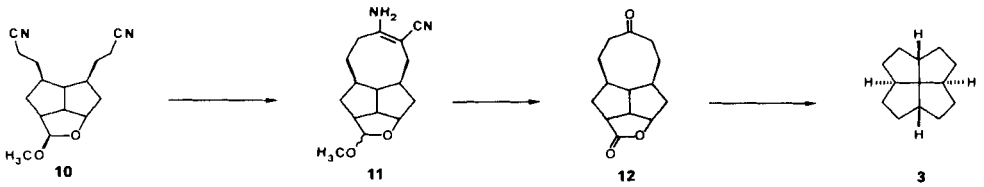
lisation, oxidation, and esterification. Based upon this reaction sequence, *'exo'*-configuration is assigned to the methoxycarbonylethyl groups in 3- and 5-position of **9** *(Scheme 1)*. *'exo'*-Configuration is also assigned to the CH_3O-group of the acetal moiety in **9**, because the acetal proton appears as a *s* in the ^{1}H-NMR spectrum.

Scheme 1



Because of earlier experience in a related case [7], we had expected that *Dieckmann* condensation of the diester **9** would give a β-ketoester, which upon further transformations could have led to the desired ketolactone **12**. Since the diester **9** gave, even under high-dilution conditions, less than 5% of the desired intramolecular condensation product, it was transformed into the dinitrile **10** by reaction of **9** with NH_3 and subsequent dehydration of the diamide [8]. Under *Ziegler-Thorpe* conditions, the dinitril **10** readily gave the β-enamino-nitrile **11**, from which the ketolactone **12** *(Scheme 2)* could be prepared.

Scheme 2



It was thought to prepare a substituted fenestrane from the ketolactone **12** by one of the well established methods for transannular carbene insertion [9]. For this purpose, the ketogroup of **12** was transformed into the corresponding (2,4,6-tri(isopropyl)phenylsulfonyl)hydrazone. However, the potassium salt of this hydrazone did not give the expected derivative of fenestrane under thermal or photolytical conditions. This result is particularly surprising because in a related case a substituted fenestrane could readily be prepared by this method [7].

Eventually, we found that the unsubstituted (all-*cis*)-[5.5.5.5]fenestrane (**3**) could be prepared directly from the ketolactone **12** by treatment with Pd/C and some H_2. The (all-*cis*)-configuration of this fenestrane **3** has been established by GC-comparison with a sample prepared by a different route [3].

Final Remarks. – (all-*cis*)-[5.5.5.5]Fenestrane (**3**) has been obtained from **4** by a reaction sequence which shows remarkable differences from that reported [3] [7]. In

view of these earlier results, the lack of *Dieckmann*-type reactions of **9** as well as the missing transannular insertion of hydrazones derived from **12** under thermal or photolytic conditions are surprising. At present, we can only speculate about the factors which give rise to this unexpected reactivity and therefore postpone a discussion until pertinent results have been obtained. The scope of the Pd-catalyzed deoxygenation with concomitant (transannular) C,C-bond formation is under active exploration.

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Experimental Part

General Remarks. See [10] [11]. Except for diisobutylaluminium hydride (DIBAH), the quality of reagents used was *purum* or *puriss.* The capillary-GC columns used has a length of 20 m.

*Ethyl 5-*exo*-(3'-Benzyloxypropyl)-9-*exo*-hydroxy-8-oxatricyclo[5.2.1.0^{4,10}]decane-3-*exo*-acrylate*[2]) (**8**) [12]. Crude 5-*exo*-(3'-benzyloxypropyl)-9-hydroxy-8-oxatricyclo[5.2.1.0^{4,10}]decane-3-*endo*-carbaldehyde[2]) (**6**) [R_f (Et_2O) 0.54; ^{1}H-NMR: 9.83 (CHO)], prepared from 2.22 g (6.0 mmol) of **5** [13], was stirred for 12 h in 20 ml of CH_2Cl_2 with a mixture of 0.24 g (6 mmol) of NaOH and 50 mg of Bu_4NI in 20 ml of H_2O. After workup, the *exo*-aldehyde **7** [R_f (Et_2O) 0.31; ^{1}H-NMR: 9.60 (CHO) [14]] containing 10% of **6** was dissolved in 10 ml of Et_2O and added at 0° to a solution, prepared from 2.69 g (12 mmol) of ethyl (diethoxyphosphoryl)acetate in 10 ml of Et_2O and 7.5 ml of 1.6N (12.0 mmol) BuLi in hexane and stirred for 2 h at 0°. After workup, the crude product was chromatographed with Et_2O to give 1.35 g (56%) of **8**. R_f (Et_2O) 0.40. IR: 3600, 2940, 1705, 1315, 1295, 1275, 1170, 1095, 1070, 1030, 995. ^{1}H-NMR: 0.89–2.30 (stack, 10H); 1.27 (*t*, *J* = 7, 3H); 2.48–2.90 (stack, 2H); 3.00–3.55 (stack, 3H); 3.72–3.90 (*m*, 1H); 4.16 (*q*, *J* = 7, 2H); 4.47 (*s*, 2H); 4.59–4.78 (*m*, 1H); 5.10–5.28 (~ *s*, br. 1H); 5.75 (*d*, *J* = 16, 1H); 6.85 (*dd*, J_{AB} = 16, J_{AX} = 7, 1H); 7.30 (*s*, 5H). MS: 400 (0.05, M^+), 92 (10), 91 (100), 79 (10), 77 (10), 73 (15), 65 (10).

