The Synthesis, Structural Characterisation and Chemical Manipulation of the [6+3]Cycloadduct Derived from α-Tropolone *O*-Methyl Ether and Trimethylenemethane

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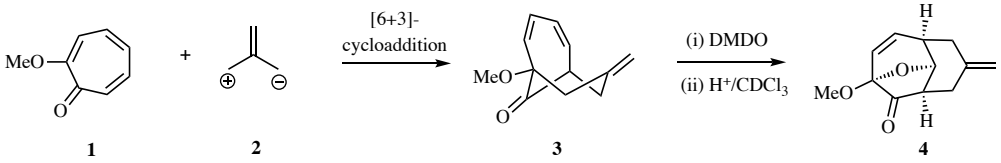

1 2 3 4

Abstract: The title bicyclic system **3**, the adduct arising from the formal [6+3]cycloaddition of 2-methoxytropone (**1**) and trimethylenemethane (**2**), has been prepared and subject to single-crystal X-ray analysis. The chemical manipulation of adduct **3** in a range of ways is reported, including through acid-catalyzed rearrangement of the derived mono-oxide to give the bicyclo[4.3.1]undecane **4**.

Keywords: [6+3]cycloaddition; oxidation, rearrangement; trimethylenemethane; troponoid.

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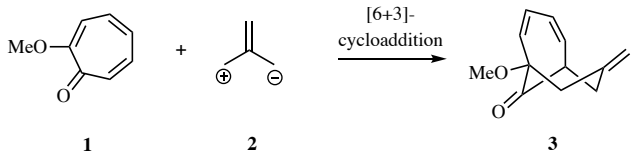
Supporting information for this article is available on the WWW under
http://dx.doi.org/10.1002/ajoc.2014XXXXX

Introduction

As a result of a re-emerging program within our group to prepare and manipulate troponoid compounds such as α-tropolone *O*-methyl ether (**1**),[1,2] we were attracted to the reports[3] of Trost and co-workers that these types of aromatic systems can engage in efficient [6+3]cycloaddition reactions with *in situ* generated trimethylenemethane (TMM, **2**) and thereby producing adducts such as **3** (Scheme 1).[4] Since these novel, readily available and polyfunctionalised reaction products could, in principle, serve as precursors to a range of intriguing molecular frameworks, investigations on the chemical manipulation of compound **3** seemed warranted. Herein, therefore, we detail the formation of adduct **3** as well as its structural characterisation and reactivity. These studies have revealed various properties of this system that should assist in its exploitation as a scaffold for the synthesis of natural products.

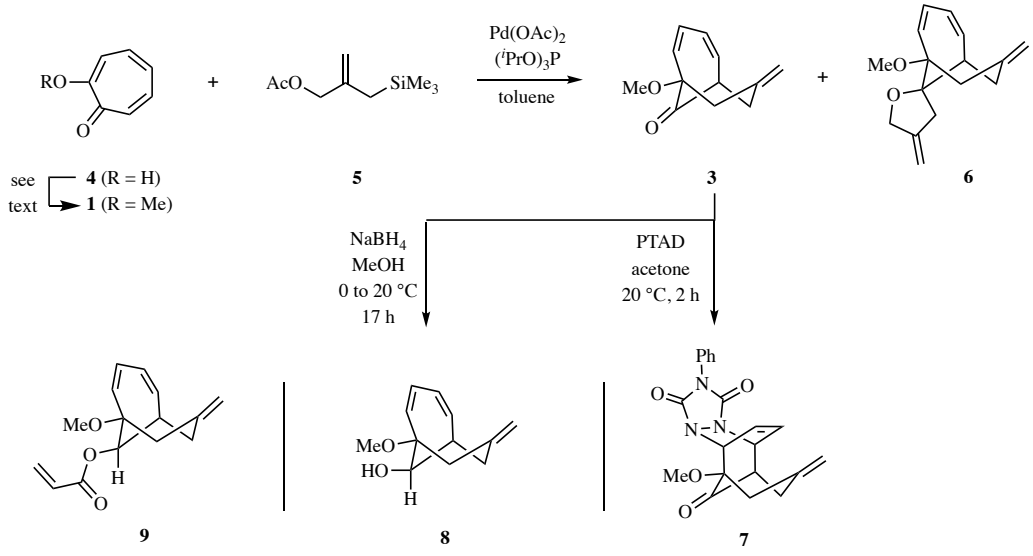


Scheme 1. The previously reported[3] [6+3]cycloaddition of troponoid **1** with TMM (**2**) leading to adduct **3**.

Results and Discussion

The reaction sequence used to obtain the target adduct **3** is shown in Scheme 2 and commenced with the *O*-methylation of readily available α-tropolone (**4**). This could be accomplished in two distinct ways. Thus, following the protocol reported by Houte and co-workers,[5] an ethereal solution substrate **4** containing methanol and triphenylphosphine was treated with diethyl azodicarboxylate (DEAD). While the anticipated Mitsunobu reaction took place and so producing the target ether **3** in 88% yield, extensive chromatography was required to separate this from co-generated triphenylphosphine oxide. Reaction of compound **4** with methyl iodide in the presence of potassium carbonate and 18-crown-6[6] provided a more practical route delivering ether **3** in 90% yield at gram scale. On treating a toluene solution of substrate **3** with 1.2 equivalents of the TMM precursor **5**[7] in the presence of $Pd(OAc)_2$ and tri-isopropylphosphite at 80 °C for 5 h the anticipated and crystalline adduct **3** was obtained in 54% yield. In an effort to improve the yield of this product, 1.5

equivalents of compound **5** was employed but this now delivered a chromatographically separable mixture of the [6+3]-adduct **3**[3] (44%) and the derivative **6** (12%) arising from a subsequent (and diastereoselective) [3+2]cycloaddition process between the carbonyl group of adduct **3** and TMM. If 2.5 equivalents of compound **5** were employed then the bis-adduct **6** (38%) became the exclusive product of reaction. The NMR, IR and mass spectral data derived from the [6+3]-adduct **3** were in complete accord with the assigned structure and matched those reported previously while a single-crystal X-ray analysis (see SI and Experimental Section for details) revealed that the associated six-membered ring adopts a near regular chair conformation. This same analysis also suggested that the face of the ketone carbonyl moiety projecting away from the bridging diene unit is the less congested/more accessible one. On this basis, the structure of the bis-adduct **6** is assigned as illustrated.



Scheme 2. The generation of target compound **3** and its engagement in Diels-Alder cycloaddition and reduction reactions.

The initial focus of our efforts to develop the chemistry of adduct **3** involved an exploration of the capacity of the embedded *s*-cissoid 1,3-diene unit to participate, as the 4π-addend, in Diels-Alder cycloaddition reactions. While a range of dienophiles, including *N*-methylmaleimide (NMM), nitroethylene (NE), methyl acrylate and 2-chloroacrylonitrile (CA) all failed to react (under forcing conditions only decomposition of compound **3** was observed), *N*-phenyltriazoline-3,5-dione (PTAD)[8] did engage in a [4+2]cycloaddition

reaction at ambient temperatures to give the crystalline adduct **7** (65%), the structure of which was established by single-crystal X-ray analysis.

The clearly limited capacity of diene **3** to participate in Diels-Alder cycloaddition reactions reflects the relatively large HOMO-LUMO gap [as determined by the outcomes of density functional theory (DFT) calculations as detailed below] that applies to such processes except when PTAD (amongst the most reactive of dienophiles)[9] is involved. This situation presumably reflects the splayed nature of the diene moiety, itself a consequence of the manner in which it is embedded within the bicyclo[4.3.1]decane framework. Indeed, the degree of deformation of this moiety is manifest in the ca. 130° angles (as discerned from the X-ray crystal structure of compound **3**) subtended by the each of the associated alkenes and the single-bond linking them.

In order to more fully understand the low intrinsic reactivity of diene **3** towards common dienophiles, DFT calculations at the M06-2X/6-31+G9d,p) level of theory in conjunction with the SMD solvent model were performed along with frontier molecular orbital (FMO) and distortion-interaction analysis. As revealed in Figure 1, these calculations predict unfeasible kinetic barriers (> 115 kJ/mol at 25 °C) for the thermal reaction of diene **3** with dienophiles such as 2-chloroacrylonitrile (CA), nitroethylene (NE) and *N*-methylmaleimide (NMM). However, with 4-phenyl-1,2,4-triazole-3,5-dione (PTAD) a substantially more modest Gibbs free energy barrier (ca. 60 kJ/mol) and a favourable reaction energy (ca. –150 kJ/mol) is observed, consistent with the successful formation of adduct **7**. The predicted reactivity difference between PTAD and the next most reactive dienophile (NE) corresponds to a difference of over 9 orders of magnitude in the addition rate coefficient at 25 °C.

