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A GENERAL SYNTHETIC APPROACH TO cis, syn, cis- TRIQUINANES via REDUCTIVE CARBON-CARBON BOND CLEAVAGE IN POLYCYCLIC FRAMES: STRATEGY FOR BIS-CYCLOPENTANE ANNULATION OF 1,3-CYCLOPENTADIENE

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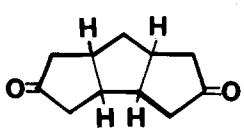
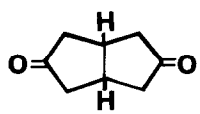
Abstract: A short, general and flexible approach to cis, syn, cis-tricyclo(6.3.0.$0^{2,6}$)undecane 4,10-dione and its derivatives from abundantly available pentacyclo (5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$)undecane-8,11-diones is described.

The intense contemporary interest in the synthetic design of linearly fused tricyclopentanoids (triquinanes) stems from their wide occurrence in Nature with promising biological profile and their likely role as the building blocks for the syntheses of 'exotic' all carbon polyhedra, e.g., dodecahedrane.[1,2] As a result, several novel approaches to this ring system have been delineated in recent years.[3] Herein, we report a simple and efficacious approach to all cis-triquinane frameworks and in particular to the cis, syn, cis-tricyclo(6.2.0.$0^{2,6}$)undecane-4,10-dione 1 and some of its derivatives. In view of the varied applications of the bicyclo(3.3.0) octane-3,7-dione 2, a bicyclic analogue of 1 in synthesis, it is anticipated that easy accessibility to 1 and its derivatives would open new avenues for further synthetic exploitation.

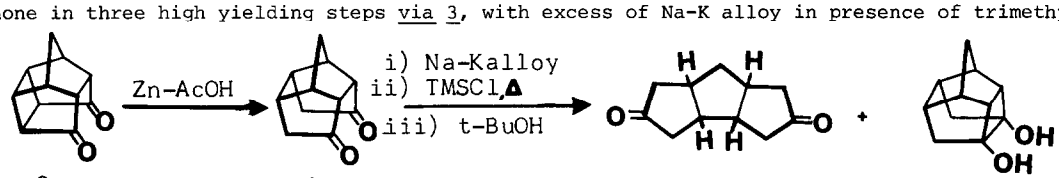


1



2

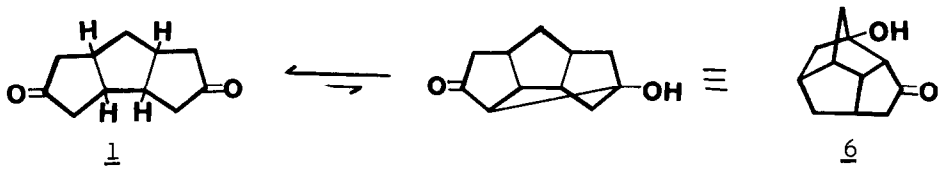
Reaction of tetracyclic dione 4, readily obtainable[4] from 1,3-cyclopentadiene and p-benzoquinone in three high yielding steps via 3, with excess of Na-K alloy in presence of trimethyl-



3 4 1 5

chlorosilane (TMSCl) and quenching with t-butanol led to the formation of 1 and 5 (8:1) in 40-45% yield.[5] Structure of 1, colorless oil, followed from its diagnostic spectral characteristics: M^+ 178, ir(CCl_4): 1750 cm^{-1}, ^1H nmr(100 MHz, $CDCl_3$): δ 0.9-3.2(m); ^{13}C nmr(25 MHz, $CDCl_3$): δ 218.9(s), 44.6(t), 43.15(d), 41.27(d), 40.45(t), 39.98(t). The tricyclic dione 1 on storage and on contact with acid established equilibrium with its trans-skeletal aldol cyclisation product 6 (^{13}C nmr: δ 222.3, 82.6, 58.35, 50.57, 50.25, 47.67, 46.46, 42.12, 40.15, 39.66, 37.89). A convincing evidence for the proposed trans-skeletal bonding emanated from the near

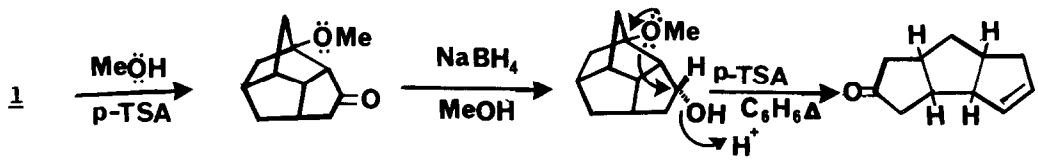
quantitative formation of the novel tetracyclic methyl ether 7 on treatment of dione 1 with methanol in presence of p-toluenesulphonic acid (p-TSA) or more conveniently and directly from 4



1 6

by treatment with Na-K alloy/TMSCl and quenching with methanol (50% yield). The tetracyclic ether turned out to be a valuable intermediate in the chemo-differentiation of the two identical carbonyl groups in 1 and its conversion to 8 is illustrative of many useful manipulations that we have carried out on 1 (Scheme 1).

