Synthesis of 6-substituted salicylates via biomimetic aromatization utilizing the cross metathesis of a vinyl dioxinone with homoallylic alcohols

Peter S. Blencowe and Anthony G.M. Barrett

Abstract: We herein report biomimetic syntheses of 6-substituted salicylates from the cross metathesis of 2,2-dimethyl-6-vinyl-1,3-dioxin-4-one with homoallylic alcohols, oxidation, and aromatization of the intermediate enone–dioxinones. Of particular note is the use of the catalyst 1,4-diazabicyclo[2.2.2]octane in the microwave thermolytic ketene generation and trapping, cyclization, and dehydration reaction sequence.

Key words: salicylates, biomimetic synthesis, dioxinone, polyketide synthesis.

Résumé : Dans ce travail, on rapporte les synthèses biomimétiques de salicylates substitués en position-6, par le biais d'une réaction de métathèse croisée de la 2,2-diméthyl-6-vinyl-1,3-dioxin-4-one avec des alcools homoallyliques, suivie d'une oxydation et d'une aromatisation de l'intermédiaire énone–dixoinones. Il est important de noter l'utilisation du 1,4-diazabicyclo[2.2.2]octane comme catalyseur dans la génération thermolytique du cétène, de son piégeage, de sa cyclisation et de sa déshydrogénation dans la séquence réactionnelle.

Mots-clés : salicylates, synthèse biomimétique, dioxinone, synthèse d'un polycétide.

[Traduit par la Rédaction]

Introduction

Salicylates have long been applied in medicine, fragrances, flavorings, and cosmetics. Simple examples include acetyl salicylic acid and methyl salicylate (oil of wintergreen).[1] 6-Substituted salicylates also occur widely in natural products, which show a wide variety of activities. These include macrocyclic salicylates such as salicylihalamide A and B;[2] apicularen A;[3] and marinomycins A–D,[4] which show anticancer activity (the latter class also displaying antibacterial activity); the fungal metabolite CJ-12 950,[5] which has the potential to treat hypercholesterolemia and hyperlipidemia; long-chain salicylic acids such as anacardic acid and derivatives that are antibiotics and antioxidants;[6] and the diacetylenic natural product frutescin.[7]

The most common syntheses of salicylates are via modification of salicylic acid (itself available from the Kolbe–Schmitt reaction)[8] by esterification or through modification via classical aromatic chemistry. De novo syntheses of these systems are less common but include methods such as oxidative cyclization,[9,10] cycloaromatization of conjugated polyenynes,[11] Diels–Alder reactions,[12] titanium(IV) chloride mediated [3 + 3] additions,[13] and domino "Michael–retro-Michael–Wittig" reactions.[14]

Previously reported biomimetic syntheses of salicylates have involved the synthesis of polycarbonyl precursors via partially reduced pyrones **2**[15] or by addition reactions to β-ketoaldehydes **4** (Scheme 1).[16] In the first case, substrates were limited to those that could be selectively reduced (i.e., not 6-phenacyl-4-hydroxy-2-pyrone), and in the second case a *tert*-butyl ester was necessary to prevent self-condensation of sodioformylacetone.

Inspired by the polyketide biosynthesis for aromatic natural products and the related biomimetic synthesis studies by Harris and Harris,[17] we sought to extend our work on the synthesis of resorcylates from diketodioxinones,[18] to the synthesis of 6-substituted salicylates. We reasoned that salicylates **7** would be available by intramolecular aldol condensation of diketo esters **8**, synthesized by ketene generation and trapping from dioxinone **9**, itself available through cross metathesis of dioxinone **10** and enone **11** (Scheme 2).

Herein, we report the concise synthesis of 6-substituted salicylates using dioxinones as stable precursors without the requirement for protecting groups or harsh reaction conditions.

Received 26 June 2012. Accepted 31 July 2012. Published at www.nrcresearchpress.com/cjc on 29 November 2012.