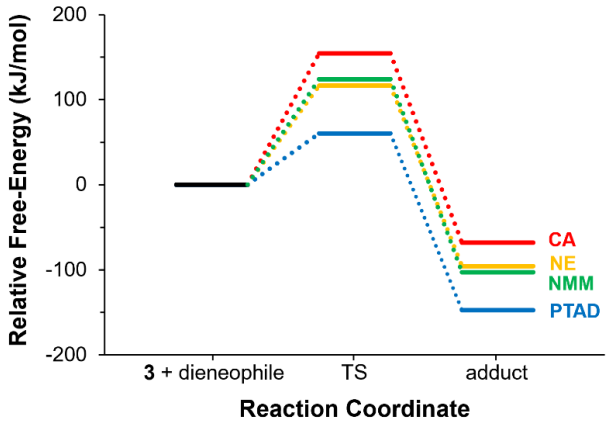


Figure 1: Calculated kinetic barriers for the thermal reaction of diene **3** with dienophiles CA, NE, NMM and PTAD

The low intrinsic Diels-Alder reactivity of **3** towards typical dienophiles is characteristic of other (simpler) large-ring cyclic dienes including cycloheptadiene and cyclooctadiene.[10] Houk and co-workers rationalised this poor reactivity, using a so-called a distortion-interaction model, in terms of out-of-plane distortions and wherein dienes embedded within larger ring systems usually need to undergo more distortion to reach synchronous transition-state geometries.[11] In the case of diene **3**, its reactivity is further reduced by the additional steric encumbrance imposed by the associated bicyclo[4.3.1]decane framework. Selecting a more electrophilic heterodienophile like PTAD offsets this poor reactivity by lowering the HOMO-LUMO gap (Figure 2a) and thereby increasing charge-transfer character at the transition-state. Distortion-interaction analysis (Figure 2b) reveals that the relative favourability of PTAD addition to diene **3** originates in the distortion rather than the interaction energy component. Compared to the other dienophiles, significantly less diene and dienophile distortion is observed with PTAD. This can be attributed to the relatively asynchronous PTAD-diene **3** transition-state, with significant out-of-plane distortion occurring around only one of the C=C bonds of diene **3**.

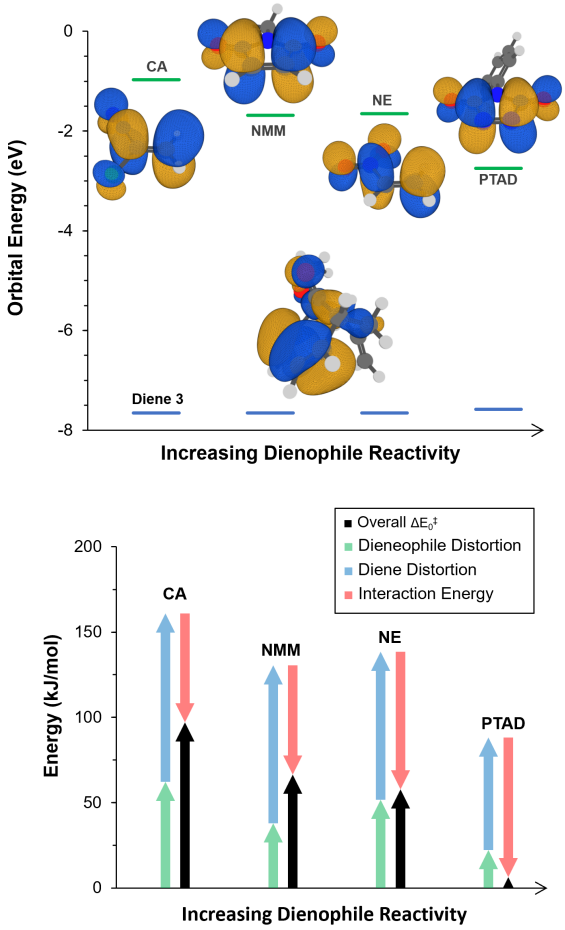
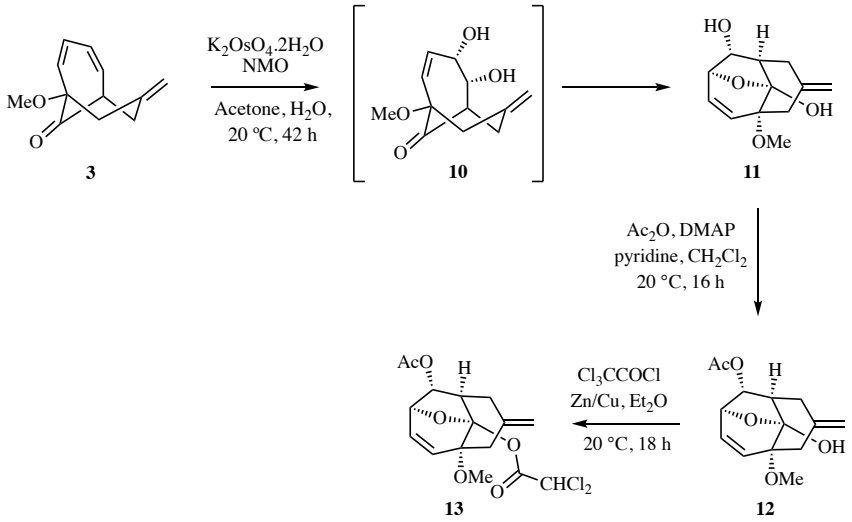


Figure 2: The FMOs (top) and energetics (bottom) involved in the Diels-Alder reactions of dienophiles CA, NMM, NE and PTAD with diene **3**

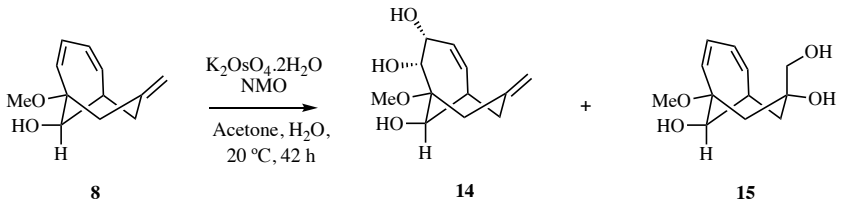
In an effort to engage the diene moiety within compound **3** in Type 1 intramolecular Diels-Alder (IMDA) cycloaddition reactions, this ketone was treated with sodium borohydride and underwent a diastereoselective reduction to give the alcohol **8** (75%) (Scheme 2). The illustrated configuration at the newly introduced stereogenic centre was confirmed thru the observation of a 1% nOe between the resonance due to the oxymethine proton and that due to the 1,3-related and axially oriented and allylic proton on the carbon remote from the bridgehead methoxy group. Various attempts were made to convert compound **8** into the corresponding acrylate **9** but while the substrate was always consumed in the attempted esterification reaction, only complex mixtures of products were observed. As such, the capacity of ester **9** to participate in IMDA reactions was not investigated any further.

The oxidative manipulation of the diene residue within the [6+3]-adduct **3** represented another aspect of our studies of the chemical behaviours of this compound. Regio- and diastereo-selective *cis*-1,2-dihydroxylation of this substrate could be accomplished under the UpJohn-type conditions[12] (Scheme 3) but the presumed primary reaction product, **10**, of this process was not observed because it was consumed in a lactol-forming process involving the ketone carbonyl residue and so leading to the crystalline compound **11** (57%), the structure of which was confirmed by a single-crystal X-ray analysis. Presumably the regio-selectivity of the initial dihydroxylation process is controlled by the bridgehead methoxy-group that serves, through inductive effects and, perhaps, steric ones as well, to inhibit electrophilic additions to the proximate double bond of the diene. Selective manipulation of the two hydroxyl groups embedded within compound **11** was readily accomplished as demonstrated by the conversion of the less hindered 2°-alcohol into the corresponding acetate **12** (94%) under standard conditions. In an effort to engage compound **12** in a [2+2]cycloaddition reaction with dichloroketene it was treated with trichloroacetyl chloride and metallic zinc. However, the only characterisable product of this process was the diester **13** (12%) arising from reaction of *in situ* generated dichloroketene with the lactol residue of compound **12**.