Scheme 1

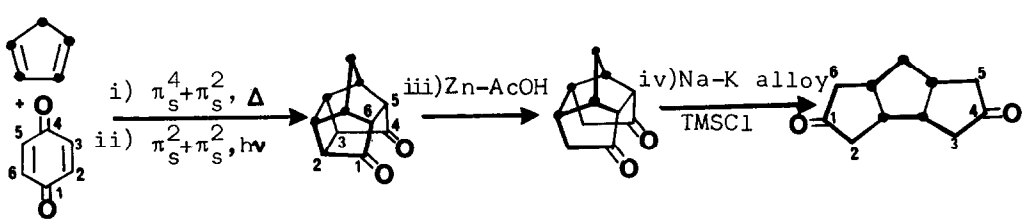


7 8

The generality of the reductive C-C bond cleavage in 4 to furnish cis, syn, cis-triquinane dione 1 was firmly demonstrated through further examples (Table 1). These useful reductions have not been subjected to any incisive mechanistic scrutiny but they appear to fall within the precedented category of reduction of 1,4-dicarbonyl systems.[9]

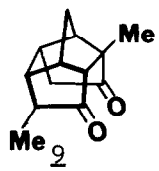
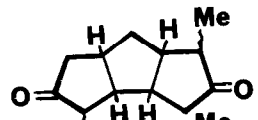
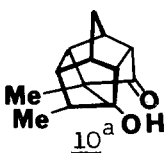
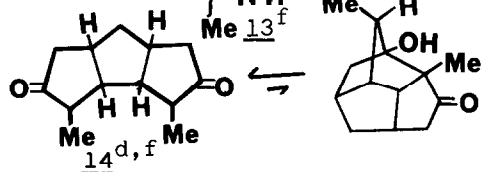
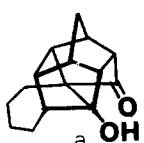
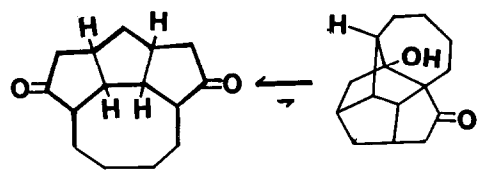
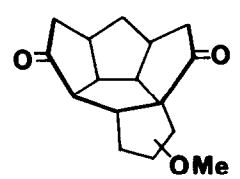
The versatility of our approach and its adaptability towards the generation of the desired substitution pattern on the triquinane framework is best appreciated by considering the origin of C-atoms of 1 from precursor 1,3-cyclopentadiene (heavy dots) and p-benzoquinone (arabic numerals). Consequently, the requisite triquinane can be simply designed, by building the comple mentary substitution pattern into 1,3-cyclopentadiene and p-benzoquinone and the sequence depicted in Scheme 2 represents a four step bis-cyclopentane annulation of 1,3-cyclopentadiene.

Scheme 2



3 4 1

Table 1

Substrate[a]	Reaction time[b]	Product(s)	Yield(%)[c]
 9	2.5 h	 13[f]	30
 10[a]	3.5 h	 14[d,f]	45-50
 11[a]	3.5 h	 15[d,f]	40-45
 12[e]	1.5 h	 16[f]	60

(a) 9 and 10 were prepared via the Zn-AcOH reduction of the precursor pentacyclic diones.[6] Compound 11 was obtained similarly from the precursor hexacyclic dione.[7] However, 10, mp.88-9° and 11, mp.119-20°, prefer stable internal aldol structures and were used as such in the reaction. (b) All reactions were essentially carried out as described for 4 in ref.5. (c) Yields based on isolated products. (d) Compounds 14 and 15 were clearly contaminated with their trans-skeletal aldol cyclisation products but could be isolated pure by column chromatography. The facility of these aldol type bonding was further established through isolation of methyl ethers on exposure to MeOH in presence of p-TSA. (e) The preparation of this compound has been reported previously by us.[8] (f) Compound 13: mixture of isomers, M^+ 206, ir(neat): 1735 cm^{-1}. Compound 14: mp.85° M^+ 206, ir(KBr); 1740 cm^{-1}, ^1H nmr (100 MHz, $CDCl_3$): δ 1.16(d,6H,J=7Hz), 1.9-2.6(m,12 H): ^{13}C nmr(25 MHz, $CDCl_3$): δ 220.4(s), 50.78(d), 44.5(d), 42.56(t), 40.92(t), 39.62(d), 15.4(q), Compound 15: mp.107-8°, M^+ 232, ir(KBr): 1735 cm^{-1}, ^1H nmr(100 MHz, $CDCl_3$): δ0.9-3.0(m), ^{13}C nmr (67.89 MHz, $CDCl_3$): δ 219.5(s), 49.6(d), 48.67(d), 40.92(t), 40.39(t), 39.86(d), 29.06(t), 25.36(t). Compound 16: mp.97-8°, M^+ 260, ir(KBr): 1730 cm^{-1}, ^1H nmr(100 MHz, $CDCl_3$): δ 0.7-3.8(m), 3.24(3H,s). ^{13}C nmr(25 MHz, $CDCl_3$): δ 222.8(s), 220.4(s), 87.4(d), 72.6(s), 62.3(d), 57.8(q), 56.0, 55.0, 54.1, 46.0(t), 45.0(t), 41.2(2c,d), 39.5(d), 30.9(t), 30.7(t).

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5. A typical procedure is provided below. In a flame dried 250 ml three-necked flask, equipped with a condenser, freshly cut sodium (0.4g, 0.017 g atom) and potassium (2 g, 0.051 g atom) in dry toluene (125 ml) were heated with vigorous stirring until a fine dispersion was formed. After cooling to ambient temp., a solution of diketone 4 (2.4 g, 13.6 mmol) in dry toluene and TMSCl (20 ml) were sequentially injected under N_2 blanket and the reaction mixture refluxed for 3 h. Filteration through celite under N_2 into t-BuOH(15 ml), concentration under vacuo and SiO_2 gel chromatography furnished 1 (950 mg, 40%) and 5(120 mg,5%).[4] From a purely preparative point of view 1 could also be obtained directly from the pentacyclic dione 3 via reiterative Na-K alloy/TMSCl/t-BuOH sequence in 50% yield. The same procedure could also be applied to the penta- and hexacyclic dione precursors of 9,10 and 11, respectively (unpublished results).
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