

## 7-(1-Acetoxyethylidene)benzonorbornadiene: A Versatile Reagent for the Synthesis of 7-Formyl and 7-Hydroxymethyl Benzonorbornadienes.

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**Abstract:** 7-(1-Acetoxyethylidene)benzonorbornadiene **3**, prepared in one step by the addition of benzyne to 6-acetoxyfulvene **2**, is hydrolysed in acid solution to form a 3:2-epimeric mixture of *syn*- and *anti*- 7-formylbenzonorbornadienes **4** and **5**, respectively; the corresponding 7-hydroxymethylbenzonorbornadienes **6** and **9** were produced by reduction of the formyl isomers with sodium borohydride.

**Keywords:** Benzyne, cycloaddition, enolacetates, fulvenes, benzonorbornadienes.

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### Introduction

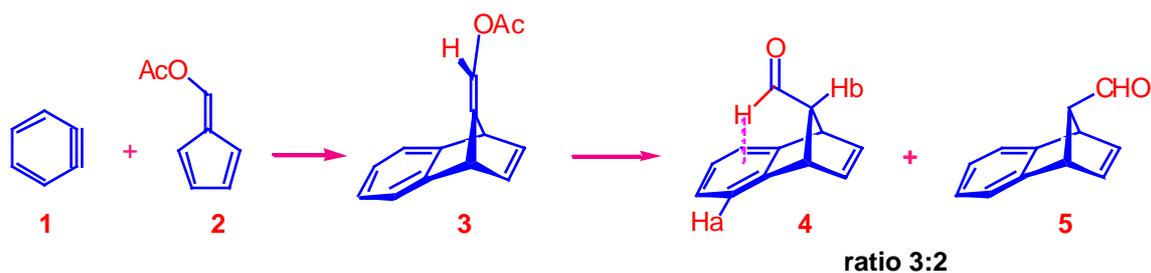
7-Substituted benzonorbornadienes are important reagents, yet simple routes for their synthesis are lacking. In principle, such compounds can be prepared by addition of benzyne to 5-substituted cyclopenta-1,3-dienes, however these isomers are themselves very unstable, being converted to the more stable 2-substituted and 3-substituted isomers during the course of benzyne addition. Further, the addition of benzyne to cyclopenta-2,4-dienones, which would circumvent the substrate isomerisation problem and provide a carbonyl group in the 7-position for subsequent modification, is

frustrated by the thermal instability of benzonorbornadien-7-ones [1]. Benzyne additions to cyclopentadienyl anions [2] and cyclopentadiene ketals [3-6] have been reported and have been used to prepare 7-substituted benzonorbornadienes.

Our answer to this issue has been to use a fulvene reagent since they have a fixed structure and can carry latent functionality to the 7-position of benzonorbornadienes. Accordingly, we investigated the addition of benzyne to 6-acetoxyfulvene **2** [7] for the synthesis of 7-(1-acetoxymethylene)-benzonorbornadiene **3**, since hydrolysis of the enol acetate group should yield the versatile formyl derivatives **4** and **5** at the 7-position. Masking of the norbornene  $\pi$ -bond of 7-(1-acetoxymethylene)benzonorbornadiene as a cycloadduct has the potential to yield products which should be capable of ozonolysis to form stable benzonorbornen-7-one derivatives suitable for CO modifications. These latter aspects have been described separately [8], while this paper concentrates on the preparation of the title compound, its hydrolysis to 7-formyl-benzonorbornadienes and reduction to the 7-hydroxymethyl derivatives.