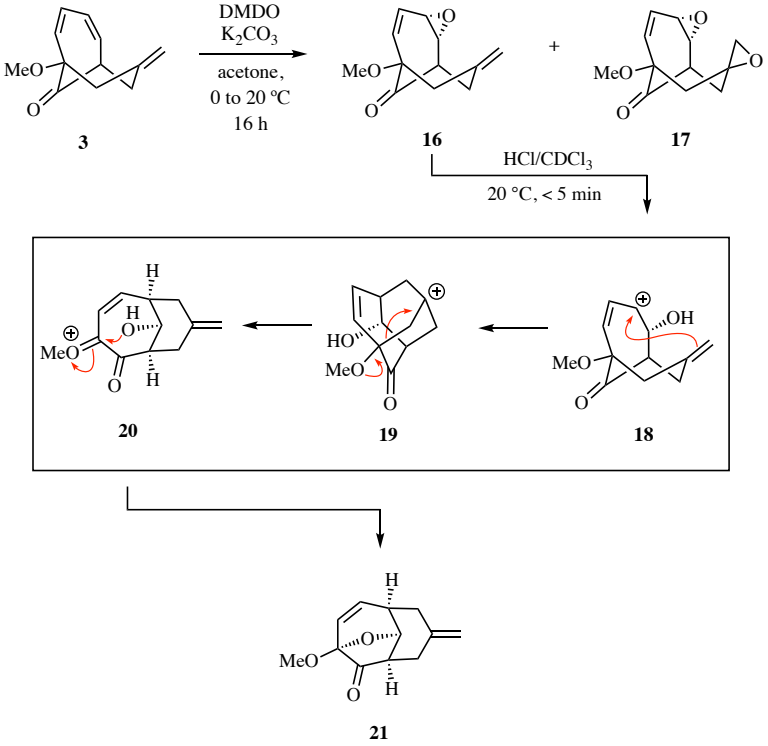
Scheme 3. The tandem *cis*-1,2-dihydroxylation/rearrangement of compound **3** leading to diol **11** and the esterification of the latter

In contrast to the outcomes shown in Scheme 3, when the alcohol **8** was subjected to the same dihydroxylation conditions as employed in the conversion **3** → **10** then, as revealed in Scheme 4, a chromatographically separable mixture of diols **14** (18%) and **15** (9%) was obtained. The structure of the former product was established using various 2D NMR experiments while the configuration of the newly introduced stereogenic centre in the latter product is assigned by analogy with the established outcomes of other electrophilic additions to the exocyclic olefinic unit in related substrates (see below). The contrasting regioselectivties associated with the mono-dihydroxylation of the diene residues within compounds **3** and **8** are noteworthy. The selectivity observed in the latter case is attributed to the vicinally related hydroxyl and methoxy groups serving as the components of a bidentate ligand that co-ordinate osmium and so directing reaction at the proximate double bond.



Scheme 4. The *cis*-1,2-dihydroxylation/rearrangement of alcohol **8** leading to triols **14** and **15**

When the dimethyldioxirane (DMDO)-mediated epoxidation[13] of diene **3** was carried out between 0 and 20 °C over 16 h (Scheme 5) then a chromatographically separable mixture of the mono-epoxide **16** (47%) and its bis-counterpart **17** (17%) was obtained. If the reaction time was reduced to 4 h then compound **16** (53%) was the sole product with 23% of the staring material being recovered. The structure of each of products **16** and **17** was established by single-crystal X-ray crystallographic methods (see Experimental Section and Supporting Information) and the configuration of the spiro-epoxide residue in latter served as the basis for the assignment of configuration at the hydroxyl-bearing stereogenic centre in congener **15**.



Scheme 5. The epoxidation of triene **3** and the acid-catalysed conversion of mono-oxide **16** into isomer **21**

On standing in $CDCl_3$ containing HCl compound **16** engaged in a smooth rearrangement process that is proposed (Scheme 5) to involve initial, proton-mediated cleavage of the epoxide ring and so affording allylic cation **18** that is immediately captured by the proximate and exocyclic double bond to give the homoadamantyl cation **19**. Methoxy-group initiated fragmentation of this last species in the illustrated manner would then afford the oxonium cation **20** that is itself trapped intramolecularly by the transannular hydroxy group to generate the observed compound **21** bearing an internal ketal residue and the structure of which was confirmed by single-crystal X-ray analysis. It should be noted that simpler 3-homoadamantyl cations have not only been invoked in various rearrangement processes[14] but the parent system has been generated and characterized by spectroscopic methods.[15]

The plausibility of this cation-based rearrangement pathway was confirmed with DFT calculations which revealed that compound **16** readily undergoes epoxide cleavage in the presence of a prototypical Bronsted acid, viz. H_3O^+ (Figure 3). This cleavage is

accompanied by concerted addition of the proximal and exo-cyclic alkene to the generated allylic carbocation and so affording the intermediate homoadamantyl cation **19** ($\Delta G^{\ddagger}$ = +30 kJ/mol, ΔG_{rxn} = –50 kJ/mol). The latter cation can then undergo nearly barrierless beta-fragmentation to yield the α,β-unsaturated oxonium ion **20** (ΔG_{rxn} = –20 kJ/mol). Following a nearly barrierless interconversion to a twist-boat type conformation (ΔG_{rxn} = –10 kJ/mol) this last species can undergo very rapid cyclisation to afford compound **21** (ΔG_{rxn} = –20 kJ/mol). Overall, compound **21** is predicted to be around 100 kJ/mol more stable than precursor **16** in the presence of H_3O^+, with the initial epoxide cleavage reaction possessing the highest barrier of any of the elementary steps ($\Delta G^{\ddagger}$ = +30 kJ/mol) involved in the overall process. The highly favourable kinetic and thermodynamic aspects of this mechanistic pathway are entirely consistent with the experimental observation that substrate **16** is readily converted into isomer **21** in acidified $CH(D)Cl_3$.

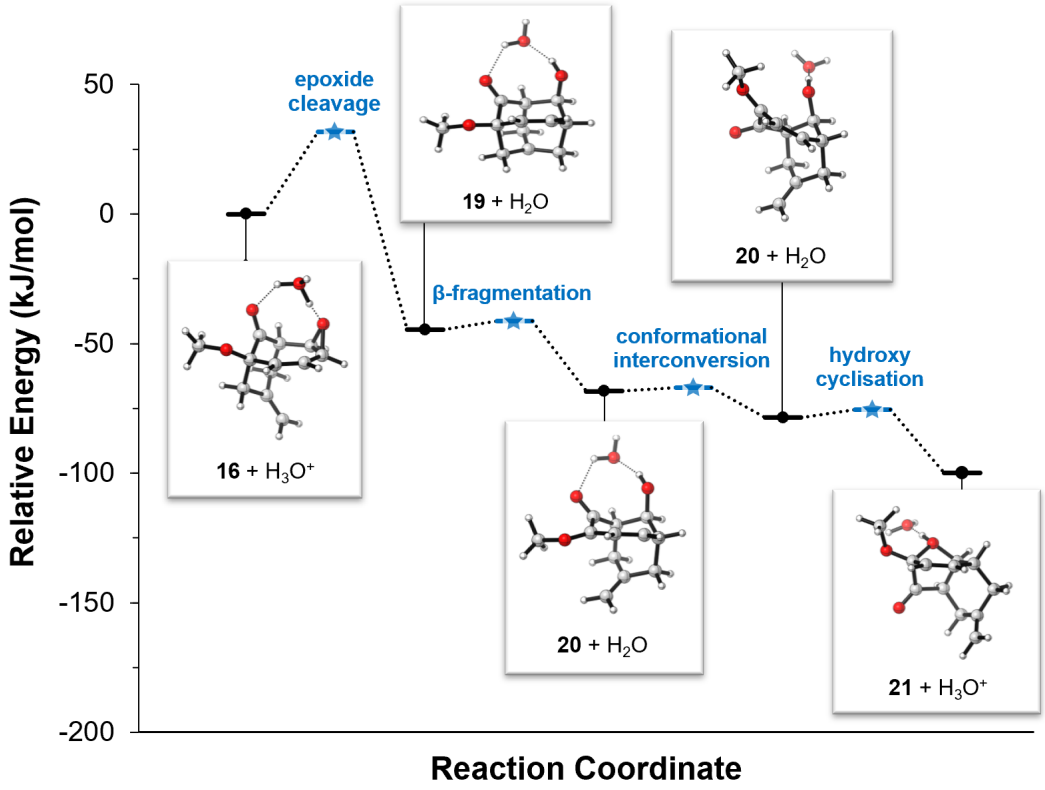
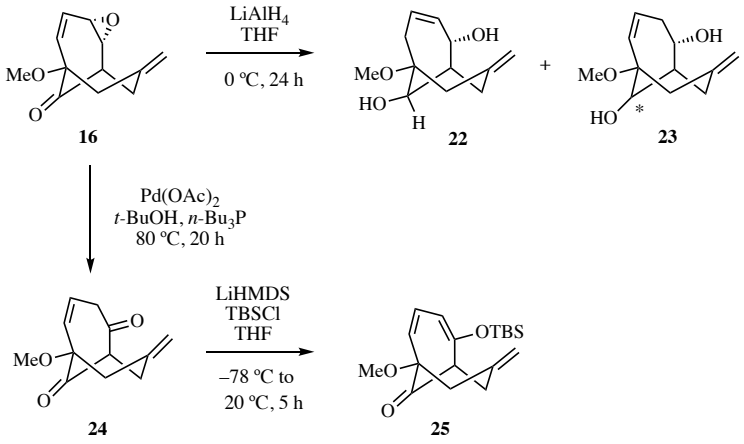


Figure 3. A potential energy surface for the rearrangement of epoxide **16** to isomer **21** [H_3O^+ was used as the model acid and the computed structures of all stable intermediates (black circles) are shown with transition state structures (blue stars) are omitted for clarity].

