One step transformation of tricyclopentabenzene (trindane) [$C_{15}H_{18}$] to 4-[1*R*,2*S*,4*R*,5*S*)-1,2,5-trihydroxy-3-oxabicyclo[3.3.0]octane-4 spiro-1′-(2′-oxocyclopentan)-2-yl]butanoic acid [$C_{15}H_{22}O_7$]

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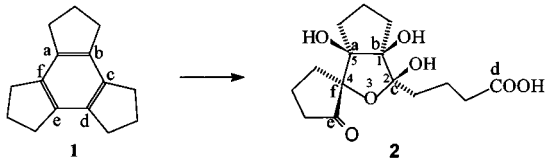
The complete, Ru(VIII) mediated oxidation of the benzene ring of trindane 1 is contained within the framework of peripheral methylenes to yield the unfragmented product 2.

This communication reports the formation of **2** on oxidation of trindane **1** with *in situ* generated Ru(VIII) species.



Trindane **1**, despite its ready availability,[1]‡ and being endowed with a three-fold symmetry, has hitherto attracted little synthetic interest.[2]§ In connection with the synthesis of benzene anchored three-fold symmetric systems, having pairs of donors and acceptors, that could lead to surfaces by self assembly, **1** was reacted with Ru(VIII) species, in anticipation of the oxidation of the six benzylic positions.§ The reaction gave no product from benzylic oxidation, but consistently afforded ~15% yields of a crystalline compound, mp 148–150 °C. The ^{13}C NMR spectrum coupled with DEPT studies suggested that the methylenes were intact and showed the presence of two types of carbonyls. The FAB (normal and negative ion) mass spectrum showed a molecular weight of 314. Elemental analysis was consistent with a molecular formula $C_{15}H_{22}O_7$ which when compared to the starting trindane ($C_{15}H_{18}$) amounts to the introduction of seven oxygens. The FTIR indicated the presence of hydroxy groups, cyclopentanone and another carbonyl peak at 1709 cm^{-1}.¶

Single crystal X-ray analysis‖ revealed the structure of the oxidation product as **2**. The crystal structure of **2** and selected interatomic parameters are presented in Fig. 1. All the bond distances and angles are within normal statistical bounds. The three five-membered rings are puckered.

A plausible reationalization of the **1** → **2** conversion, where oxidation is contained by the peripheral methylenes, is presented in Scheme 1.**

The basic framework of **2** is similar to that of ginkgolides,[3] a class of cytotoxic substances having therapeutic value. The one step transformation of hydrocarbon trindane to such condensed, highly oxygenated systems is noteworthy.

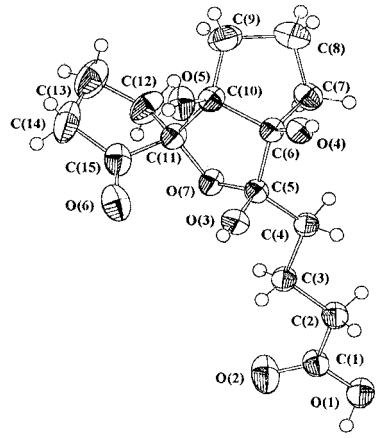
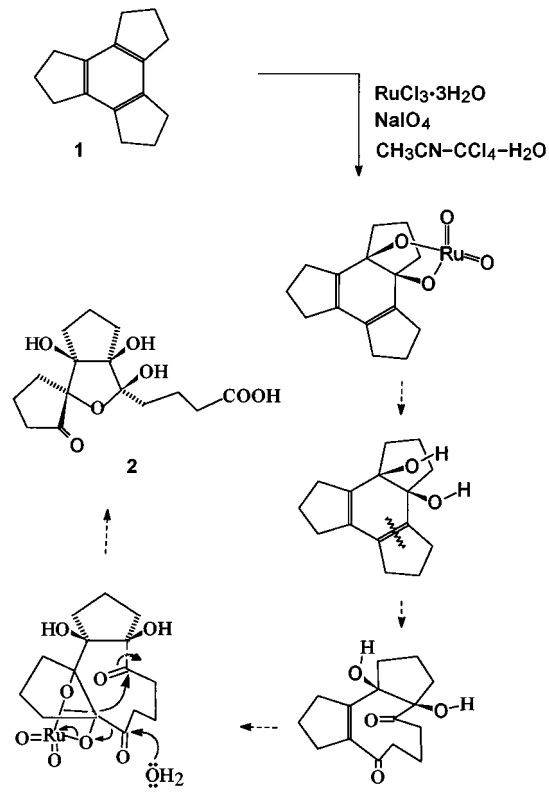
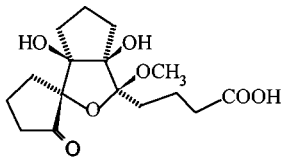