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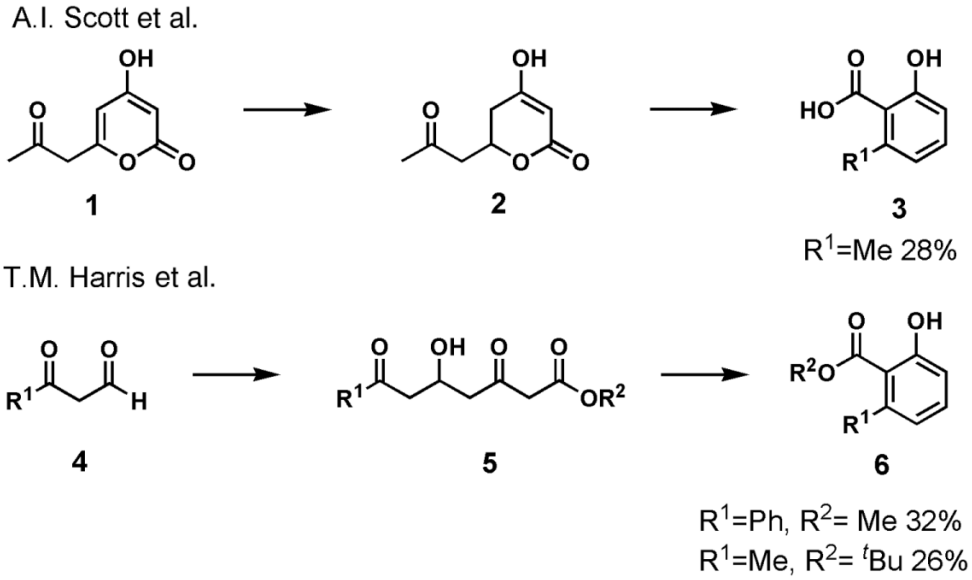
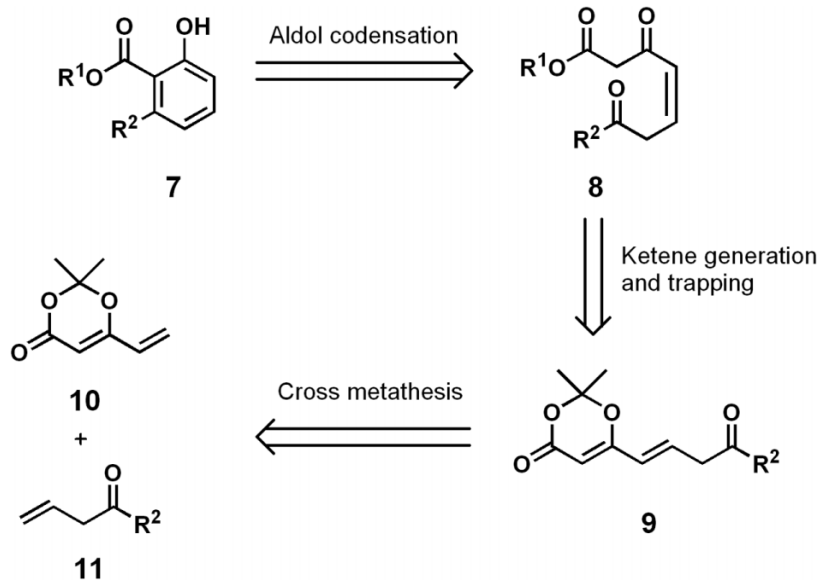
This article is part of a Special Issue dedicated to Professor Derrick Clive. Dedicated to Derrick Clive in recognition of his scholarship and original elegant contributions to synthetic organic chemistry.

Scheme 1. Previous biomimetic routes to 6-substituted salicylic acid derivatives.



Scheme 2. Retrosynthesis of salicylates from dioxinone precursor **10**.



Results and discussion

Vinyl dioxinone **10** was prepared by the procedure of Gebauer and Blechert[19] from *tert*-butyl 5-chloro-3-oxopentanoate[20] in a 72% yield over two steps. The homoallylic alcohols **14a**–**14k** were synthesized in 82%–94% yields by reaction of allylmagnesium bromide with the corresponding aldehydes.[21] Oxidation of homoallylic alcohol **14a** with pyridinium chlorochromate (PCC)[22] gave the enone **11** in a 64% yield, but attempted cross metathesis of **11** with vinyl dioxinone **10** using the Grubbs–Hoveyda II catalyst **12** was unsuccessful and only gave rise to the enedione **13** in a poor yield. In contrast, cross metathesis of homoallylic alcohol **14a** with vinyl dioxinone **10** gave dioxinone **15a** in an 81% yield (Scheme 3).[23]