The reductive cleavage of epoxide **16** could be effected using $LiAlH_4$ and this was accompanied by reduction of the associated ketone carbonyl group (Scheme 6) and such that a partially chromatographically separable mixture of the isomeric diols **22** (43%) and **23** (19%) was obtained. The structure of the former product was secured through a single-crystal X-ray analysis (see Experimental Section and Supporting Information for Details). While the configuration at the marked (*) carbon center in the second product, the structure of which is only tentatively assigned, could not be determined unequivocally it is assumed to be the same as that at the analogous center in congener **22**.

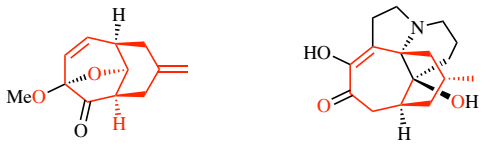


Scheme 6. The reductive cleavage of mono-oxide **16** and its conversion into the oxygenated diene **25**

On treating a solution of epoxide **16** in *tert*-butanol with palladium diacetate and tri-*n*-butylphosphine then a Meinwald rearrangement[16] reaction took place to give the crystalline dione **24** (8%), the structure of which was also confirmed by single-crystal X-ray analysis. Compound **24** could itself be converted, under standard conditions, into the corresponding silyl enol ether **25** (96%). Despite being an an oxygenated analogue of the title diene **3** and, potentially therefore, a more activated form of it (in terms of its capacity for engagement in normal-electron demand Diels-Alder cycloaddition reactions), compound **25** also failed to react with dienophiles such as *N*-methylmaleimide, nitroethylene, methyl acrylate and 2-chloroacrylonitrile.

Conclusions

The [6+3]-adduct **3** arising from the addition of troponoid **1** to *in situ* generated TMM (**2**) is not a particularly effective diene for normal-electron demand Diels-Alder reactions and neither is its oxygenated derivative **25**. However, compound **3** does engage in a range of selective oxidation reactions and the mono-oxide arising from its treatment with DMDO engages in a novel rearrangement reaction, probably involving the intermediate 3-homoadamantyl cation **19**, and so forming the oxygen-bridged bicyclo[4.3.1]decadienone **21**. A related compound, **11**, is obtained through the regioselective dihydroxylation of adduct **3**. Such systems, or related ones, could serve as precursors to a range of natural products including, for example, the novel alkaloid lycojaponicumin D (**26**).[17]



21 **26**

Figure 4. A comparison of the structures of compound **21** and the natural product lycojaponicumin D (**26**)

Experimental Section

General Experimental Procedures.

Unless otherwise specified, proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded at room temperature in base-filtered $CDCl_3$ on a spectrometer operating at 400 MHz for proton and 101 MHz for carbon nuclei. The signal due to residual $CHCl_3$ appearing at δ_H 7.26 and the central resonance of the $CDCl_3$ "triplet" appearing at δ_C 77.20 were used to reference ^{1}H and ^{13}C NMR spectra, respectively. ^{1}H NMR data are recorded as follows: chemical shift (δ) [multiplicity, coupling constant(s) *J* (Hz), relative integral] where multiplicity is defined as: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet or combinations of the above. Infrared spectra (ν_{max}) were recorded on a FTIR spectrometer. Samples were analyzed as thin films. Low-resolution ESI mass spectra were recorded on a single quadrupole liquid chromatograph-mass spectrometer, while high-resolution measurements were conducted on a time-of-flight instrument. Low- and high-resolution EI mass spectra were recorded on a magnetic-sector machine. Analytical thin layer chromatography (TLC)

was performed on aluminum-backed 0.2 mm thick silica gel 60 F_{254} plates. Eluted plates were visualized using a 254 nm UV lamp and/or by treatment with a suitable dip followed by heating. These dips included phosphomolybdic acid : ceric sulfate : sulfuric acid (conc.) : water (37.5 g : 7.5 g : 37.5 g : 720 mL) or potassium permanganate : potassium carbonate : 5% sodium hydroxide aqueous solution : water (3 g : 20 g: 5 mL : 300 mL). Flash chromatographic separations were carried out following protocols defined by Still *et al*.[18] with silica gel 60 (40–63 μm) as the stationary phase and using the AR- or HPLC-grade solvents indicated. Starting materials, reagents, drying agents, and other inorganic salts were generally commercially available and used as supplied. Tetrahydrofuran (THF), methanol and dichloromethane were dried using a solvent purification system that is based upon a technology originally described by Grubbs *et al*.[19] Where necessary, reactions were performed under an atmosphere of nitrogen.

Specific Chemical Transformations

(±)-(1*R*,6*R*)-1-Methoxy-8-methylenebicyclo[4.3.1]deca-2,4-dien-10-one (3) and (±)-(1*R*,6*R*,10*S*)-1-Methoxy-4',8-dimethylene-4',5'-dihydro-3'*H*-spiro[bicyclo[4.3.1]deca-ne -10,2'-furan]-2,4-diene (6). A magnetically stirred mixture of α-tropolone methyl ether (**3**)[6] (29 mg, 0.21 mmol) and $Pd(OAc)_2$ (11.9 mg, 0.053 mmol) in toluene (1 mL, anhydrous and degassed with argon) maintained at 20 ºC under an atmosphere of nitrogen, was treated with $(Pr^iO)_3P$ (96 mg, 0.46 mmol), at which point the mixture turned from orange to pale-yellow. Compound **5**[7] (59 mg, 0.32 mmol) was then added in one portion and the resulting solution was heated at 80 ºC for 3 h. The cooled reaction mixture was concentrated under pressure, and the residue thus obtained was subjected to flash chromatography (silica, 1:9 v/v ethyl acetate/hexane elution) and so affording two fractions, A and B.

Concentration of fraction A (R_f = 0.3) afforded compound **6** (6 mg, 12%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.90 (dd, *J* = 12.5 and 7.4 Hz, 1H), 5.80 (dd, *J* = 11.7 and 7.4 Hz, 1H), 5.51 (m, 2H), 5.07 (m, 1H), 4.96 (m 1H), 4.75 (m, 1H), 4.72 (m, 1H), 4.49 (d, *J* = 12.9 Hz, 1H), 4.32 (dd, *J* = 12.9 and 2.4 Hz, 1H), 3.47 (s, 3H), 3.27 (d, *J* = 15.6 Hz, 1H), 2.76-2.62 (complex m, 2H), 2.38 (dd, *J* = 14.1 and 6.5 Hz, 1H), 2.31-2.06 (complex m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 141.4, 133.9, 132.7, 125.3, 124.4, 114.6, 105.0, 87.0, 81.8, 69.7, 54.1, 46.4, 44.5, 38.3, 37.9; IR ν_{max} 2937, 1656, 1621, 1447,

1104, 1078, 1062, 893, 754 cm^{-1}; MS (EI, 70 eV) *m/z* 244 ($M^{+\bullet}$, 78%), 209 (60), 173 (100), 91 (98), 73 (77); HRMS Calculated for $C_{16}H_{20}O_2$ [$M^{+\bullet}$] 244.1463, found 244.1466.

