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SYNTHESIS OF cis-BICYCLO|3.3.0|OCT-3-ENE-2,7-DIONE, A HIGHLY FUNCTIONALIZED CYCLOPENTANOID INTERMEDIATE

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Summary.- *cis*-Bicyclo|3.3.0|oct-3-ene-2,7-dione (1) has been synthesized either from *cis*-bicyclo|3.3.0|octane-3,7-dione (2) or the |2+2|-cycloadduct 10 of 5-trimethylsilylcyclopentadiene with dichloroketene. As anticipated, the conjugated double bond of acetal 9 acts as a Michael acceptor in front of nucleophiles such as PhSeCH$_2$Li to give the *exo*-1,4-addition derivative 16, from which intermediates with functionalized *endo*-side chains are easily worked up.

cis-Bicyclo|3.3.0|oct-3-ene-2,7-dione (1) is an interesting synthetic intermediate in which all eight carbon atoms are properly activated and ready to undergo a series of *chemo, regio,* and *stereoselective* reactions very useful for the synthesis of either natural[1,2] or non natural[2] polyfused cyclopentanoid systems. Bi-[3] and tricyclooctane[4] derivatives of similar complexity have recently been described.

The starting point of our synthesis is the readily available *cis*-bicyclo|3.3.0|octane-2,7-dione (2)[5] that may be now prepared in good yield by the procedure described by Bertz, Rihs, and Woodward[6]. Although symmetry is usually a simplifying factor in retrosynthetic analysis, it may be sometimes a complicating factor, as Bertz has recently emphasized[3b], in the factual realization of the synthesis. Such is the case for the starting diketone 2, in which symmetry must be broken in order to differentiate two identical moities.

Acetalization of 2 with 1 equiv. of 2,2-dimethylpropane-1,3-diol results in a mixture[7] that, after chromatographic separation on silica gel, gave 13% yield of the starting diketone, 53% of monoacetal 3, and 15% of bisacetal. The yield of monoacetal could be increased up to nearly 80% by refluxing the recovered diketone and bisacetal (1:1 molar mixture), under equilibrating acid conditions, to give a roughly 1:2:1 statistical mixture of the three components, which were separated by column chromatography on silica gel, and the process repeated once again.

Monoacetal **3** was readily converted in 50% overall yield to bicyclic olefin **6** through a series of conventional transformations involving $NaBH_4$ reduction of the free carbonyl group, mesylation of the resulting *endo*-alcohol (**3** → **4** → **5**) and elimination of the mesyloxy group either with $KOBu^t$/DMSO or neutral alumina (**5** → **6**)(Scheme 1).[8]

Bicyclic olefin **6** gave, after treatment with MCPBA, in CH_2Cl_2 soln, a 1:3 mixture of *endo*:*exo*-epoxides **7** in 87-93% yield, the base induced isomerization to allylic alcohol **8** being thoroughly and carefully studied. The best results were obtained by using either $LiNEt_2$ in ether or $LiNPr^i_2$ in THF. However, the yields of isolated product were only 45-55%, in contrast with 93% yield reported by Whitesell *et al.*[9] in the closely related *endo*2-methyl derivative of **6**, which gives only the *exo*-epoxide.

Oxidation of allylic alcohol **8** with PCC gave the α,β-unsaturated ketone **9** in 79-85% yield, which was hydrolized to *cis*-bicyclo|3.3.0|oct-3-ene-2,7-dione (**1**) (76% yield). The whole transformation, from diketone **2** to diketone **1**, implies the conversion of a readily accesible 1,5-consonant dicarbonyl system into a 1,4-dissonant relationship by means of a formal 1,2-carbonyl transposition[10] in an overall yield of 8-10%.

A second route to diketone **1**, that starts from the well known |2+2|-cycloadduct **10** of 5-trimethylcyclopentadiene with dichloroketene[11] and proceeds through the sequence of reactions shown in Scheme 2[*Cf.* 8], gave lower overall yields owing to the competitive formation of ketonic products observed in the isomerization of epoxysilane **13**[12], which gave only 33% yield of the desired allylic alcohol **15**.

Treatment of enone acetal **9** with $PhSeCH_2Li$ (in THF/HMPT;-78°to RT)[13] afforded the expected *exo*-1,4-addition product **16** (Scheme 3) from which intermediates with conveniently functionalized *endo*-side chains are easily worked up (**16** → **17** → **18** → **19**).[14] Application of these transformations to the synthesis of triquinacene derivatives and related polyquinanes will be reported in full elsewhere[15].