Subsequently, we examined the oxidation of the cross metathesis product **15a** to give enone–dioxinone **16a** (Table 1). Our initial attempts involving pyridinium chlorochromate and manganese dioxide were unsuccessful with unreacted starting material being recovered (Table 1, entries 1 and 2). Modified Oppenauer oxidation[24] was of limited use owing to contamination of the product with the hydrogen acceptor 2,4-dinitrobenzaldehyde. Swern conditions gave an intractable mixture of products possibly because of chlorination as has been observed for aryl vinyl ketones.[25]

In contrast to these failures, oxidations with hypervalent iodine reagents were more useful. While oxidation with iodoxybenzoic acid (IBX) in dimethyl sulfoxide (DMSO)[26] resulted in overoxidation, reaction in ethyl acetate[27] gave

Scheme 3. Cross metathesis reactions of vinyl dioxinone **10**.

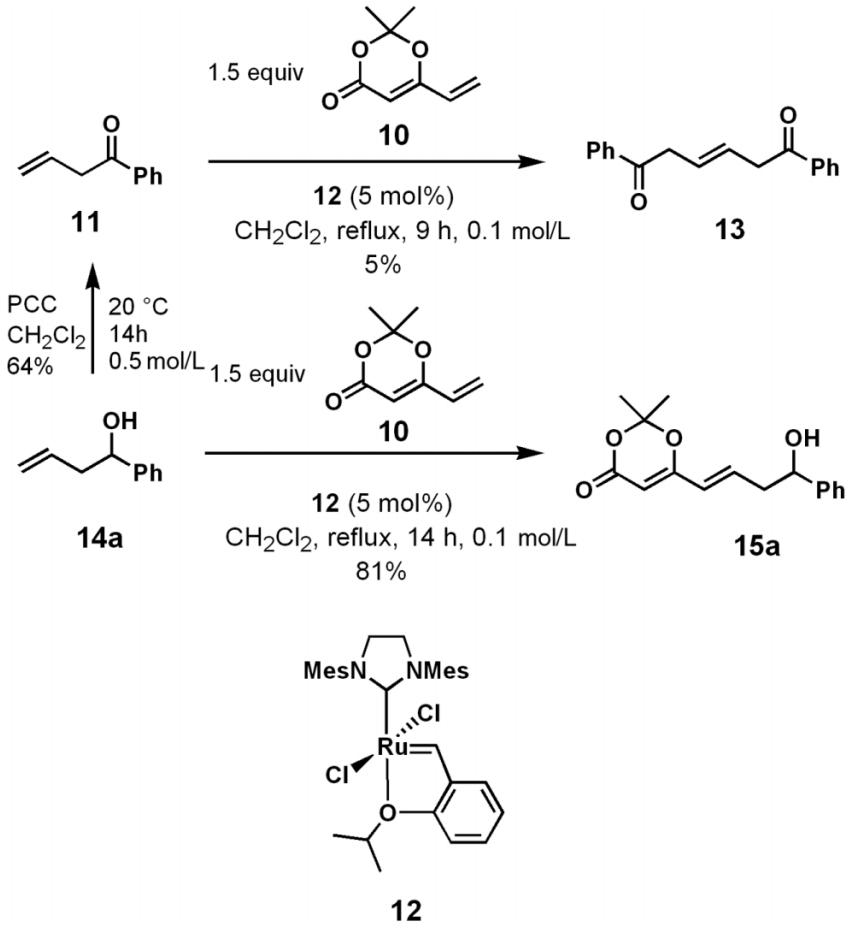
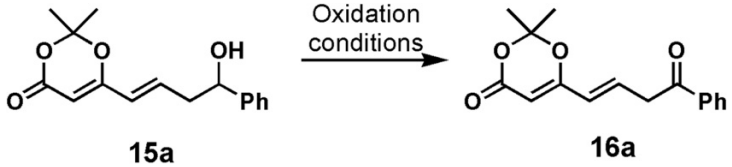


Table 1. Conditions for the oxidation of **15a**.



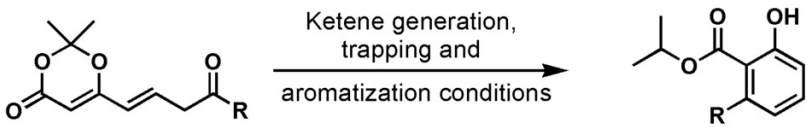
Entry	Oxidation conditions	Yield of **16a** (%)
1	PCC, CH_2Cl_2, 20 °C	0
2	MnO_2, CH_2Cl_2, 20 °C	0
3	IBX, EtOAc, 80 °C	67
4	DMP, CH_2Cl_2, 20 °C	40
5	DMP, CH_2Cl_2, 0 °C	77

Note: PCC, pyridinium chlorochromate; IBX, iodoxybenzoic acid; DMP, Dess–Martin periodinane.

enone–dioxinone **16a** in a 67% yield (Table 1, entry 3). Dess–Martin periodinane (DMP)[28] was found to be most efficient and oxidation at 0 °C gave enone **16a** in a 77% yield (Table 1, entries 4 and 5).