## Results and Discussion

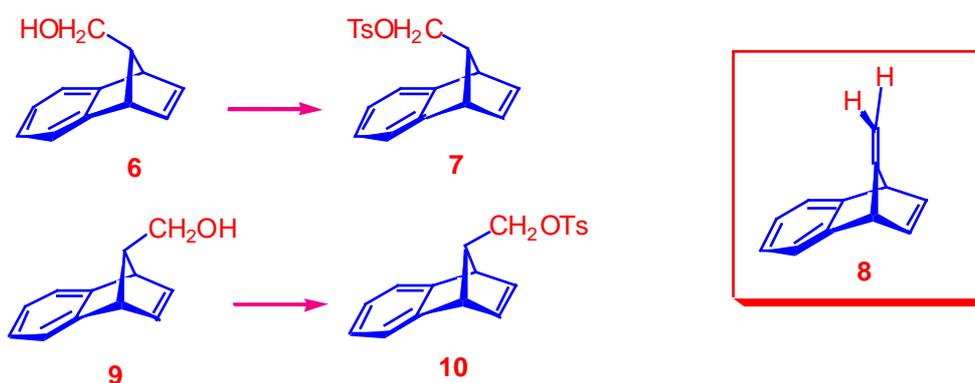
The reaction of benzyne **1**, generated from diazotisation of anthranilic acid [9], to 6-acetoxyfulvene **2** proceeded without significant deacetylation to form 7-(acetoxymethylidene)-benzonorbornadiene **3** in 45% yield (Scheme 1). The  $^1\text{H-NMR}$  of **3** confirmed the presence of the acetate group (methyl resonance at  $\delta$  2.40), while the unsymmetrical nature of the structure was evident from the bridgehead protons which appeared as well separated resonances ( $\delta$  4.16, 4.56). The aromatic and norbornene  $\pi$ -bond resonances overlapped to produce an unresolved multiplet at  $\delta$  6.80-7.40. The resonance for the exocyclic vinylidene proton in **3** occurred as a singlet at  $\delta$  6.58, considerably downfield from that observed for 7-methylidenebenzonorbornadiene **8** ( $\delta$  4.12), consistent with the electron-withdrawing capacity of the acetoxy substituent.



Scheme 1

Acid hydrolysis of **3** was conducted in acetone containing concentrated hydrochloric acid [10] and produced the *syn*-isomer **4** (stereochemical designations have been made relative to the benzene ring) and the *anti*-isomer **5** as an oily mixture (3:2, as determined by  $^1\text{H-NMR}$ ) in 69% yield. The individual isomers, which were separated by chromatography, each displayed a characteristic low-field resonance for the aldehyde proton. Significantly, there was a difference of 0.42 ppm in the chemical shifts of the two isomers, and this was used to help make their structure assignments. The

higher field resonance ( $\delta$  9.18) of the major isomer **4** also displayed a vicinal coupling ( $J = 2.5$  Hz), which was not observed with its isomer **5** (slightly broadened singlet at  $\delta$  9.60). The shift to high field of the major *syn*-isomer was consistent with the aldehyde being positioned above the benzenoid ring and this was confirmed by the presence of an NOE between the formyl proton and the aromatic proton  $H_a$ . The stabilisation afforded by the interaction of the formyl proton and the benzene ring fixed the formyl group in **4** in the transoid configuration. This proposal is supported by the 2.5 Hz coupling of the former proton with the bridge proton  $H_b$ . The lack of coupling in the *anti*-isomer **5** suggested that free rotation was occurring. Neither aldehyde could be obtained crystalline, so the *syn*-isomer **4** was converted to its pale yellow-coloured 2,4-dinitrophenyl hydrazone derivative for characterisation.



Scheme 2

Reduction of the aldehydes **4** and **5** to their respective hydroxymethyl compounds **6** and **9** was achieved in quantitative yield using sodium borohydride. When conducted on a mixture, the generated alcohols were separated by chromatography on silica and the *syn*-isomer **6** eluted first, suggesting there might be some H-bonding with the aromatic. In keeping with the assignments made for the aldehydes, the methylene protons of *syn*-isomer **6** occurred at higher field ( $\delta$  3.08) than the *anti*-isomer **9** ( $\delta$  3.60) which reflected the fact that the methylene protons were positioned closer to the shielding zone of the aromatic ring. The oily alcohol **6** was characterised as its 3,5-dinitrobenzoyl derivative [11].

