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GENERAL APPROACH FOR THE SYNTHESIS OF POLYQUINENES *VIA* THE WEISS REACTION
XII. THE CHUGAEV APPROACH TO ELLACENE (1,10-CYCLODODECANOTRIQUINANCENE)

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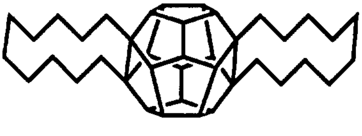
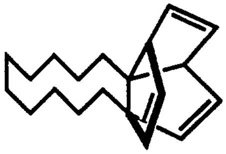
SUMMARY: The synthesis of ellacene (1,10-cyclododecanotriquinancene) **2** has been achieved *via* the Weiss reaction. The regiospecific monoallylation of **6** to provide **7**, and the pyrolysis of tris xanthate **11** in HMPA at 220°C to furnish **2** represent the key steps in the sequence. The HMPA-mediated dehydration of triol **10** to form the ethers **12** and **13** in preference to the desired **2** has also been observed.

Since the first synthesis of triquinacene by Woodward et al[1], the preparation of this molecule and its dimerization to dodecahedrane proposed independently by Woodward[1], Müller[2] and Jacobson[3] have attracted the interests of many organic chemists[4,5] All attempts, however, to dimerize triquinacene into dodecahedrane have failed, presumably, because of the difficulty in effecting reaction between the concave faces of the two molecules[5].



