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Tetrahedron
Tetrahedron 63 (2007) 12026–12036

Bargellini condensation of coumarins. Expeditious route to *o*-carboxyvinylphenoxyisobutyric acids and application to the synthesis of sesquiterpenes helianane, heliannuol A and heliannuol C

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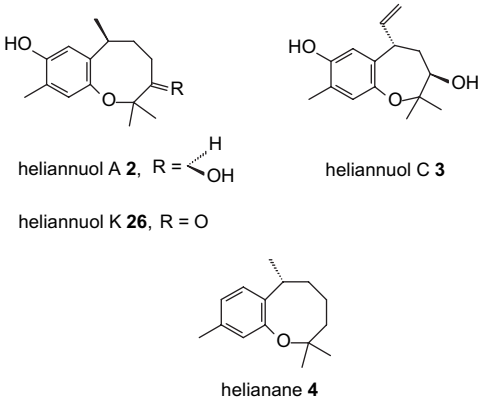
Received 16 April 2007; revised 22 August 2007; accepted 6 September 2007
Available online 11 September 2007

Abstract—The direct Bargellini condensation of coumarins involving reaction with chloroform and acetone in the presence of aqueous sodium hydroxide furnished *o*-carboxyvinylphenoxyisobutyric acids in good yields. The utility of this new useful protocol was demonstrated by the transformation of the three diesters **9b**, **9f** and **9g** to the sesquiterpenes helianane **4**, heliannuol A **2** and heliannuol C **3**, respectively.

1. Introduction

A century ago Bargellini reported the interesting condensation of phenols with chloroform and acetone in the presence of sodium hydroxide to furnish α-phenoxyisobutyric acids **1** (Scheme 1).[1] In fact, however, he was modifying the structure attributed to this condensation product by Link[2] a few years earlier. Although initial studies were confined to phenolic substrates, later investigators have extended this to aliphatic alcohols and with better yields from condensation with acetonechloroform (chloretone).[3] Thus, a simple methodology for the general conversion of alcohols to α-alkoxyisobutyric acid systems was developed. Dealkoxylation of these products provided an access to methacrylic acids. Besides acetone, other ketonic substrates were also found to respond identically to this reaction condition.[3] Further transformations of the phenoxyisobutyric acids to amides for possible exploration as plant hormones[4] and also to provide an alternative to Birch reduction have been described.[5] In the case of aminoethanols, the amine functionality served as the nucleophile and the resultant acids underwent an intramolecular lactonisation to afford 2-oxomorpholines.[6] An unusual case of a *para*-carbon atom functioning as a nucleophile in a hindered phenol has also been reported.[7] Despite the ready incorporation of an isobutyric acid system onto an alcoholic oxygen, the demonstration of its utility in synthesis had not been forthcoming. A recent report discloses application to the synthesis of a dual PPARα/γ agonist by employing this condensation in a sterically congested phenol.[8] However, the acceptability of this method as a useful protocol in synthesis came with the recent isolation of heliannuol A **2** and heliannuol C **3**,[9] important allelochemicals from cultivar sunflowers and the related sesquiterpene helianane **4**,[10] from marine sponge. These compounds contain an α-phenoxyisobutyl component and can readily serve as appropriate target molecules to attest to the viability of Bargellini condensation for incorporation of this unit. Indeed the early approaches to these sesquiterpenes featuring a novel benzoxocane ring system have employed this condensation to install the crucial *gem*-dimethyl functionality in a suitable substrate that was



Keywords: Bargellini condensation; *o*-Carboxyvinylphenoxyisobutyric acids; Heliannuols; Helianane; Ring-closing metathesis.
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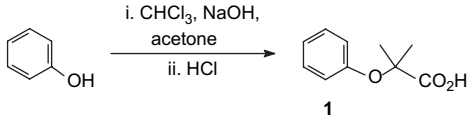
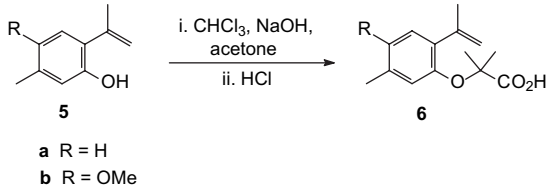
0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.09.006

expanded to the requisite ring system.[11] Our previous synthesis of **2** and **4** also had relied on this condensation to transform the styrenol(s) **5** to the phenoxyisobutyric acid(s) **6**, which were subsequently elaborated to the natural products (Scheme 2).[12] The styrenols **5a** and **5b** were obtained from decarboxylative alkaline hydrolysis of coumarins **7b** and **7f**. Coumarins undergo an initial ring opening under alkaline hydrolytic conditions to generate an intermediate phenolate. Hence it occurred to us that if coumarins are subjected to Bargellini reaction conditions involving the use of base, the intermediate phenolates on further reaction with acetone and chloroform will finally provide a novel one-step route to α-phenoxyisobutyric acids with the additional advantage of an acrylic acid functionality on the adjacent carbon atom of the phenyl ring for further useful transformations. We describe in this article the successful realization of this strategy[13] and demonstrate the utility of the methodology by applying it to the synthesis of helianane **4**, heliannuol A **2** and heliannuol C **3**.



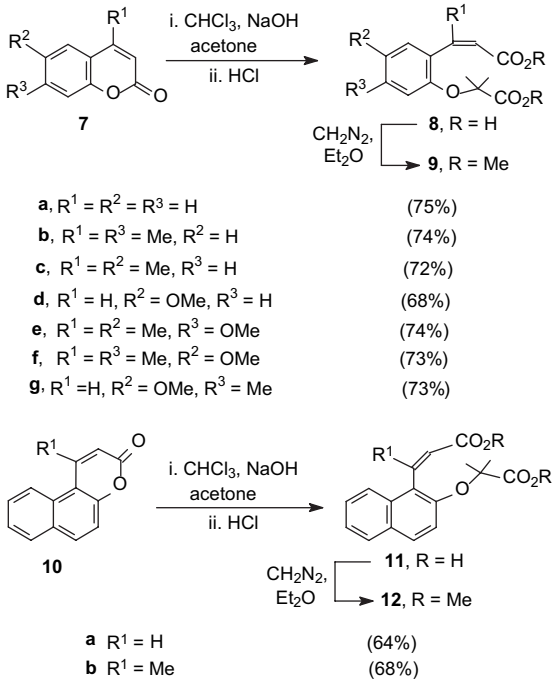
Scheme 1.



Scheme 2.

2. Results and discussion

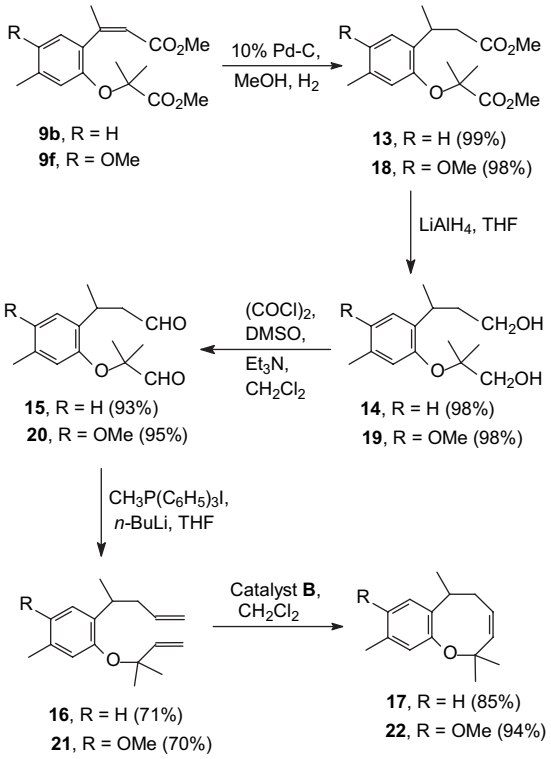
Coumarin **7a** was subjected to reaction with chloroform and acetone in the presence of sodium hydroxide under Bargellini conditions and the product acidified to afford the diacid **8a** in 75% yield as a crystalline solid. The structural assignment was adequately supported by analytical and spectral data. The HRMS showed a molecular weight correlating to the desired molecular formula and the ^{1}H NMR spectrum showed a 6 proton singlet at δ 1.57 for the *gem*-dimethyl group along with other associated features further attesting to the assigned structure. This diacid **8a** was additionally characterized as the dimethyl ester **9a**, obtained on treatment with diazomethane. The double bond in **8a** was assigned the cis stereochemistry based on the coupling constant value in the ^{1}H NMR spectrum (12 Hz). The trans product shows a much higher value for the coupling constant.[14] The methodology was extended to a variety of coumarins **7a–g** and in all cases the desired diacids **8a–g** were obtained in yields ranging from 70–75% and were characterized as the corresponding dimethyl esters **9a–g**. The benzocoumarins **10a** and **10b** also responded similarly to the reaction conditions affording the expected diacids **11a** and **11b** in 65–70% yields and were characterized as dimethyl esters **12a** and **12b** (Scheme 3). Thus, the direct Bargellini condensation with coumarins provided a useful single-step protocol for the preparation of functionalized phenoxy acids. To underscore the preparative utility of this novel procedure, appropriately substituted products were transformed to the natural products, helianane **4**, heliannuols A **2** and C **3** as detailed below.



Scheme 3. Yields reported are overall for **9** and **12**.