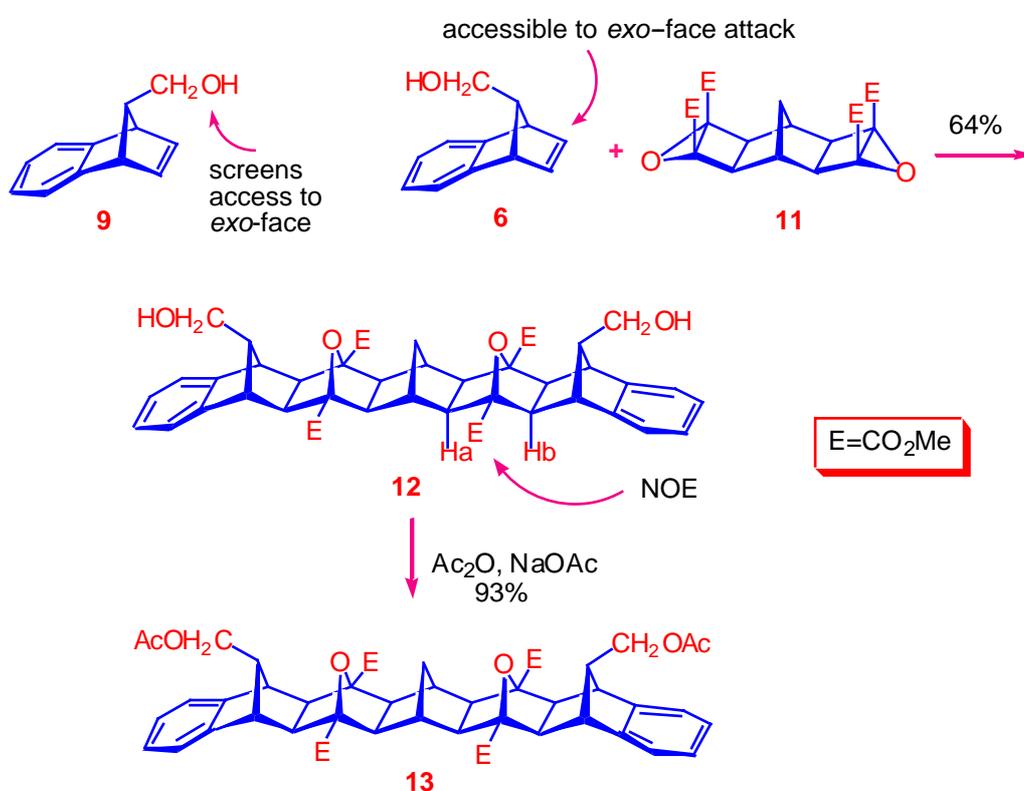
Tosylation of a mixture of **6** and **9** was achieved by treatment with tosyl chloride in pyridine and formed a mixture of **7** and **10** that was recrystallised slowly from alcohol to yield two types of crystals. The larger prisms were shown to be the *syn*-isomer **7**, while the colourless needles, which were separated manually from the mixture, corresponded to the *anti*-isomer **10**.

### BLOCK Coupling of *Syn*-7-hydroxymethyl-benzonorbornadiene **6**.

A special feature of the different isomers of the 7-hydroxymethyl-benzonorbornadienes **6** and **9** as substrates for BLOCK coupling reactions [12], is the accessibility of the  $\pi$ -bond for reagent attack at the *exo*-face. This difference is attributed to the screening effect of the hydroxymethyl group when it

is on the same side as the  $\pi$ -bond (the *anti*-isomer **9**) thereby precluding attack at that dienophilic centre. Thus, treatment of a mixture of alcohols **6** and **9** with the *bis*-epoxide **11** [13] gave only one coupled product **12**, that derived from alcohol **6**, while unchanged alcohol **9** was recovered from the reaction mixture (Scheme 3). The structure of the coupled product **12** was supported by spectroscopy in which the bridge methine proton ( $\delta$  3.51) was typically downfield-shifted owing to its proximity to the adjacent oxabridge. The NOE between protons  $H_a$  and  $H_b$  fully confirmed the *exo,exo*-stereochemistry.

For molecule **12** to be an effective spacer system, then attachment of functionality at the hydroxymethyl groups must be easy to achieve. In this case, acylation of the pendant hydroxyl groups was readily achieved by acetylation with acetic anhydride containing sodium acetate as base, to thus form the diacetate **13** in 93% yield. This derivatisation is a marked improvement over spacer units in which the hydroxyl group is directly attached to the methano-bridge [14].



Scheme 3

## Conclusions

A direct entry to 7-formyl benzonorbornadienes by hydrolysis of 7-(1-acetoxymethylene)-benzonorbornadiene has provided access to a versatile set of *syn*- and *anti*- starting materials that can be readily transformed to other 7-substituted benzonorbornadienes, many of which are difficult to prepare by other methods.