*Dimethyl 9-*exo*-Methoxy-8-oxatricyclo[5.2.1.0^{4,10}]decane-3-*exo*,5-*exo*-dipropionate*[2]) (**9**). Hydrogenation of 2 g (5.0 mmol) of **8** over Pd/C gave an oil, which was refluxed with MeOH and a trace of TsOH as catalyst. Subsequent oxidation with $RuCl_3$ (0.156 g) and $NaIO_4$ (2.88 g, 13.57 mmol) gave an acid, which was esterified with MeOH. After workup, the crude diester was chromatographed with Et_2O and gave 0.71 g (42%) of **9**. Capillary-GC (*SE 52*, 180°, 13.9 min) revealed the presence of *ca.* 10% of the 3-*endo*-isomer (15.2 min). An anal. pure sample was obtained by HPLC purification (hexane/*t*-Bu(Me)O 2:1). R_f (Et_2O) 0.57. IR: 2950, 1730, 1436, 1200, 1100. ^{1}H-NMR: 1.05–2.81 (stack, 16H); 2.90–3.21 (*m*, 1H); 3.23 (*s*, 3H); 3.62 (*s*, 6H); 4.37–4.56 (*m*, 1H); 4.62 (*s*, 1H). MS: 339 (1, $M^+ - 1$), 309 (25), 248 (47), 207 (23), 206 (100), 204 (31), 133 (22), 121 (35), 119 (30), 105 (22), 79 (29). Anal. calc. for $C_{18}H_{28}O_6$: C 63.51, H 8.29; found: C 63.52, H 8.39.

*9-*exo*-Methoxy-8-oxatricyclo[5.2.1.0^{4,10}]decane-3-*exo*,5-*exo*-dipropiononitrile*[2]) (**10**). A mixture of 1 g (2.92 mmol) of **9** and 0.8 g of liquid NH_3 in 1 ml of MeOH was heated in a pressure bomb to 160° for 17 h. The foamy diamide was transformed into **10** by the method of *Saraie et al.* [8]. After workup with CH_2Cl_2, the crude material was chromatographed with Et_2O to give 0.58 g (72%) of **10** as colourless oil. Pure **10** was obtained by HPLC (CH_2Cl_2/MeOH 99:1). According to capillary-GC (*SE 54*, 225°, 11.1 min), **10** contained *ca.* 7% of the 3-*endo*-isomer (12.3 min). R_f (Et_2O) 0.29. IR: 3010, 2955, 2930, 2245, 1450, 1425, 1100, 1060, 1045, 1000, 985, 970, 950. ^{1}H-NMR: 1.02–3.22 (stack, 17H); 3.26 (*s*, 3H); 4.37–4.60 (*m*, 1H); 4.67 (*s*, 1H). GC/MS: 273 (1, $M^+ - 1$), 243 (32), 174 (39), 160 (39), 132 (29), 120 (87), 119 (22), 105 (19), 95 (39), 93 (31), 91 (63), 79 (100), 77 (39), 67 (34). Anal. calc. for $C_{16}H_{22}N_2O_2$: C 70.04, H 8.08, N 10.21; found: C 70.15, H 8.16, N 10.22.

Ziegler-Thorpe *Reaction of* **10** [15]. A solution of 2.93 g (18.2 mmol) of hexamethyldisilazane in 150 ml of THF was treated with 18.15 mmol of BuLi at 0°. After heating to reflux, a solution of 1.0 g (3.64 mmol) of **10** in 100 ml of THF was added during 22 h. After heating for 1 h, the turbid solution was worked up. Flash chromatography [16] with Et_2O gave crude material which was further purified by low-pressure chromatography [17] with CH_2Cl_2/MeOH 97.5:2.5 giving *11-amino-5-methoxy-4-oxatetracyclo[6.5.1.1^{3,6}.0^{14,15}]pentadec-11-ene-12-carbonitrile* (**11**; 0.593 g, 59%) as colorless crystals. For analysis, a sample was recrystallized twice from THF/Et_2O/pentane. M.p. 154–159° (dec.). R_f (Et_2O) 0.34. IR: 3510, 3405, 3010, 2920, 2860, 2180, 1630,

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[2]) The configurational descriptors *exo* and *endo* are used as in the related bicyclo[X.Y.Z]alkanes in which $X \geq Y > Z > 0$.

