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# Palladium-catalyzed carbonylation of halo arene-*cis*-dihydrodiols to the corresponding carboxylates. Access to compounds unavailable by toluene dioxygenase-mediated dihydroxylation of the corresponding benzoate esters

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***The authors wish to dedicate this paper to the memory of David Gibson (deceased July 24, 2014) and in recognition of his lifetime contributions to the field of biocatalysis.***

**Abstract**

A series of arene-*cis*-dihydrodiol carboxylates was prepared by palladium-catalyzed carbonylation of (1*S*, 2*S*-cis)-3-iodo-3,5-cyclohexadiene-1,2-diol, which is obtained in high titers by enzymatic dihydroxylation of iodobenzene. Both the free diol and the corresponding acetonide were subjected to this protocol to produce various arene-*cis*-dihydrodiol carboxylates that are unavailable by fermentations of the corresponding benzoates or are produced in low yields. The comparison of yields obtained from fermentations versus carbonylation was made for all compounds investigated. Experimental and spectral data are provided for all new compounds.

## Introduction

The enzymatic dihydroxylation of aromatic compounds to the corresponding arene-*cis*-dihydrodiols such as **1**, Figure 1, was discovered by Gibson in 1968.[1] In the last 25 years many new metabolites resulting form this enzymatic oxidation were discovered and catalogued[2] and used in enantioselective synthesis of natural products.[3]

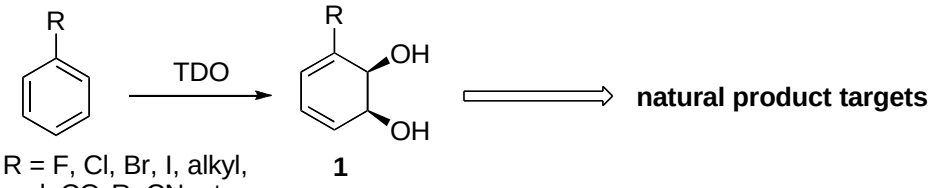
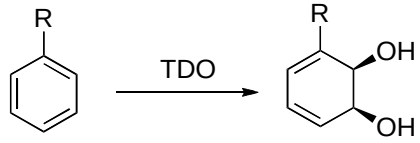


**Figure 1**. Enzymatic dihydroxylation of arenes by toluene dioxygenase (TDO).

The diols derived from single ring aromatics and various benzoate esters are available in multigram quantities by fermentation with recombinant organisms such as *E. coli* JM109 (pDTG601A), which overexpresses toluene dioxygenase. This organism, and others, expressing related dioxygenases for dihydroxylation of fused aromatics or biphenyls, were also developed by Gibson in 1989.[4]

The yields of arene-*cis*-dihydrodiols vary from milligrams/L to 30 or more grams/L. Whole-cell fermentation of aromatics with the JM109 clone was investigated at medium scales (10 to 15L fermentors) for several common substrates.[5] In addition, a procedure was published in *Organic Syntheses*[6] for the preparation of several halo arene-*cis*-dihydro diols by employing the blocked mutant, *Pp*39D, and common equipment, such as is found in any laboratory engaged in organic synthesis. The most commonly used metabolites are shown in Table 1, along with the yields of fermentation.

**Table 1**. Comparison of yields of enzymatic dihydroxylation of various substrates.




**1**

| Entry | R = | organism | Yield (g/L) or (%) | ee (%) | Reference |
|---|---|---|---|---|---|
| 2 | Me | *Pp*39D | 0.93 | - | 1[b], 7, 8[c] |
| | | *Pp*UV4 | (~60%) | >98 | 9, 10[c] |
| | | JM109 | 12-15 [16][a] | - | 4, 5 |
| 3 | F | *Pp*UV4 | - | ~60 | 9[b] , 10[c] |
| 4 | Cl | *Pp*39D | 0.3-1 | - | 1[b], 8, 11[c] |
| | | *Pp*UV4 | (80%) | >98 | 9, 10[c] |
| | | JM109 | 9-11 [12][a] | - | 5 |
| 5 | Br | *Pp*39D | - | - | 1, 12[b] |
| | | *Pp*UV4 | (77%) | >98 | 10[c], 13 |

| | | | | | |
|---|---|---|---|---|---|
| | | JM109 | 9-12 [20][a] | - | 5 |
| 6 | I | *Pp*39D | - | - | 1 |
| | | *Pp*UV4 | (85%) | >98 | 10[c], 13, 14[b] |
| | | JM109 | 7-9 [10][a] | >98 | 5, 14[b] |
| 7 | $CH=CH_2$ | *Pp*39D | (>95%) | >98 | 8[b], 15[c], 16 |
| | | *Pp*UV4 | (~30%) | >98 | 10[c] |
| | | JM109 | 6-8 [12][a] | - | 5 |
| 8 | CCH | *Pp*39D | 0.05 | - | 8[b] |
| | | *Pp*UV4 | (~10%) | >98 | 10[c] |
| | | JM109 | 3-3.5 | - | 5 |
| 9 | $CH_2CH_2OAc$ | JM109 | 3-5 [5][a] | >98 | 5, 17[b,c] |
| 10 | $CH_2CH_2Br$ | *Pp*39D | 0.2 | 96 | 18[b,c] |
| | | JM109 | 6-9 [9][a] | - | 5 |
| 11 | $CO_2Me$ | *Pp*39D | 2.25 | - | 19[b] |
| | | JM109 | 1.3 [1.5][a] | >98 | 20[c] |
| 12 | $CO_2Et$ | JM109 | 0.8 [1.0][a] | >98 | 20[bc], 21 |
| 13 | $CO_2nPr$ | JM109 | 0.07 | >98 | 20[bc] |
| 14 | $CO_2iPr$ | JM109 | 0.05 | >98 | 20[bc] |
| 15 | $CO_2tBu$ | JM109 | - | - | 20[bc] |
| 16 | $CO_2CH_2CHCH_2$ | JM109 | 0.6 | >98 | 20[bc] |
| 17 | $CO_2CH_2CCH$ | JM109 | 1.0 | >98 | 20[bc] |
| 18 | $CO_2CH_2(C_6H_5)$[d] | JM109 | - | - | - |
| 19 | cyclopropyl | JM109 | 2.5 [8-10][a] | >98 | 22[b,c] |

Legend: [a]Current yield on 10-15L scale as obtained in the Hudlicky group; [b]reference to isolation, [c]reference to full characterization, [d]Attempted fermentation of this ester, performed as part of this study, did not provide the diol metabolite.

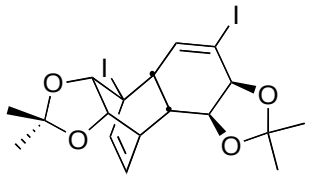
From the Table it is clear that only a few substrates produce yields upward of 10 grams/L. Moreover, the recently investigated dihydroxylation of various benzoate esters (Me, Et, *n*-Pr, *i*-Pr, allyl, propargyl) revealed that these are poor substrates, as evidenced by the low yields of metabolites **11-17**.[20] This study was extended to dihydroxylation of

methyl halobenzoates [23] and, most recently, to various alkyl halobenzoates in order to compare regioselectivity of dihydroxylation as a function of both, halogen and alkoxy functionalities.[24]

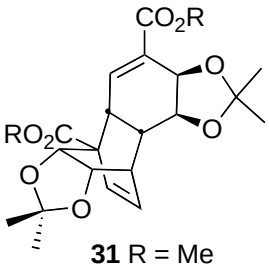
The diol derived from ethyl benzoate, **12**, was used in a very efficient synthesis of oseltamivir[21] and its production at higher titers would be beneficial. For any future refinement of the published synthesis of oseltamivir and its derivatives the availability of **12** in larger amounts would be essential. In this paper we report a simple palladium-catalyzed carbonylation protocol for the preparation of various carboxylates from iodo- or bromoarene cis-dihydrodiols (entry **6** and **5**, respectively).