## Acknowledgements

PF thanks CQU for the award of a PhD scholarship while GC acknowledges the award of a MSc scholarship from ANU. Funding support through the Centre for Molecular Architecture at CQU has enabled this work, which had its origins at ANU in the 1980s, to be completed. Several compounds described herein are presently being used in ARC-funded projects at CQU.

## Experimental

### General

Microanalyses were carried out by the ANU Microanalytical Service. Melting points, which are uncorrected, were determined with a Reichert melting point apparatus. IR spectra were recorded on a Unicam SP200G infrared spectrophotometer. UV spectra were recorded with a Unicam SP800 spectrophotometer. Mass spectra were recorded on a Varian Mat CH7 or an A.E. I. MS902 spectrometer. EI or ESMS (electrospray mass spectrometry) were conducted on a Micromass Platroem II single quadrupole mass spectrometer.  $^1\text{H-NMR}$  (100 MHz) spectra were recorded on a Jeolco Minimar 100-MHz spectrometer.  $^1\text{H-NMR}$  (400 MHz) and  $^{13}\text{C-NMR}$  (75 MHz) were recorded on a Bruker Avance DPX 400-MHz spectrometer. All data was acquired using  $\text{CDCl}_3$  solutions with TMS as an internal standard and are reported in ppm on the appropriate  $\delta_{\text{H}}$  and  $\delta_{\text{C}}$  scales. Coupling constants are reported in Hz. The silica gel used for column chromatography was silica gel 60 (230-400 mesh). TLC was performed on Merck aluminium sheets coated with silica gel 60 F<sub>254</sub>. Radial chromatography was carried out with a Chromatotron, Model No 7924T, using 1 mm plates coated with silica gel 60 F<sub>254</sub>. All preparative thin-layer chromatography was carried out on plates using 2 mm layers of silica gel (Merck GF<sub>254</sub>). All solvents were removed under reduced pressure.

### ***9-(Acetoxymethylidene)-1,4-dihydro-1,4-methanonaphthalene (3).***

Solutions of anthranilic acid (55.4 g, 0.4 mol) in tetrahydrofuran (200 mL) and isopentyl nitrite (47.3 g, 0.4 mol) in tetrahydrofuran (200 mL) were added dropwise and simultaneously to a refluxing solution of 6-acetoxyfulvene (55 g, 0.4 mol) in tetrahydrofuran (100 mL) over a period of about 1 h. The solution was refluxed for a further 1 h cooled, made alkaline with aqueous sodium hydroxide (4%, 500 mL), and extracted with petroleum spirit (3 x 500 mL). The dried extracts were freed of solvent and the residue recrystallised from n-hexane to yield the title product as pale yellow crystals (38 g, 45%), m.p. 78-79 °C; Found: C, 79.2; H, 5.8.  $\text{C}_{14}\text{H}_{12}\text{O}_2$  requires C, 79.2; H, 5.7%;  $^1\text{H-NMR}$  (100 MHz): 2.40 (s, 3H,  $\text{CH}_3$ ), 4.16 (br m, 1H, bridgehead), 4.56 (br m, 1H, bridgehead), 6.58 (s, 1H, methylene proton), 6.80-7.40 (m, 6H, aromatic and  $\text{H}_{2,3}$ ); UV (ethanol) nm: ( $\epsilon$ ) 225 (3950), 265 (680), 272 (850), 279 (800); IR (nujol)  $\text{cm}^{-1}$ : 1080, 1740; MS:  $m/z$  212( $\text{M}^+$ , 25%), 171 (10), 170 (72), 169 (66), 152 (12), 142 (41), 141 (100), 140 (10), 139 (25), 116 (19), 115 (53), 63 (10), 43 (51). The other peaks were less than 10%.