Reflux of a toluene solution of dioxinone **16a** and in situ trapping of the resultant ketene with 2-propanol gave the salicylate **17a** in a 53% yield (Table 2, entry 1). When heating of **16a** was carried out under microwave conditions, ketene generation and trapping was complete within 45 min (as observed by ^{1}H NMR spectroscopy), and heating of the intermediate for a further 8 h to effect aromatization gave salicylate **17a** in a 14% yield (Table 2, entry 2).[29] It was found that the microwave reaction of **16a** in the presence of 1,4-diazabicyclo [2.2.2]octane (DABCO) was more rapid and gave salicylate **17a** in a 55% yield after 1.5 h (Table 2, entry 3). Excess DABCO was not required for the acceleration (Table 2, entry

Table 2. Optimization of ketene generation, trapping by isopropanol, and aromatization.

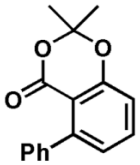


16a **17a**

Entry	Additive (equiv)	Temperature (°C)[a]	Solvent[b]	Time (h)	Yield of **17a** (%)
1	—	Reflux[c]	PhMe	26	53
2	—	120	EtOAc	8	14
3	DABCO (10)	120	EtOAc	1.5	55
4	DABCO (1)	120	EtOAc	2	47
5	DABCO (1)	120	EtOAc	8	51

[a]Microwave heating.
[b]*i*-PrOH (40 equiv.) was added as the trapping agent.
[c]Conventional heating.

Fig. 1. Possible benzodioxinone product.



18

4) and prolonged heating failed to give any further conversion (Table 2, entry 5). The mechanism of rate enhancing action by DABCO is yet to be determined, though alkene (trans to cis) isomerization is a possibility.[30]

As has been shown previously, reaction of diketodioxinones with triethylamine smoothly gave the corresponding benzodioxinones.[31] In contrast, we have now found that the reaction of enone–dioxinone **16a** with triethylamine, Hünig's base, 5 mol/L hydrochloric acid, or ammonium acetate resulted only in decomposition and the arene **18** was not formed. No reaction was observed with acetic acid (Fig. 1).

The optimized reaction conditions for the cross metathesis, oxidation, and aromatization were applied to synthesize a range of salicylates **17a**–**17i** in good yields (Scheme 4). Efficient cross metathesis in some cases required the use of an increased amount (10 mol %) of catalyst **12** to achieve an acceptable yield. In these cases, some self-metathesis of vinyl dioxinone **10** was observed (<10%). The homoallylic alcohol **15k** failed to undergo cross metathesis, presumably because of coordination of the pyridine nitrogen to ruthenium, resulting in catalyst deactivation.

In all cases, aromatization proceeded in good yield except in one instance (**16j** → **17j**). In this example, steric hindrance presumably suppressed the initial intramolecular aldol reaction. Notably, the nature of the para substituent on the aryl unit (R) had little effect with both electron-donating groups (**16e**) and electron-withdrawing groups (**16b**) undergoing aromatization with comparable efficiency.

Conclusion

A range of isopropyl 6-aryl and 6-alkyl salicylate esters were prepared from the vinyl dioxinone **10** by cross metathesis with the homoallylic alcohols **14a**–**14i**, Dess–Martin periodinane (DMP) oxidation, and aromatization via generation and trapping of enedione–ketenes. The methodology is a mild and convenient process for the preparation of salicylates with these substitution patterns. Further aspects of this methodology will be reported in due course. ^{1}H and ^{13}C NMR spectra for all new compounds can be found in the Supplementary data.

