A Short Synthesis of a Useful C_{19} Heptaquinane

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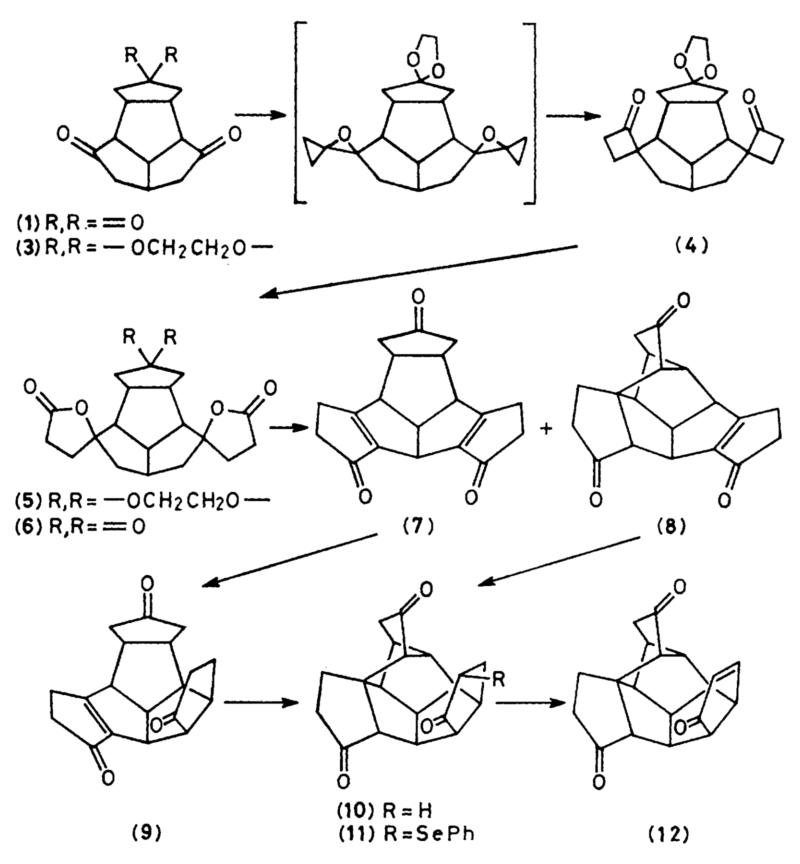
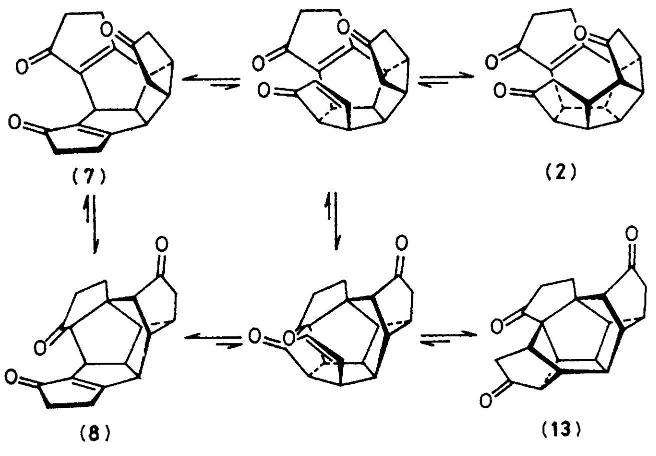
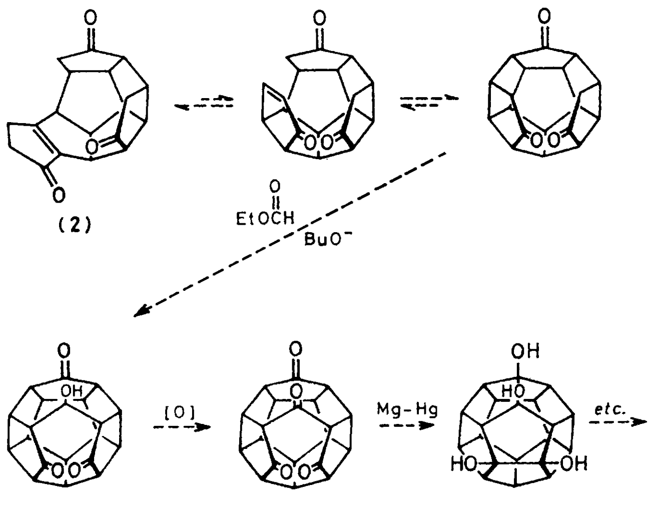
A simple six-step route from *endo*-tetracyclo[5.5.1.0^{2,6}.0^{10,13}]tridecane-4,5,12-trione to heptacyclo[11.5.1.0^{2,6}.0^{5,9}.0^{7,19}.0^{8,12}.0^{14,18}]nonadec-14(18)-ene-3,10,17-trione, a heptaquinane closely related to dodecahedrane, is described.