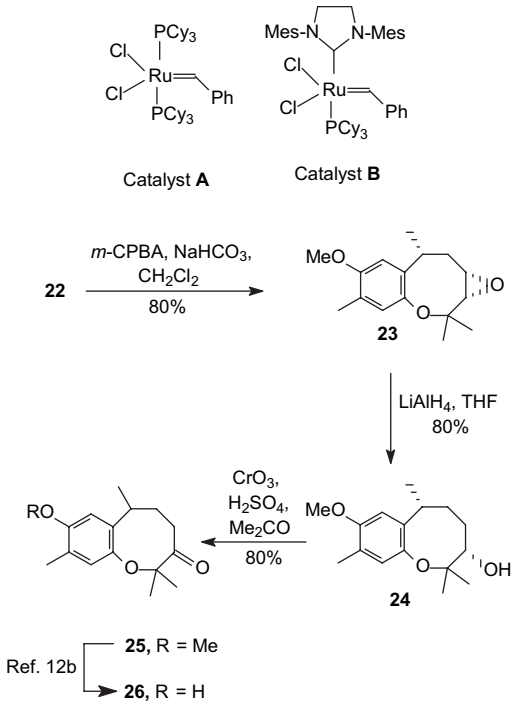
Catalytic hydrogenation of the diester **9b** furnished the saturated diester **13** in quantitative yield. This diester **13** was then reduced to the diol **14** with lithium aluminium hydride in refluxing ether in excellent yield (98%). This diol **14** underwent smooth oxidation under Swern conditions to the dialdehyde **15** (93%), which was subjected to a double Wittig reaction with triphenylmethylene phosphorane to afford the diene **16** in 70% yield. This diene **16** had previously been taken to helianane **4** by Snieckus and Stefinovic,[11b] thus concluding in the present case a formal synthesis of this sesquiterpene. We also carried out the reported steps to complete the synthesis. However, our efforts on cyclization by employing Grubbs first generation catalyst (**A**) were unsuccessful and furnished only a complex product profile. The second generation of Grubbs catalyst (**B**) proved successful and led to a smooth ring-closure furnishing the cyclized alkene **17** in 85% yield (Scheme 4). This alkene was spectroscopically identical to a sample previously synthesized in this laboratory and which had been hydrogenated to helianane **4**.[12b]

The above sequence of reactions starting with hydrogenation was applied on the diester **9f** to eventually afford the benzoxocene **22**, incorporating the basic structural framework of heliannuol A **2** (Scheme 4). Shishido et al. had, in their enantioselective synthesis of **2**, employed a similar substrate having a different protecting group for the C-5 hydroxy function to elaborate to the final compound.[15] Thus, treatment of this benzoxocene **22** with *m*-chloroperbenzoic acid in the presence of $NaHCO_3$ in dichloromethane



Scheme 4.

furnished a single epoxide **23**. This was reduced with lithium aluminium hydride to furnish *O*-methyl heliannuol A **24** in 80% yield (Scheme 5). This was spectroscopically identical to the sample previously prepared in this laboratory.[12] Jones oxidation of this alcohol afforded *O*-methyl heliannuol K **25**, which had been converted to heliannuols K **26** and A **2** concluding another useful approach to their synthesis.[12b]

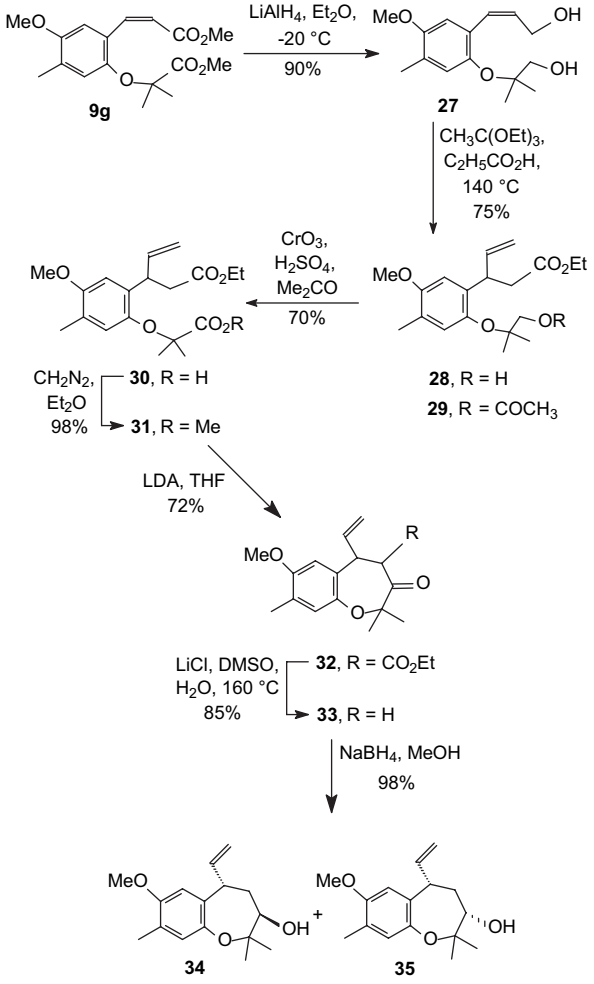


Scheme 5.

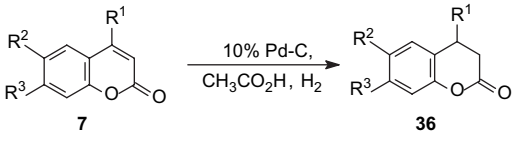
The direct Bargellini condensation of coumarins resulted in the generation of an acrylic acid functionality on the adjacent carbon of the phenolic group, which takes part in the reaction. This feature was advantageously exploited to install the crucial vinyl moiety in a synthesis of heliannuol C **3**.[16]

The diester **9g** was reduced with lithium aluminium hydride in ether at −20 °C to furnish the diol **27** in 90% yield. In the next step of the synthesis the differential status of the two hydroxyl groups present in **27** was suitably exploited to install the vinyl group through an *ortho*-ester Claisen rearrangement. Thus, refluxing a mixture of the diol with triethyl orthoacetate in the presence of a catalytic amount of propionic acid smoothly afforded the rearranged ester **28** in good yield. The acetate **29** was obtained as a minor component in some of the runs. This could be easily separated and mild base treatment (aqueous methanolic potassium hydroxide) of this acetate **29** hydrolyzed it back to the hydroxyester **28**. The ester alcohol **28** was subjected to Jones oxidation to furnish the carboxylic acid **30** (70%), which on treatment with diazomethane afforded the diester **31**. When this diester **31** was treated with LDA in THF, it underwent the expected Dieckmann cyclization to deliver the β-ketoester **32**, which on heating in dimethyl sulfoxide with added lithium chloride and water resulted in a smooth Krapcho deethoxycarbonylation[17] to furnish the benzoxepanone **33** in an overall yield of 61% from **31**. In contrast to the hydride reduction of the heliannuol A precursor **25**, reduction of ketone **33** with sodium borohydride in methanol was non-stereoselective and afforded a mixture of *O*-methyl heliannuol C **34** and its epimer **35** in a 1:3 proportion in 98% yield. An efficient separation of the components could be achieved by preparative thin layer chromatography and the spectral data of **34** and **35** fully matched with those reported previously (Scheme 6).[18] Since **34** had been demethylated to heliannuol C **3**,[18] the present efforts concluded a synthesis of this allelochemical. The larger presence of the undesired epimer **35** in the final step of reduction adversely affected the overall yield. Hence efforts were directed for inversion of the configuration of the hydroxyl group in **35**. Various experimental conditions involving the application of the Mitsunobu reaction for effecting this inversion were unfruitful. Hence, as a viable alternative **35** was oxidized back to the ketone **33** in near quantitative yield employing Jones reagent and reduced with sodium borohydride as before to yield a mixture of **34** and **35**. This sequence of oxidation and reduction was repeated and after four such runs the combined yields of the desired **34** was improved to 62–65%.

The direct Bargellini condensation of coumarins was then extended to dihydrocoumarins also. Catalytic hydrogenation of coumarins **7a–d**,**f**,**g** in acetic acid furnished the corresponding dihydrocoumarins **36a–f** in excellent yield (Scheme 7). When these dihydro derivatives, **36a–f** were subjected to interaction with chloroform and acetone in the presence of sodium hydroxide as per already established conditions, they afforded the expected diacids in yields ranging between 70 –75% and were fully characterized as the corresponding dimethyl esters **37a–d**, **13** and **18** obtained from reaction with diazomethane (Scheme 8). The diesters **13** and **18** were identical in all respects with the corresponding diesters obtained from hydrogenation of the unsaturated diesters **9b** and **9f**, respectively.



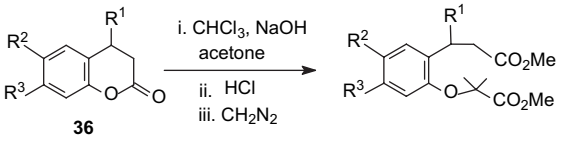
Scheme 6.



a, $R^1 = R^2 = R^3 = H$ → **36a** (99%)
b, $R^1 = R^3 = Me$, $R^2 = H$ → **36e** (97%)
c, $R^1 = R^2 = Me$, $R^3 = H$ → **36b** (98%)
d, $R^1 = H$, $R^2 = OMe$, $R^3 = H$ → **36d** (99%)
f, $R^1 = R^3 = Me$, $R^2 = OMe$ → **36f** (98%)
g, $R^1 =H$, $R^2 = OMe$, $R^3 = Me$ → **36c** (98%)

Scheme 7.

In summary we have developed a novel one-step protocol for the generation of functionalized phenoxy acids from the direct Bargellini condensation of coumarins and dihydrocoumarins and demonstrated the synthetic utility through application to the synthesis of the sesquiterpenes, helianane **4** and heliannuols A **2** and C **3**. It is expected that more varied applications of this useful observations will be forthcoming in future directed towards the development of more complex natural product structural frameworks.



a, $R^1 = R^2 = R^3 = H$ **37a** (75%)
b, $R^1 = R^2 = Me$, $R^3 = H$ **37b** (74%)
c, $R^1 =H$, $R^3 = Me$, $R^2 = OMe$ **37c** (72%)
d, $R^1 = H$, $R^2 = OMe$, $R^3 = H$ **37d** (70%)
e, $R^1 = R^3 = Me$, $R^2 = H$ **13** (75%)
f, $R^1 = R^3 = Me$, $R^2 = OMe$ **18** (75%)

Scheme 8.

3. Experimental

3.1. General

All non-aqueous reactions were carried out under an inert atmosphere (nitrogen). Melting points were taken in open capillary tubes in a sulfuric acid bath and are uncorrected. Dry solvents and reagents were prepared from reagent grade materials by conventional methods. Petroleum ether refers to the fraction of bp. 60–80 °C. The purity of the products was routinely monitored by TLC. Preparative TLC was performed with silica gel HF_{254} (E. Merck) plates of 1-mm thickness. Drying of organic layers was done with sodium sulfate. ^1H NMR spectra were recorded at 300 MHz in $CDCl_3$ solutions. ^{13}C NMR spectra were recorded in $CDCl_3$ solution at 75 MHz. Peak positions are indicated in parts per million downfield from an internal TMS standard. IR spectra of liquid products were recorded as thin films or in $CHCl_3$ solution. IR spectra of solids were recorded as KBr pellets.