## Results and discussion

Cross-coupling strategies have been used in order to obtain homochiral *cis*-diols that would not be available from the corresponding aromatic substrates. Thus Boyd prepared a number of compounds via cross-coupling of various vinyl halides derived from arene *cis*-dihydrodiols, in some cases with the diene unit being partially saturated (potassium azodicarboxylate (PAD) reduction).[25] Banwell successfully performed $sp^2$-$sp^3$ cross-coupling of the vinyl iodide in diol **6 (**protected as acetonide) at elevated temperatures without detriment to the otherwise labile diene functionality.[26] It is well known that the diene diols of type **1** are prone to stereoselective Diels-Alder type dimerization even at low temperatures, with the dimerization proceeding much faster when the diols are protected as their corresponding acetonides.[27] We have prepared dimers from the acetonide-protected diols **20, 22** and **23**, namely the pentacyclic compounds **30, 31** and **32**, shown in Figure 2, in order to assess their presence in the carbonylation reaction mixture.



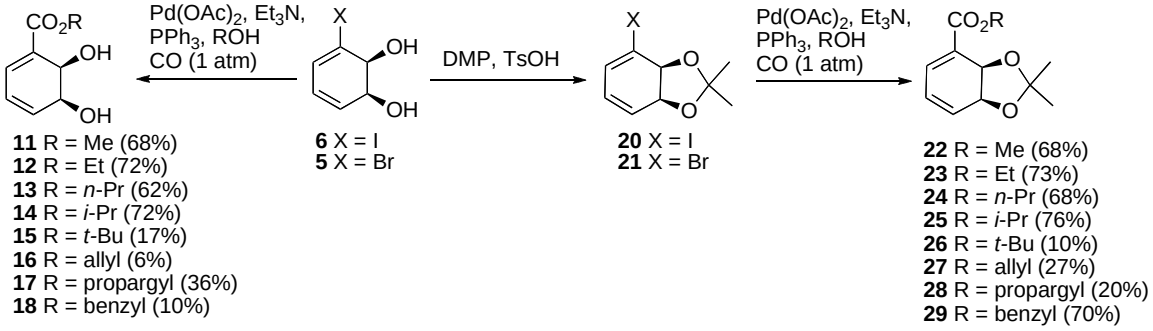

**30**




**31** R = Me
**32** R = Et

**Figure 2**. Diels-Alder dimers produced from the acetonide-protected diols **20**, **22** and **23**

These compounds were prepared in reasonable yields (**30** = 38%, **31**, = 42%, **32** = 64%) by refluxing a solution of the corresponding acetonides in xylene for 24-40 hours.
We investigated the palladium-catalyzed carbonylation with the acetonide-protected diol **20** (EtOH, 40 °C) and were delighted to find that ethyl ester **23** was produced with high conversions and good isolated yields at multigram scales, Scheme 1. The carbonylation of the bromo derivative **21** also yielded the corresponding ethyl ester **23**, although in lower yield than that obtained with the carbonylation of vinyl iodide **20**. As well, the free diols **6** and **5** were subjected to the same conditions. The carbonylation of **6** (EtOH, 40 °C) produced **12** in good yields, far exceeding those obtained from the biotransformation of ethyl benzoate, Table 2. The substrate scope was subsequently expanded, and the carbonylation procedure was utilized to produce the acetonide-protected compounds **22-29**, Table 2. Despite initial concerns, little or no dimerization was observed under the carbonylation reaction conditions.




**11** R = Me (68%)
**12** R = Et (72%)
**13** R = *n*-Pr (62%)
**14** R = *i*-Pr (72%)
**15** R = *t*-Bu (17%)
**16** R = allyl (6%)
**17** R = propargyl (36%)
**18** R = benzyl (10%)

**6** X = I
**5** X = Br

**20** X = I
**21** X = Br

**22** R = Me (68%)
**23** R = Et (73%)
**24** R = *n*-Pr (68%)
**25** R = *i*-Pr (76%)
**26** R = *t*-Bu (10%)
**27** R = allyl (27%)
**28** R = propargyl (20%)
**29** R = benzyl (70%)

**Scheme 1**

Both the free diol **6** and the acetonide-protected diol **20** were subjected to carbonylation in the presence of various alcohols, to produce ester derivatives which were previously obtained in low yields by fermentation.[20] Furthermore, it was previously shown that compound **15** was unavailable through biotransformation [20], and it was demonstrated, as part of this study, that compound **18** was similarly unavailable through biotransformation. Compounds **15** and **18**, as well as their corresponding acetonide-protected derivatives **26** and **29**, were accessed through the carbonylation of **6** and **20** respectively . The comparison of isolated yields is shown in Table 2.

**Table 2**. Comparison of the yields of benzoate metabolites obtained by fermentation with those from the carbonylation of free halodiene **6** or acetonide **20**.

| Entry | Yield of free diol by fermentations of benzoate (%) (g/L)[20] | Yield of benzoate by carbonylation of free diol **6** (%) (g/L)[a] | Entry | Yield of benzoate by carbonylation of acetonide **20** (%) (g/L)[b] |
|---|---|---|---|---|
| **11** R = Me | 19.2% (1.3) | 68% (6.8) | **22** R = Me | 68% (6.8) |
| **12** R = Et | 43.4% (0.8) | 72% (7.2) | **23** R = Et | 73% (7.3) |
| **13** R = *n*-Pr | 5.8% (0.07) | 62% (6.2) | **24** R = *n*-Pr | 64% (6.4) |
| **14** R = *i*-Pr | 4.1% (0.05) | 72% (7.2) | **25** R = *i*-Pr | 76% (7.6) |
| **15** R = *t*-Bu | - | 17% (1.7) | **26** R = *t*-Bu | 10% (1.0) |
| **16** R = allyl | 52.0% (0.6) | 7% (0.7) | **27** R = allyl | 27% (2.7) |
| **17** R = $CH_2CCH$ | 69.1% (1.0) | 36% (3.6) | **28** R = $CH_2CCH$ | 22% (2.2) |
| **18** R = benzyl | - | 10% (1.0) | **29** R = benzyl | 71% (7.1) |

[a]Hypothetical yield for comparison. Biotransformation of iodobenzene affords up to 10 g/L of diol **6**. This yield was multiplied by the yield of the subsequent carbonylation step to reflect the relative amount of compounds **11**-**18** available through this method. (Ex. 10 g/L (biotransformation yield of **6**) x 72% (carbonylation yield of **12**) = 7.2 g/L of compound **12**)

[b]Hypothetical yield for comparison. Biotransformation of iodobenzene affords up to 10 g/L of diol **6**. This yield was multiplied by the yield of the subsequent carbonylation step

to reflect the relative amount of compounds **22-29** available through this method. (Ex. 10 g/L (biotransformation yield of **6**) x 73% (carbonylation yield of **23**) = 7.3 g/L of compound **23**)

From Table 2, it is clear that the carbonylation of the readily available enzymatic metabolite, namely vinyl iodide **6**, provides a much more efficient access to esters **11**-**14**, **17**, **18** than would a direct fermentation of the corresponding benzoates. This is also true for the carbonylation of the acetonide-protected diol **20**, which provided efficient access to compounds **22-29**.

## Conclusions

Palladium-catalyzed carbonylation of (1*S*, 2*S*-*cis*)-3-iodo-3,5-cyclohexadiene-1,2-diol, as well as its acetonide, in the presence of an appropriate alcohol led to the synthesis of various arene-*cis*-diol carboxylates that are not readily available by enzymatic dihydroxylation of the parent benzoate esters. The carbonylation protocol provided the known metabolites of alkyl benzoates in much higher yields than those obtained in fermentations. In addition, this protocol provided several new compounds previously unavailable by fermentation. The higher yields of benzoate-derived metabolites obtained by the carbonylation protocol will make it easier to provide improvements in the synthesis of oseltamivir analogs and other compounds derived from arene-*cis*-diol carboxylates. Finally, the combination of biocatalysis and traditional synthesis clearly provides a more effective access to compounds of interest; this has been articulated in several recent reviews.[3c,3d,28]

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Partnership for Innovation and Commercialization (OPIC), and The Advanced Biomanufacturing Centre (Brock University).
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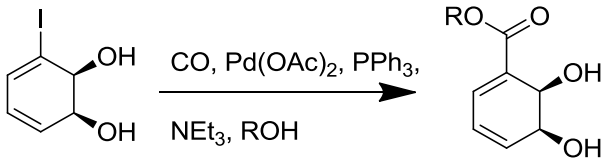
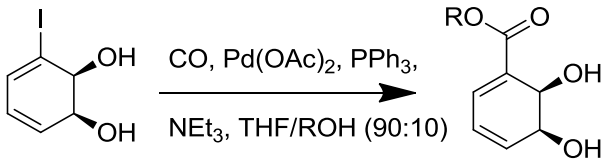
## Experimental section

