Synthesis of Ditwistane and Bisnorditwistane: Novel Ring Systems

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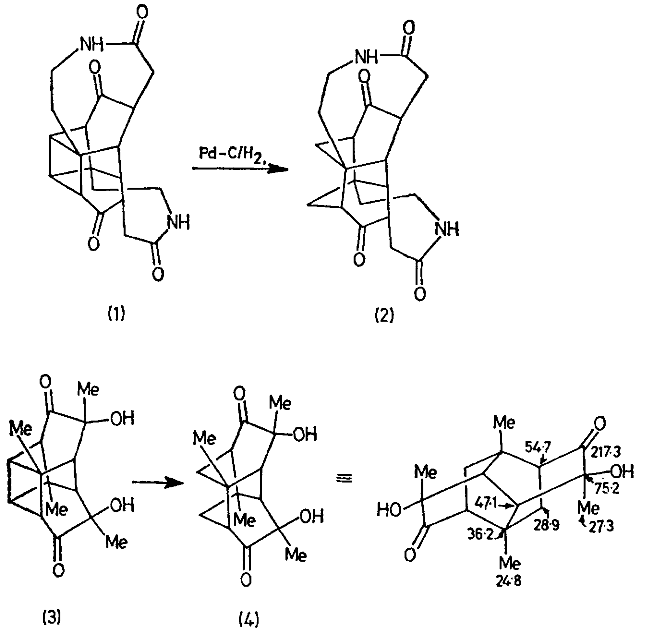
Summary Catalytic hydrogenation of the central bond in the bicyclo[2,2,0]hexane system is applied to the synthesis of ditwistane and bisnorditwistane.

In the course of studies on the properties of the dimeric cage compound (**1**), which was synthesized photochemically from *N*-chloroacetyltyramine,[1] we found that catalytic hydrogenation of (**1**) with 10% Pd–C in MeOH (3 kg/cm^2) gave a dihydrocompound (**2**) (53%; m.p. >270°). Although the ^{1}H n.m.r. spectrum is too complex to elucidate the structure, hydrogenolysis at the central bond in the bicyclo-[2,2,0]hexane system of (**1**) into (**2**) is expected to release most of the strain energy of (**1**). A few precedents of this type of hydrogenolysis have been reported,[2] though four-membered rings usually remain unchanged under catalytic reduction conditions.[3]

In order to clarify the hydrogenation, a model cage compound (**3**)[4] was hydrogenated as described above for 24 h to give (**4**) (92·5%; m.p. 231—233°; M^+ 278). The ^{1}H n.m.r. spectrum, in which four methyl groups appear as two sharp singlets at δ 1·12 and 1·52, shows that (**4**) is a symmetrical molecule. No C–H bonds were exchanged for D by treatment of (**4**) with NaOMe in MeOD at 50° showing that (**4**) has no methylene groups adjacent to the carbonyl groups. If no unexpected rearrangement took place, the above data show the correct structure to be (**4**), which was confirmed by the ^{13}C n.m.r. spectrum and finally by *X*-ray analysis.

The ^{13}C n.m.r. spectrum of (**4**) in $CDCl_3$ exhibits eight different types of carbon atoms (Scheme 1, values in p.p.m. downfield from Me_4Si).

Compound (**4**) crystallized in the monoclinic space group $P2/c$ with two molecules per cell unit and cell parameters $a = 14{\cdot}962(6)$, $b = 7{\cdot}011(2)$ and $c = 8{\cdot}521(5)$ Å, and $\beta = 122{\cdot}92(2)°$. A computer-controlled four-circle diffractometer with Cu-K_α radiation collected 991 independent non-zero reflections. The molecular structure was revealed by the symbolic addition procedure for centrosymmetric crystals[5] and refined by the block-diagonal matrix least-squares method. The final *R*-factor was 4·6%. The molecule has a two-fold symmetry. All the rings are six-membered and in the distorted twist-boat conformation (Figure).