1



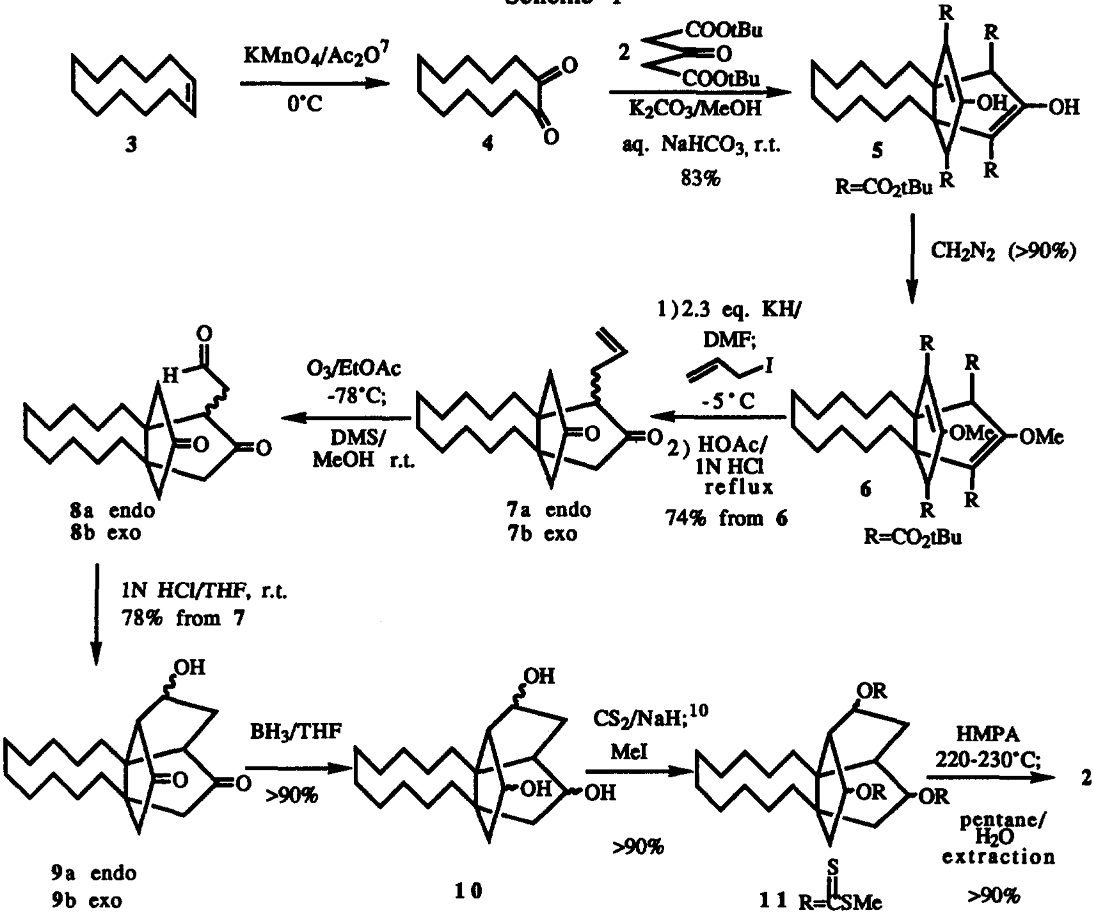
2

In keeping with our interest in the preparation of polyquinenes[4d,6] and polyquinanes we envisaged the synthesis of 1,2,16,17-biscyclododecanododecahedrane **1** from ellacene **2** since the 12-membered cyclododecyl ring would block the convex faces of the molecule from attack. Presumably, this would increase the opportunity for the two molecules of the triene to react in the desired concave-concave fashion (see also the aldol approach of Serratosa[4e]). In this communication, we wish to report the successful synthesis of tetracyclo[11.5.2.0^{1,8}.0^{4,8}]eicosa-2,5,19-triene **2** *via* the Chugaev (HMPA, 220°C) approach to the desired olefinic system.

The α-diketone **4** prepared by the Sharpless procedure[7] from cyclododecene **3** was allowed to stir with two equivalents of di-t-butyl-3-ketoglutarate in CH_3OH under aqueous alkaline conditions at room temperature. This process gave the tetra-t-butyl ester **5** isolated as the bisenol in 83% yield. The enolic hydroxyl groups were protected by converting **5** into the dimethyl bisenol ether **6** (>90%). This material was then subjected to the monoallylation sequence with allyl iodide at -5°C. The monoallyl

[10.3.3]propellanedione 7 isolated in 74% overall yield (from 6) was oxidized to the diketoaldehyde 8 *via* ozonolysis. Aldol cyclization of 8 to 9 was executed under acidic conditions to permit the exo-isomer 8b to epimerize to the endo-isomer 8a, the endo stereochemistry of which is necessary for cyclization. The diketoalcohol 9 was obtained as a mixture of exo- and endo- stereoisomers from which the endo-isomer was separated and crystallized. The exo-isomer was obtained in only 85% purity. Both alcohols were characterized by NMR studies[8]. The reduction of a mixture of 9a and 9b was carried out using a Lewis acid mediated sequence (THF-BH_3) to prevent retroaldol reactions[6] in the process.

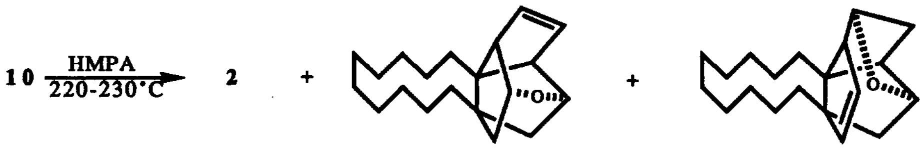
Scheme 1



Examination of the mixture of triols by ^{13}C-NMR spectroscopy indicated the presence of at least three diasteromeric triols indicative of attack (BH_3) on the carbonyl groups from both the concave and convex faces of the cis-bicyclo[3.3.0]octane-3,7-dione unit.

In contrast to the HMPA-mediated dehydration of perhydrotriquinacene triol and perhydrocyclohexanotriquinacene triol to the desired trienes[4d], dehydration of **10** provided only 10% yield of the desired ellacene **2** accompanied by the two ethers[9] **12** and **13** in 30% yield (Scheme 2). The structures of the two ethers were deduced by NMR spectroscopy (^{1}H, ^{13}C and 2D-COSY). The formation of both the exo- and endo-hydroxyl groups from the carbonyl reduction sequence, and a buttressing interaction effected by the 12-membered ring presumably result in the formation of **12** and **13** in preference to **2**. In order to circumvent this difficulty the Chugaev approach[10] was employed and eventually resulted in the synthesis of ellacene **2** in high yield. Initial difficulties in the preparation of the tris xanthate **11**[10] were overcome by replacing THF with CS_2 in the reaction mixture. This gave the xanthate **11** in >90% yield. Pyrolysis of **11** in HMPA at 220-230°C furnished ellacene[11] in 90% overall yield from **10**. This procedure was superior to the pyrolysis under neat conditions since dilution of the triene formed in HMPA limited intermolecular reactions which provide polymeric material.