3.1.1. General procedure for Bargellini condensation of coumarins. Powdered NaOH (4.56 g, 114 mmol) was added in small portions with stirring to a solution of the required coumarin (11.4 mmol) in acetone (50 mL). The mixture became warm and was cooled to about 35 °C by immersing in a water bath. To this stirred solution, chloroform (10 mL) was added within 10 min. The reaction mixture was then refluxed for 5 h, cooled, concentrated to one-third of its volume and diluted with water (20 mL). It was acidified with 6 N HCl and extracted thoroughly with ether (3×30 mL). The combined ethereal extracts were further extracted with saturated $NaHCO_3$ (3×25 mL). The alkaline aqueous part was neutralized with cold 6 N HCl and then extracted with ether (3×30 mL). The organic layer was washed with saturated brine (25 mL), dried, filtered and evaporated under reduced pressure. The diacids were characterized as dimethyl esters, which were obtained on reaction with diazomethane in ether and purified by column chromatography over silica gel.

3.1.1.1. Methyl 3-[2-(1-methoxycarbonyl-1-methylethoxy)-phenyl]-acrylate (9a). Following the general procedure, coumarin **7a** (1.90 g, 13.01 mmol), furnished the diacid **8a** (2.44 g, 75%) as a white solid, crystallized from ether/petroleum ether. Mp 114–116 °C. IR (KBr) 1695 (br), 1715, 2974 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.57

(6H, s, –C*Me*$_2$–), 5.99 (1H, d, *J* 12.0 Hz, =C*H*–), 6.80 (1H, d, *J* 8.2 Hz, Ar*H*), 6.97 (1H, t, *J* 7.4, Ar*H*), 7.24 (1H, d, *J* 12.0 Hz, –C*H*=) mixed with 7.19–7.25 (1H, m, Ar*H*), 7.47 (1H, d, *J* 8.2 Hz, Ar*H*), 8.76 (2H, br s, –COO*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.3 (2C), 79.8, 117.4, 119.7, 121.9, 127.2, 130.1, 131.2, 142.4, 152.8, 171.7, 179.3. HRMS (ES +ve) calcd for $C_{13}H_{14}O_5Na$ $[M+Na]^+$ 273.0739, found 273.0736.

This diacid **8a** was esterified with diazomethane. The product was purified by column chromatography (10% EtOAc/petroleum ether) to furnish the dimethyl ester **9a** as a colourless oil (2.66 g, 98%). R_f (10% EtOAc/petroleum ether) 0.52. IR ($CHCl_3$) 1715, 1738 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.58 (6H, s, –C*Me*$_2$–), 3.69 (3H, s, O*Me*), 3.76 (3H, s, O*Me*), 5.97 (1H, d, *J* 12.4 Hz, =C*H*–), 6.96 (1H, d, *J* 8.2 Hz, Ar*H*), 6.97 (1H, t, *J* 7.5 Hz, Ar*H*), 7.21 (1H, t, *J* 7.5 Hz, Ar*H*) mixed with 7.20 (1H, d, *J* 12.4 Hz, –C*H*=), 7.56 (1H, dd, *J* 8.2, 1.0 Hz, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.2 (2C), 51.1, 52.3, 79.6, 116.6, 119.3, 121.2, 127.1, 129.6, 130.7, 139.7, 153.1, 166.5, 174.6. HRMS (ES +ve) calcd for $C_{15}H_{19}O_5$ $[M+H]^+$ 279.1233, found 279.1231.

3.1.1.2. Methyl 3-[2-(1-methoxycarbonyl-1-methyl-ethoxy)-4-methylphenyl]-but-2-enoate (9b). Coumarin **7b** (2 g, 11.49 mmol) furnished the diacid **8b** (2.4 g, 75%) as a colourless solid, crystallized from ether/petroleum ether. Mp 164–166 °C. IR (KBr) 1695 (br), 1712, 2975 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.59 (6H, s, –C*Me*$_2$–), 2.17 (3H, s, *Me*), 2.29 (3H, s, *Me*), 5.99 (1H, s, =C*H*–), 6.53 (1H, s, Ar*H*), 6.80 (1H, d, *J* 7.8 Hz, Ar*H*), 6.97 (1H, d, *J* 7.8 Hz, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.4, 24.8, 25.0, 27.1, 79.0, 116.5, 117.6, 122.3, 127.9, 128.4, 138.7, 150.3, 155.1, 169.8, 177.3. HRMS (ES +ve) calcd for $C_{15}H_{19}O_5$ $[M+H]^+$ 279.1237. Found 279.1236.

This diacid **8b** was esterified with diazomethane. The product was purified by column chromatography over silica gel (10% EtOAC/petroleum ether) to furnish the dimethyl ester **9b** as a colourless oil (2.6 g, 98%). R_f (10% EtOAc/petroleum ether) 0.54. IR ($CHCl_3$) 1713, 1737 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.52 (6H, s, –C*Me*$_2$–), 2.16 (3H, s, *Me*), 2.28 (3H, s, *Me*), 3.55 (3H, s, O*Me*), 3.75 (3H, s, O*Me*), 5.91 (1H, s, =C*H*–), 6.53 (1H, s, Ar*H*), 6.78 (1H, d, *J* 7.8 Hz, Ar*H*), 6.92 (1H, d, *J* 7.8 Hz, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3, 25.1, 25.9 (2C), 50.6, 52.2, 79.2, 117.9, 118.1, 122.4, 128.3, 130.1, 138.1, 151.2, 154.4, 165.8, 174.9. HRMS (ES +ve) calcd for $C_{17}H_{23}O_5$ $[M+H]^+$ 307.1546. Found 307.1540.

3.1.1.3. Methyl 3-[2-(1-methoxycarbonyl-1-methyl-ethoxy)-5-methylphenoxy]-but-2-enoate (9c). Coumarin **7c** (1 g, 5.747 mmol) was subjected to Bargellini condensation following the general procedure and the resultant diacid **8c** (1.18 g, 74%) obtained as a sticky material was esterified with diazomethane and purified by column chromatography over silica gel (12% EtOAc/petroleum ether) to give the diester **9c** (1.27 g, 98%) as a colourless liquid. R_f (12% EtOAc/petroleum ether) 0.51. IR ($CHCl_3$) 1715, 1738 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.50 (6H, s, –C*Me*$_2$–), 2.16 (3H, s, *Me*), 2.26 (3H, s, *Me*), 3.54 (3H, s, O*Me*), 3.76 (3H, s, O*Me*), 5.92 (1H, s, =C*H*–), 6.61 (1H, d, *J* 8.3 Hz, Ar*H*), 6.84 (1H, s, Ar*H*), 6.95 (1H, d, *J* 8.3 Hz, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.4, 25.0, 25.9 (2C), 50.7, 52.2, 79.2, 117.1, 117.9, 128.6, 128.9, 130.8, 132.9, 148.9, 154.1, 165.8, 175.0. Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.62; H, 7.25.

3.1.1.4. Methyl 3-[5-methoxy-2-(1-methoxycarbonyl-1-methyl-ethoxy)-phenyl]-acrylate (9d). Coumarin **7d** (1 g, 5.682 mmol) furnished the diacid **8d** (1.12 g, 70%) as a gummy oil. This was esterified with diazomethane to furnish the diester **9d** (1.2 g, 97%) as a colourless liquid after chromatographic purification over silica gel (10% EtOAc/petroleum ether). R_f (10% EtOAc/petroleum ether) 0.51. IR ($CHCl_3$) 1715, 1738 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44 (6H, s, –C*Me*$_2$–), 3.61 (3H, s, O*Me*), 3.69 (3H, s, O*Me*), 3.70 (3H, s, O*Me*), 5.89 (1H, d, *J* 12.6 Hz, =C*H*–), 6.67–6.69 (2H, m, Ar*H*), 7.14 (1H, d, *J* 12.6 Hz, –C*H*=), 7.11–7.13 (1H, m, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.3 (2C), 51.4, 52.6, 55.7, 80.5, 115.4, 115.7, 119.7, 119.9, 129.1, 139.6, 147.3, 154.3, 166.7, 174.9. Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54. Found: C, 62.31; H, 6.52.

3.1.1.5. Methyl 3-[4-methoxy-2-(1-methoxycarbonyl-1-methyl-ethoxy)-5-methylphenyl]-but-2-enoate (9e). Coumarin **7e** (1 g, 4.90 mmol) furnished the diacid **8e** (1.13 g, 75%) as a gummy product and was esterified with diazomethane. The product was purified by column chromatography over silica gel (10% EtOAc/petroleum ether) to furnish the diester **9e** as a colourless liquid (1.21 g, 98%). R_f (10% EtOAc/petroleum ether) 0.53. IR ($CHCl_3$) 1715, 1738 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.49 (6H, s, –C*Me*$_2$–), 2.12 (3H, s, *Me*), 2.15 (3H, s, *Me*), 3.56 (3H, s, O*Me*), 3.73 (3H, s, O*Me*), 3.77 (3H, s, O*Me*), 5.89 (1H, s, =C*H*–), 6.35 (1H, s, Ar*H*), 6.80 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.6, 25.3, 26.4 (2C), 50.9, 52.5, 55.3, 80.2, 102.0, 118.2, 120.3, 125.3, 130.4, 150.5, 153.9, 157.6, 166.4, 175.4. Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 64.26; H, 7.20.

3.1.1.6. Methyl 3-[5-methoxy-2-(1-methoxycarbonyl-1-methyl-ethoxy)-4-methylphenyl]-but-2-enoate (9f). Coumarin **7f** (2 g, 9.804 mmol) furnished the diacid **8f** (2.26 g, 75%) as a viscous product. This was esterified with diazomethane and subjected to column chromatography over silica gel (12% EtOAc/petroleum ether) to furnish the dimethyl ester **9f** as a colourless oil (2.4 g, 97%). R_f (10% EtOAc/petroleum ether) 0.51. IR ($CHCl_3$) 1715, 1738 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.47 (6H, s, –C*Me*$_2$–), 2.18 (3H, s, *Me*), 2.20 (3H, s, *Me*), 3.63 (3H, s, O*Me*), 3.73 (3H, s, O*Me*), 3.78 (3H, s, O*Me*), 5.92 (1H, s, =C*H*–), 6.50 (1H, s, Ar*H*), 6.62 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.1, 24.2, 24.8, 24.9, 50.6, 51.9, 55.3, 79.8, 110.2, 118.3, 121.3, 126.4, 131.6, 144.3, 152.6, 154.1, 165.8, 175.0. Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 64.25; H, 7.18.

