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Permethylpentalene Chemistry

Andrew E. Ashley,[a] Andrew R. Cowley,[a] and Dermot O'Hare*[a]

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A rational solution-phase synthesis of a permethylpentalene (Pn*) ligand precursor for use in organometallic chemistry has been devised through the novel peripheral alkylation of the bicyclo[3.3.0]octane ring system. Tetramethylation of tetramethyl 3,7-dihydroxybicyclo[3.3.0]octa-2,6-diene-2,4,6,8-tetracarboxylate (**1**) forms sterically encumbered **2** which exhibits fluxionality. Decarboxylation to **3** followed by facile double dehydrogenation using Br_2 affords **4**. Nucleophilic addition of the final two methyl groups necessitates the use of an organocerium reagent and work-up yields the hexamethylated hydroxy-fulvene **5**. Dehydration is achieved using aprotic conditions (LiCl/DMSO) to afford the tetraene **6**, an exocyclic isomer of Pn*. **6** incorporates a bicyclic vinylfulvene unit, avoiding an 8π anti-aromatic structure. Both **3** and **4** have been structurally characterised.

Introduction

Pentalene (C_8H_6, Pn) has fascinated theoretical and synthetic chemists alike for over 80 years since it was first proposed that the structure might have aromatic characteristics[1] and a resonance energy greater than that of benzene.[2] However, early attempts to isolate the species through the manipulation of bicyclo[3.3.0]octane precursors using conventional techniques were fraught with failure.[3,4] The isolation of Pn was finally achieved by Hafner from photolysis of the [2+2] dimer at –196 °C (Figure 1).[5] Recent electronic and IR data suggest the molecule to have a bond-alternant C_{2h} structure and an 8π anti-aromatic ground state.[6] Katz discovered that the double deprotonation of a dihydropentalene (PnH_2) affords the aromatic 10π dianion (Pn^{2-})[7] which corresponds to a formal two-electron reduction of Pn and this species has been the most common entry point into organometallic pentalene chemistry to date.[8]

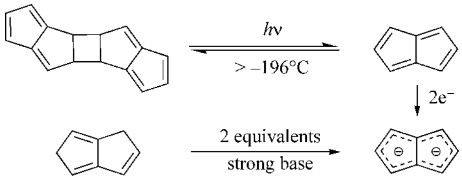

Figure 1. Reversible formation of pentalene from [2+2] dimer and synthesis of pentalene dianion through deprotonation of 1,5-dihydropentalene.

The past decade has seen a resurgence of activity in this area due to the applicability of the bicyclic framework in the construction of organometallic macromolecules[9,10] and the discovery that the ligand may fold about the bridgehead bond to deliver a novel η^8-coordination mode which effectively "caps" an entire face of a metal's coordination sphere.[11–13] Given the ubiquitous occurrence of cyclopentadienyl (Cp) complexes and their derivatives, it might at first appear surprising that those of Pn are not nearly as extensive. However, this disparity can be traced to the difficulties associated with efficient syntheses of organic precursors, namely PnH_2, which is commonly derived using pyrolytic methods and specialised expensive equipment,[14,15] which has stilted the development of this potentially rich and diverse field. Furthermore, existing methods for the substitution around the ring system rely upon double silylation of the dianion,[14] or the use of mono-alkylated PnH_2 precursors[16] which limit applications where polysubstitution may be desirable. In particular, having seen the remarkable effects demonstrated in the properties of complexes from the replacement of Cp with permethylcyclopentadienyl (Cp*) (enhanced stability, solubility, crystallisability and electronic effects due to the augmented donor capacity of the ligator),[17–19] the potential that a new ligand, permethylpentalene (Pn*), could offer is outstanding. In this communication we report the first synthesis and characterisation of an unusual polyolefinic precursor to this ligand. The polyalkylation of the pentalene unit has been achieved through the unique peripheral functionalisation of the bicyclo[3.3.0]octane skeleton. The protocol employs a facile and entirely solution-phase route from readily available starting materials, proceeding in yields comparable to those reported for the permethylcyclopentadienyl precursor Cp*H.

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[a] Chemistry Research Laboratory, University of Oxford,
Mansfield Rd, Oxford, OX1 3TA, UK
E-mail: dermot.ohare@chem.ox.ac.uk

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Results and Discussion

The natural regiochemical polarities of the tetramethyl 3,7-dihydroxybicyclo[3.3.0]octa-2,6-diene-2,4,6,8-tetracarboxylate (WeissH$_4$, **1**, Figure 2)[20] starting material in this synthesis are ideally suited to the peripheral functionalistion of the ring system, requiring four "Me$^+$" and two "Me$^-$" synthons to effect overall permethylation of non-bridgehead positions.