### General procedure for the carbonylation of compound 6 to corresponding esters (11-15)



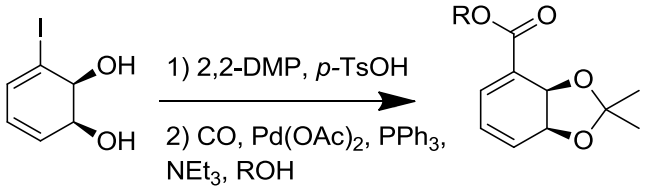

A solution of **6**[10] (500 mg, 2.10 mmol) was dissolved in alcohol (30 mL), and carbon monoxide was bubbled through the reaction mixture for 15 minutes, after which triethylamine (0.59 mL, 4.2 mmol) was added followed by solid triphenylphosphine (110 mg, 0.42 mmol) and palladium (II) acetate (47 mg, 0.21 mmol). The orange suspension was heated to 40 ºC. The reaction was monitored by TLC [hexanes/EtOAc (1:1)] and consumption of the starting material was observed after 1-2.5 hours. Upon cooling to room temperature, the crude reaction mixture was concentrated to dryness under reduced pressure. The residue was then dissolved in diethyl ether, filtered through a plug of Celite, and concentrated. The crude material was purified by flash column chromatography [hexanes/EtOAc (1:1)] to yield the corresponding ester.

**General procedure for the carbonylation of compound 6 to corresponding esters (16-18)**




A solution of **6**[10] (500 mg, 2.10 mmol) was dissolved in a solution of THF/alcohol (9:1) (30 mL), and carbon monoxide was bubbled through the reaction mixture for 15 minutes, after which triethylamine (0.59 mL, 4.2 mmol) was added followed by solid triphenylphosphine (110 mg, 0.42 mmol) and palladium (II) acetate (47 mg, 0.21 mmol). The orange suspension was heated to 40 ºC. The reaction was monitored by TLC [hexanes/EtOAc (1:1)] and consumption of the starting material was observed after 4-6 hours. Upon cooling to room temperature, the crude reaction mixture was concentrated to dryness under reduced pressure. The residue was then dissolved in diethyl ether, filtered through a plug of Celite, and concentrated. The crude material was purified by flash column chromatography [hexanes/EtOAc (1:1)] to yield the corresponding ester.

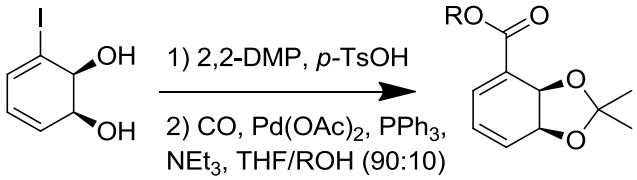
**General procedure for the acetonide protection of compound 6 and subsequent carbonylation of compound 20 to corresponding esters (22-26)**




A solution of **6**[10] (500 mg, 2.10 mmol) was dissolved in 2,2-dimethoxypropane (10 mL), to which was added a catalytic amount of *p*-toluenesulfonic acid. The reaction was monitored by thin layer chromatography (TLC), and was observed to be complete after 0.5 hours. The reaction mixture was concentrated under reduced pressure, diluted with EtOAc (15 mL) and washed with a saturated solution of sodium bicarbonate (2 x 3 mL)

and brine (1 x 2 mL). The reaction mixture was concentrated under reduced pressure, and dissolved in alcohol (30 mL). Carbon monoxide was bubbled through the reaction mixture for 15 minutes, after which triethylamine (0.59 mL, 4.2 mmol) was added followed by solid triphenylphosphine (110 mg, 0.42 mmol) and palladium (II) acetate (47 mg, 0.21 mmol). The orange suspension was heated to 40 ºC. The reaction was monitored by TLC [hexanes/EtOAc (4:1)] and consumption of the starting material was observed after 1-2.5 hours. Upon cooling to room temperature, the crude reaction mixture was concentrated to dryness under reduced pressure. The residue was then dissolved in diethyl ether, filtered through a plug of Celite, and concentrated under reduced pressure. The crude material was purified by flash column chromatography [hexanes/EtOAc (9:1)] to yield the corresponding ester.

**General procedure for the acetonide protection of compound 6 and subsequent carbonylation of compound 20 to corresponding esters (27-29)**

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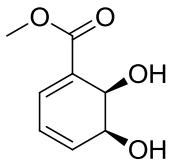
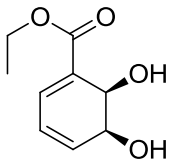
starting material was observed after 4-6 hours. Upon cooling to room temperature, the crude reaction mixture was concentrated to dryness under reduced pressure. The residue was then dissolved in diethyl ether, filtered through a plug of Celite, and concentrated under reduced pressure. The crude material was purified by flash column chromatography [hexanes/EtOAc (9:1)] to yield the corresponding ester.

**(+)-Methyl (5*S*,6*R*)-5,6-Dihydroxycyclohexa-1,3-dienecarboxylate (11)** [20]




**11**: (68%); Pale yellow oil; $R_f$ = 0.33 [hexanes/EtOAc (1:2)]; $[\alpha]_D^{20}$ = +68.8 (*c* = 0.8, $CHCl_3$) [lit.[20] $[\alpha]_D^{23}$ = +71.3 (*c* = 1.6, $CHCl_3$)]; IR (film) *v* 3412, 2098, 1690, 1639, 1291, 820, 772 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.05 (d, *J* = 5.3 Hz, 1H, CH-2), 6.17 (dd, *J* = 10.3, 0.6 Hz, 1H, CH-4), 6.05 (qd, *J* = 5.1, 2.2 Hz, 1H, CH-3), 4.53 (m, 1H, CH-6), 4.45 (m, 1H, CH-5), 3.77 (s, 3H, $OCH_3$), ; $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 167.5 (C=O), 138.6 (CH-4), 134.3 (CH-2), 128.4 (C-1), 122.6 (CH-3), 69.5 (COH-5), 64.8 (COH-6), 52.1 ($OCH_3$); MS (EI) *m/z* (%) 170 (33), 152 (61), 139 (22), 138 (96), 136 (71), 121 (100), 110 (95), 109 (66), 105 (23), 93 (42), 92 (22) 82 (57), 81 (56), 65 (59), 5 3(49), 51 (22); HRMS (EI) calcd for $C_8H_{10}O_4$: 170.0579. Found: 170.0580.

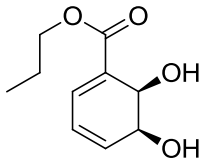
**(+)-Ethyl (5*S*,6*R*)-5,6-Dihydroxycyclohexa-1,3-dienecarboxylate (12)** [20]




**12**: (72%); Colourless crystals; $R_f$ = 0.31 [hexanes/EtOAc (1:2)]; mp 49-50 $^oC$ (pentane) [lit.[20] mp 48 $^oC$ (EtOAc/hexanes)]; $[\alpha]_D^{20}$ = +53.5 (*c* = 1.6, $CHCl_3$) [lit.[20] $[\alpha]_D^{23}$ = +54.7

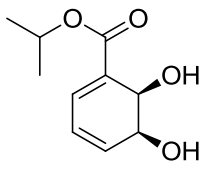
($c$ = 3.8, $CHCl_3$)]; IR (film) $\nu$ 3385, 2981, 2934, 1700, 1280, 1243, 1104, 1068, 825, 771 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.04 (d, $J$ = 5.3 Hz, 1H, CH-2), 6.15 (dt, $J$ = 9.4, 1.1 Hz, 1H, CH-4), 6.03 (dq, $J$ = 9.2, 2.3 Hz, 1H, CH-3), 4.52 (m, 1H, CH-6), 4.44 (m, 1H, CH-5), 4.22 (q, $J$ = 7.0 Hz, 2H, $OCH_2$), ), 1.28 (t, $J$ = 7.2 Hz, 3H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 167.1 (C=O), 138.7 (CH-4), 134.1 (CH-2), 128.7 (C-1), 122.5 (CH-3), 69.8 (COH-5), 64.5 (COH-6), 60.9 ($OCH_2$), 14.2 ($CH_3$); MS (EI) *m/z* (%) 184 (9), 166 (20), 138 (26), 122 (33), 121 (52), 105 (100), 77 (39), 51 (21), 45 (20); HRMS (EI) calcd for $C_9H_{12}O_4$: 184.0736. Found: 184.0731; Anal. calcd for $C_9H_{12}O_4$: C, 58.69; H 6.57. Found C, 58.77; H, 6.60.