3.1.1.7. Methyl 3-[5-methoxy-2-(1-methoxycarbonyl-1-methyl-ethoxy)-4-methylphenyl]-acrylate (9g). Coumarin **7g** (2.0 g, 10.53 mmol) furnished the diacid **8g** (2.30 g, 75%) as a colourless solid, crystallized from ether/petroleum ether. Mp 142–144 °C. IR (KBr) 1695 (br), 1715, 2974 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.54 (6H, s,

–C*Me*$_2$–), 2.17 (3H, s, *Me*), 3.75 (3H, s, O*Me*), 5.96 (1H, d, *J* 12.0 Hz, =C*H*–), 6.72 (1H, s, Ar*H*), 7.13 (1H, s, Ar*H*), 7.26 (1H, d, *J* 12.0 Hz, –C*H*=); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.8, 25.5 (2C), 55.9, 80.2, 112.6, 119.9, 121.5, 126.2, 128.9, 138.9, 147.4, 152.5, 166.8, 176.8. Anal. Calcd for $C_{15}H_{18}O_6$: C, 61.22; H, 6.16. Found: C, 61.20; H, 6.17.

This diacid **8g** was esterified with diazomethane to furnish the dimethyl ester **9g** (2.5 g, 98%) as a colourless oil after purification by column chromatography over silica gel (12% EtOAc/petroleum ether). R_f (12% EtOAc/petroleum ether) 0.53. IR ($CHCl_3$) 1716, 1737 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.51 (6H, s, –C*Me*$_2$–), 2.16 (3H, s, *Me*), 3.70 (3H, s, O*Me*), 3.78 (3H, s, O*Me*), 3.79 (3H, s, O*Me*), 5.92 (1H, d, *J* 12.7 Hz, =C*H*–), 6.61 (1H, s, Ar*H*), 7.19 (1H, d, *J* 12.7 Hz, –C*H*=), 7.32 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.4, 25.0 (2C), 51.1, 52.2, 55.4, 80.2, 111.8, 118.3, 121.2, 125.9, 128.9, 139.4, 146.8, 152.3, 166.6, 174.6. HRMS (ES +ve) Calcd for $C_{17}H_{23}O_6$ $[M+H]^+$ 323.1495. Found 323.1492.

3.1.1.8. Methyl-3-[2-(1-methoxycarbonyl-1-methyl-ethoxy)-naphthalen-1-yl]-acrylate (12a). Coumarin **10a** (1 g, 5.102 mmol) furnished the diacid **11a** (0.99 g, 65%) as a gummy liquid and was esterified with diazomethane. The product was purified by column chromatography (12% EtOAc/petroleum ether) to furnish the diester **12a** as a colourless liquid (1.06 g, 98%). R_f (12% EtOAc/petroleum ether) 0.49. IR ($CHCl_3$) 1715, 1738 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.56 (6H, s, –C*Me*$_2$–), 3.47 (3H, s, O*Me*), 3.79 (3H, s, O*Me*), 6.33 (1H, d, *J* 12.0 Hz, =C*H*–), 7.05 (1H, d, *J* 9.0 Hz, Ar*H*), 7.27 (1H, d, *J* 12.0 Hz, –C*H*=), 7.33–7.45 (2H, m, Ar*H*), 7.70 (1H, d, *J* 9.0 Hz, Ar*H*), 7.76 (2H, d, *J* 9.0 Hz, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.5 (2C), 51.0, 52.3, 79.9, 118.3, 123.9, 124.0, 124.1, 124.1, 126.3, 128.0, 128.9, 129.27, 131.7, 137.9, 149.6, 166.2, 174.9. Anal. Calcd for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14. Found: C, 69.51; H, 6.13.

3.1.1.9. Methyl-3-[2-(1-methoxycarbonyl-1-methyl-ethoxy)-naphthalen-1-yl]-but-2-enoate (12b). Coumarin **10b** (1 g, 4.76 mmol) furnished the diacid **11b** (1.05 g, 70%), which was esterified with diazomethane to furnish the diester **12b** (1.11 g, 97%) as a colourless liquid after purification by column chromatography over silica gel (10% EtOAc/petroleum ether). R_f (10% EtOAc/petroleum ether) 0.52. IR ($CHCl_3$) 1716, 1739 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.53 (3H, s, –C*Me*$_2$–), 1.60 (3H, s, –C*Me*$_2$–), 2.25 (3H, s, *Me*), 3.37 (3H, s, O*Me*), 3.79 (3H, s, O*Me*), 6.24 (1H, s, =C*H*–), 7.15 (1H, d, *J* 9.0 Hz, Ar*H*), 7.30–7.41 (2H, m, Ar*H*), 7.62 (1H, d, *J* 8.4 Hz, Ar*H*), 7.67 (1H, d, *J* 9.0 Hz, Ar*H*), 7.76 (1H, d, *J* 8.4 Hz, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.1, 25.6, 26.8, 50.6, 52.3, 79.4, 117.9, 119.8, 123.8, 123.8, 126.3, 127.8, 127.9, 129.2, 130.9, 147.7, 153.2, 153.2, 165.3, 175.2. Anal. Calcd for $C_{20}H_{22}O_5$: C, 70.16; H, 6.48. Found: C, 70.14; H, 6.45.

3.1.1.10. Methyl-3-[2-(1-methoxycarbonyl-1-methyl-ethoxy)-4-methylphenoxy]-butanoate (13). A methanolic solution of the ene-diester **9b** (1.0 g, 3.268 mmol) containing Pd–C (10%, 50 mg) was stirred under a hydrogen atmosphere (1 atm) until hydrogen uptake was completed. The catalyst was filtered off, the solvent removed and the residue was purified by column chromatography (10% EtOAc/petroleum ether) to furnish the saturated diester **13** (0.99 g, 99%) as a colourless oil. R_f (10% EtOAc/petroleum ether) 0.56. IR ($CHCl_3$) 1739 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (3H, d, *J* 6.9 Hz, –HC*Me*), 1.63 (6H, s, –C*Me*$_2$–), 2.24 (3H, s, *Me*), 2.45 (1H, dd, *J* 9.1, 15.0 Hz, –CHMeC*H*$_2$–), 2.70 (1H, dd, *J* 5.5, 15.0 Hz, –CMeC*H*$_2$–), 3.51–3.88 (1H, m, ArC*H*Me), 3.64 (3H, s, O*Me*), 3.76 (3H, s, O*Me*), 6.40 (1H, s, Ar*H*), 6.73 (1H, d, *J* 7.8 Hz, Ar*H*), 7.04 (1H, d, *J* 7.8 Hz, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.8, 21.0, 25.1, 25.1, 29.8, 41.1, 51.2, 52.2, 78.5, 116.5, 122.1, 126.7, 132.9, 136.3, 152.5, 173.1, 175.0. HRMS (ES +ve) calcd for $C_{17}H_{25}O_5$ $[M+H]^+$ 309.1703. Found 309.1719.

3.1.1.11. 3-[2-(2-Hydroxy-1,1-dimethylethoxy)-4-methylphenoxy]-1-butanol (14). To a magnetically stirred slurry of $LiAlH_4$ (230 mg, 6.06 mmol) in dry ether (15 mL) was added dropwise a solution of the diester **13** (1 g, 3.25 mmol) in dry ether (10 mL) and the reaction mixture was heated to reflux for 4 h, cooled and then quenched with cold aqueous saturated Na_2SO_4 solution (5 mL). The ether layer was separated and the aqueous layer was extracted with ether (3×20 mL). The combined ether extracts were washed with saturated brine (20 mL), dried and concentrated. The residual oil was purified by column chromatography over silica gel (50% EtOAc/petroleum ether) to furnish the diol **14** (800 mg, 98%) as a colourless solid. Mp 96–98 °C. R_f (50% EtOAc/petroleum ether) 0.47. IR (KBr) 3400 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16 (3H, d, *J* 6.5 Hz, –CH*Me*), 1.17 (3H, s, –C*Me*$_2$–), 1.29 (3H, s, –C*Me*$_2$–), 1.37–1.46 (1H, m, –CHMeC*H*$_2$–), 1.64–1.71 (1H, m, ArCHMeC*H*$_2$–), 2.21 (3H, s, *Me*), 3.17–3.25 (1H, m, ArC*H*Me–), 3.38–3.64 (4H, m, –C*H*$_2$OH), 6.77 (1H, s, Ar*H*), 6.78 (1H, d, *J* 7.6 Hz, Ar*H*), 7.01 (1H, d, *J* 7.6 Hz, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.9, 21.6, 22.4, 24.3, 27.2, 42.5, 60.6, 71.1, 81.5, 122.8, 124.7, 126.8, 136.3, 137.4, 153.1. HRMS (ES +ve) calcd for $C_{15}H_{25}O_3$ $[M+H]^+$ 253.1804. Found 253.1797.

3.1.1.12. 3-[2-(1,1-Dimethyl-2-oxo-ethoxy)-4-methylphenyl]-butyraldehyde (15). To a magnetically stirred and cooled (−78 °C) solution of oxalyl chloride (530 mg, 4.17 mmol) in dichloromethane (8 mL), a solution of dimethyl sulfoxide (640 mg, 8.12 mmol) in dichloromethane (2 mL) was added dropwise. After stirring at −78 °C for 15 min a solution of the diol **14** (260 mg, 1.032 mmol) in dichloromethane (5 mL) was added and stirred for 45 min, at this temperature. Triethylamine (1.4 mL, 10 mmol) was then added and stirring was continued for another 2 h at −78 °C. The reaction mixture was allowed to warm to room temperature. After 2 h, the reaction mixture was poured into cold water (10 mL) and the organic layer separated. The aqueous part was extracted with dichloromethane (3×25 mL). The combined organic layers were washed with water (20 mL), dried and concentrated. The residual oil was subjected to column chromatography. Elution with EtOAc/petroleum ether (1:9) afforded the dialdehyde **15** (240 mg, 93%) as a colourless oil. R_f (10% EtOAc/petroleum ether) 0.48. IR (Neat) 1732 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (3H, d, *J* 6.9 Hz, –CH*Me*), 1.46 (6H, s, –C*Me*$_2$–), 2.22 (3H, s, *Me*), 2.55–2.75 (2H, m, –CHMeC*H*$_2$–), 3.69–3.76 (1H, m, ArC*H*Me), 6.39 (1H, s, Ar*H*), 6.77 (1H, d, *J* 7.7 Hz, Ar*H*), 7.07 (1H, d, *J* 7.7 Hz, Ar*H*), 9.69 (1H, t,

J 1.9 Hz, –CH_2CHO), 9.82 (1H, s, –C*H*O); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0, 21.8, 22.2, 22.4, 28.1, 51.3, 83.3, 117.1, 123.4, 127.7, 132.9, 137.4, 152.8, 202.6, 204.0. Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.53; H, 8.13.