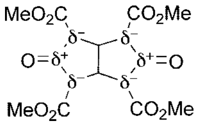

Figure 2. Regiochemical polarities of tetramethyl 3,7-dihydroxybicyclo[3.3.0]octa-2,6-diene-2,4,6,8-tetracarboxylate (WeissH$_4$, **1**).

Thus, reaction of WeissH$_4$ with an excess of MeI and K$_2$CO$_3$ in acetone gave a near quantitative yield of **2** [2,4,6,8-tetramethyl (tetramethyl-3,7-bicyclo[3.3.0]octane-3,7-dione-2,4,6,8-tetracarboxylate), WeissMe$_4$] as a white crystalline solid after work-up (Figure 3). Crystals suitable for X-ray crystallography were obtained from a saturated MeOH solution at –10 °C and a view is depicted in Figure 4.

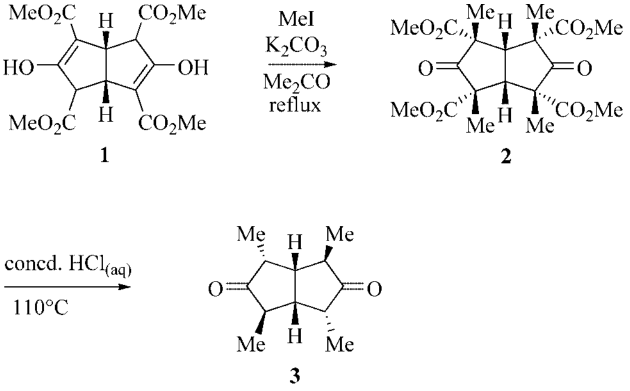

Figure 3. Syntheses of **2** and **3** from WeissH$_4$.

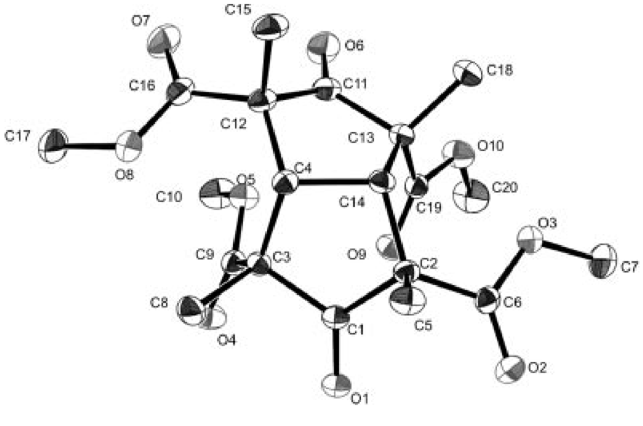

Figure 4. ORTEP view of **2** (hydrogen atoms excluded for clarity).

The molecule has approximate C_2 symmetry with a rotation axis through the central C–C bond. At first glance it can be seen that all four of the ester groups are *endo*, having been forced into the envelope of the *cis*-fused ring system. The ester groups do not fill the cavity formed by the two rings equally because it is extremely crowded; two point inwards, whilst the other two are forced outwards. This is unusual because these functionalities have a larger steric requirement than the alkyl substituents. This result can be explained by the alkylation mechanism, whereby an intermediate enolate can be attacked by MeI either *exo* or *endo* with respect to the ring "pocket". Because the least hindered approach is the former, this is the site of reaction which forces the ester group into the *endo* position. As more of these groups are pushed inwards, the steric bias in favour of further *exo* attack increases and results in tetramethylation occurring exclusively in this manner. The process is irreversible and the outcome is the kinetic product, with the accommodation of the ester groups leading to a highly distorted pentalenic framework. The bond lengths for all alkyl-Me and ester environments remain largely unaffected by the distortion of the rings, and along with the ketonic carbonyl groups are typical for C–C, C–O, C=O distances. The central C(4)–C(14) bond is the longest in the molecule and is an indication of the strain which exists in the fusion of two five-membered rings in this system. It can be seen that C(2)–C(14) is rather shorter than the C(3)–C(4) bond and supports a "push-pull" mechanism about the bridgehead for the exchange of ester and alkyl-Me environments; this is evidenced from ^{1}H and ^{13}C NMR spectroscopy. Where the ring positions are sp^3 hybridised, it would be expected that the angles should correspond closely to tetrahedral values; however many do not. The largest deviations are for C(3)–C(4)–C(12) and C(13)–C(14)–C(2), with an average 13.36° departure from the standard tetrahedral angle of 109.47°, which exemplifies the degree of molecular twisting experienced in **2**. The room temperature ^{1}H and ^{13}C NMR spectra demonstrate that **2** is fluxional; the former displays two very broad resonances for the ester-Me and alkyl-Me environments and a sharp singlet for the bridgehead protons. At low-temperature these signals sharpen and produce a spectrum consistent with the solid-state structure, i.e. two peaks for each of the former positions. The dynamics may be modelled successfully using a two-site exchange and the thermodynamic values obtained for the process are $\Delta H^{\ddagger} = 1.12\times10^{-3}\,\mathrm{J\,mol^{-1}}$, $\Delta S^{\ddagger} = -197.50\,\mathrm{J\,K^{-1}\,mol^{-1}}$ and $\Delta G^{\ddagger}_{298} = 58.86\,\mathrm{kJ\,mol^{-1}}$. The significant entropic contribution can be rationalised if it is presumed that the transition state has the ester functionalities almost symmetrically placed in the bicyclic fold; in this conformation rotational motion is likely to be highly restricted.