**(+)-*n*-Propyl (5*S*,6*R*)-5,6-Dihydroxycyclohexa-1,3-dienecarboxylate (13)** [20]



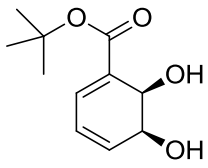

**13**: (62%); Waxy solid; $R_f$ = 0.15 [hexanes/EtOAc (1:1)]; $[\alpha]_D^{20}$ = +55.2 ($c$ = 1.4, $CHCl_3$) [lit.[20] $[\alpha]_D^{22}$ = +58.8 ($c$ = 1.1, $CHCl_3$)]; IR (film) $\nu$ 3398, 2968, 1700, 1280, 1240 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.08 (d, $J$ = 5.4 Hz, 1H, CH-2), 6.20 (dd, $J$ = 9.5, 2.5 Hz, 1H, CH-4), 6.09 (ddd, $J$ = 9.5, 5.4, 2.2 Hz, 1H, CH-3), 4.58 (d, $J$ = 6.3 Hz, 1H, CH-6), 4.48 (ddd, $J$ = 6.3, 2.5, 2.2 Hz, 1H, CH-5), 4.16 (t, $J$ = 6.7 Hz, 2H, $OCH_2$), 1.72 (qt, $J$ = 7.4, 6.7 Hz, 2H, $CH_2$), 0.98 (t, $J$ = 7.4 Hz, 3H, $CH_3$); $^{13}C$ NMR (75MHz, $CDCl_3$) $\delta$ 167.1 (C=O), 138.4 (CH-4), 133.9 (CH-2), 128.7 (C-1), 122.6 (CH-3), 69.4 (COH-5), 66.6 ($OCH_2$), 64.8 (COH-6), 22.0 ($CH_2$), 10.4 ($CH_3$); MS (EI) *m/z* (%): 198 (18), 180 (22), 138 (100), 121 (81), 110 (54), 105 (77); HRMS (EI) calcd for $C_{10}H_{14}O_4$: 198.0892. Found: 198.0892.

**(+)-*i*-Propyl (5*S*,6*R*)-5,6-Dihydroxycyclohexa-1,3-dienecarboxylate (14)** [20]



**14**: (72%); Colourless crystals; $R_f$ = 0.31 [hexanes/EtOAc (2:3)]; mp 80-82 $^{o}$C (pentane) [lit.[20] mp 83-85 $^{o}$C (EtOAc/hexanes)]; $[\alpha]_D^{22}$ = +66.5 (*c* = 1.0, $CHCl_3$) [lit.[20] $[\alpha]_D^{22}$ = +64.7 (*c* = 1.1, $CHCl_3$)]; IR (film) *v* 3274, 2981, 1698, 1263, 1241 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.05 (ddd, *J* = 5.5, 1.0, 0.5 Hz, 1H, CH-2), 6.20 (ddt, *J* = 9.6, 2,7, 0.9 Hz, 1H, CH-4), 6.08 (ddd, *J* = 9.6, 5.5, 2.2 Hz, 1H, CH-3), 5.12 (hept, *J* = 6.3 Hz, 1H, OCH), 4.58 (dd, *J* = 6.4, 0.5 Hz, 1H, CH-6), 4.48 (br m, 1H, CH-5), 1.30 (d, *J* = 6.3 Hz, 6H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 166.5 (C=O), 138.2 (CH-4), 133.6 (CH-2), 128.9 (C-1), 122.63 (CH-3), 69.2 (COH-5), 68.5 (OCH), 64.9 (COH-6), 21.8 ($CH_3$); MS (EI) *m/z* (%): 198 (19), 180 (16), 156 (14), 138 (100); HRMS (EI) calcd for $C_{10}H_{14}O_4$: 198.08921. Found: 198.08896; Anal. calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found C, 60.68; H, 7.19.

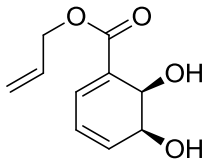
**(+)-*t*-Butyl (5*S*,6*R*)-5,6-Dihydroxycyclohexa-1,3-dienecarboxylate (15)**



**15**: (17%); White crystalline solid; $R_f$ = 0.31 [hexanes/EtOAc (1:1)]; mp 88-90 $^{o}$C (pentane); $[\alpha]_D^{20}$ = +53.3 (*c* = 0.3, $CHCl_3$); IR (film) *v* 3382, 2977, 2932, 1699, 1639, 1575, 1477, 1456, 1393, 1368, 1290, 1253, 1159, 1106, 1066, 1024, 993, 889, 849, 826, 783, 770 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.95 (d, *J* = 5.6 Hz, 1H, CH-2), 6.22 (dd, *J* = 9.5, 2.8 Hz, 1H, CH-4), 6.11 (ddd, *J* = 9.5, 5.7, 1.9 Hz, 1H, CH-3), 4.51 (dd, *J* = 6.4, 4.0 Hz, 1H, CH-6), 4.47 (m, 1H, CH-5), 1.59 (s, 9H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 166.4 (C=O), 137.3 (CH-4), 132.9 (CH-2), 129.8 (CH-1), 123.0 (CH-3), 87.5 (OC), 68.6 (COH-5), 65.7 (COH-6), 28.1 ($CH_3$); MS (EI) *m/z* (%): 195 (15), 194 (100), 165 (6), 162

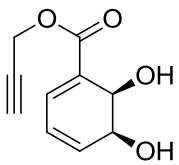
(5), 157 (10), 156 (96), 154 (21), 152 (6); HRMS (EI) 212.1049 = $C_{11}H_{16}O_4$; calcd for $C_{11}H_{14}O_3$ [(M-18)$^+$, $H_2O$]: 194.0943. Found: 194.0944.

**(+)-Allyl (5*S*,6*R*)-5,6-Dihydroxycyclohexa-1,3-dienecarboxylate (16)** [20]




**16**: (6%); Colourless crystals; $R_f$ = 0.23 [hexanes/EtOAc (1:1)]; mp 44-47 $^o$C (pentane) [lit.[20] mp 48-50 $^o$C (EtOAc/hexane)]; $[\alpha]_D^{20}$ = +67.4 (*c* = 0.2, $CHCl_3$) [lit.[20] $[\alpha]_D^{22}$ = +72.5 (*c* = 1.6, $CHCl_3$)]; IR (film) *v* 3394, 1704, 1273, 1238 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.12 (d, *J* = 5.5 Hz, 1H, CH-2), 6.23 (ddt, *J* = 9.6, 2,7, 1.0 Hz, 1H, CH-4), 6.11 (ddd, *J* = 9.5, 5.5, 2.2 Hz, 1H, CH-3), 5.98 (ddt, *J* = 17.2, 10.4, 5.7Hz, 1H, allyl CH), 5.37 (dt, *J* = 17.2, 1.5Hz, 1H, allyl $CH_2$), 5.28 (dt, *J* = 10.4, 1.3 Hz, 1H, allyl $CH_2$), 4.72 (ddd, *J* = 5.7, 1.5, 1.3 Hz, 2H, $OCH_2$), 4.61 (br s, 1H, COH), 4.50 (br s, 1H, COH); $^{13}$C NMR (75MHz, $CDCl_3$) $\delta$ 166.6 (C=O), 138.8 (CH-4), 134.4 (CH-2), 131.9 (allyl CH), 128.4 (C-1), 122.4 (CH-3), 118.3 (allyl $CH_2$), 69.6 ($OCH_2$), 65.5 (COH-5), 64.5 (COH-6); MS (EI) *m/z* (%): 196 (20), 178 (18), 138 (80), 121 (95), 41 (100). HRMS (EI) calcd for $C_{10}H_{12}O_4$: 196.07356. Found: 196.07364; Anal. calcd for $C_{10}H_{12}O_4$ + 1/8 $H_2O$: C, 60.52; H, 6.22. Found C, 60.52; H, 6.26.