3.1.1.13. 2-[2-(1,1-Dimethylallyloxy)-4-methylphenyl]-pent-4-ene (16). *n*-BuLi (0.7 mL of 1.6 M solution in hexane, 1.12 mmol) was added dropwise to a solution of methyltriphenylphosphonium iodide (486 mg, 1.20 mmol) in freshly distilled THF (8 mL) at 0 °C under argon. The mixture was stirred for 1 h at the same temperature. A solution of the dialdehyde **15** (100 mg, 0.403 mmol) in THF (8 mL) was charged into the solution at 0 °C and the resulting solution was stirred overnight. The reaction mixture was quenched with saturated NH_4Cl (5 mL) and extracted with ether (3×20 mL). The organic layer was washed with brine (30 mL) and dried over Na_2SO_4. The residual oil was subjected to column chromatography. Elution with EtOAc/petroleum ether (1:100) afforded the diene **16** (70 mg, 71%) as a colourless oil. R_f (1% EtOAc/petroleum ether) 0.71; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.18 (3H, d, *J* 6.9 Hz, –CH*Me*), 1.48 (6H, s, –C*Me*$_2$–), 2.10–2.43 (2H, m, –CHMeCH_2–), 2.25 (3H, s, *Me*), 3.20–3.27 (1H, m, ArC*H*Me–), 4.93 (1H, d, *J* 11.3 Hz, –CH_2CH=CH_2), 5.00 (1H, d, *J* 18.8 Hz, –CH_2CH=CH_2), 5.14 (1H, d, *J* 10.9 Hz, –CMe_2CH=CH_2), 5.22 (1H, d, *J* 17.6 Hz, –CMe_2CH=CH_2), 5.69–5.89 (1H, m, –CH_2CH=CH_2), 6.16 (1H, dd, *J* 10.9, 17.6 Hz, –CMe_2CH=CH_2), 6.74 (1H, d, *J* 7.8 Hz, Ar*H*), 6.86 (1H, s, Ar*H*), 7.04 (1H, d, *J* 7.8 Hz, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.6, 21.6, 27.8, 27.8, 32.4, 42.0, 79.6, 113.2, 115.7, 120.0, 122.5, 126.9, 135.8, 135.8, 138.3, 145.5, 153.9. HRMS (ES +ve) calcd for $C_{17}H_{25}O$ $[M+H]^+$ 245.1905. Found 245.1901.

3.1.1.14. 2,2,6,9-Tetramethyl-5,6-dihydro-2*H*-benzo[*b*]oxocene (17). A round bottom flask charged with second generation Grubbs catalyst (catalyst **B**) (16 mg, 0.018 mmol) was evacuated and filled with argon gas three times before the addition of a solution of the diene **16** (60 mg, 0.246 mmol) in degassed dichloromethane (20 mL). The resulting solution was stirred at room temperature for 6 h. The solvent was removed under reduced pressure, and the dark residue was purified by preparative thin layer chromatography (1% EtOAc/petroleum ether) to give the benzoxocene **17** (45 mg, 85%) as a colourless liquid. R_f (1% EtOAc/petroleum ether) 0.64. The spectral data of **17** were identical with the reported values.[12b]

3.1.1.15. Methyl 3-[5-methoxy-2-(1-methoxycarbonyl-1-methyl-ethoxy)-4-methylphenyl]-butanoate (18). The ene-diester **9f** (1.2 g, 3.57 mmol) was hydrogenated as for **9b** to furnish the saturated diester **18** (1.18 g, 98%) as a colourless oil. R_f (10% EtOAc/petroleum ether) 0.54. IR ($CHCl_3$) 1738 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (3H, d, *J* 6.9 Hz, –CH*Me*), 1.56 (3H, s, –C*Me*$_2$–), 1.57 (3H, s, –C*Me*$_2$–), 2.11 (3H, s, *Me*), 2.47 (1H, dd, *J* 16.3, 9.3 Hz, –CHMeCH_2–), 2.68 (1H, dd, *J* 16.3, 5.7 Hz, –CHMeCH_2–), 3.63 (1H, m, ArC*H*Me), 3.65 (3H, s, O*Me*), 3.72 (3H, s, O*Me*), 3.77 (3H, s, O*Me*), 6.48 (1H, s, Ar*H*), 6.68 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.9, 20.1, 25.2, 25.3, 30.0, 41.3, 51.2, 52.2, 55.5, 79.0, 108.8, 119.9, 124.4, 134.6, 145.7, 152.6, 172.9, 175.2. HRMS (ES +ve) calcd for $C_{18}H_{27}O_6$ $[M+H]^+$ 339.1809. Found 339.1807.

3.1.1.16. 3-[2-(2-Hydroxy-1,1-dimethylethoxy)-5-methoxy-4-methylphenyl]-1-butanol (19). The diester **18** (500 mg, 1.49 mmol) was subjected to reduction with $LiAlH_4$ (112 mg, 2.96 mmol) following conditions as for **13** and afforded the diol **19** (410 mg, 98% yield) as a colourless solid after purification by column chromatography (50% EtOAc/petroleum ether), crystallized from ether/petroleum ether. Mp 58–60 °C. R_f (50% EtOAc/petroleum ether) 0.45. IR (KBr) 3380 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22 (3H, s, –C*Me*$_2$–), 1.26 (3H, d, *J* 7.0 Hz, –CH*Me*), 1.31 (3H, s, –C*Me*$_2$–), 1.42–1.50 (1H, m, CHMeCH_2–), 1.77–1.86 (1H, m, CHMeCH_2–), 2.16 (3H, s, *Me*), 3.23–3.30 (1H, m, ArC*H*Me), 3.50–3.61 (4H, m, CH_2OH), 3.71–3.79 (2H, m, O*H*), 3.87 (3H, s, O*Me*), 6.64 (1H, s, Ar*H*), 6.81 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.8, 20.5, 21.7, 23.7, 27.2, 41.8, 55.4, 60.1, 70.2, 80.1, 107.6, 124.2, 124.8, 137.9, 145.2, 154.1. HRMS (ES +ve) calcd for $C_{16}H_{27}O_4$ $[M+H]^+$ 283.1910. Found 283.1911.

3.1.1.17. 3-[2-(1,1-Dimethyl-2-oxo-ethoxy)-5-methoxy-4-methylphenyl]-butyraldehyde (20). Oxidation of the diol **19** (230 mg, 0.816 mmol) was carried out following the procedure for **14** and furnished the dialdehyde **20** (220 mg, 95%) as a colourless oil. R_f (10% EtOAc/petroleum ether) 0.51. IR (Neat) 1732 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30 (3H, d, *J* 6.9 Hz, –CH*Me*), 1.39 (3H, s, –C*Me*$_2$–), 1.41 (3H, s, –C*Me*$_2$–), 2.11 (3H, s, *Me*), 2.61–2.76 (2H, m, CHMeCH_2–), 3.71–3.78 (1H, m, ArC*H*Me), 3.86 (3H, s, O*Me*), 6.45 (1H, s, Ar*H*), 6.64 (1H, s, Ar*H*), 9.72 (1H, t, *J* 2.1 Hz, –C*H*O), 9.86 (1H, s, –C*H*O); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.8, 20.5, 21.5, 21.8, 27.7, 50.9, 55.6, 83.0, 109.0, 120.2, 125.1, 134.1, 145.3, 153.0, 201.9, 203.4. Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.05; H, 7.96.

3.1.1.18. 2-[2-(1,1-Dimethylallyloxy)-5-methoxy-4-methylphenyl]-pent-4-ene (21). The dialdehyde **20** (210 mg, 0.755 mmol) was subjected to a double Wittig reaction as for **15** to afford the diene **21** (145 mg, 70%) as a colourless oil. R_f (1% EtOAc/petroleum ether) 0.74; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.87 (3H, d, *J* 6.6 Hz, –CH*Me*), 1.41 (6H, s, –C*Me*$_2$–), 2.11 (3H, s, *Me*), 2.14–2.25 (1H, m, CHMeCH_2–), 2.31–2.40 (1H, m, CHMeCH_2–), 3.20–3.30 (1H, m, ArC*H*Me), 3.78 (3H, s, O*Me*), 4.93–5.21 (4H, m, =CH_2), 5.72–5.77 (1H, m, –C*H*=), 6.08–6.17 (1H, m, –C*H*=), 6.54 (1H, s, Ar*H*), 6.83 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.9, 20.4, 27.1, 27.2, 32.1, 41.9, 55.6, 79.1, 108.5, 112.7, 115.5, 122.9, 123.5, 137.3, 137.7, 145.1, 146.5, 152.0. Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.75; H, 9.57.

3.1.1.19. 8-Methoxy-2,2,6,9-tetramethyl-5,6-dihydro-2*H*-benzo[*b*]oxocene (22). Ring-closing metathesis of the diene **21** (25 mg, 0.091 mmol) was carried out using second generation Grubbs catalyst (catalyst B) as per conditions for **17** to give the benzoxocene **22** (21 mg, 94%) as a colourless liquid. R_f (1% EtOAc/petroleum ether) 0.70; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (3H, d, *J* 6.0 Hz, –CH*Me*), 1.39 (3H, s, –C*Me*$_2$–), 1.58 (3H, s, –C*Me*$_2$–), 2.13 (3H, s, *Me*), 2.89 (1H, m, –CHMeCH_2–), 3.28 (1H, m, –CHMeCH_2–),

3.79 (3H, s, O*Me*), 3.82 (1H, m, ArC*H*Me–), 5.26 (1H, d, *J* 9.0 Hz, –OCMe$_2$C*H*═), 5.64–5.73 (1H, m, –CMe$_2$CH═C*H*–), 6.48 (1H, s, Ar*H*), 6.70 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, CDCl$_3$) δ 15.7, 25.1, 26.9, 28.4, 29.6, 34.2, 55.3, 80.9, 123.9, 126.4, 127.6, 128.6, 128.9, 134.9, 137.6, 154.2. Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.98; H, 8.99.