Scheme 1

Ditwistane (**8**),† the parent compound of this type of new symmetrical cage compounds, was synthesized from (**6**)[7] derived from (**5**) (Scheme 2).[4] After hydrogenation of (**6**) in AcOH for 7 days, the product mixture, mainly diacetates of hexahydro-compounds, was treated with NaOH in aq. MeOH and then oxidized with CrO_3 in 90% AcOH to give ditwistanedione (**7**) (47%; m.p. 223—227°; M^+ 190). Compound (**7**) was converted into the bisthioacetal (70·3%; m.p. 199—203°), which was desulphurised with Raney Ni to ditwistane (**8**) (crude yield 95%). Recrystallisation from MeOH and sublimation gave fine prisms [m.p. 117—118·5° (sealed capillary); sublimation at 75—85° (bath temp.); M^+ 162]. The ^{1}H n.m.r. spectrum is quite similar to that of twistane.[8] The ^{13}C n.m.r. spectrum in $CDCl_3$ has six sharp signals at 23·0, 25·2, 26·2, 29·7, 31·2, and 32·3 p.p.m. showing the correct structure to be (**8**)

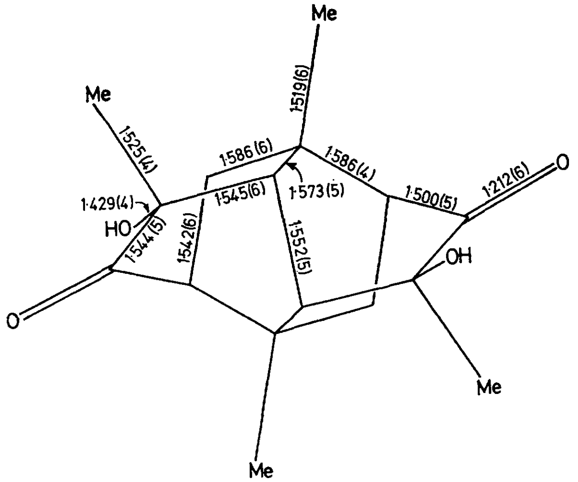
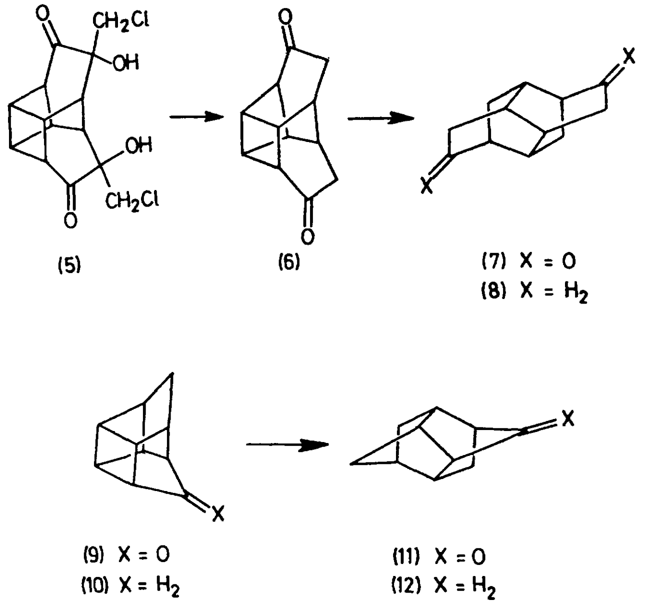


Figure. Bond lengths (Å) of 6,12-dihydroxy-2,6,9,12-tetramethyltetracyclo[6,2,2,0^{2,7},0^{4,9}]dodecane-5,11-dione (4).



Scheme 2

Similarly, (**9**)[9] was reduced to (**10**) (78%), which was recently synthesized photochemically from *endo*-tricyclo-[5,2,1,0^{2,6}]dec-8-en-3-one.[10] Thioacetalisation of (**11**) (80%) and desulphurisation (43·3%) gave bisnorditwistane (**12**) as fine plates [m.p. 160—161° (sealed capillary); sublimation at 75—80° (bath temp.); M^+ 134; δ (CCl_4) 0·6—2·3 (complex)]. Compound (**12**) was also synthesised directly from (**10**)[11] by reduction in AcOH (10 h) in 74% yield.

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† According to the proposed nomenclature,[6] (8) is named [8]-ditwistane.

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