Concentration of fraction B (R_f = 0.2) afforded a a solid, recrystallization (dichloromethane) of which afforded compound **3** (18 mg, 44%) as colorless masses, m.p = 57-58 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 (m, 1H), 5.79 (m, 1H), 5.48 (m, 1H), 5.34 (d, *J* = 12.1 Hz, 1H), 4.96 (m, 1H), 4.93 (m, 1H), 3.52 (s, 3H), 3.35 (m, 1H), 2.75-2.62 (complex m, 2H), 2.57 (dd, *J* = 13.1 and 2.8 Hz, 1H), 2.43 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.5, 139.9, 129.7, 127.7, 125.1, 124.3, 117.0, 87.9, 54.3, 52.5, 48.2, 41.3; IR ν_{max} 2948, 2936, 1712, 1657, 1134, 1079, 968, 913, 901, 847, 756, 696 cm^{-1}; MS (EI, 70 eV) *m/z* 190 ($M^{+\bullet}$, 80%), 175 (45), 162 (52), 147 (100), 91 (99); HRMS Calculated for $C_{12}H_{14}O_2$ [$M^{+\bullet}$] 190.0994, found 190.0995.

(±)-(4*S*,5*R*,6*R*,10*R*,11*S*,12*R*)-6-Methoxy-8-methylene-2-phosphanyl-6,7,8,9,10,11-hexahydro-1*H*,5*H*-5,11-etheno-6,10-methano[1,2,4]triazolo[1,2-*a*][1,2]diazonine-1,3,15(2*H*)-trione (7). A magnetically stirred solution of compound **3** (86 mg, 0.46 mmol) in acetone (1 mL) maintained at 20 °C was treated with PTAD (123 mg, 0.703 mmol). The ensuing red solution was stirred at 20 °C for 2 h and during which time a solid precipitated. The resulting mixture was concentrated under reduced pressure, and the residue thus obtained subjected to flash chromatography (silica, 1:1 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_f = 0.4), a tan-coloured solid that upon recrystallization (ethyl acetate/hexane) afforded compound **7** (108 mg, 65%) as white, crystalline masses, m.p. = 197-198 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.40 (complex m, 4H), 7.35 (m, 1H), 6.45 (m, 2H), 5.26 (m, 1H), 5.20 (m, 1H), 4.76 (m, 2H), 3.68 (s, 3H), 3.43 (m, 1H), 2.91-2.79 (complex m, 2H), 2.74 (m, 1H), 2.65 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13C NMR (101 MHz, $CDCl_3$) δ 207.5, 153.0, 152.9, 140.7, 131.8, 131.3, 129.5, 129.3, 128.6, 125.7, 114.1, 84.4, 57.2, 53.5, 52.8, 51.5, 45.8, 38.0; IR ν_{max} 2936, 1769, 1707, 1409, 1265, 1096, 887, 770, 690, 646 cm^{-1}; MS (ESI, +ve) *m/z* 753 [$(2M + Na)^+$, 10%], 388 [$(M + Na)^+$, 100]; HRMS (ESI, +ve): calculated for $C_{20}H_{19}N_3O_4{}^{23}Na$ $(M + Na)^+$ 388.1273, found 388.1274.

(±)-(1*R*,6*R*,10*S*)-1-Methoxy-8-methylenebicyclo[4.3.1]deca-2,4-dien-10-ol (8). A magnetically stirred solution of compound **11** (86 mg, 0.45 mmol) in methanol maintained at 0 ºC was treated with $NaBH_4$ (45 mg, 1.2 mmol) and the ensuing clear, colorless solution was allowed to warm, with stirring, to 20 ºC over 17 h then treated with $NaHCO_3$ (5 mL of a

sat. aq. solution) and the separated aqueous phase extracted with dichloromethane (3 x 8 mL). The combined organic phases were then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The yellow oil thus obtained was subjected to flash chromatography (silica, ethyl acetate elution) and concentration of the relevant fractions (R_f = 0.3 in 3:7 v/v ethyl acetate/Hexane) afforded the alcohol **8** (65 mg, 75%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (m, 2H), 5.61 (m, 2H), 4.75 (m, 1H), 4.73 (m, 1H), 4.23 (m, 1H), 3.46 (s, 3H), 2.97 (m, 1H), 2.45-2.31 (complex m, 3H), 2.21 (m, 1H), 2.14 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 132.7, 132.5, 125.3, 124.1, 114.8, 81.8, 72.4, 51.6, 43.8, 42.9, 38.7; IR ν_{max} 3452, 2936, 1446, 1076, 994, 894, 755 cm^{-1}; MS (EI, 70 eV) *m/z* 192 ($M^{+\bullet}$, 42%), 177 (35), 149 (75), 137 (77), 91 (100); HRMS (EI, 70 eV) calculated for $C_{12}H_{16}O_2$ $M^{+\bullet}$ 192.1150, found 192.1151.

(±)-(2*S*,4a*R*,8*R*,8a*S*,9*R*)-4a-Methoxy-6-methylene-2,4a,5,6,7,8-hexahydro-8a*H*-2,8-methanochromene-8a,9-diol (11). A magnetically stirred solution of compound **3** (48 mg, 0.25 mmol) in acetone/H_2O (2.5 mL of a 4:1 v/v mixture) maintained at 20 ºC was treated with K_2OsO_4•$2H_2O$ (9 mg, 0.024 mmol) then *N*-methylmorpholine-*N*-oxide (30 mg, 0.26 mmol). The resulting black solution was stirred for 42 h before being treated with Na_2SO_3 (20 mL of a sat. aq. solution) then extracted with ethyl acetate (3 x 5 mL). The combined organic phases were dried (Na_2SO_4), filtered and then concentrated under reduced pressure and the yellow oil thus obtained was subjected to flash chromatography (silica, ethyl acetate elution). Concentration of the relevant fractions (R_f = 0.6) afforded a white solid, recrystallization (ethanol) of which gave compound **11** (32 mg, 57%) as white crystalline masses, m.p. = 178-180 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.30 (dd, *J* = 9.6 and 4.8 Hz, 1H), 5.50 (d, *J* = 9.6 Hz, 1H), 4.76 (broad s, 1H), 4.73 (broad s, 1H), 4.65 (s, 1H), 4.33 (dd, *J* = 4.8 and 1.1 Hz, 1H), 3.59 (m, 1H), 3.43 (s, 3H), 2.46-2.33 (complex m, 3H), 2.22 (m, 1H), 2.18 (m, 1H), 2.14 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.1, 134.8, 127.9, 113.1, 103.9, 80.7, 80.4, 75.5, 53.9(8), 53.9(6), 42.5, 32.5; IR ν_{max} 3419, 3292, 2939, 1650, 1277, 1081, 1057, 1004, 952, 895, 889, 761, 650, 602 cm^{-1}; MS (ESI, +ve) *m/z* 471 [$(2M + Na)^+$, 10%], 247 [$(M + Na)^+$, 100]; HRMS (ESI, +ve) calculated for $C_{12}H_{16}O_4{}^{23}Na$ $(M + Na)^+$ 247.0946, found 247.0947.

(±)-(2*S*,4a*R*,8*R*,8a*S*,9*R*)-8a-Hydroxy-4a-methoxy-6-methylene-4a,5,6,7,8,8a-hexahydro-2*H*-2,8-methanochromen-9-yl acetate (12). A magnetically stirred solution of compound **11** (9 mg, 0.040 mmol), and acetic anhydride (40 mg, 0.40 mmol) in

dichloromethane (6 mL) maintained at 20 ºC was treated with pyridine (32 mg, 0.40 mmol) then 4-(*N*,*N*-dimethylamino)pyridine (1 mg, 0.008 mmol). The resulting mixture was stirred for 16 h then treated with NH_4Cl (10 mL of a sat. aq. solution) and the separated aqueous phase extracted with dichloromethane (3 x 5 mL). The combined organic phases were then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give compound **12** (10 mg, 94%) as a clear, colorless oil (R_f = 0.3 in 3:7 v/v ethyl acetate/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.35 (dd, *J* = 9.6 and 4.8 Hz, 1H), 5.55 (d, *J* = 9.6 Hz, 1H), 4.79 (broad s, 1H), 4.76 (broad s, 1H), 4.65 (s, 1H), 4.41 (m, 1H), 4.35 (d, *J* = 3.8 Hz, 1H), 3.43 (s, 3H), 2.58 (m, 1H), 2.48-2.34 (complex m, 2H), 2.28- 2.14 (complex m, 2H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 140.7, 134.3, 128.7, 113.6, 103.6, 81.5, 77.2, 75.6, 54.0, 49.4, 42.5, 32.2, 21.2; IR ν_{max} 3466, 2943, 1734, 1656, 1235 cm^{-1}; MS (ESI, +ve) *m/z* 289 [$(M + Na)^+$, 100%]; HRMS (ESI, +ve) calculated for $C_{14}H_{18}O_5{}^{23}Na$ $(M + Na)^+$ 289.1052, found 289.1055.