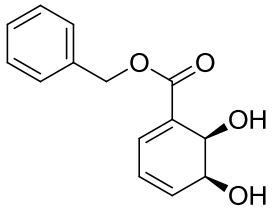
**(+)-Propargyl (5*S*,6*R*)-5,6-Dihydroxycyclohexa-1,3-dienecarboxylate (17)** [20]




**17**: (36%); Colourless crystals; $R_f$ = 0.31 [EtOAc/hexanes (3:2)]; mp 67-69 $^o$C (pentane) [lit.[20] mp 70-72◦C (EtOAc/Hexanes)]; $[\alpha]_D^{20}$ = +74.3 (*c* = 0.2, $CHCl_3$) [lit.[20] $[\alpha]_D^{22}$ =

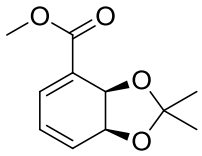
+88.20 (*c* = 1.6, $CHCl_3$)]; IR(film) *v* 3385, 3291, 1707, 1270, 1234 $cm^{-1}$; $^1H$ NMR (300 MHz, acetone-$d_6$) $\delta$ 7.15 (dd, *J* = 5.7, 0.8 Hz, 1H, CH-2), 6.25 (dd, *J* = 9.7, 2.7 Hz, 1H, CH-4), 6.12 (ddd, *J* = 9.8, 5.6, 2.2 Hz, 1H, CH-3), 4.82 (d, *J* = 2.5 Hz, 2H, $OCH_2$), 4.62 (dd, *J* = 6.8, 4.7 Hz, 1H, CH-6), 4.54 (m, 1H, CH-5), 2.50 (t, *J* = 2.5 Hz, 1H, CH); $^{13}C$ NMR (75 MHz, acetone-$d_6$) $\delta$ 167.2 (C=O), 142.5 (CH-4), 136.3 (CH-2), 131.1 (C-1), 123.5 (CH-3), 80.0 (propargyl C), 77.3 (propargyl CH), 72.5 (COH-5), 65.5 (COH-6), 53.4 ($OCH_2$); MS (EI) *m/z* (%): 194 (7), 176 (28), 138 (47), 121 (100); HRMS (EI) calcd for $C_{10}H_{10}O_4$: 194.0579. Found: 194.0581; Anal. calcd for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19. Found: C, 62.08; H, 5.18.

**(+)-Benzyl (5*S*,6*R*)-5,6-Dihydroxycyclohexa-1,3-dienecarboxylate (18)**



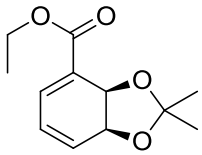

**18**: (10%); Pale yellow oil; $R_f$ = 0.30 [hexanes/EtOAc (1:1)]; $[\alpha]_D^{20}$ = +48.8 (*c* = 0.2, $CHCl_3$); IR (film) *v* 3390, 2959, 1704, 1639, 1575, 1498, 1455, 1395, 1260, 1164, 1104, 1066, 1027, 995, 915, 811, 757, 697; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 7.38 (d, *J* = 4.5 Hz, 1H, $C_6H_5$), 7.35 (m, 4H, $C_6H_5$), 7.12 (d, *J* = 5.6 Hz, 1H, CH-2), 6.23 (dd, *J* = 9.7, 2.8 Hz, 1H, CH-4), 6.12-6.09 (m, 1H, CH-3), 5.25 (s, 2H, $OCH_2$), 4.62 (m, 1H, CH-6), 4.49 (m, 1H, CH-5); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 166.8 (C=O), 138.5 (CH-4), 135.7 (CH-2), 134.3 (benzyl C), 128.7 (C-1), 128.4 (benzyl CH), 128.3 (benzyl CH), 128.2 (benzyl CH), 122.8 (CH-3), 68.9 (COH-5), 66.8 ($OCH_2$), 65.2 (COH-6); MS (EI) *m/z* (%): 246 (13), 244 (58), 238 (24), 228 (28), 221 (13), 220 (100), 213 (19), 212 (99), 210 (12), 207 (12), 204 (17), 201 (10), 200 (49), 199 (16), 197 (13), 195 (15), 194 (36), 192 (12), 183 (15), 182 (14), 181 (19), 179 (15), 172 (12), 169 (10), 168 (11), 167 (30), 166 (14), 165 (20), 159 (11), 157 (22), 156 (31), 155 (45), 154 (13), 153 (20), 152 (18), 151 (15); HRMS (EI) 246.0892 = $C_{14}H_{14}O_4$; calcd for $C_{14}H_{12}O_3$ [$(M-18)^+$, $H_2O$]: 228.0786. Found: 228.0787.

**(+)-Methyl (3a*R*,7a*S*)-2,2-Dimethyl-3a,7a-dihydrobenzo[*d*][1,3]dioxole-4-carboxylate (22)** [19, 25d]



**22**: (68%); Colourless oil; $R_f$ = 0.45 [hexanes/EtOAc (4:1)]; $[\alpha]_D$ = +88.5 (*c* = 0.2, $CHCl_3$); IR (film) *v* 2988, 2952, 1715, 1651, 1589, 1437, 1371, 1260, 1160, 1108, 1081, 1030, 881, 864, 762, 707, 631, 522 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 7.14 (m, 1H, CH-5), 6.11 (m, 2H, CH-6/CH-7), 4.94 (d, *J* = 8.4 Hz, 1H, CO-3a), 4.87 (dd, *J* = 8.5, 1.9 Hz, 1H, CO-7a), 3.83 (s, 3H, $OCH_3$), 1.46 (s, 3H, $CH_3$), 1.40 (s, 3H, $CH_3$); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 166.7 (C=O), 134.0 (CH-6), 133.9 (CH-5), 126.1 (C-4), 121.3 (CH-7), 105.6 (OCO-2), 72.5 (CO-7a), 68.2 (CO-3a), 52.0 ($OCH_3$), 26.7 ($CH_3$), 25.1 ($CH_3$); MS (EI) *m/z* (%) 195 (68), 163 (11), 153 (100), 152 (39), 121 (90), 120 (16), 109 (57), 105 (21), 94 (21), 93 (27), 92 (18), 79 (12), 77 (32), 65 (44), 63 (10), 59 (37), 51 (11); HRMS (EI) 210.0892 = $C_{11}H_{14}O_4$; calcd $C_{10}H_{11}O_4$ $[(M-15)^+, CH_3]$: 195.0657. Found: 195.0655.

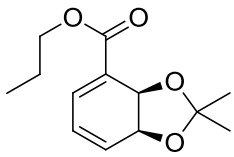
**(+)-Ethyl (3a*R*,7a*S*)-2,2-Dimethyl-3a,7a-dihydrobenzo[*d*][1,3]dioxole-4-carboxylate (23)** [20]



**23**: (73%); Colourless oil; $R_f$ = 0.56 [hexanes/EtOAc (1:1)]; $[\alpha]_D^{20}$ = +76.2 (*c* = 1.3, $CHCl_3$) [lit.[20] $[\alpha]_D^{23}$ = +74.6 (*c* = 4.0, $CHCl_3$)]; IR (film) *v* 3018, 2987, 2936, 1712, 1651, 1425, 1380, 1259, 1155, 1031, 917, 856, 697, 667, 512 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.06 (dd, *J* = 5.6, 0.8 Hz, 1H, CH-5), 6.24 (dd, *J* = 9.5, 2.8, 1H, CH-6), 6.13 (ddd, *J* = 9.9, 5.7, 2.1, 1H, CH-7), 4.62 (d, *J* = 6.4 Hz, 1H, CH-3a), 4.50 (m, 1H, CH-7a),

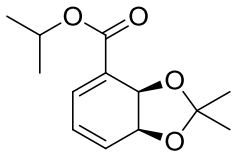
4.29 (q, J = 7.2, 2H, $OCH_2$), 1.35 (t, *J* = 7.2 Hz, 3H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 166.2 (C=O), 142.3 (CH-6), 130.0 (CH-5), 126.4 (C-4), 121.3 (CH-7), 108.5 (OCO-2), 72.6 ($OCH_2$), 70.4 (CO-7a), 60.5 (CO-3a), 26.2 ($CH_3$), 25.1 ($CH_3$), 14.2 ($CH_3$); MS (EI) *m/z* (%): 211 (77), 181 (15), 169 (17), 123 (100), 105 (17), 95 (13), 83 (11), 79 (76), 67 (14), 59 (10), 55 (11), 43 (82), 41 (14); HRMS (EI) 224.1049 = $C_{12}H_{16}O_4$; calcd $C_{11}H_{13}O_4$ [$(M-15)^+$, $CH_3$]: 211.0970. Found: 211.0969; Anal. calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found C, 64.52; H, 7.08.