**Syn- and anti- 9-Formyl-tricyclo[6.2.1.0<sup>2,7</sup>]undeca-2,4,6,9-tetraene (4,5).**

A solution of enol acetate **3** (2 g, 9.4 mmol) in concentrated hydrochloric acid (4 mL) and acetone (16 mL) was refluxed for 0.5 h. After cooling, water (20 mL) was added and the mixture extracted with ether (2 x 20 mL). The ethereal extract was washed with water (30 mL), dried and freed of solvent. The <sup>1</sup>H-NMR spectrum of the crude product indicated a 3:2 mixture of the *syn*-isomer **4** and *anti*-isomer **5**. The residue was distilled (approx. 80 °C, 0.1 mbar) to give the products as a colourless liquid (1.1 g, 69%). The two isomers were separated by preparative TLC (silica, 1:1 chloroform and petroleum spirit).

The *syn*-aldehyde **4**, was recovered from the least polar band as a colourless oil (0.4 g, 25%). <sup>1</sup>H-NMR (100 MHz): 3.25 (m, 1H, H<sub>11</sub>), 4.15 (m, 2H, H<sub>1,8</sub>), 6.88 (t, 2H, H<sub>9,10</sub>), 6.90-7.40 (m, 4H, aromatic protons), 9.18 (d, 1H, *J* = 2.5 Hz, formyl proton); IR (nujol) cm<sup>-1</sup>: 1730 cm<sup>-1</sup> (carbonyl stretch); MS: *m/z* 170 (M<sup>+</sup>, 50%), 169 (17), 142 (16), 141 (100), 115 (41), 63 (12), 21 (45). The other peaks were less than 10%.

The 2,4-dinitrophenylhydrazone derivative was recrystallised from ethyl acetate giving bright yellow crystals, m.p. 177-178 °C; Found: C, 61.7; H, 4.0; N, 15.9. C<sub>18</sub>H<sub>14</sub>O<sub>4</sub>N<sub>4</sub> requires C, 61.7; H, 4.0; N, 16.0%

The *anti*-aldehyde **5** was recovered as a colourless oil (0.2 g, 12%); <sup>1</sup>H-NMR (100 MHz): 3.20 (m, 1H, H<sub>11</sub>), 4.20 (m, 2H, H<sub>1,4</sub>), 6.74 (t, 2H, H<sub>9,10</sub>), 6.9-7.4 (m, 4H, aromatic protons), 9.60 (br s, 1H, formyl proton); IR (nujol) cm<sup>-1</sup>: 1725 cm<sup>-1</sup> (carbonyl stretch); MS: *m/z* 170 (M<sup>+</sup>, 12%), 169 (11), 142 (16), 141 (100), 115 (26). The other peaks were less than 10%.

**Syn- and anti- 9-(hydroxymethyl)-tricyclo[6.2.1.0<sup>2,7</sup>]undeca-2,4,6,9-tetraene (6,9).**

A mixture of the *syn*-aldehyde **4** and *anti*-aldehydes **5** (0.6 g, 3.5 mmol) in the ratio of 3:2 and sodium borohydride (0.2 g, 6.7 mmol) were stirred in ethanol (10 mL) for 1 h. Water was added and the solution extracted with ether. The ethereal extracts were dried, the solvent removed and the residual mixture of alcohols separated by preparative thin-layer chromatography (silica, 7% ethyl acetate in petroleum spirit, 10 developments).

The *syn*-alcohol **6** was recovered from the least polar band as a colourless liquid (0.25 g, 42%). <sup>1</sup>H-NMR (100 MHz): 2.50 (br s, 1H, OH), 2.84 (t, 1H, *J* = 8 Hz, H<sub>11</sub>), 3.08 (d, 2H, *J* = 8 Hz, OCH<sub>2</sub>), 3.67 (m, 2H, H<sub>1,8</sub>), 6.80 (t, 2H, H<sub>9,10</sub>), 6.9-7.5 (m, 4H, aromatic protons).