(±)-(2*S*,4a*R*,8*R*,8a*R*,9*R*)-9-Acetoxy-4a-methoxy-6-methylene-2,4a,5,6,7,8-hexahydro-8a*H*-2,8-methanochromen-8a-yl 2,2-dichloroacetate (13). A magnetically stirred mixture of compound **12** (6 mg, 0.023 mmol) and zinc (56 mg, 0.86 mmol) in anhydrous diethyl ether (5 mL) maintained at 20 ºC was treated, dropwise, with trichloroacetyl chloride (*ca.* 100 µL). The resulting yellow solution was stirred for 18 h before being concentrated under reduced pressure. The brown residue thus obtained was diluted with dichloromethane (3 mL) and the resulting solution treated with H_2O (5 mL) then extracted with dichloromethane (3 x 5 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give a yellow residue that was subjected to flash chromatography (silica, 1:4 v/v ethyl acetate/hexane elution). Concentration of the relevant fractions (R_f = 0.6 in 3:7 v/v ethyl acetate/hexane) gave compound **13** (1 mg, 12%) as clear, colorless oil. ^{1}H NMR (800 MHz, $CDCl_3$) δ 6.33 (dd, *J* = 9.7 and 4.7 Hz, 1H), 6.04 (s, 1H), 5.45 (d, *J* = 9.7 Hz, 1H), 4.84 (m, 1H), 4.80 (m, 1H), 4.60 (broad s, 1H), 4.39 (d, *J* = 3.4 Hz, 1H), 3.39 (s, 3H), 3.33 (m, 1H), 2.56 (m, 1H), 2.49 (m, 2H), 2.19 (dd, *J* = 12.9 and 2.1 Hz, 1H), 2.11 (s, 3H); ^{13}C NMR (200 MHz, $CDCl_3$) δ 171.3, 161.4, 139.5, 131.8, 130.4, 113.8, 110.6, 81.3, 78.2, 75.2, 64.9, 54.2, 47.2, 42.6, 32.2, 21.0; IR ν_{max} 2932, 2850, 1737, 1236 cm^{-1}; MS (ESI, +ve) *m/z* 403 [$(M + Na)^+$, 10%], 401 [$(M + Na)^+$, 65], 399 [$(M + Na)^+$, 100]; HRMS (ESI): calculated for $C_{16}H_{18}O_6{}^{23}Na^{35}Cl_2$ $(M + Na)^+$ 399.0378, found 399.0378.

(±)-(1*S*,2*R*,3*R*,6*R*,10*R*)-1-Methoxy-8-methylenebicyclo[4.3.1]dec-4-ene-2,3,10-triol (14) and **(±)-(1*R*,6*R*,10*R*)-8-(hydroxymethyl)-1-methoxybicyclo[4.3.1]deca-2,4-diene-8,10-diol (15).** A magnetically stirred solution of compound **8** (19 mg, 0.099 mmol) in acetone/water (2.5 mL of a 4:1 v/v mixture) maintained at 20 ºC was treated with K_2OsO_4•$2H_2O$ (7 mg, 0.019 mmol) then *N*-methylmorpholine-*N*-oxide (12 mg, 0.10 mmol). The resulting black solution was stirred for 120 h before being treated with Na_2SO_3 (5 mL of a sat. aq. solution) then extracted with ethyl acetate (3 x 5 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated under reduced pressure and the residue thus obtained subjected to flash chromatography (silica, 1:19 v/v methanol/ethyl acetate elution) to afford two fractions, A and B.

Concentration of fraction A (R_f = 0.4) afforded compound **14** (4 mg, 18%) as a clear, colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.66 (app. dt, *J* = 13.3 and 2.0 Hz, 1H), 5.57 (app. dt, *J* = 13.3 and 2.5 Hz, 1H), 4.91 (broad s, 1H), 4.82 (broad s, 1H), 4.63 (m, 2H), 4.13 (m, 1H), 3.84 (m, 1H), 3.32 (s, 3H), 3.29 (d, *J* = 11.1 Hz, 1H), 3.18 (s, 1H), 2.95 (m, 1H), 2.63 (dd, *J* = 12.9 and 2.1 Hz, 1H), 2.49 (m, 1H), 2.34 (m, 1H), 2.21 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.2, 134.5, 128.2, 115.2, 80.8, 78.0, 76.4, 71.9, 49.4, 42.0, 39.6, 35.5; IR ν_{max} 3351, 2924, 1070 cm^{-1}; MS (ESI, +ve) *m/z* 475 [(2M + Na)$^+$, 20%], 249 [(M + Na)$^+$, 100]; HRMS (ESI, +ve) calculated for $C_{12}H_{18}O_4{}^{23}Na$ (M + Na)$^+$ 249.1103, found 249.1102.

Concentration of fraction B (R_f = 0.3) afforded compound **15** (2 mg, 9%) as a clear, colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.17-6.04 (complex m, 2H), 5.99 (m, 1H), 5.78 (m, 1H), 4.38 (m, 1H), 3.50 (s, 3H), 3.43 (m, 1H), 3.22 (dd, *J* = 11.1 and 7.2 Hz, 1H), 2.97 (s, 1H), 2.85 (m, 1H), 2.06 (m, 2H), 1.96 (m, 1H), 1.92 (d, *J* = 10.8 Hz, 1H), 1.64 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.0(63), 137.0(61), 124.0, 123.9, 81.9, 71.9, 69.3, 69.1, 52.5, 41.6, 40.7, 38.0; IR ν_{max} 3392, 2923, 1078 cm^{-1}; MS (ESI, +ve) *m/z* 475 [(2M + Na)$^+$, 10%], 249 [(M + Na)$^+$, 100]; HRMS (ESI, +ve) calculated for $C_{12}H_{18}O_4{}^{23}Na$ (M + Na)$^+$ 249.1103, found 249.1105.

(±)-(1*R*,2*R*,4*S*,7*R*)-7-Methoxy-9-methylene-3-oxatricyclo[5.3.1.0^{2,4}]undec-5-en-11-one (16) and (±)-(1'*R*,2*S*,2'*R*,4'*S*,7'*R*)-7'-Methoxy-3'-oxaspiro[oxirane-2,9'-tricyclo-[5.3.1.0^{2,4}]undecan]-5'-en-11'-one (17). A magnetically stirred mixture of compound **3** (49 mg, 0.26 mmol) and K_2CO_3 (25 mg, 0.18 mmol) maintained at 0 ºC was treated with DMDO (9.0 mL of a 36 mM solution in acetone, 0.32 mmol) that had been cooled to 0 ºC. The

resulting pale-yellow reaction mixture was stirred at 20 ºC for 24 h before being concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 1:4 v/v ethyl acetate/hexane elution) and thus affording two fractions, A and B.

Concentration of fraction A (R_f = 0.6 in 2:3 v/v ethyl acetate/hexane) afforded a white solid that upon recrystallization (ethyl acetate/hexane) gave compound **16** (25 mg, 47%) as clear, colorless crystals, m.p. = 66-68 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.15 (dd, *J* = 12.5 and 5.8 Hz, 1H), 5.74 (dd, *J* = 12.5 and 0.9 Hz, 1H), 4.97 (broad s, 1H), 4.86 (broad s, 1H), 3.53 (m, 1H), 3.49 (s, 3H), 3.35 (m, 1H), 3.16 (m, 1H), 2.68 (m, 1H), 2.60 (m, 1H), 2.54 (m 1H), 2.44 (dd, *J* = 12.9 and 2.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.4, 138.7, 135.4, 125.6, 116.2, 86.2, 57.0, 54.6, 52.1, 50.0, 48.1, 36.3; IR ν_{max} 2930, 2935, 1718, 1659, 1445, 1115, 1083, 988, 915, 776 cm^{-1}; MS (EI, 70 eV) *m/z* 206 ($M^{+\bullet}$, 5%), 178 (55), 141 (88), 91 (100); HRMS (EI, 70 eV) calculated for $C_{12}H_{14}O_3$ ($M^{+\bullet}$) 206.0943, found 206.0944.