**(+)-*n*-Propyl (3a*R*,7a*S*)-2,2-Dimethyl-3a,7a-dihydrobenzo[*d*][1,3]dioxole-4-carboxylate (24)**



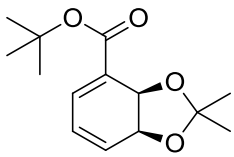
**24**: (68%); Clear colourless oil; $R_f$ = 0.46 [hexanes/EtOAc (4:1)]; $[\alpha]_D^{20}$ = +72.6 (*c* = 1.2, $CHCl_3$); IR (film) *v* 2974, 2937, 1713, 1589, 1460, 1379, 1370, 1256, 1160, 1107, 1080, 1052, 1027, 863, 705 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.16-7.14 (m, 1H, CH-5), 6.11 (m, 2H, CH-6/CH-7), 4.95 (d, *J* = 8.3 Hz, 1H, CH-7a), 4.87 (dd, *J* = 8.3, 1.4 Hz, 1H, CH-3a), 4.19 (t, *J* = 6.6 Hz, 2H, $OCH_2$), 1.74 (m, 2H, $CH_2$), 1.46 (s, 3H, $CH_3$), 1.41 (s, 3H, $CH_3$), 1.00 (t, *J* = 7.4 Hz, 3H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 166.2 (C=O), 133.8 (CH-6), 133.6 (CH-5), 126.4 (C-4), 121.3 (CH-7), 105.5 (OCO-2), 72.6 (CO-7a), 68.2 (CO-3a), 66.4 ($OCH_2$), 26.7 ($CH_3$), 25.0 ($CH_3$), 22.0 ($CH_2$), 10.5 ($CH_3$); MS (EI) *m/z* (%) 223 (27), 181 (72), 180 (18), 179 (17), 163 (11), 139 (100), 138 (42), 137 (18), 122 (11), 121 (69), 120 (15), 110 (18), 105 (21), 95 (65), 94 (18), 93 (15), 82 (12), 77 (24), 66 (11), 65 (28), 58 (49); HRMS (EI) 238.1205 = $C_{13}H_{18}O_4$; calcd $C_{12}H_{15}O_4$ [$(M-15)^+$, $CH_3$]: 223.0970. Found: 223.0968.

**(+)-*i*-Propyl (3a*R*,7a*S*)-2,2-Dimethyl-3a,7a-dihydrobenzo[*d*][1,3]dioxole-4-carboxylate (25)**



**25**: (76%); Clear colourless oil; $R_f$ = 0.51 [hexanes/EtOAc (4:1)]; $[\alpha]_D^{20}$ = +94.8 (*c* = 0.1, $CHCl_3$); IR (film) *v* 2983, 2935, 1710, 1589, 1455, 1372, 1261, 1160, 1106, 1027, 927, 862, 803, 706 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.12 (m, 1H, CH-5), 6.10 (m, 2H, CH-6/CH-7), 5.16 (hept, *J* = 6.4, 1H, OCH), 4.94 (d, *J* = 8.3 Hz, 1H, CH-3a), 4.87 (dd, *J* = 8.3, 1.4 Hz, 1H, CH-7a), 1.47 (s, 3H, $CH_3$), 1.41 (s, 3H, $CH_3$), 1.31 (d, *J* = 6.3, 6H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 165.6 (C=O), 133.7 (CH-6), 133.4 (CH-5), 126.7 (C-4), 121.3 (CH-7), 105.5 (OCO-2), 72.6 (CO-7a), 68.2 (OCH), 68.1 (CO-3a), 26.7 ($CH_3$), 25.0 ($CH_3$), 21.9 ($CH_3$), 21.9 ($CH_3$); MS (EI) *m/z* (%) 223 (19), 181 (68), 180 (19), 179 (19), 139 (100), 138 (55), 137 (20), 122 (14), 121 (96), 120 (22), 110 (17), 105 (18), 95 (49), 94 (21), 93 (19), 92 (12), 82 (18), 77 (24), 66 (15), 65 (35), 59 (16); HRMS (EI) 238.1205 = $C_{13}H_{18}O_4$; calcd $C_{12}H_{15}O_4$ $[(M-15)^+, CH_3]$: 223.0970. Found: 223.0966.

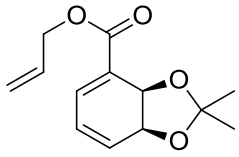
**(+)-*t*-Butyl (3a*R*,7a*S*)-2,2-Dimethyl-3a,7a-dihydrobenzo[*d*][1,3]dioxole-4-carboxylate (26)**



**26**: (10%); Clear colourless oil; $R_f$ = 0.63 [hexanes/EtOAc (4:1)]; $[\alpha]_D^{20}$ = +81.3 (*c* = 0.6, $CHCl_3$); IR (film) *v* 2981, 2933, 1707, 1589, 1456, 1368, 1275, 1255, 1160, 1109, 1050, 1025, 905, 848, 704 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.06 (m, 1H, CH-5), 6.08 (m, 2H, CH-6/CH-7), 4.87 (d, *J* = 8.2 Hz, 1H, CH-3a), 4.85 (d, *J* = 8.3, 1H, CH-7a), 1.54 (s, 9H, $CH_3$), 1.46 (s, 3H, $CH_3$), 1.41 (s, 3H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 165.4 (C=O), 133.5 (CH-6), 133.1 (CH-5), 127.6 (C-4), 121.3 (CH-7), 105.5 (OCO-2), 81.0 (OC), 72.8 (CO-7a), 68.2 (CO-3a), 28.2 ($CH_3$), 26.7 ($CH_3$), 25.0 ($CH_3$); MS (EI) *m/z* (%) 181 (25), 179 (14), 139 (46), 138 (40), 121 (46), 95 (19), 94 (21), 93 (13), 77 (14), 65

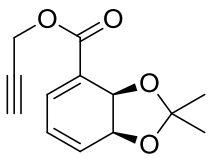
(24), 57 (100); HRMS (EI) 252.1361 = $C_{14}H_{20}O_4$; calcd $C_{13}H_{17}O_4$ [(M-15)$^+$, $CH_3$]: 237.1122. Found: 237.1127.

**(+)-Allyl (3a*R*,7a*S*)-2,2-Dimethyl-3a,7a-dihydrobenzo[*d*][1,3]dioxole-4-carboxylate (27)**



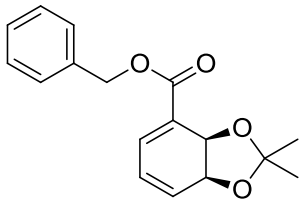
**27**: (27%); Clear colourless oil; $R_f$ = 0.65 [hexanes/EtOAc (4:1)]; $[\alpha]_D^{20}$ = +79.3 (*c* = 0.2, $CHCl_3$); IR (film) *v* 2987, 2935, 1715, 1649, 1589, 1455, 1404, 1371, 1252, 1161, 1109, 1029, 993, 923, 863, 706 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.18 (m, 1H, CH-5), 6.12 (m, 2H, CH-6/CH-7), 5.98 (m, 1H, allyl CH), 5.38 (dq, *J* = 17.4, 1.7 Hz, 1H, allyl $CH_2$), 5.26 (dq, *J* = 10.6, 1.6 Hz, 1H, allyl $CH_2$), 4.96 (d, *J* = 8.5 Hz, 1H, CH-3a), 4.88 (dd, *J* = 8.5, 2.1 Hz, 1H, CH-7a), 4.74 (dt, *J* = 5.5, 1.5 Hz, 2H, $OCH_2$), 1.46 (s, 3H, $CH_3$), 1.41 (s, 3H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 165.8 (C=O), 134.0 (CH-6), 134.0 (CH-5), 132.2 (allyl $CH_2$), 126.1 (C-4), 121.3 (CH-7), 118.0 (allyl CH), 105.6 (OCO-2), 72.5 (CO-7a), 68.1 (CO-3a), 65.4 ($OCH_2$), 26.7 ($CH_3$), 25.0 ($CH_3$); MS (EI) *m/z* (%) 221 (22), 220 (14), 179 (57), 163 (13), 161 (30), 137 (15), 135 (17), 122 (14), 121 (100), 109 (11), 107 (23), 105 (32), 94 (15), 93 (18), 77 (25), 65 (31); HRMS (EI) 236.1049 = $C_{13}H_{16}O_4$; calcd $C_{12}H_{13}O_4$ [(M-15)$^+$, $CH_3$]: 221.0814. Found: 221.0810.