The hydrolysis-decarboxylation of **2** proved to be difficult, with the conditions for the analogous process on **1** (1–3 M HCl$_{(aq)}$, reflux)[20] resulting in the extremely slow evolution of CO$_{2(g)}$. This has been previously observed for other substituted keto esters of bicyclo[3.3.0]octane.[21] In this instance, it can be envisaged that the formation of a tetrahedral intermediate in the $A_{AC}2$[22] process for the hydrolysis under these conditions is severely retarded due to the steric encumbrance within the molecular cleft in which the esters reside. However, use of concentrated HCl$_{(aq)}$ at 110 °C as the reaction medium permitted the isolation of **3** (2,4,6,8-tetramethylbicyclo[3.3.0]octane-3,7-dione) in excellent yield as a white flaky solid. Compound **3** has been characterised by ^{1}H and ^{13}C NMR spectroscopy.

Double-resonance experiments and ^{1}H-^{1}H COSY NMR confirmed that H_a and H_b (Figure 5) have rather different chemical shifts (separated by 0.88 ppm) and this is probably due to unusual shielding effects within the envelope structure for the *endo* protons. Furthermore, the magnetic inequivalence of the bridgehead protons and long-range coupling (over three bonds) results in the resonances for $H_{a/a'}$, $H_{b/b'}$ and $H_{e/e'}$ having a complex multiplet appearance. The *exo*/*endo* environments for the methyl substituents are more readily apparent from the spectrum as two overlapping doublets for $Me_{c/c'}$ and $Me_{d/d'}$, which do not show further splitting. These findings, coupled with the detection of a single peak for the bridgehead-C atoms, suggest that the stereoisomer formed has a C_2 axis of symmetry perpendicular to the ring fusion; the only possible structure is that shown in Figure 3. Although the methyl substituents now occupy both *endo* and *exo* sites in the molecule in contrast to **1** (the latter bulkier), it is assumed that this is the thermodynamic product since acid-catalysed keto-enol tautomerism would allow rapid interconversion between all possible stereoisomers.

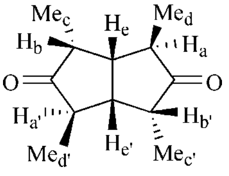

Figure 5. Magnetic inequivalence of hydrogen atoms in **3**.

The oxidation of **3** using excess Br_2 in methanol proved to be intriguing for two reasons (Figure 6). First of all, the bromination-dehydrobromination sequence was remarkably smooth to afford **4** in good yield after a high-vacuum distillation, with no intermediate bromoketones isolated from the reaction mixture at any point. Secondly, no mono-oxidation product could be furnished under these conditions, even if an equimolar ratio of reagents is utilised; in this case a 50:50 mixture of **3** and **4** was retrieved. This is believed to arise due to kinetic factors; the second bromination–elimination reaction results in a highly conjugated π system and this process is presumably much faster than the first. However, Bertz has documented similar findings on the unsubstituted analogue of **3** and concludes that the high symmetry of these species precludes a chemical transformation (e.g. enolisation) in which the symmetry would be broken.[23] **4** is found to be a colourless crystalline and sublimable substance which has been structurally characterised by X-ray crystallography (Figure 7), enabling the relative configuration of the alkyl-Me substituents to be ascertained. Treatment of this material with strong bases results in its decomposition, via a deep purple and unidentifiable species in agreement with the behaviour reported for the unmethylated counterpart.[24]

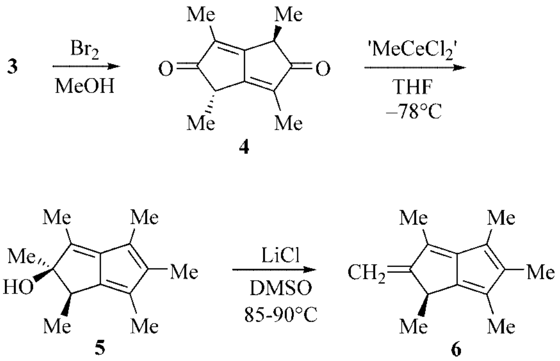

Figure 6. Syntheses of **4**, **5** and **6**.