The ready accessibility of the all-*cis* C_{13} tetraquinane (**1**) (in two steps from glyoxal and dimethyl β-oxoglutarate)[1] makes this compound a worthy potential starting material for the synthesis of highly convex polyquinanes. We report a simple six-step route from (**1**) to a C_{19} heptacycle (**2**) which provides the shortest entry to such highly developed polycycles[2] yet described and offers the potential for a significantly simpler synthesis of dodecahedrane than that described recently.[3]





Scheme 1



Scheme 2

The tetracycle (**1**) was selectively protected at the less hindered C-4 carbonyl by acetalization† (ethylene glycol, benzene, $MeC_6H_4SO_3H$, Dean and Stark, 8 min). Addition of Trost's diphenylsulphonium cyclopropylide[4] to (**3**) in acetonitrile (rather than the recommended solvent, dimethyl sulphoxide, which caused difficulties in the work-up) followed by rearrangement of the oxaspiropentanes over silica gel gave the bis-spirobutane (**4**) in 70% yield. Baeyer–Villiger ring expansion to (**5**) (H_2O_2, OH^-, MeOH) and deprotection to (**6**) proceeded smoothly (91%). Exposure of the bis-lactone (**6**) to P_2O_5 in $MeSO_3H$ furnished the key hexacycle (**7**) (55%) under exceptionally mild conditions (40 °C, 4 h).[5] Careful chromatography of the by-products gave also the heptacycle (**8**) (10%) which proved to be equivalent to (**7**) in terms of synthetic utility.

Hydrogenation of the double bonds of (**7**) could not be induced beyond the dihydro-adduct (**9**). Steric hindrance within the cavity of (**9**) twists the skeleton such that mild acid or base treatment (*e.g.*, Na_2CO_3, H_2O, MeOH) effects a rapid and quantitative internal Michael addition, affording (**10**). The formation of the superficially undesirable transannular bond allows differentiation of the three carbonyls with respect to electrophilic attack, those in the twisted rings being less

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† All new compounds have been fully characterized by analysis and spectroscopy.

reactive. Thus, treatment of (**10**) with phenylselenyl chloride in ethyl acetate gave selectively the desired adduct, (**11**), albeit in modest yield (47% after recovery of starting material). Careful oxidative elimination afforded the enone (**12**). Unfortunately, the planned retro-Michael cleavage, to liberate an enolate capable of adding to the newly formed enone to furnish (**2**), could not be effected. Mild acid or base treatment simply caused isomerization of the enone to the more stable tetrasubstituted position, generating (**8**), which is readily reduced, by hydrogenation, to (**10**). This result, although disappointing, did suggest that under more forcing conditions a series of equilibria might be set up in which the heptacycle (**2**) would participate, as illustrated in Scheme 1. In fact, treatment of (**7**) with methanolic sodium hydroxide (sealed tube, 100 °C), with strict oxygen exclusion, gave three products, the expected heptacycle (**2**) (22%), the Michael adduct (**8**) of (**7**) (22%), and the octacycle (**13**) (35%). Identical treatment of (**8**) or (**13**) gives the same, evidently equilibrium, ratio of products. The octacycle (**13**) presumably arises *via* addition of the enolate at C-6 to the enone. The nearly equivalent stabilities of the three major products, which this result implies, is rather remarkable. The very high angle strain of the octacycle (**13**), for example, is evidently balanced by the high steric strain of the more regular heptacycle (**2**).‡

This heptacycle (**2**) is, we believe, suitably functionalized for further elaboration towards dodecahedrane. Scheme 2 outlines one promising potential route.

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References

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2 For an extensive review see: P. E. Eaton, *Tetrahedron*, 1979, **35**, 2189.

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5 P. E. Eaton, G. R. Carlson, and J. T. Lee, *J. Org. Chem.*, 1973, **38**, 4071.

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‡ The structures of (**2**), (**4**), (**9**), (**10**), (**12**), and (**13**) have been confirmed by *X*-ray crystallography: *cf.* J. E. Baldwin, P. L. M. Beckwith, J. D. Wallis, A. P. K. Orrell, and K. Prout, in preparation.