The 3,5-dinitrobenzoyl derivative was recrystallised again from a mixture of benzene and petroleum spirit (twice) to give pale yellow crystals, m.p. 137-140 °C; Found: C, 62.6; H, 4.1; N, 7.7. C<sub>19</sub>H<sub>14</sub>O<sub>6</sub>N<sub>2</sub> requires C, 62.3; H, 3.9; N, 7.7%

The *anti*-alcohol **9** was recrystallised from a mixture of benzene and petroleum spirit as white needles (0.15 g, 25%) m.p. 50-51.5 °C; Found: C, 83.1; H, 7.5. C<sub>12</sub>H<sub>12</sub>O requires C, 83.7; H, 7.0% <sup>1</sup>H-NMR (100 MHz): 2.65 (br s, 1H, OH), 2.80 (t, 1H, *J* = 8 Hz, H<sub>11</sub>), 3.60 (d, 2H, *J* = 8 Hz, OCH<sub>2</sub>), 3.76 (m, 2H, H<sub>1,8</sub>), 6.58 (t, 2H, H<sub>9,10</sub>), 6.8-7.3 (m, 4H, aromatic protons); UV (ethanol) nm: (ε) 274 (430), 267 (500), 260 (430), 235 (930), 213 (4500); IR (nujol) cm<sup>-1</sup>: 695, 735, 1010, 1020, 3300; MS:

$m/z$  172 ( $M^+$ , 35%), 154 (18), 153 (16), 142 (17), 141 (100), 129 (11), 128 (33), 115 (32). The other peaks were less than 10%.

***Syn- and anti- 9-(tosyloxymethyl)-tricyclo[6.2.1.0<sup>2,7</sup>]undeca-2,4,6,9-tetraene (7, 10).***

A solution of the *syn*-alcohol **6** and *anti*-alcohol **9** (0.4 g, 2.3 mmol) in the ratio of 3:2 and tosyl chloride (0.36 g, 1.9 mmol) in anhydrous pyridine (3 mL) was stirred under nitrogen for 3 days. Water (10 mL) was added and the solution extracted with ether (3 x 5 mL). The combined ethereal extract was dried and freed of solvent. The residue was allowed to slowly crystallise from ethanol over a period of several days giving two crystal forms which were separated manually.

The *syn*-tosylate **7**, crystallised as large, colourless prisms (0.25g, 33%) m.p. 106-108 °C. Found C, 69.9; H, 5.5; S, 9.8.  $C_{19}H_{18}O_3S$  requires C, 69.9; H, 5.6; S, 9.8%;  $^1H$ -NMR (100 MHz): 2.48 (s, 3H,  $CH_3$ ), 3.04 (br t, 1H,  $J = 7.5$  Hz,  $H_{11}$ ), 3.62 (d, 2H,  $J = 7.5$  Hz,  $CH_2$ ), 3.72 (m, 2H,  $H_{1,8}$ ), 6.88 (t, 2H,  $H_{9,10}$ ), 6.96-7.74 (m, 8H, aromatic protons); UV (ethanol) nm: ( $\epsilon$ ) 274 (440), 269 (530), 227 (10000), 213 (9300); IR (nujol)  $cm^{-1}$ : 660, 700, 765, 835, 955, 1175; MS:  $m/z$  326 ( $M^+$ , 28%), 155 (23), 154 (100), 153 (31), 152 (10), 142 (14), 141 (99), 128 (25), 115 (26), 91 (25). The other peaks were less than 10%.

The *anti*-tosylate **10**, crystallised as colourless needles (0.15 g, 20%) m.p. 105-105 °C; Found: C, 69.8; H, 6.0; S, 9.5.  $C_{19}H_{18}O_3S$  requires C, 69.9; H, 5.6; S, 9.8%;  $^1H$ -NMR (100 MHz): 2.48 (s, 3H,  $CH_3$ ), 2.96 (t, 1H,  $H_{11}$ ), 3.78 (m, 2H,  $H_{1,8}$ ), 4.16 (d, 2H,  $J = 7.5$  Hz,  $CH_2$ ), 6.58 (t, 2H,  $H_{9,10}$ ), 6.90-7.84 (m, 8H, aromatic protons); UV (ethanol) nm: ( $\epsilon$ ) 274 (460), 269 (610), 226 (11400), 221 (14300); IR (nujol)  $cm^{-1}$ : 950, 1175; MS:  $m/z$  326 ( $M^+$ , 21%), 155 (22), 154 (100), 153 (36), 152 (10), 142 (12), 141 (81), 128 (28), 115 (28), 91 (29), 65 (15). The other peaks were less than 10%.