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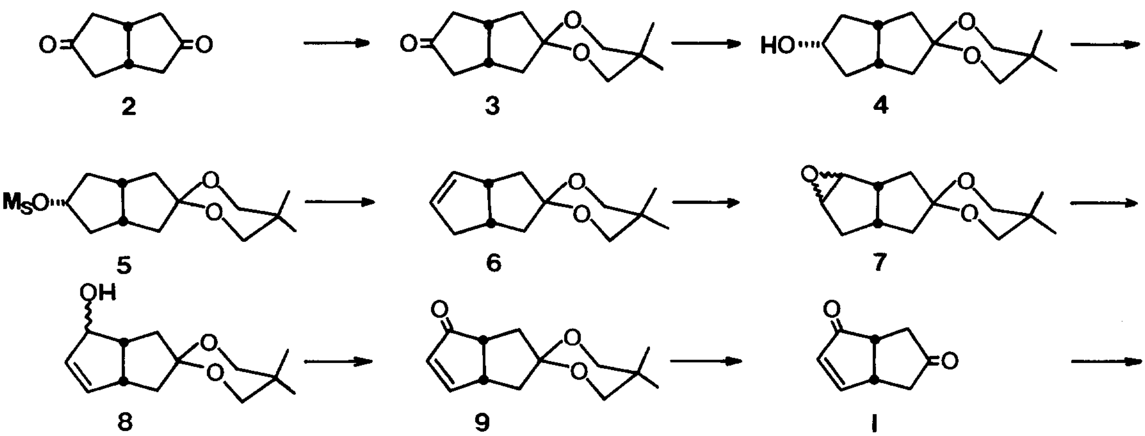
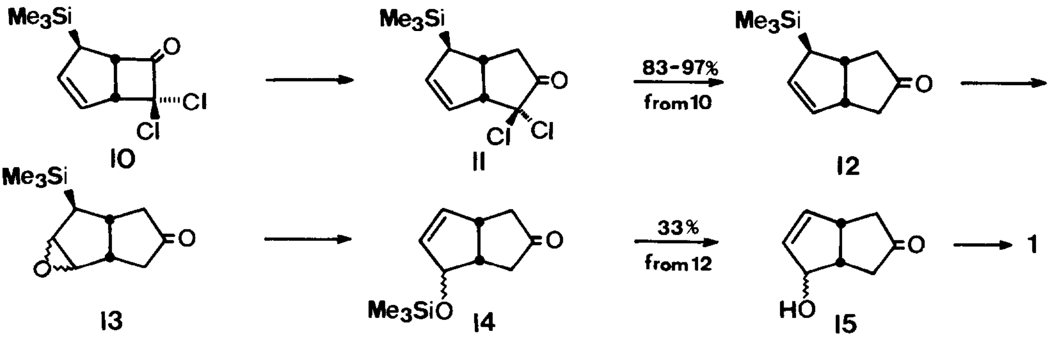
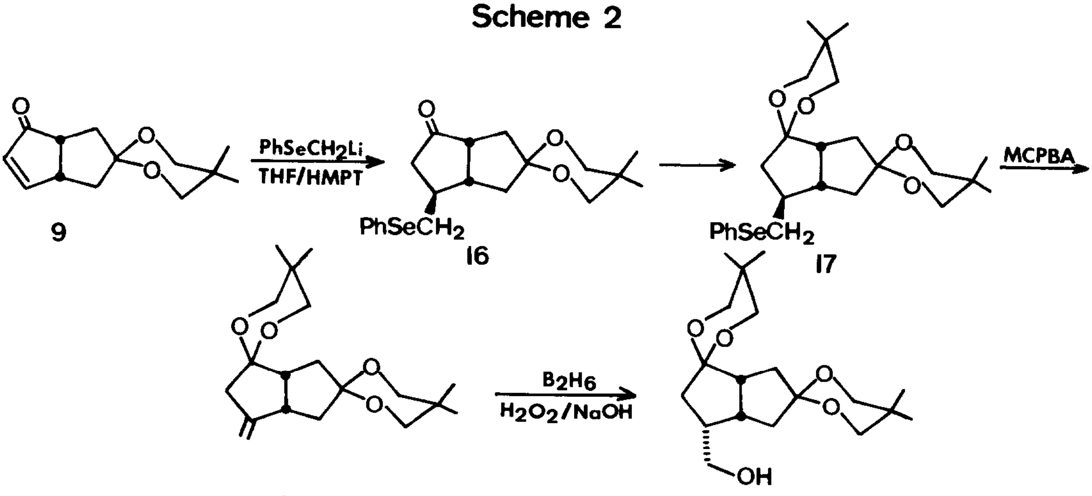


Scheme 1



Scheme 2



Scheme 3

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15. All new compounds were completely characterized and gave satisfactory analytical and/or spectral data. Compound 9, white crystals , m.p. 76-77°; has been studied by X ray analysis and the results will be reported in a separate paper. The structure is also consistent with ^{1}H NMR spectrum: (CCl$_4$) 1.80 (s, 3H); 2.00 (s, 3H); 1.4-3.0 (m, 6H); 3.23 (s, 2H); 3.35 (s, 2H); 5.90 (d, J = 5.5 Hz, 1H); 7.40 (dd, J = 5.5 Hz, J' = 2.5 Hz, 1H); ^{13}C NMR (CDCl$_3$): 22.2 (q), 22.7 (q), 29.9 (s), 34.0 (t), 38.3 (t), 42.7 (d), 71.1 (t), 72.6 (t), 107.8 (s), 133.4 (d), 166.8 (d), 212.0 (s); IR (KBr): 3060, 2965, 2870, 1715, 1590, 1110, 1025, 935, 880, 820 and 770 cm^{-1}; M.S.: 222 (M$^{+\cdot}$), 207, 194, 179, 128, 69.

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