3.1.1.20. 5-Methoxy-3,6,9,9-tetramethyl-2,3,9,9a-tetrahydro-1a*H*-1,8-dioxabenzo[*a*]cyclopropa[*e*]-cyclooctene (23). A stirred mixture of the alkene **22** (20 mg, 0.0812 mmol) and NaHCO$_3$ (55 mg, 0.655 mmol) in dry dichloromethane (2 mL) was cooled to 0 °C and slowly treated with *m*-CPBA (41.14 mg, 0.32 mmol) such that temperature never rose above 0 °C. Stirring was continued for 12 h at room temperature. The reaction mixture was quenched with water (5 mL) and extracted with ether (3×10 mL). The organic layer was washed with saturated aqueous Na$_2$CO$_3$ solution (10 mL), saturated brine (10 mL) and dried over Na$_2$SO$_4$. The residual oil was subjected to column chromatography (petroleum ether/EtOAc 19:1) to give the epoxide **23** (16 mg, 80%) as a colourless liquid. R_f (5% EtOAc/petroleum ether) 0.51; ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.20 (3H, d, *J* 6.9 Hz, –CH*Me*–), 1.44 (3H, s, –C*Me*$_2$–), 1.55 (3H, s, –C*Me*$_2$–), 2.16 (3H, s, *Me*), 2.26–2.33 (2H, m, –CHMeC*H*$_2$–), 2.54–2.56 (1H, m, –OC*H*), 2.93–2.99 (1H, m, –OC*H*), 3.08–3.13 (m, 1H), 3.80 (3H, s, O*Me*), 6.52 (1H, s, Ar*H*), 6.74 (1H, s, Ar*H*); ^{13}C NMR (300 MHz, CDCl$_3$) δ 16.2, 25.4, 27.8, 29.9, 34.6, 37.8, 55.9, 58.1, 59.7, 80.0, 112.4, 124.9, 129.1, 137.7, 145.6, 154.7. Anal. Calcd for $C_{16}H_{22}O_3$: C 73.25; H 8.45. Found: C 73.22; H 8.46.

3.1.1.21. *O*-Methyl heliannuol A (24). To a magnetically stirred slurry of LiAlH$_4$ (5.8 mg, 0.152 mmol) in dry THF (1 mL) was added dropwise a solution of the epoxide **23** (20 mg, 0.076 mmol) in dry THF (1 mL). The reaction mixture was refluxed for 8 h, cooled and then decomposed with cold saturated aqueous Na$_2$SO$_4$ solution (2 mL). The ether layer was separated and the aqueous layer extracted with ether (3×5 mL). The combined ether extracts were washed with saturated brine (5 mL), dried and concentrated. The residual oil was purified by column chromatography over silica gel (petroleum ether/EtOAc 19:1) to furnish *O*-methyl heliannuol A **24** (16 mg, 80%) as a colourless oil. R_f (5% EtOAc/petroleum ether) 0.35.

The spectral data of **24** were identical with the reported values.[12b]

3.1.1.22. *O*-Methyl heliannuol K (25). Jones reagent (aqueous solution of CrO$_3$ and H$_2$SO$_4$) was added dropwise to a cooled (ice) solution of the alcohol **24** (16 mg, 0.061 mmol) in acetone (0.5 mL) until orange colour persisted. Stirring was continued at room temperature for 2 h. Acetone was removed by distillation. The residue was extracted with ether (3×10 mL), dried and solvent removed and the product purified by column chromatography over silica gel (petroleum ether/EtOAc 19:1) to furnish the ketone, *O*-methyl heliannuol K **25** (12.7 mg, 80%) as a colourless liquid. R_f (5% EtOAc/petroleum ether) 0.46. The spectral data of **25** were identical with the reported values.[12b]

3.1.1.23. 3-[2-(2-Hydroxy-1,1-dimethylethoxy)-5-methoxy-4-methylphenyl]-prop-2-en-1-ol (27). A suspension of LiAlH$_4$ (570 mg, 15.02 mmol) in ether (15 mL) was stirred for 1 h and allowed to settle. The clear solution (13 mL) was removed via syringe and added dropwise to a stirred and cooled (−20 °C) solution of the diester **9g** (1.0 g, 3.76 mmol) in ether (15 mL). After stirring for 4 h at this temperature, the reaction mixture was quenched by addition of aqueous saturated Na$_2$SO$_4$ solution (5 mL). The ether layer was carefully decanted. The residue after removal of solvent was subjected to column chromatography over silica gel. Elution with EtOAc/petroleum ether (1:1) furnished the diol **27** (750 mg, 90%) as a gummy oil. R_f (50% EtOAc/petroleum ether) 0.41; ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.20 (6H, s, –C*Me*$_2$–), 2.18 (3H, s, *Me*), 3.53 (2H, s, –CMe$_2$C*H*$_2$OH), 3.78 (3H, s, O*Me*), 4.18 (2H, d, *J* 6.9 Hz, ═CHC*H*$_2$OH), 5.89–5.92 (1H, m, ═C*H*–), 6.56 (1H, s, Ar*H*), 6.57 (1H, d, *J* 9.9 Hz, ArC*H*═CH–), 6.81 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, CDCl$_3$) δ 15.9, 22.9 (2C), 55.4, 59.6, 70.0, 81.7, 111.1, 126.0, 126.3, 128.2, 129.2, 131.0, 144.9, 153.4. HRMS (ES +ve) calcd for $C_{15}H_{22}O_4Na$ [M+Na]$^+$ 289.1416. Found 289.1416.

3.1.1.24. Ethyl 3-[2-(2-hydroxy-1,1-dimethylethoxy)-5-methoxy-4-methylphenyl]-4-pentenoate (28) and ethyl 3-[2-(2-acetoxy-1,1-dimethylethoxy)-5-methoxy-4-methylphenyl]-4-pentenoate (29). A mixture of the diol **27** (500 mg, 1.88 mmol), triethyl orthoacetate (3.0 g, 18.8 mmol) and propionic acid (5 mg, 0.07 mmol) was heated with stirring maintaining the temperature of the liquid at 138–142 °C. Heating was continued for 24 h, the reaction mixture was allowed to cool to room temperature and excess orthoacetate was removed by distillation under reduced pressure (~50–60 °C at 20 mmHg). The residue was purified by column chromatography. Elution with EtOAc/petroleum ether (1:19) afforded the acetoxyester **29** (100 mg, 14%) as a colourless oil. R_f (5% EtOAc/petroleum ether) 0.61. IR (Neat) 1738 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.22 (3H, t, *J* 7.1 Hz, –OCH$_2$*Me*), 1.34 (6H, s, –C*Me*$_2$–), 2.15 (6H, s, *Me* and OCO*Me*), 2.57–2.71 (2H, m, –C*H*$_2$CO$_2$Et), 3.77 (3H, s, O*Me*), 4.10 (2H, q, *J* 7.1 Hz, OC*H*$_2$CH$_3$), 4.18 (2H, d, *J* 2.5 Hz, –CMe$_2$C*H*$_2$OAc), 4.40 (1H, dd, *J* 6.6, 14.9 Hz, ArC*H*(CH═CH$_2$)CH$_2$–), 5.07 (1H, d, *J* 16.7 Hz, ═C*H*$_2$), 5.08 (1H, d, *J* 11.0 Hz, ═C*H*$_2$), 5.91–6.03 (1H, m, –C*H*═), 6.58 (1H, s, Ar*H*), 6.83 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, CDCl$_3$) δ 14.2, 16.1, 20.9, 24.0 (2C), 38.4, 39.7, 55.6, 60.3, 70.6, 78.7, 109.2, 114.7, 124.9, 125.1, 133.9, 139.9, 145.4, 153.6, 171.0, 171.9. Anal. Calcd for $C_{21}H_{30}O_6$: C, 66.65; H, 7.99. Found: C, 66.62; H, 8.01.

Further elution with EtOAc/petroleum ether (1:9) afforded the hydroxyester **28** (480 mg, 75%) as a colourless oil. R_f (10% EtOAc/petroleum ether) 0.42. IR (Neat) 1735, 3450 (br) cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.20 (3H, t, *J* 7.2 Hz, –OCH$_2$*Me*), 1.27 (3H, s, –C*Me*$_2$–), 1.34 (3H, s, –C*Me*$_2$–), 2.16 (3H, s, *Me*), 2.59 (1H, dd, A of ABX, J_{AB} 14.4 Hz, J_{AX} 6.5 Hz, –C*H*$_A$H$_B$CO$_2$Et), 2.65 (1H, dd, B of ABX, J_{BA} 14.4 Hz, J_{BX} 8.5 Hz, –CH$_A$*H*$_B$CO$_2$Et), 3.57 (1H, dd, *J* 11.5, 4.8 Hz, –CMe$_2$C*H*$_2$OH), 3.70 (1H, d, *J* 11.5 Hz, –CMe$_2$C*H*$_2$OH), 3.77 (3H, s, O*Me*), 4.11 (2H, q, *J* 7.2 Hz, OC*H*$_2$Me), 4.35–4.42 (1H, m, X of ABX, ArC*H*(CH═CH$_2$)CH$_2$–), 5.08–5.15 (2H, m, ═C*H*$_2$),

5.93–6.05 (1H, m, –C*H*═), 6.58 (1H, s, Ar*H*), 6.83 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 15.9, 22.3, 23.8, 38.5, 39.8, 55.4, 60.5, 70.8, 80.8, 109.1, 114.8, 124.2, 125.0, 133.6, 139.4, 145.4, 153.3, 172.6. HRMS (ES +ve) calcd for $C_{19}H_{28}O_5Na$ $[M+Na]^+$ 359.1835. Found 359.1834.

3.1.1.25. Ethyl 3-[5-methoxy-2-(1-methoxycarbonyl-1-methyl-ethoxy)-4-methylphenyl]-4-pentenoate (31). Jones reagent (aqueous solution of CrO_3 and H_2SO_4) was added dropwise to a cooled (ice) and stirred solution of the hydroxyester **28** (200 mg, 0.59 mmol) in acetone (4 mL) until the orange colour persisted. It was then allowed to stir at room temperature for 12 h. Excess reagent was decomposed by addition of few drops of methanol and acetone was removed by distillation under reduced pressure. The residue was diluted with water (10 mL) and extracted with ether (3×20 mL). The ethereal extract was washed with brine (15 mL), dried and the solvent removed to furnish the acid **30** (145 mg, 70%) as a viscous material and was esterified with diazomethane and purified by column chromatography over silica gel eluting with EtOAc/petroleum ether (1:9) to give the diester **31** (150 mg, 98%) as a colourless oil. R_f (10% EtOAc/petroleum ether) 0.61. IR (Neat) 1735 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21 (3H, t, *J* 7.2 Hz, OCH_2*Me*), 1.53 (3H, s, –C*Me*$_2$–), 1.56 (3H, s, –C*Me*$_2$–), 2.11 (3H, s, *Me*), 2.69 (2H, d, *J* 7.5 Hz, –CH_2CO_2Et), 3.76 (3H, s, O*Me*), 3.79 (3H, s, O*Me*), 4.10 (2H, q, *J* 7.2 Hz, OCH_2Me), 4.25–4.28 (1H, m, ArC*H*(CH═CH_2)CH_2–), 5.05–5.12 (2H, m, ═CH_2), 5.95–6.06 (1H, m, –C*H*═), 6.49 (1H, s, Ar*H*), 6.59 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 16.0, 25.0, 25.5, 39.2, 39.4, 52.3, 55.6, 60.2, 79.2, 110.0, 114.7, 120.2, 125.0, 131.7, 139.6, 145.9, 152.7, 172.0, 175.3. HRMS (ES +ve) calcd for $C_{20}H_{29}O_6$ $[M+H]^+$ 365.1965. Found 365.1959.