Scheme 2



10% **12** (15%) **13** (15%)

During the syntheses of triquinacene and cyclohexanotriquinacene[4d], isomeric olefins were observed from the HMPA-mediated dehydration sequence of the corresponding triol[4d], although these isomeric trienes could be isomerized to the desired triquinacene. In contrast, ellacene **2**, a viscous oil, was isolated as a single compound (GC: R_t=6.67min, HP5880 with a capillary columm at 200°C) *via* the syn elimination (pyrolysis) in HMPA. As expected from the C_2 symmetry of **2**, only three olefinic carbon signals were observed in its ^{13}C-NMR spectrum, and five sets of signals were found in the ^{1}H-NMR spectrum of this centrosubstituted triquinacene. Studies with **2** in regard to **1** will be reported in due course.

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8. **9a** (endo): The endo hydroxyl group can form an intramolecular hydrogen bond with the carbonyl group which shifts the signals of the corresponding carbon and the proton attached to that carbon to lower field[4d]. These characteristic signals (underlined) were used to distinguish the endo isomer from the exo isomer. ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.43-1.70 (20H, m), 2.03-2.86 (9H, m), 4.49 (1H, m). ^{13}C-NMR (62.86 MHz, $CDCl_3$) δ 22.46, 22.71, 23.12, 23.45, 25.94, 26.27, 26.86, 27.49, 33.34, 35.11, 42.22, 47.20, 50.87, 54.24, 57.20, 60.71, 65.45, 74.20, 218.36, 220.30. Mass spectrum (EI, 15ev): 318 (M^+, 78.1), 300 (M^+-H_2O, 75.0), 233 (100.0).

9b (exo): ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.40-1.80 (20H, m), 1.90-2.80 (9H, m), 4.28 (1H, d, J=5.0 Hz). ^{13}C-NMR (62.86 MHz, $CDCl_3$) δ 22.83, 23.05, 23.19, 23.57, 25.66, 26.57, 26.90, 27.45, 34.12, 34.77, 40.04, 47.00, 52.04, 57.63, 60.87, 67.50, 217.84, 219.31. Mass spectrum (EI): 318 (M^+, 78.1), 300 (M^+-H_2O, 75.0).

9. **12** and **13**: The two ethers were not separable by capillary GC. The ^{1}H-NMR signals were assigned by 2-D COSY experiments, and the ^{13}C-NMR of the triquinacene ring system by off-resonance experiments and relative intensities. **12**: ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.30-1.60 (20H, m) 1.70 (2H, d, J=11Hz), 1.82 (2H, d, J=11Hz), 2.39 (2H, s), 3.82 (2H, s), 5.80 (2H, t, J=1.4Hz); ^{13}C-NMR (62.86 MHz, $CDCl_3$) δ 45.05 (s), 48.03 (t), 58.30 (s), 58.68 (d), 73.14 (d), 128.62 (d). **13**: ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.30-1.60 (21H, m), 1.86 (2H, m), 2.01 (2H, tt, J=10.2, 1.9, 1.8Hz), 2.30 (1H, s), 2.62 (1H, s), 4.07 (1H, d, J=3Hz), 4.15 (1H, t, J=2.7Hz), 5.36 (1H, dd, J=5.7, 2.8Hz), 5.74 (1H, d, J=5.7Hz); ^{13}C-NMR (62.86 MHz, $CDCl_3$) δ 39.69 (t), 44.76 (t), 51.36 (d), 61.07(s), 63.60 (d), 66.63 (s), 77.72(d), 81.80 (d), 123.56 (d), 141.44(d). The unassigned signals (in the mixture) for the twelve-membered rings of **12** and **13**: 22.81, 23.88, 24.21, 24.49, 24.56, 26.27,26.98, 27.41, 27.78, 28.32, 29.57, 33.27, 34.81, 35.01. High resolution mass spectrum: Calcd. for $C_{20}H_{30}O$: 286.2297. Found: 286.2285.

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11. **2**: ^{1}H-NMR(250 MHz, $CDCl_3$) δ 1.21-1.75 (20H, m), 3.33 (2H, s), 5.45 (2H, dd, J=5.69, 2.00Hz), 5.50 (2H, dd, J=5.69, 2.01Hz), 5.57 (2H, s). ^{13}C-NMR (62.86 MHz, $CDCl_3$) δ 22.90 (1C, t), 23.92 (1C, t), 24.37 (1C, t), 24.60 (1C, t), 25.92 (1C, t), 26.92 (1C, t), 27.58 (1C, t), 28.13 (1C, t), 33.48 (1C, t), 36.04 (1C, t), 63.50 (1C, s), 63.92 (2C, d), 68.30 (1C, s), 129.64 (2C, d), 132.22 (2C, d), 138.05 (2C, d). High-resolution mass spectrum: Calcd. for $C_{20}H_{28}$ 268.2191. Found: 268.2178.

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