**(+)-Propargyl (3a*R*,7a*S*)-2,2-Dimethyl-3a,7a-dihydrobenzo[*d*][1,3]dioxole-4-carboxylate (28)** [20]



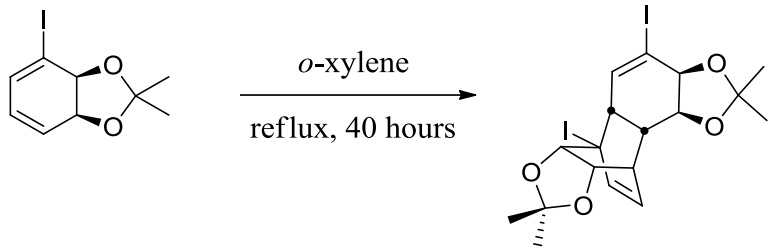
**28**: (20%); Colourless oil; $R_f$ = 0.54 [hexanes/EtOAc (4:1)]; $[\alpha]_D^{20}$ = +110.6 (*c* = 0.2, $CHCl_3$) [lit.[20] $[\alpha]_D^{22}$ = +112.7 (*c* = 1.3, $CHCl_3$)]; IR (film) *v* 2987, 2935, 1718, 1030 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.22 (dd, *J* = 5.3, 1.1 Hz, 1H, CH-5), 6.14 (m, 2H, CH-6/CH-7), 4.95 (d, *J* = 8.4 Hz, 1H, CH-3a), 4.89 (dd, J = 8.4, 2.4 Hz, 1H, CH-7a), 4.84 (dd, *J* = 2.5, 1.0 Hz, 2H, $OCH_2$), 2.50 (t, *J* = 2.5 Hz, 1H, propargyl CH), 1.47 (s, 3H, $CH_3$), 1.41 (s, 3H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 165.3 (C=O), 134.8 (CH-6), 134.4 (CH-5), 125.5 (C-4), 121.2 (CH-7), 105.7 (OCO-2), 77.7 (propargyl C), 74.9 (propargyl CH), 71.8 (CO-7a), 68.0 (CO-3a), 52.3 ($OCH_2$), 26.7 ($CH_3$), 25.0 ($CH_3$); MS (EI) *m/z* (%) 219 (42), 177 (41), 163 (17), 121 (83), 43 (100); HRMS (EI) calcd for $C_{12}H_{11}O_4$: 219.0657. Found: 219.0659; Anal. calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.68; H, 6.08.

(+)-**Benzyl (3a*R*,7a*S*)-2,2-Dimethyl-3a,7a-dihydrobenzo[*d*][1,3]dioxole-4-carboxylate (29)**



**29**: (70%); Clear colourless oil; $R_f$ = 0.53 [hexanes/EtOAc (4:1)]; $[\alpha]_D^{20}$ = +75.8 (*c* = 1.5, $CHCl_3$); IR (film) *v* 3034, 2987, 2935, 1712, 1588, 1455, 1371, 1253, 1161, 1108, 1028, 864, 737, 698 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 7.39 (m, 5H, $C_6H_5$), 7.19 (m, 1H, CH-5), 6.12 (m, 2H, CH-6/CH-6), 5.28 (s, 2H, $OCH_2$), 4.98 (d, *J* = 8.4 Hz, 1H, CH-3a), 4.88 (dd, *J* = 8.4, 2.2 Hz, 1H, CH-7a), 1.48 (s, 3H, $CH_3$), 1.42 (s, 3H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 166.0 (C=O), 136.0 (CH-6), 134.2 (CH-5), 134.1 ($C_6H_5$), 128.5 ($C_6H_5$), 128.2 ($C_6H_5$), 128.1 ($C_6H_5$), 126.1 (C-4), 121.3 (CH-7), 105.6 (OCO-2), 72.5 (CO-7a), 68.2 (CO-3a), 66.5 ($OCH_2$), 26.7 ($CH_3$), 25.1 ($CH_3$); MS (EI) *m/z* (%) 105 (15), 91 (100), 77 (14), 65 (25), 58 (11), 52 (15); HRMS (EI) 286.1205 = $C_{17}H_{18}O_4$; calcd $C_{11}H_{13}O_4$ $[(M-15)^+, CH_3]$: 271.0965. Found: 271.0966.

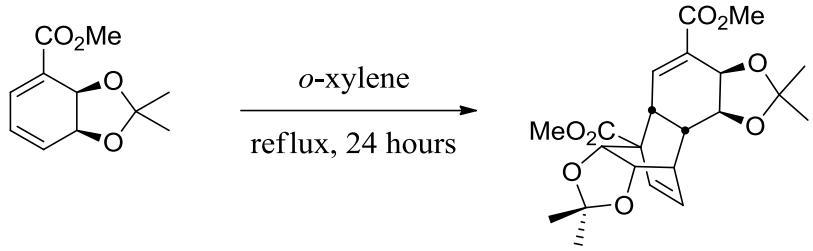
**(+)-(3a*S*,5a*S*,6*S*,6a*S*,9a*S*,10*R*,10a*R*,10b*S*)-4,6-Diiodo-2,2,8,8-tetramethyl-3a,5a,6,6a,9a,10,10a,10b-octahydro-6,10-ethenonaphtho[1,2-*d*:6,7-*d'*]bis([1,3]dioxole) (30)**




Acetonide **20**[29] was dissolved in *o*-xylene and heated to reflux for 40 hours. The solution was concentrated under reduced pressure and purified via flash column chromatography [hexanes/EtOAc (4:1)] to obtain 0.19 g (38%) of **2** as a white solid.

**30**: $R_f$ = 0.39 [hexanes/EtOAc (4:1)]; mp 220-224 °C (EtOAc/pentane); $[\alpha]_D^{20}$ = +106.5 (*c* = 1.0, $CHCl_3$); IR (film) *v* 2984, 2933, 2898, 1455, 1380, 1280, 1262, 1236, 1225, 1209, 1160, 1082, 1068, 1012 $cm^{-1}$; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 6.89 (d, *J* = 3.7 Hz, 1H, CH-5), 6.25 (d, *J* = 8.6 Hz, 1H, CH-11), 5.79 (t, *J* = 7.3 Hz, 1H, CH-12), 4.49 (d, *J* = 7.2 Hz, 1H, CH-6a), 4.38 (dd, *J* = 7.2, 3.6 Hz, 1H, CH-9a), 4.18 (d, *J* = 4.6 Hz, 1H, CH-3a), 4.15 (d, *J* = 4.1 Hz, 1H, CH-10b), 2.91 (m, 1H, CH-10), 2.71 (dd, *J* = 8.7, 3.6 Hz, 1H, CH-5a), 2.49 (d, *J* = 9.2 Hz, 1H, CH-10a), 1.47 (s, 3H, $CH_3$), 1.40 (s, 3H, $CH_3$), 1.38 (s, 3H, $CH_3$), 1.36 (s, 3H, $CH_3$); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 140.1 (CH-5), 139.0 (CH-11), 128.7 (CH-12), 109.3 (OCO-2), 108.7 (OCO-8), 103.9 (C-4), 84.7 (CO-6a), 79.1 (CO-9a), 78.6 (CO-3a), 75.2 (CO-10b), 48.3 (C-6), 45.6 (CH-5a), 38.4 (CH-10), 35.2 (CH-10a), 27.9 ($CH_3$), 26.7 ($CH_3$), 25.5 ($CH_3$), 25.1 ($CH_3$); MS (EI) *m/z* (%) 122 (11), 107 (14), 105 (11), 104 (43), 93 (11), 91 (26), 79 (23), 78 (10), 77 (23), 75 (27), 70 (12), 69 (11), 61 (14), 57 (18), 55 (15), 45 (19), 43 (100), 42 (11), 41 (18), 39 (15); HRMS (EI) calcd for $C_{18}H_{22}O_4$: 555.9607. Found: 555.9602; Anal. calcd for $C_{18}H_{22}I_2O_4$: C, 38.87; H, 3.99. Found: C, 39.14; H, 4.04.