Fig. 1 The single-crystal X-ray structure of **2** with ellipsoids shown at 50% probability. For clarity the hydrogen atoms are not labelled. Selected bond lengths (Å) and angles (°): O(1)–C(1) 1.314(7), O(2)–C(1) 1.20(1), O(3)–C(5) 1.385(7), O(4)–C(6) 1.426(7), O(5)–C(10) 1.435(8), O(6)–C(15) 1.201(8), O(7)–C(5) 1.419(7), O(7)–C(11) 1.435(6); O(1)–C(1)–O(2) 122.6(6), O(1)–C(1)–C(2) 112.9(6), O(2)–C(1)–C(2) 124.5(5), O(3)–C(5)–O(7) 110.9(5), O(3)–C(5)–C(4) 108.1(4), O(3)–C(5)–C(6) 110.5(5), O(4)–C(6)–C(5) 110.0(4), O(4)–C(6)–C(7) 109.3(5), O(4)–C(6)–C(10) 112.7(5), O(5)–C(10)–C(6) 112.9(4), O(5)–C(10)–C(9) 112.9(5), O(5)–C(10)–C(11) 104.9(5), O(6)–C(15)–C(11) 124.6(5), O(6)–C(15)–C(14) 107.2(6), O(7)–C(11)–C(10) 106.3(4), O(7)–C(11)–C(12) 110.5(5), O(7)–C(11)–C(15) 110.2(5).



Scheme 1

The resemblance of **2** to sugars was highlighted by simultaneous isolation of **3**, by replacement of the anomeric hydroxy group during workup.††



3

The formation of highly functionalized complex condensed systems in one step, by the containment of aromatic ring oxidation within peripheral, methylene groups should be a general reaction. The unpredictable course of such reactions coupled with the delineation of their structures, largely by X-ray crystallography, should provide incentives for exploration along these lines, and which are currently being pursued.‡‡

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Notes and References

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‡ A standardized procedure for **1** based on early reports (ref. 1) is given below:

Cyclopentanone (16 ml, 0.18 mol) in dry EtOH (18 ml) was mixed with conc. H_2SO_4 (8 ml dropwise), refluxed for 15 h, poured on to ice (~70 g), neutralised with sodium carbonate and extracted with CH_2Cl_2 (3 × 30 ml), washed with water, dried ($MgSO_4$), evaporated and chromatographed on a silica gel column using petroleum ether to get 4.0 g (33%) of **1** [mp 92 °C (lit.[1] 95–97 °C)].

§ To the best of our knowledge, the only report (ref. 2) pertains to benzylic hexabromination followed by zinc reduction to afford mixtures of dehydrogenated tricyclopentabenzenes.