***The tosylhydrazone of 9-formyl-tricyclo[6.2.1.0<sup>2,7</sup>]undeca-2,4,6,9-tetraene (4).***

A solution of the *syn*-aldehyde **4** (0.5 g, 2.90 mmol) and *N*-tosylhydrazine (0.54 g, 2.9 mmol) in methanol (10 mL) containing two drops of concentrated hydrochloric acid was stirred for 1 h. The solvent was removed and the product dissolved in hot benzene (20 mL). On cooling the excess *N*-tosylhydrazine was removed by filtration and the filtrate freed of solvent. The residue was recrystallised from ethanol to give the product as colourless needles (0.6 g, 61%) m.p. 134-135 °C. Found: C, 67.4; H, 5.7; N, 8.2; S, 9.5.  $C_{19}H_{18}N_2SO_2$  requires C, 67.4; H, 5.4; N, 8.3; S, 9.5%;  $^1H$ -NMR (100 MHz): 2.44 (s, 3H,  $CH_3$ ), 3.40 (dd, 1H,  $H_{11}$ ), 3.88 (m, 2H,  $H_{1,8}$ ), 6.50 (d, 1H,  $H_a$ ), 6.84 (m, 2H,  $H_{9,10}$ ), 6.8-7.8 (m, 8H, aromatic protons); UV (ethanol) nm: ( $\epsilon$ ) 276 (1000), 271 (1500), 244 (7800); IR (nujol)  $cm^{-1}$ : 1165, 1360; MS:  $m/z$  338 ( $M^+$ , 5%), 184 (15), 183 (100), 167 (17), 166 (27), 156 (16), 153 (15), 152 (13), 141 (10), 129 (11), 128 (25), 115 (15), 91 (17). The other peaks were less than 10%.

***Tetramethyl (1 $\alpha$ ,2 $\beta$ ,3 $\alpha$ ,4 $\beta$ ,5 $\alpha$ ,12 $\alpha$ ,13 $\beta$ ,14 $\alpha$ ,15 $\beta$ ,16 $\alpha$ ,17 $\beta$ ,18 $\alpha$ ,19 $\beta$ ,20 $\alpha$ ,27 $\alpha$ ,28 $\beta$ ,29 $\alpha$ ,30 $\beta$ ) 32,34-dioxa- 33,35-dihydroxymethyldodecacyclo[14.14.1.1<sup>3,14</sup>.1<sup>5,12</sup>.1<sup>18,29</sup>.1<sup>20,27</sup>.0<sup>2,15</sup>.0<sup>4,13</sup>.0<sup>6,11</sup>.0<sup>17,30</sup>.0<sup>19,28</sup>.***

***0<sup>21,26</sup>*]pentatriaconta-6,8,10,21,23,25-hexaene-3,14,18,29-tetracarboxylate (12).**

A mixture of alcohol mixture **6** and **9** (*syn:anti* = 2:1), (168 mg, 0.98 mmol) and *bis*-epoxide **11** (133 mg, 0.33 mmol) was dissolved in acetonitrile (5.0 mL) and transferred to a thick-walled glass tube which was cooled, sealed and placed in an oven at 140 °C for 3.5 h. After evaporation of the solvent under reduced pressure, the crude product was purified by radial chromatography. Elution using a solvent system of petroleum ether : EtOAc = 1:3 gave unreacted *anti*-alcohol **9**. Increasing the polarity to MeOH : EtOAc = 1 : 9 afforded **12** as a colourless solid (156 mg, 64%), m.p. 221-223 °C. <sup>1</sup>H-NMR (400 MHz): 1.83 (s, 4H, H<sub>2,15,17,30</sub>), 1.95 (br s, 2H, H<sub>31</sub>), 2.08 (br s, 2H, H<sub>1,16</sub>), 2.15 (s, 4H, H<sub>4,13,19,28</sub>), 3.05 (d, 4H, *J* = 6.9 Hz, H<sub>1',2'</sub>), 3.09 (s, 4H, H<sub>5,12,20,27</sub>), 3.45 (t, 2H, *J* = 7.3 Hz, H<sub>33,35</sub>), 3.91 (s, 12H, OCH<sub>3</sub>), 7.05-7.08 (m, 4H, H<sub>8,9,23,24</sub>), 7.10-7.13 (m, 4H, H<sub>7,10,22,25</sub>); <sup>13</sup>C-NMR (75 MHz): 28.88 (C<sub>31</sub>), 40.65 (C<sub>1,16</sub>), 47.53 (C<sub>5,12,20,27</sub>), 52.33 (OCH<sub>3</sub>), 55.31 (C<sub>33,35</sub>), 55.31 (C<sub>2,15,17,30</sub>), 56.24 (C<sub>4,13,19,28</sub>), 61.04 (C<sub>1',2'</sub>), 89.39 (C<sub>3,14,18,29</sub>), 122.19 (C<sub>7,10,22,25</sub>), 126.42 (C<sub>8,9,23,24</sub>), 145.43 (C<sub>6,11,21,26</sub>), 169.20 (carbonyl). HRMS (EI) for C<sub>43</sub>H<sub>44</sub>O<sub>12</sub> Calc. 752.2833; Found 752.2833.