Experimental

General methods

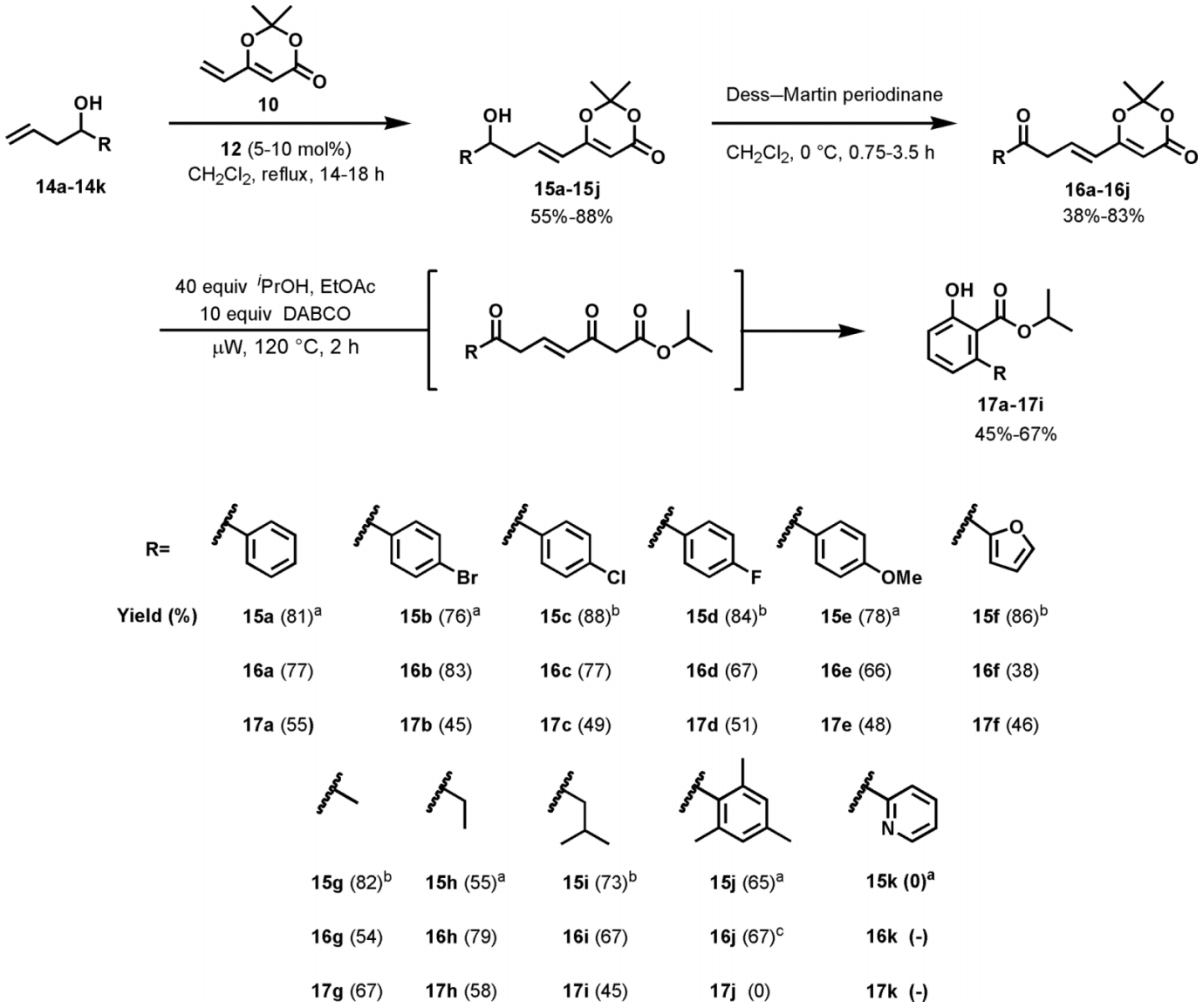
All reactions were carried out in oven-dried glassware under N_2, using commercially supplied solvents and reagents unless otherwise stated. CH_2Cl_2 was redistilled from CaH_2. Flash chromatography was carried out on silica gel (eluents are given in parentheses). Analytical TLC was performed on precoated silica gel F_{254} aluminum plates with visualization under UV light and by staining with acidic vanillin or acidic potassium permanganate solutions. Melting points were determined using a hot-stage microscope and are uncorrected. ^{1}H and ^{13}C NMR spectra were, respectively, recorded at 400 and 101 MHz with the solvent used in each case specified and spectra referenced to residual solvent peaks. Elemental analysis was carried out by the London Metropolitan elemental analysis service.