Concentration of fraction B (R_f = 0.2 in 2:3 v/v ethyl acetate/hexane) afforded afforded a white solid that upon recrystallization (ethyl acetate/hexane) gave compound **17** (10 mg, 17%) %) as clear, colorless crystals, m.p. = 155-156 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.21 (ddd, *J* = 12.5, 5.9 and 0.8 Hz, 1H), 5.87 (d, *J* = 12.5 Hz, 1H), 3.63 (m, 1H), 3.46 (s, 3H), 3.44 (m, 1H), 3.23 (dd, *J* = 4.6 and 3.9 Hz, 1H), 2.79 (dd, *J* = 4.9 and 2.1 Hz, 1H), 2.75 (dd, *J* = 4.9 and 1.4 Hz, 1H), 2.59 (m, 1H), 2.50 (dd, *J* = 13.1 and 1.8 Hz, 1H), 1.64 (m, 1H), 1.61 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.0, 136.7, 125.5, 84.4, 56.6, 56.0, 54.3, 54.2, 51.8, 48.3, 45.2, 34.5; IR ν_{max} 3060, 2841, 1723, 1651, 1447, 1406, 1317, 1203, 1120, 1088, 1002, 899, 788 cm^{-1}; MS (EI, 70 eV) *m/z* 222 ($M^{+\bullet}$, 15%), 191 (23), 139 (68), 111 (100), 91 (82); HRMS (EI, 70 eV) calculated for $C_{12}H_{14}O_4$ ($M^{+\bullet}$) 222.0892, found 222.0892.

(±)-(2*R*,4a*R*,8*R*,8a*S*)-2-Methoxy-6-methylene-4a,5,6,7,8,8a-hexahydro-2*H*-2,8-methanochromen-9-one (21). A solution of epoxide **16** (15 mg, 0.073 mmol) in $CDCl_3$ (500 μL) maintained at 20 ºC was treated with concentrated HCl (*ca.* 5 μL). Immediately thereafter, the reaction mixture was subjected to ^{1}H NMR analysis and so revealing that the starting material had been completely consumed. Accordingly, the entire reaction mixture was subjected to flash chromatography (silica, 1:4 v/v ethyl acetate/hexane elution). Concentration of the appropriate fractions (R_f = 0.7 in 2:3 v/v ethyl acetate/hexane) gave a

white solid that upon recrystallization (ethyl acetate/hexane) gave compound **21** (21 mg, 73%) as clear, colorless crystals, m.p. = 114-115 °C. ^{1}H NMR (800 MHz, $CDCl_3$) δ 5.81 (dd, *J* = 9.9 and 2.1 Hz, 1H), 5.78 (ddd, *J* = 9.9, 2.5 and 1.3 Hz, 1H), 4.79 (broad s, 1H), 4.76 (ddd, *J* = 8.3, 5.5 and 1.3 Hz, 1H), 4.73 (broad s, 1H), 3.46 (s, 3H), 3.00 (broad s, 1H), 2.84 (td, *J* = 8.3 and 1.4 Hz, 1H), 2.71 (dt, *J* = 14.6 and 1.8 Hz, 1H), 2.37 (m, 1H), 2.22 (m, 1H), 2.16 (m, 1H); ^{13}C NMR (200 MHz, $CDCl_3$) δ 205.1, 138.2, 136.1, 127.0, 113.7, 100.7, 72.4, 52.8, 46.6, 35.8, 35.6, 31.8; IR ν_{max} 2918, 1759, 1653, 1443, 1383, 1266, 1231, 1111 1055, 1020, 985 cm^{-1}; MS (ESI, +ve) *m/z* 245 [(M + K)$^+$, 90%], 229 [(M + Na)$^+$, 100], 207 [(M + H)$^+$, 15]; HRMS (ESI, +ve) calculated for $C_{12}H_{14}O_3{}^{23}Na$ (M + Na)$^+$ 229.0841, found 229.0839.

(±)-(1*R*,2*S*,6*S*,10*R*)-6-Methoxy-8-methylenebicyclo[4.3.1]dec-3-ene-2,10-diol (22) and (±)-(1*R*,2*S*,6*R*,10*R*)-6-Methoxy-8-methylenebicyclo[4.3.1]dec-4-ene-2,10-diol (23). $LiAlH_4$ (860 μL of a 1.0 M solution in THF, 0.86 mmol) was added, dropwise, to a magnetically stirred solution of compound **16** (43 mg, 0.21 mmol) in anhydrous THF (5 mL) maintained at –78 ºC under a nitrogen atmosphere. The resulting mixture was left to warm, with stirring, to 20 ºC, over 24 h. The resulting pale-yellow solution was then treated with water (6 mL) (CAUTION: possibility of hydrogen evolution) and the separated aqueous phase extracted with dichloromethane (3 x 6 mL). The combined organic phases were then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 7:3 v/v ethyl acetate/hexane elution) to give two fractions, A and B.

Concentration of fraction A (R_f = 0.3) afforded gave a white solid that upon recrystallization (ethyl acetate/hexane) gave compound **22** (6 mg, 14%) as clear, colorless crystals, m.p. = 83-84 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.77 (m, 1H), 5.57 (m, 1H), 4.66 (broad s, 1H), 4.54 (broad s, 1H), 4.25 (m, 1H), 4.05 (m, 1H), 3.74 (d, *J* = 9.3 Hz, 1H), 3.26 (s, 3H), 3.18 (d, *J* = 2.4 Hz, 1H), 2.83 (m, 1H), 2.72 (dq, *J* = 16.7 and 2.8 Hz, 1H), 2.55 (dd, *J* = 13.4 and 2.2 Hz, 1H), 2.51-2.37 (complex m, 2H), 2.27 (m, 1H), 2.16 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1, 132.0, 127.0, 111.7, 78.9, 77.0, 73.2, 49.0, 43.0, 40.8, 36.6, 34.3; IR ν_{max} 3339, 2930, 1651, 1445, 1422, 1258, 1071, 1002, 983, 891, 710, 652 cm^{-1}; MS (ESI, +ve) *m/z* 443 [(2M + Na)$^+$, 10%], 233 [(M + Na)$^+$, 100]; **HRMS** (ESI, +ve) calculated for $C_{12}H_{18}O_3{}^{23}Na$ (M + Na)$^+$ 233.1154, found 233.1153.

Concentration of fraction B (R_f = 0.3) gave a 3:2 mixture of two compounds identified as **22** and (tentatively) **23** (21 mg, 0.10 mmol, 48%) as a clear, colorless oil. ^{13}C NMR (100 MHz, $CDCl_3$) δ (for compound **23**) 142.8, 131.3, 126.9, 114.2, 81.4, 77.7, 73.6, 49.6, 42.5, 40.9, 36.2, 35.7.

(±)-(1*R*,6*R*)-6-Methoxy-8-methylenebicyclo[4.3.1]dec-4-ene-2,10-dione (24). A magnet -ically stirred mixture of the epoxide **16** (100 mg, 0.485 mmol) and $Pd(OAc)_2$ (22 mg, 0.98 mmol) in *t*-BuOH (10 mL, degassed with argon) maintained at 20 ºC under an atmosphere of nitrogen, was treated with *n*-Bu_3P (98 mg, 0.48 mmol) and so resulting in the reaction mixture turning from orange to pale-yellow. This mixture was heated at 80 ºC for 20 h then the cooled reaction mixture was concentrated under reduced pressure and the residue was subjected to flash chromatography (silica, 1:4 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_f = 0.4 in 1:4 v/v EtOAc/hexane), a white solid that upon recrystallization (ethyl acetate/hexane) gave compound **24** (7 mg, 7%) as clear, colorless crystals, m.p. = 116-118 °C. ^{1}H NMR (800 MHz, $CDCl_3$) δ 5.90 (ddd, *J* = 11.4, 9.6 and 3.8 Hz, 1H), 5.54 (dd, *J* = 11.4 and 3.1 Hz, 1H), 4.92 (broad s, 1H), 4.88 (broad s, 1H), 3.51 (s, 3H), 3.36 (dd, *J* = 7.0 and 1.7 Hz, 1H), 3.28 (m, 1H), 3.07 (m, 1H), 2.91 (dd, *J* = 13.5 and 9.6 Hz, 1H), 2.60-2.54 (complex m, 2H), 2.50 (m, 1H); ^{13}C NMR (200 MHz, $CDCl_3$) δ 210.3, 200.4, 138.4, 134.6, 123.6, 116.5, 85.6, 63.1, 54.1, 48.6, 41.9, 37.8; IR ν_{max} 2960, 1732, 1700, 1448, 1285, 1224, 1113, 1084, 1004, 980, 910, 847, 756, 709, 605 cm^{-1}; MS (ESI, +ve) *m/z* 229 [$(M + Na)^+$, 47%], 207 [$(M + H)^+$, 20], 175 (50), 147 (100); HRMS (ESI, +ve) calculated for $C_{12}H_{14}O_3{}^{23}Na$ $(M + Na)^+$ 229.0841, found 229.0837.