***Tetramethyl (1 $\alpha$ ,2 $\beta$ ,3 $\alpha$ ,4 $\beta$ ,5 $\alpha$ ,12 $\alpha$ ,13 $\beta$ ,14 $\alpha$ ,15 $\beta$ ,16 $\alpha$ ,17 $\beta$ ,18 $\alpha$ ,19 $\beta$ ,20 $\alpha$ ,27 $\alpha$ ,28 $\beta$ , 29 $\alpha$ ,30 $\beta$ ) 32,34-dioxa-33,35-diacetoxymethyl dodecacyclo [14.14.1.1<sup>3,14</sup>.1<sup>5,12</sup>.1<sup>18,29</sup>.1<sup>20,27</sup>.0<sup>2,15</sup>.0<sup>4,13</sup>.0<sup>6,11</sup>.0<sup>17,30</sup>.0<sup>19,28</sup>.0<sup>21,26</sup>]pentatriaconta-6,8,10,21,23,25-hexaene-3,14,18,29-tetracarboxylate (13).***

A solution of diol **12** (70 mg, 0.09 mmol), acetic anhydride (300  $\mu$ L, 2.9 mmol) and sodium acetate (7 mg, 0.08 mmol) in chloroform (5.0 ml) was refluxed for 4 h. The reaction mixture was allowed to cool and poured onto cold water (8 ml). The organic layer was washed with sodium bicarbonate (saturated solution), (2 x 8 ml), dried (MgSO<sub>4</sub>), and concentrated by removal of solvent under reduced pressure. The crude product was recrystallised from methanol as a colourless solid; yield: 72 mg, (93 %), mp 245-247 °C; <sup>1</sup>H-NMR (400 MHz): 1.84 (s, 4H, H<sub>2,15,17,30</sub>), 1.93 (s, 6H, OAc), 1.95 (br s, 2H, H<sub>31</sub>), 2.10 (br s, 2H, H<sub>1,16</sub>), 2.15 (s, 4H, H<sub>4,13,19,28</sub>), 3.07 (s, 4H, H<sub>5,12,20,27</sub>), 3.51 (m, 6H, H<sub>1',2',33,35</sub>), 3.92 (s, 12H, OCH<sub>3</sub>), 7.05-7.07 (m, 4H, H<sub>8,9,23,24</sub>), 7.09-7.12 (m, 4H, H<sub>7,10,22,25</sub>); <sup>13</sup>C-NMR (75 MHz): 20.76 (OAc), 28.87 (C<sub>31</sub>), 40.62 (C<sub>1,16</sub>), 48.00 (C<sub>5,12,20,27</sub>), 51.64 (C<sub>33,35</sub>), 52.29 (OCH<sub>3</sub>), 55.24 (C<sub>2,15,17,30</sub>), 56.21 (C<sub>4,13,19,28</sub>), 63.10 (C<sub>1',2'</sub>), 89.38 (C<sub>3,14,18,29</sub>), 122.29 (C<sub>7,10,22,25</sub>), 126.67 (C<sub>8,9,23,24</sub>), 145.01 (C<sub>6,11,21,26</sub>), 169.15, 170.77 (carbonyl); HRMS (ES) for [C<sub>47</sub>H<sub>48</sub>O<sub>14</sub> + Na]<sup>+</sup> Calc. 859.2942; Found 859.2945.

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*Sample Availability:* Samples not available.