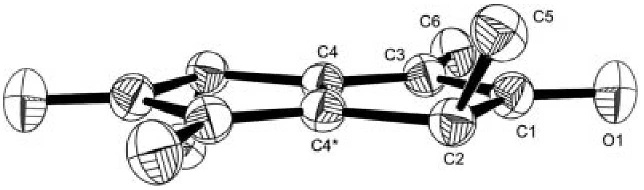

Figure 7. ORTEP view of **4** (hydrogen atoms excluded for clarity).

The effects of steric bulk upon the thermal stability and longevity of pentalenes is evidenced from the synthesis and structural determination of 1,3,5-tri-*tert*-butylpentalene.[25] In the context of the present study, the oxidation state of **4** upon methylation-dehydration is equivalent to that of the tetraene Pn* and permits an investigation into whether the six methyl groups bestow enough protection around the ring system to enable its full characterisation and reduction to Pn^{*2-}. Reaction of **4** with MeLi or MeMgI in THF solvent at –78 °C led to immediate formation of a purple colour and destruction of the starting material. This behaviour is characteristic of readily enolisable bicyclo[3.3.0]octanediones[26,27] and has been circumvented through the use of organocerium reagents.[28] Treatment of **4** with three equivalents of "$MeCeCl_2$" (formed from MeLi·LiBr and $CeCl_3$[29]) in THF solvent followed by an aqueous work-up led to 1,2,3,4,5,6-hexamethyl-1,2-dihydropentalen-2-ol (**5**), the mono-dehydration product from the expected diene-diol. Dihydropentalene **5** is sensitive to polymerisation upon concentration which precludes purification by crystallisation, distillation or chromatography. It is also extremely unstable towards acid degradation, turning deep green upon exposure to protic environments. It has been characterised using high-resolution mass spectrometry (HRMS) and $^{1}H/^{13}C$ NMR spectroscopy in [D$_6$]DMSO. This solvent allows the observation of the hydroxy resonance as a sharp feature, which is supported by a well-defined absorption in the IR spectrum at 3609 cm^{-1}.

The final dehydration of **5** required a novel aprotic method to be devised. It was discovered that the use of excess LiCl in molecular-sieves-dried DMSO was extremely effective at achieving this transformation, which can be conveniently monitored by ^{1}H NMR spectroscopy in [D$_6$]-DMSO and shows the disappearance of the alcohol peak in the starting material with concomitant formation of

1,3,4,5,6-pentamethyl-2-methylene-1,2-dihydropentalene (**6**, Pn*′). Compound **6** has been studied by ^{1}H and ^{13}C NMR spectroscopy which confirm the vinyl-fulvene structural moiety and the molecule is expected to exist as a racemate. As for **5**, this species is very acid-sensitive, and its stability in solution is concentration dependent. The elemental composition has been established by HRMS and the IR spectrum again contains bands attributable to the fulvene unit as well as the exocyclic C=C bond. Presumably, Pn* is not formed in this process since there at least two available transition states for elimination and these would likely reflect the energies of the products. Deposition of the olefin bond into the ring would ultimately result in an 8π anti-aromatic system and is least favourable. However, alternative loss of a proton from a Me group to produce **6** avoids this pathway and therefore leads to the isomer isolated. Using an internal ^{1}H NMR standard the yield of **6** from **4** is found to be 60%, and overall the conversion from one mol of WeissH$_4$ is 43.3% and on a scale of some 75 g.

In summary, we have succeeded in the large-scale synthesis of a hydrocarbon precursor to the permethylpentalene ligand which is an unexpected exocyclic isomer of the polyalkylated tetraene, and have consequently developed further the chemistry of unsaturated bicyclo[3.3.0]octane systems. Furthermore, the route avoids complex pyrolytic transformations commonly associated with the formation of unsubstituted Pn starting materials and should be amenable to every laboratory. Preliminary investigations have also shown that Pn*′, in conjunction with homoleptic metal carbonyl groups, form bimetallic compounds containing the Pn* moiety and has thus demonstrated its usefulness as a synthon for organometallic pentalene chemistry.[30] Our current research is now focussed on exploring the complexation chemistry of Pn* on metal centres.

CCDC-628489 and -628490 contain the supplementary crystallographic details for compounds **2** and **4**, respectively. This data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see also the footnote on the first page of this article): Full experimental details and the spectroscopic data for all new compounds.

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