3.1.1.26. Ethyl-7-methoxy-2,2,8-trimethyl-3-oxo-5-vinyl-2,3,4,5-tetrahydrobenzo[*b*]oxepane-4-carboxylate (32). To a well stirred solution of LDA [prepared from *n*-butyl lithium (0.6 mL of 1.6 M solution in hexane, 0.96 mmol) and diisopropylamine (110 mg, 1.09 mmol)] in THF (1 mL) at –20 °C, a solution of diester **31** (130 mg, 0.36 mmol) in THF (1 mL) was added dropwise under argon atmosphere. The reaction mixture was stirred for 2 h at that temperature and then allowed to warm to room temperature and stirred for 12 h. It was then quenched with dilute HCl (6 N) (5 mL) and extracted with ether (3×15 mL). The combined ethereal extract were washed with water (10 mL), dried and the solvent removed. The residue was subjected to column chromatography over silica gel. Elution with EtOAc/petroleum ether (1:9) afforded the β-ketoester **32** (86 mg, 72%) as a viscous oil. R_f (10% EtOAc/petroleum ether) 0.51. IR (Neat) 1722, 1753 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (3H, s, –C*Me*$_2$–), 1.26 (3H, t, *J* 7.4 Hz, OCH_2*Me*), 1.50 (3H, s, –C*Me*$_2$–), 2.13 (3H, s, *Me*), 3.74 (3H, s, O*Me*), 4.05 (1H, t, *J* 9.0 Hz, ArC*H*(CH═CH_2)CH_2–), 4.23 (2H, q, *J* 7.4 Hz, OCH_2Me), 4.69 (1H, d, *J* 9.9 Hz, C*H*CO_2Et), 5.04 (1H, d, *J* 10.2 Hz, ═CH_2), 5.11 (1H, d, *J* 16.2 Hz, ═CH_2), 5.79–5.90 (1H, m, ═CH_2), 6.49 (1H, s, Ar*H*), 6,72 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.5, 16.2, 21.7, 25.8, 46.4, 55.9, 56.7, 61.7, 89.4, 112.8, 116.4, 126.9, 127.1, 128.6, 140.5, 146.7, 155.2, 169.5, 208.7. HRMS (ES +ve) calcd for $C_{19}H_{25}O_5$ $[M+H]^+$ 333.1703. Found 333.1696.

3.1.1.27. 7-Methoxy-2,2,8-trimethyl-5-vinyl-4,5-dihydrobenzo[*b*]oxepan-3-one (33). A mixture of the β-ketoester **32** (40 mg, 0.12 mmol), dimethyl sulfoxide (0.4 mL), water (1 drop), and lithium chloride (6 mg, 0.14 mmol) was heated with stirring in an oil bath at 150–160 °C for 5 h. The reaction mixture was cooled, diluted with water (5 mL) and extracted with ether (3×15 mL) after saturation with sodium chloride. The organic extract was dried and concentrated. The residual oil was purified by preparative thin layer chromatography (petroleum ether/EtOAc 49:1) to afford the ketone **33** (27 mg, 85%) as a colourless oil. R_f (5% EtOAc/petroleum ether) 0.62. IR (Neat) 1720 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (3H, s, –C*Me*$_2$–), 1.40 (3H, s, –C*Me*$_2$–), 2.14 (3H, s, *Me*), 2.85 (1H, dd, *J* 10.8, 5.8 Hz, ArCH(CH═CH_2)CH_2–), 3.42 (1H, t, *J* 10.8 Hz, –CH(CH═CH_2)CH_2–), 3.63–3.75 (1H, m, ArC*H*(CH═CH_2)CH_2–), 3.75 (3H, s, O*Me*), 5.08 (1H, d, *J* 10.0 Hz, ═CH_2), 5.13 (1H, d, *J* 17.0 Hz, ═CH_2), 5.83–5.95 (1H, m, –C*H*═), 6.50 (1H, s, Ar*H*), 6.74 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.7, 22.6, 25.1, 42.7, 43.9, 55.5, 87.9, 111.9, 114.9, 126.4, 126.6, 129.0, 141.3, 146.7, 154.4, 214.1. HRMS (ES +ve) calcd for $C_{16}H_{21}O_3$ $[M+H]^+$ 261.1491. Found 261.1485.

3.1.1.28. *O*-Methyl heliannuol C (34) and *epi*-*O*-methyl heliannuol C (35). To a stirred and cold (0 °C) solution of the ketone **33** (27 mg, 0.104 mmol) in methanol (0.5 mL), $NaBH_4$ (5 mg, 0.13 mmol) was added portionwise and stirring continued for 5 min at that temperature. The reaction mixture was then quenched with twice its volume of water and extracted with ether (3×15 mL). The ethereal extract was washed with water, dried and concentrated. The residual oil was purified by preparative thin layer chromatography (petroleum ether/EtOAc 19:1) to afford *O*-methyl heliannuol C **34** (7 mg, 26%) and its epimer **35** (19 mg, 70%) as viscous liquids.

Spectral data for **34**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.15 (3H, s, –C*Me*$_2$–), 1.30 (3H, s, –C*Me*$_2$–), 1.95 (1H, ddd, *J* 13.8, 9.0, 3.3 Hz, –CH(CH═CH_2)CH_2–), 2.02 (1H, ddd, *J* 13.8, 7.7, 3.3 Hz, –CH(CH═CH_2)CH_2–), 2.14 (3H, s, *Me*), 3.62 (1H, br m, ArC*H*(CH═CH_2)CH_2–), 3.78 (3H, s, O*Me*), 3.81 (1H, m, C*H*OH), 5.02 (1H, d, *J* 17.1 Hz, ═CH_2), 5.11 (1H, d, *J* 10.2 Hz, ═CH_2), 6.13 (1H, ddd, *J* 17.2, 10.2, 7.3 Hz, C*H*═), 6.53 (1H, s, Ar*H*), 6.72 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.6, 21.2, 26.7, 36.2, 42.7, 55.6, 74.7, 79.6, 110.2, 115.2, 125.2, 126.3, 133.8, 139.7, 147.3, 153.9.

Spectral data for **35**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.13 (3H, s, –C*Me*$_2$–), 1.31 (3H, s, –C*Me*$_2$–), 1.92 (1H, m, ArCH(CH═CH_2)CH_2–), 2.08 (1H, dt, *J* 13.8, 3.3 Hz, ArCH(CH═CH_2)CH_2–), 2.15 (3H, s, Me), 3.53 (1H, br m, ArC*H*(CH═CH_2)CH_2–), 3.76 (1H, m, C*H*OH), 3.77 (3H, s, O*Me*), 4.96 (1H, d, *J* 17.1 Hz, ═CH_2), 5.15 (1H, d, *J* 10.5 Hz, ═CH_2), 6.13 (1H, ddd, *J* 17.1, 10.5, 6.9 Hz, C*H*═), 6.52 (1H, s, Ar*H*), 6.75 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.7, 21.7, 26.5, 35.8, 43.1, 55.6, 78.1, 79.3, 109.9, 114.9, 125.2, 126.3, 133.6, 141.0, 147.5, 153.9.

The spectral data of **34** and **35** were in agreement with the reported values.[17]

3.1.2. General procedure for the preparation of dihydrocoumarins from coumarins. A solution of coumarin (5 mmol, 1 equiv) in acetic acid (15 mL) containing Pd–C (10%, 50 mg) was stirred under a hydrogen atmosphere (1 atm) until hydrogen uptake was completed (~12 h). The catalyst was filtered and acetic acid was neutralized by addition of solid Na_2CO_3, diluted with water (30 mL) and extracted with chloroform (3×40 mL). The organic layer was washed with water (25 mL), dried and evaporated. The residue was subjected to column chromatography over silica gel (petroleum ether/EtOAc 9:1) to furnish the dihydrocoumarins.

3.1.2.1. 4,6-Dimethyl-dihydrocoumarin (36b). Coumarin **7c** (1 g, 5.747 mmol) on hydrogenation furnished the dihydrocoumarin **36b** (0.99 g, 98%) as a colourless oil. R_f (15% EtOAc/petroleum ether) 0.51. IR ($CHCl_3$) 1768 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.30 (3H, d, *J* 6.96, ArCH*Me*CH_2–), 2.31 (3H, s, Me), 2.53 (1H, dd, *J* 15.7, 7.1 Hz, –CHMeC*H*$_2$–), 2.79 (1H, dd, *J* 15.7, 5.4 Hz, –CHMeC*H*$_2$–), 3.11 (1H, m, ArC*H*Me), 6.90 (1H, d, *J* 7.9 Hz, Ar*H*), 7.01 (1H, s, Ar*H*) 7.02 (1H, d, *J* 7.9 Hz, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.9, 20.8, 29.5, 36.9, 116.7, 127.0, 127.6, 128.7, 134.2, 149.2, 168.6. Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.99; H, 6.87.

3.1.2.2. 6-Methoxy-7-methyl-dihydrocoumarin (36c). Coumarin **7g** (1 g, 5.263 mmol) on hydrogenation furnished dihydrocoumarin **36c** (0.99 g, 98%) as a colourless solid, crystallized from ether/petroleum ether. Mp 88–90 °C. R_f (15% EtOAc/petroleum ether) 0.54. IR ($CHCl_3$) 1767 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.17(3H, s, *Me*), 2.75 (2H, t, *J* 7.0 Hz, ArCH$_2$C*H*$_2$–), 2.94 (2H, t, *J* 7.0 Hz, ArC*H*$_2$CH$_2$–), 3.79 (3H, s, O*Me*), 6.60 (1H, s, Ar*H*), 6.80 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.7, 23.6, 29.2, 55.6, 108.9, 118.6, 119.8, 126.4, 145.1, 154.1, 168.9. Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.68; H, 6.58.