(±)-(1*R*,6*R*)-5-((*tert*-Butyldimethylsilyl)oxy)-1-methoxy-8-methylenebicyclo[4.3.1]-deca-2,4-dien-10-one (25). Lithium hexamethyldisilazide (39 μL of a 1.0 M solution in THF, 0.039 mmol) was added dropwise to a magnetically stirred solution of compound **24** (4 mg, 0.019 mmol) in anhydrous THF (1 mL) maintained at –78 ºC under a nitrogen atmosphere. The resulting mixture was stirred for 2 h, treated with TBSCl (5.9 mg, 0.39 mmol) then allowed to warm, with stirring, to 20 ºC over 3 h. The resulting solution was concentrated under reduced pressure and the residue thus obtained subjected to flash chromatography (silica, 1:9 v/v ethyl acetate/hexane elution) to afford, after concentration of the relevant fractions (R_f = 0.4), compound **25** (6 mg, 96%) as a clear, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.72 (dd, *J* = 12.5 and 8.5 Hz, 1H), 5.10 (d, *J* = 12.5 Hz, 1H),

5.01 (m, 2H), 4.95 (m, 1H), 3.51 (s, 3H), 3.21 (dd, J = 6.8 and 2.1 Hz, 1H), 2.76-2.64 (m, 3H), 2.61 (m, 1H), 0.92 (s, 9H), 0.19 (s, 3H), 0.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.3, 152.0, 139.9, 124.3, 123.8, 116.2, 103.9, 86.3, 58.5, 53.9, 49.1, 39.5, 25.5, 18.0, –4.4, –4.8; IR ν_{max} 2931, 1724, 1615, 1235, 1179, 1135, 1090, 848 cm^{-1}; MS (ESI, +ve) *m/z* 663 [(2M + Na)$^+$, 20%], 343 [(M + Na)$^+$, 100]; HRMS (ESI, +ve) calculated for $C_{18}H_{28}O_3Si^{23}Na$ (M + Na)$^+$ 343.1705, found 343.1703.

Crystallographic Studies on Compounds 3, 7, 11, 16, 17, 21, 22 and 24

Crystal data

Compound 3: $C_{12}H_{14}O_2$, M = 190.24, T = 150 K, monoclinic, space group $P2_1/c$, Z = 4, a = 7.0201(1), b = 20.3175(3), c = 7.4430(2) Å, β = 112.540(3)°, V = 980.51(3) Å^3, D_x = 1.289 g.cm^{-3}, 1930 unique data ($2\theta_{max}$ = 145°), 1785 with $I > 2.0\sigma(I)$; R = 0.033, Rw = 0.082, S = 1.00.

Compound 7: $C_{20}H_{19}N_3O_4$, M = 365.39, T = 150 K, monoclinic, space group $P2_1/c$, Z = 4, a = 13.5538(1), b = 7.5734(1), c = 17.1890(2) Å, β = 94.1831(10)°, V = 1759.72(2) Å^3, D_x = 1.379 g.cm^{-3}, 3490 unique data ($2\theta_{max}$ = 145°), 3219 with $I > 2.0\sigma(I)$; R = 0.035, Rw = 0.090, S = 1.00.

Compound 11: $C_{12}H_{16}O_4$, M = 224.26, T = 150 K, trigonal, space group $R\bar{3}$, Z = 18, a = 27.8145(3), c = 7.2697(1) Å, V = 4870.68(7) Å^3, D_x = 1.376 g.cm^{-3}, 2135 unique data ($2\theta_{max}$ = 144.4°), 2077 with $I > 2.0\sigma(I)$; R = 0.032, Rw = 0.076, S = 1.01.

Compound 16: $C_{12}H_{14}O_3$, M = 206.24, T = 150 K, orthorhombic, space group $Pbca$, Z = 8, a = 10.2381(1), b = 8.4009(1), c = 24.1004(2) Å, V = 2072.86(2) Å^3, D_x = 1.322 g.cm^{-3}, 2059 unique data ($2\theta_{max}$ = 144.6°), 1993 with $I > 2.0\sigma(I)$; R = 0.037, Rw = 0.098, S = 1.01.

Compound 17: $C_{24}H_{28.55}O_{8.27}$, M = 449.39, T = 150 K, monoclinic, space group $P2_1/c$, Z = 4, a = 8.2892(1), b = 25.1452(3), c = 10.2313(1) Å, β = 90.4873(11)°, V = 2132.47(2) Å^3, D_x = 1.400 g.cm^{-3}, 4214 unique data ($2\theta_{max}$ = 144.6°), 4077 with $I > 2.0\sigma(I)$; R = 0.061, Rw = 0.142, S = 1.06.

Compound 21: $C_{12}H_{14}O_3$, M = 206.24, T = 150 K, monoclinic, space group $P2_1/n$, Z = 4, a = 7.3469(1), b = 7.6646(1), c = 18.4587(2) Å, β = 97.9441(12)°, V = 1029.45(1) Å^3, D_x = 1.331 g.cm^{-3}, 2033 unique data ($2\theta_{max}$ = 144.8°), 1972 with $I > 2.0\sigma(I)$; R = 0.032, Rw = 0.077, S = 1.04.

Compound 22: $C_{12}H_{18}O_3$, M = 210.27, T = 150 K, monoclinic, space group $P2_1/n$, Z = 4, a = 6.9287(1), b = 9.2358(1), c = 17.2307(2) Å, β = 100.0258(11)°, V = 1085.79(1) Å^3, D_x = 1.286 g.cm^{-3}, 2153 unique data ($2\theta_{max}$ = 144.8°), 2094 with $I > 2.0\sigma(I)$; R = 0.033, Rw = 0.084, S = 1.01.

Compound 24: $C_{12}H_{14}O_3$, M = 206.24, T = 150 K, triclinic, space group $P\bar{1}$, Z = 2, a = 6.8638(2), b = 7.5915(3), c = 10.2836(5) Å, α = 84.717(4)°, β = 82.352(3)°, γ = 75.871(3)°, V = 514.02(2) Å^3, D_x = 1.332 g.cm^{-3}, 2024 unique data ($2\theta_{max}$ = 144.8°), 1869 with $I > 2.0\sigma(I)$; R = 0.035, Rw = 0.091, S = 1.03.

Structure Determinations

Images were measured on an SuperNova diffractometer (CuKα, mirror monochromator, λ = 1.54184 Å) and data extracted using the CrysAlis PRO package.[20] Structure solution was by ShelXT,[21] and the structures of compounds **3**, **7**, **11**, **16**, **17**, **21**, **22** and **24** were all refined using ShelXL[22] in the OLEX2 program package.[23] Atomic coordinates, bond lengths and angles, and displacement parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC deposition numbers 1909496-1909503). These data can be obtained free-of-charge *via* www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

Computational Procedures

All standard *ab initio* molecular orbital theory and density functional theory (DFT) calculations were carried out using the Gaussian 09[24] software package. Geometries were optimized at the M06-2X/6-31+G(d,p)[25] level of theory, and frequencies were also calculated at this level. For the Diels Alder calculations, Gibbs free energies in solution were calculated via a thermocycle in which Gibbs free energies in the gas phase, as calculated via standard ideal gas partition functions, were combined with Gibbs free energies of solvation and the necessary phase change correction term.[26] The SMD solvent model[27] was used to correct for implicit solvent effects, with toluene and acetone as solvents. For this purpose, geometries were fully optimized in solution at the M06-2X/6-31+G(d,p) level of theory. For the cation rearrangement calculations, Gibbs free energies

in solution were calculated via the direct method[28] utilizing solution-phase partition functions, calculated using the SMD model at the M06-2X/6-31+G(d,p) level of theory with chloroform as the solvent. For all the species investigated, a full conformational search was performed, at a resolution of 120° about sp^3-sp^3 bonds and 180° about sp^3-sp^2 and sp^2-sp^2 bonds. For the Diels Alder reactions, all possible product diastereoisomers were investigated, with barriers and reaction energies reflecting formation of the most (kinetically and thermodynamically) favorable product diastereoisomer.

Associated Content

Supporting Information

Anisotropic displacement ellipsoid plots from the single-crystal X-ray analysis of compounds **3**, **7**, **11**, **16**, **17**, **21**, **22** and **24**. ^{1}H and ^{13}C NMR spectra of compounds **3**, **6**, **7**, **8**, **11**, **12**, **13**, **14**, **15**, **16**, **17**, **21**, **22**, **23**, **24** and **25**. Raw energies of species involved in the Diels-Alder and carbocationic rearrangement reactions as well as gas and solution phase geometries for the same. This material is available free-of-charge via the Internet at http://XXXXX…….

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Notes

The authors declare no competing financial interest.

Acknowledgements

We thank the Australian Research Council and the Institute of Advanced Studies for financial support.

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