¶ A mixture of trindane (0.495 g, 2.5 mmol), CH_3CN–CCl_4–H_2O (10 : 10 : 20 ml), $NaIO_4$ (9.63 g, 45 mmol), $RuCl_3{\cdot}3H_2O$ (2.2 mol%, ~0.015 g) was sealed, shaken for 3 h, cautiously opened, filtered, the residue washed with EtOAc (3 × 20 ml), the organic layers washed with water, dried, evaporated and chromatographed on a silica gel column. Elution with EtOAc–hexane (1 : 1) gave fractions containing **2** (TLC: R_f 0.25, $CHCl_3$–MeOH 9 : 1) which on concentration deposited crystals, mp 148–150 °C (0.120 g, ~15%), Anal. Found: C, 57.55; H, 7.33%. Calc. for $C_{15}H_{22}O_7$: C, 57.32; H, 7.00. ν(KBr, cm^{-1}) 3396, 2972, 1736, 1709, 1432, 1143; δ_H(300 MHz, $CDCl_3$–DMSO-d_6) 1.6–2.5 (m, CH_2), 4.4 (br, OH × 2), 5.9 (br, OH × 1), 7.7 (s, COOH); δ_C($CDCl_3$–DMSO-d_6) 16.19–34.66 (9 × CH_2), 85.99, 87.32, 93.04, 103.78 (4 × C-O), 174.40 (CO), 221.01 (CO); *m/z* (FAB) (neg) 313 (78%), *m/z* (FAB) (pos) + Na^+ 337 (77%).

‖ *Crystal data*: $C_{15}H_{22}O_7$, M_r = 314.332, triclinic, $P\bar{1}$, a = 7.510(4), b = 10.465(1), c = 10.624(4) Å, α = 110.62(4), β = 99.42(8), γ = 91.12(4)°, U = 768.2(6) $Å^3$, Z = 2, D_x = 1.359 g cm^{-3}, μ(Mo-Kα) 0.11 mm^{-1}. Data were collected at 298(1) K, for a crystal of dimensions 0.20 × 0.20 × 0.30 mm, on an Enraf–Nonius CAD4-mach 2 diffractometer. A total of 2939 unique data were collected. The data were corrected for Lorentz polarisation and decay. The structure was solved by the direct method and refined on F using the full matrix least-squares technique using XTAL 3.2 program package and a total of 2195 reflections [$I \geqslant 3\,\sigma(I)$]. The final R,R_w indices were 0.061 and 0.067 for 205 parameters (non-hydrogen atoms, anisotropic hydrogen atoms in idealized positions, C–H 0.96 Å, O–H 0.87 Å with a fixed U_{iso} of 0.10. CCDC 182/1018.

** The nature of **2** would need the oxidation of each carbon centre of the aromatic ring. However, the sequence of events envisaged in Scheme 1 is largely notional. The step leading to *cis* hydroxylation, envisaged as the first step, is required to control the stereochemical outcome of the reaction. Preference, if any, of the reagent addition in the second step is obliterated since the process leads to oxidative C–C scission. Molecular models clearly show that the critical third step requires addition of the reagent from the side *anti* to the *cis* hydroxy grouping—which seem to be dictated by steric factors—to enable the generation of the oxabicyclooctane unit in **2** by transannular addition with correct stereochemical disposition at centres 2 and 4 (Scheme 1).

†† The formation of **3**, which was isolated as a gum, in ~7% yield has been traced to the use of small amounts of MeOH as the co-eluent. A spectral comparison of **2** with this compound indicated a simple replacement of a HO group by MeO, which was confirmed by analytical and detailed spectral studies. ν (neat)/cm^{-1} 3434, 1735, 1445, 1175; δ_H(300 MHz, $CDCl_3$) 1.4–2.4 (m, CH_2), 3.48, 4.21 (s, s, OH × 2, exchangeable), 6.42 (s, COOH, exchangeable), 3.66 (OMe); δ_C($CDCl_3$) 17.05–38.05 (9 × CH_2), 51.48 (CH_3O), 85.95, 88.35, 95.17, 105.00 (4 × C-O), 174.00, 222.90 (2 × CO) (DEPT studies showed 9 × CH_2 and 1 × CH_3]; *m/z* (FAB) (neg) 327.

‡‡ The immediate higher homologues of trindane can be readily prepared from the cyclanones (ref. 1). They would be the natural targets of further studies.

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