3.1.2.3. 4,7-Dimethyl-dihydrocoumarin (36e). Coumarin **7b** (1 g, 5.75 mmol) furnished dihydrocoumarin **36e** (0.98 g, 97%) on hydrogenation as a colourless oil. R_f (15% EtOAc/petroleum ether) 0.52. IR ($CHCl_3$) 1767 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.31 (3H, d, *J* 6.9 Hz, CH*Me*), 2.34 (3H, s, *Me*), 2.55 (1H, dd, *J* 15.7, 7.3 Hz, –CHMeC*H*$_2$–), 2.81 (1H, dd, *J* 15.7, 5.4 Hz, –CHMeC*H*$_2$–), 3.15 (1H, m, ArC*H*Me), 6.87 (1H, s, Ar*H*), 6.93 (1H, d, *J* 7.7 Hz, Ar*H*), 7.09 (1H, d, *J* 7.7 Hz, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.4, 21.4, 29.5, 37.4, 117.8, 125.2, 125.7, 126.6, 138.9, 151.5, 169.0. Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.97; H, 6.87.

3.1.2.4. 6-Methoxy-4,7-methyl-dihydrocoumarin (36f). Hydrogenation of coumarin **7f** furnished dihydrocoumarin **36f** as a colourless crystalline solid. Mp 76–78 °C. R_f (15% EtOAc/petroleum ether) 0.53. IR ($CHCl_3$) 1767 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.24 (3H, d, *J* 6.8 Hz, CH*Me*), 2.11 (3H, s, *Me*), 2.47 (1H, dd, *J* 6.8, 15.8 Hz, ArCHMeC*H*$_2$–), 2.73 (1H, dd, *J* 6.8, 15.8 Hz, ArCHMeC*H*$_2$–), 3.01–3.07 (1H, m, ArC*H*MeCH$_2$–), 3.82 (3H, s, O*Me*), 6.56 (1H, s, Ar*H*), 6.70 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.8,19.9, 29.5, 36.8, 55.6, 107.5, 118.8, 125.2, 126.6, 144.3, 154.3, 168.66. Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.84; H, 6.85.

3.1.2.5. Bargellini condensation of dihydrocoumarins. Following the general procedure for Bargellini condensation of coumarins, dihydrocoumarins **36a–e** furnished the saturated diacids and were characterized as dimethyl esters **13**, **18** and **37a—d**, which were obtained on reaction with diazomethane and purified by column chromatography over silica gel.

3.1.2.6. Methyl-2-[2-(2-methoxycarbonyl-ethyl)-phenoxy]-2-methylpropionate (37a). Dihydrocoumarin **36a** (500 mg, 3.38 mmol) furnished the diacid, which was esterified with diazomethane. The product was purified by column chromatography (12% EtOAc/petroleum ether) to furnish the diester **37a** (710 mg, 75%) as a colourless liquid. R_f (12% EtOAc/petroleum ether) 0.56. IR ($CHCl_3$) 1738 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.26 (6H, s, –C*Me*$_2$–), 2.56 (2H, t, *J* 8.0 Hz, ArCH$_2$C*H*$_2$–), 2.95 (2H, t, *J* 8.0 Hz, ArC*H*$_2$CH$_2$–), 3.67 (3H, s, O*Me*), 3.76 (3H, s, O*Me*), 6.59 (1H, d, *J* 7.5 Hz, Ar*H*), 6.89 (1H, d, *J* 7.3 Hz, Ar*H*), 7.08 (1H, t, *J* 7.3 Hz, Ar*H*), 7.19 (1H, d, *J* 7.5 Hz, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.4 (2C), 26.4, 34.0, 51.4, 52.4, 78.6, 115.4, 121.4, 127.0, 130.3, 131.1, 153.4, 173.7, 174.9. Anal. Calcd for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.22; H, 7.16.

3.1.2.7. Methyl-2-[4-methoxy-2-(2-methoxycarbonyl-ethyl)-5-methylphenoxy]-butanoate (37b). Dihydrocoumarin **36b** (500 mg, 2.84 mmol) furnished the saturated diester **37b** (650 mg, 74%) as a colourless liquid after purification by column chromatography (12% EtOAc/petroleum ether). R_f (12% EtOAc/petroleum ether) 0.55. IR ($CHCl_3$) 1738 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.32 (3H, d, *J* 6.8 Hz, ArC*H*Me–), 1.60 (6H, s, –C*Me*$_2$–), 2.25 (3H, s, *Me*), 2.46 (1H, dd, *J* 9.2, 15.0 Hz, –CHMeC*H*$_2$–), 2.70 (1H, dd, *J* 5.4, 15.0 Hz, –CHMeC*H*$_2$–), 3.61 (1H, m, ArC*H*Me), 3.63 (3H, s, O*Me*), 3.76 (3H, s, O*Me*), 6.49 (1H, d, *J* 8.3 Hz, Ar*H*), 6.86 (1H, d, *J* 8.3 Hz, Ar*H*), 6.97 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.6, 21.1, 25.2, 31.5, 40.5, 52.3, 52.3, 78.6, 115.8, 121.1, 126.9, 127.6, 130.8, 135.8, 150.4, 173.1, 175.1. HRMS (ES +ve) calcd for $C_{17}H_{25}O_5$ $[M+H]^+$ 309.1703. Found 309.1719.

3.1.2.8. Methyl-2-[4-methoxy-2-(2-methoxycarbonyl-ethyl)-5-methylphenoxy]-2-methylpropionate (37c). Dihydrocoumarin **36c** (500 mg, 2.60 mmol) furnished the diester **37c** (610 mg, 72%) as a colourless liquid after purification by column chromatography (12% EtOAc/petroleum ether). R_f (12% EtOAc/petroleum ether) 0.56. IR ($CHCl_3$) 1738 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.55 (6H, s, –C*Me*$_2$–), 2.10 (3H, s, *Me*), 2.59–2.64 (2H, m, ArCH$_2$C*H*$_2$–), 2.87–2.92 (2H, m, ArC*H*$_2$CH$_2$–), 3.67 (3H, s, O*Me*), 3.72 (3H, s, O*Me*), 3.78 (3H, s, O*Me*), 6.48 (1H, s, Ar*H*), 6.63 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.0, 25.1, 25.3, 26.9, 34.4, 51.7, 52.2, 55.6, 79.1, 112.0, 120.0, 124.8, 129.8, 146.5, 152.5, 172.2, 175.2. Anal. Calcd for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46. Found: C, 62.92; H, 7.44.

3.1.2.9. Methyl 2-[4-methoxy-2-(2-methoxycarbonyl-ethyl)-phenoxy]-2-methylpropionate (37d). Dihydrocoumarin **36d** (500 mg, 2.81 mmol) furnished the saturated

diester **37d** (615 mg, 71%) as a colourless liquid after purification by column chromatography (12% EtOAc/petroleum ether). R_f (12% EtOAc/petroleum ether) 0.53. IR ($CHCl_3$) 1738 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.49 (6H, s, –C*Me*$_2$–), 2.55 (2H, t, *J* 7.5 Hz, ArCH$_2$C*H*$_2$–), 2.84 (2H, t, *J* 7.5 Hz, ArC*H*$_2$CH$_2$–), 3.60 (3H, s, O*Me*), 3.67 (3H, s, O*Me*), 3.70 (3H, s, O*Me*), 6.53 (2H, s, Ar*H*), 6.65 (1H, s, Ar*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.7 (2C), 27.0, 51.9, 52.9, 55.9, 79.6, 111.9, 116.3, 118.1, 133.4, 147.7, 154.8, 174.1, 175.6. Anal. Calcd for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15. Found: C, 61.93; H, 7.15.

Acknowledgements

We sincerely thank the Department of Science and Technology, Government of India for financial support. B.B. thanks the CSIR for a research fellowship. P.K.S. thanks the UGC for a Minor Research Grant.

References and notes

1. Bargellini, G. *Gazz. Chim. Ital.* **1906**, *36*, 329–339.
2. Link, B. 28. R 665-D.R.P 80986.
3. Weizmann, C.; Sulzbacher, M.; Bergmann, E. *J. Am. Chem. Soc.* **1948**, *70*, 1153–1158.
4. Gilman, H.; Wilder, G. R. *J. Am. Chem. Soc.* **1955**, *77*, 6644–6646.
5. Corey, E. J.; Barcza, S.; Klotmann, G. *J. Am. Chem. Soc.* **1969**, *91*, 4782–4786.
6. Lai, J. T. *Synthesis* **1984**, 122–123.
7. Lai, J. T. *Tetrahedron Lett.* **2001**, *42*, 557–560.
8. Cvetovich, R. J.; Chung, J. Y. L.; Kress, M. H.; Amato, J. S.; Matty, L.; Weingarten, M. D.; Tsay, F.-R.; Li, Z.; Zhou, G. *J. Org. Chem.* **2005**, *70*, 8560–8563.
9. Macias, F. A.; Varela, R. M.; Torres, A.; Molinillo, J. M. G.; Fronzek, F. R. *Tetrahedron Lett.* **1993**, *34*, 1999–2002.
10. Harisson, B.; Crews, P. *J. Org. Chem.* **1997**, *62*, 2646–2648.
11. (a) Grimm, E. L.; Levac, S.; Trimble, L. A. *Tetrahedron Lett.* **1994**, *35*, 6847–6850; (b) Stefinovic, M.; Snieckus, V. *J. Org. Chem.* **1998**, *63*, 2808–2809.
12. (a) Tuhina, K.; Bhowmik, D. R.; Venkateswaran, R. V. *Chem. Commun.* **2002**, 634–635; (b) Ghosh, S.; Tuhina, K.; Bhowmik, D. R.; Venkateswaran, R. V. *Tetrahedron* **2007**, *63*, 644–651.
13. Preliminary report: Sen, P. K.; Biswas, B.; Venkateswaran, R. V. *Tetrahedron Lett.* **2005**, *46*, 8741–8743.
14. Imashiro, R.; Seki, M. *J. Org. Chem.* **2004**, *69*, 4216–4226.
15. Kishuku, H.; Shindo, M.; Shishido, K. *Chem. Commun.* **2003**, 350–351.
16. Preliminary report: Biswas, B.; Sen, P. K.; Venkateswaran, R. V. *Tetrahedron Lett.* **2006**, *47*, 4019–4021.
17. Krapcho, A. P. *Synthesis* **1982**, 805–822, 893–914.
18. Vyvyan, J. R.; Oaksmith, J. M.; Parks, B. W.; Peterson, E. M. *Tetrahedron Lett.* **2005**, *46*, 2457–2460.