1590, 1190, 1090, 1040, 1005, 990, 970, 955. ^{1}H-NMR: 1.0–3.15 (stack, 15H); 3.27, 3.31 (2*s*, ratio 1.3:1, 3H); 4.25–4.8 (stack, 4H). MS: 274 (100, M^+), 243 (40), 221 (46), 161 (48), 133 (29), 132 (29), 120 (27), 117 (26), 107 (27), 95 (21), 91 (36), 79 (29), 70 (48). Anal. calc. for $C_{16}H_{22}N_2O_2$: C 70.04, H 8.08, N 10.21; found: C 70.11, H 8.00, N 10.25.

4-Oxatetracyclo[6.5.1.1^{3,6}.0^{14,15}]pentadecane-5,11-dione (**12**). A solution of 0.3 g (1.09 mmol) of **11** in 8 ml of glacial AcOH and 0.5 ml of H_2O was refluxed for 45 min. After addition of 3 ml of H_3PO_4 (85%), the mixture was refluxed for 22 h. Extraction with CH_2Cl_2 and treatment with 2N NaOH gave material, which was dissolved in 5 ml of acetone and 2 ml of 2N $HClO_4$. After 45 min, the org. product was oxidized at 0° with *Jones* reagent to give crude **12**. After low-pressure chromatography [17] with CH_2Cl_2 Et_2O 4:1, **12** was obtained in 17% yield. Alternatively, a solution of 0.2 g (0.72 mmol) of **11** in 7 ml of toluene was treated with 1.6 ml of 1M DIBAH in toluene at −70°. After 2.5 h, 2 ml of 10% aq. KOH was added, the mixture stirred for 30 min at r.t. and refluxed in presence of 10 ml of CH_2Cl_2 for 45 min. The org. layer was separated and the aq. phase again triturated with CH_2Cl_2. The yellow oil isolated was refluxed in 7 ml of acetone and 3 ml of 2N H_2SO_4 for 2.5 h. Subsequent *Jones* oxidation at 0° gave, after extraction with CH_2Cl_2 and workup, a crystalline material that was purified twice by low-pressure chromatography [17] with CH_2Cl_2/Et_2O 3:1 and *t*-Bu(Me)O/CH_2Cl_2 1:1, resp., to give 35 mg (20%) of **12** (86% purity). An anal. pure sample was obtained by HPLC (*t*-Bu(Me)O/CH_2Cl_2 1:7). M.p. 184–185°. R_f (*t*-Bu(Me)O/CH_2Cl_2) 0.39. IR: 1765, 1700, 1185, 1160, 995. ^{1}H-NMR: 1.1–3.47 (stack, 17H); 4.62–4.82 (*m*, 1H). ^{13}C-NMR: 34.4 (*t*), 34.6 (*t*), 41.0 (*t*), 43.3 (*t*), 44.6 (*t*), 44.7 (*t*), 45.7 (*d*), 47.9 (*d*), 49.0 (*d*), 53.1 (*d*), 54.9 (*d*), 83.1 (*d*), 179.7 (*s*), 218.7 (*s*). MS: 335 (8), 334 (50, M^+), 216 (23), 206 (37), 190 (55), 177 (100), 176 (36), 145 (23), 133 (21), 131 (27), 105 (34), 93 (23), 91 (43), 79 (47), 77 (24). Anal. calc. for $C_{14}H_{18}O_3$: C 71.77, H 7.74; found: C 71.59, H 7.62.

*(all-*cis*)-[5.5.5.5]Fenestrane* (=cis-*transoid*-cis-*transoid*-cis-*transoid*-cis-*transoid*-*Tetracyclo[5.5.1.0^{4,13}.0^{10,13}]-tridecane;* **3**). To a mixture of 5.4 mg (0.023 mmol) of **12** and 30 mg of 10% Pd/C in an ampoule under N_2 was added 4 ml of H_2. The sealed ampoule was heated in a metal bath to 320° for 5 h. The mixture was extracted with CH_2Cl_2, and the oil isolated was analyzed by capillary-GC. Apart from 20% **12**, 40% of **3** was detected. It was identified by co-injection with a sample prepared by a different route [3]; a 1:1 mixture of **3** and an authentic sample gave a single peak on 3 different capillary-GC columns (*OV 1701*, temp. 3°/min, 80–220°, ret. time 14.8 min; *CW 20M*, 65–220°, 14.3 min; *SE 54*, 120°, isothermal, 3.2 min). CAS-Registry-Number of **3**: 67 490-05-5.

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