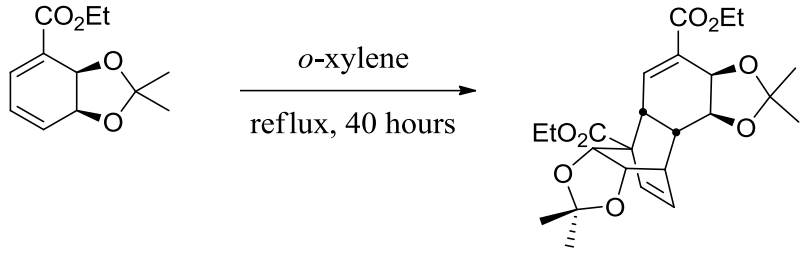
**(+)-(3a*R*,5a*R*,6*S*,6a*R*,9a*S*,10*R*,10a*S*,10b*S*)-Dimethyl 2,2,8,8-tetramethyl-3a,5a,6,6a,9a,10,10a,10b-octahydro-6,10-ethenonaphtho[1,2-*d*:6,7-*d'*]bis([1,3]dioxole)-4,6-dicarboxylate (31)**




Acetonide **22**[19, 25d] was dissolved in *o*-xylene and heated to reflux for 24 hours. The solution was concentrated under reduced pressure and purified via flash column chromatography [hexanes/EtOAc (6:1)] to obtain 34 mg (42%) of **31** as white powdery solid.

**31**: $R_f$ = 0.33 [hexanes/EtOAc (3:1)]; mp 180-183 °C (pentane); $[\alpha]_D^{20}$ = +50.3 (*c* = 0.4, $CHCl_3$); IR (film) *v* 2932, 1737, 1436, 1379, 1283, 1262, 1210, 1164, 1060, 882, 804, 742 $cm^{-1}$; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 6.45 (d, *J* = 8.3 Hz, 1H, CH-5), 6.20 (t, *J* = 7.2 Hz, 1H, CH-11), 5.40 (t, *J* = 2.6 Hz, 1H, CH-12), 4.63 (dd, *J* = 7.2, 1.4 Hz, 1H, CH-6a), 4.40 (dd, *J* = 7.3, 3.2 Hz, 1H, CH-9a), 4.29 (t, *J* = 7.6 Hz, 1H, CH-3a), 3.90 (s, 3H, $OCH_3$), 3.79 (s, 3H, $OCH_3$), 3.63 (t, *J* = 8.2, 1H, CH-10b), 3.37 (m, 1H, CH-10), 3.11 (dt, *J* = 7.4, 2.5 Hz, 1H, CH-5a), 1.94 (dd, *J* = 8.3, 1.9 Hz, 1H, CH-10a), 1.51 (s, 3H, $CH_3$), 1.35 (s, 6H, $CH_3$), 1.30 (s, 3H, $CH_3$); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 173.0 (C=O), 171.2 (C=O), 138.8 (CH-5), 129.7 (CH-11), 128.5 (CH-12), 117.8 (C-4), 110.0 (OCO-2), 109.9 (OCO-8), 79.0 (CO-6a), 78.4 (CO-9a), 77.3 (CO-3a), 56.3 (C-6), 52.6 ($OCH_3$), 52.5 ($OCH_3$), 48.9 (CH-5a), 42.6 (CH-10), 38.3 (CH-10a), 27.2 ($CH_3$), 25.4 ($CH_3$), 25.0 ($CH_3$), 24.6 ($CH_3$); MS (EI) *m/z* (%) 213 (8), 157 (6), 131 (6), 121 (7), 100 (13), 97 (6), 95 (6), 83 (6), 81 (4), 77 (7), 71 (6), 70 (5), 69 (15), 61 (5), 59 (5), 58 (100), 57 (12), 55 (9); HRMS (EI) calcd for $C_{22}H_{28}O_8$: 420.1784. Found: 420.1801; Anal. calcd for $C_{22}H_{28}O_8$: C, 62.85; H, 6.71. Found: C, 63.10; H, 6.79.

**(+)-(3a*R*,5a*R*,6*S*,6a*R*,9a*S*,10*R*,10a*S*,10b*S*)-Diethyl 2,2,8,8-tetramethyl-3a,5a,6,6a,9a,10,10a,10b-octahydro-6,10-ethenonaphtho[1,2-*d*:6,7-*d'*]bis([1,3]dioxole)-4,6-dicarboxylate (32)**




A solution of acetonide **23**[20] was dissolved in *o*-xylene and heated to reflux for 40 hours. The solution was concentrated under reduced pressure and purified via flash column chromatography [hexanes/EtOAc (4:1)] to obtain 0.34 g (68%) of **32** as pale yellow solid.

**32**: $R_f$ = 0.24 [hexanes/EtOAc (4:1)]; mp 91-93 °C (pentane); $[\alpha]_D^{20}$ = +47.8 (*c* = 1.0, $CHCl_3$); IR (film) *v* 2984, 2937, 1721, 1458, 1380, 1262, 1221, 1163, 1072, 1026 $cm^{-1}$; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 6.43 (d, *J* = 3.8 Hz, 1H, CH-5), 6.38 (d, *J* = 8.8 Hz, 1H, CH-11), 6.04 (t, *J* = 7.0 Hz, 1H, CH-12), 4.60 (d, *J* = 7.0 Hz, 1H, CH-6a), 4.58 (d, *J* = 4.8 Hz, 1H, CH-9a), 4.43 (dd, *J* = 7.0, 3.3 Hz, 1H, CH-3a), 4.37 (q, *J* = 13.9 Hz, 2H, $OCH_2$), 4.22 (m, 2H, $OCH_2$), 4.16 (dd, *J* = 4.6, 1.9 Hz, 1H, CH-10b), 3.01 (m, 1H, CH-10), 2.95 (dd, *J* = 9.0, 3.3 Hz, 1H, CH-5a), 2.32 (d, *J* = 9.1, 1H, CH-10a), 1.35 (s, 3H, $CH_3$), 1.33 (t, *J* = 7.1 Hz, 3H, $CH_3$), 1.29 (s, 3H, $CH_3$), 1.28 (s, 3H, $CH_3$), 1.27 (s, 3H, $CH_3$), 1.26 (s, 3H, $CH_3$); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 171.5 (C=O), 165.9 (C=O), 136.5 (CH-5), 131.5 (CH-11), 130.2 (CH-12), 128.8 (C-4), 109.7 (OCO-2), 108.2 (OCO-8), 80.7 (CO-6a), 78.3 (CO-9a), 76.9 (CO-3a), 69.2 (CO-10b), 61.5 ($OCH_2$), 60.7 ($OCH_2$), 53.9 (C-6), 40.4 (CH-10), 38.6 (CH-5a), 34.9 (CH-10a), 28.1 ($CH_3$), 26.5 ($CH_3$), 25.4 ($CH_3$), 25.1 ($CH_3$), 14.2 ($CH_3$), 14.2 ($CH_3$); MS (EI) *m/z* (%) 433 (22), 390 (27), 375 (22), 287 (22), 286 (25), 285 (65), 273 (14), 272 (27), 269 (53), 259 (20), 258 (17), 257 (26), 245 (17), 244 (22), 241 (32), 229 (26), 228 (14), 227 (100), 217 (14), 213 (27); HRMS (EI) 448.2097 = $C_{24}H_{32}O_8$; calcd $C_{23}H_{29}O_8$ $[(M-15)^+, CH_3]$: 433.1857. Found: 433.1857; Anal. calcd for $C_{24}H_{32}O_8$: C, 64.27; H, 7.19. Found C, 63.99; H, 7.30.

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