With the exception of commercially available pent-4-en-2ol (**14g**) the homoallylic alcohols **14a**,[32] **14b**,[33] **14c**,[34] **14d**,[34] **14e**,[32] **14f**,[32] **14h**,[35] **14i**,[35] **14j**,[32] and **14k**,[36] were prepared as described in the literature from the corresponding aldehydes by reaction with allylmagnesium bromide.[21]

General procedure A for cross metathesis of homoallylic alcohols 14a–14k

Catalyst **12** (5–10 mol %) was added with stirring to vinyl dioxinone **10** (1.5–2 equiv) and homoallylic alcohol (**14a**–**14k**, 0.1 mol/L) in CH_2Cl_2 at reflux and heating was continued for

Scheme 4. Synthesis of 6-aryl and 6-alkyl salicylates.



14–18 h. The mixture was rotary evaporated and chromatographed to give the corresponding dioxinone (**15a**–**15j**).

General procedure B for oxidation of dioxinones 15a–15j

DMP (1.4 equiv) was added with stirring to dioxinone (**15a**–**15j**, 0.1 mol/L) in CH_2Cl_2 at 0 °C and stirring continued at this temperature for 0.75–3.5 h. The mixture was chromatographed eluting with Et_2O, and the fractions containing product were rotary evaporated. Chromatography of the residue gave the enone–dioxinone (**16a**–**16j**).

General procedure C for aromatization of enone–dioxinones 16a–16j

Molecular sieves (100 mg per 0.1 mmol **16a**–**16j**), DABCO (10 equiv), *i*-PrOH (40 equiv), and enone-dioxinone (**16a**–**16j**) in EtOAc (0.02 mol/L) were placed in a 10 mL microwave vial and microwave heated at 120 °C for 2 h. The resulting mixture was filtered and rotary evaporated. The residue was taken up in EtOAc (10 mL) and washed with 1 mol/L aqueous HCl. The aqueous layer was extracted further with EtOAc (2 × 10 mL), and the combined organic layers were dried ($MgSO_4$), rotary evaporated, and chromatographed to give the salicylates **17a**–**17i**.

***(E)-6-(4-Hydroxy-4-phenylbut-1-enyl)-2,2-dimethyl-4H-1,3-dioxin-4-one* (15a)**

According to general procedure A, reaction of alcohol **14a** (210 mg, 1.42 mmol) and dioxinone **10** (328 mg, 2.13 mmol) with catalyst **12** (45 mg, 0.071 mmol) for 14 h and chromatography (hexanes–Et_2O, 7:3 to 1:1) gave dioxinone **15a** (315 mg, 81%) as a brown oil. IR (thin film, cm^{-1}): 3422, 1703, 1649, 1589, 1389, 1373, 1273, 1252, 1200, 1018, 967, 903, 757, 700. ^1H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.40–7.32 (m, 5H), 6.64–6.55 (m, 1H), 6.02–5.95 (m, 1H), 5.25 (s, 1H), 4.84 (dd, J = 7.8, 4.9 Hz, 1H), 2.70–2.60 (m, 2H), 2.27 (br s, 1H), 1.70 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 162.9,

162.0, 143.5, 137.9, 128.6, 128.0, 125.6, 125.0, 106.4, 93.9, 73.3, 42.3, 25.0. MS (EI) *m/z*: 275 $[M + H]^+$. HR-MS (EI) *m/z* calcd for $C_{16}H_{19}O_4$: 275.1283 $[M + H]^+$; found: 275.1288. Anal. calcd for $C_{16}H_{18}O_4$: C 70.06, H 6.61; found: C 70.15, H 6.71.

***(E)-6-(4-(4-Bromophenyl)-4-hydroxybut-1-enyl)-2,2-dimethyl-4H-1,3-dioxin-4-one* (15b)**

According to general procedure A, reaction of alcohol **14b** (491 mg, 2.16 mmol) and dioxinone **10** (500 mg, 3.25 mmol) with catalyst **12** (68 mg, 0.11 mmol) for 16 h and chromatography (hexanes–Et_2O, 7:3 to 1:3) gave dioxinone **15b** (577 mg, 76%) as a brown solid; mp 85–90 °C (Et_2O–pentane). IR (thin film, cm^{-1}): 3451, 1689, 1651, 1590, 1391, 1375, 1275, 1201, 1010, 971, 820, 600. ^1H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.49 (d, J = 8.3 Hz, 2H), 7.23 (d, J = 8.3 Hz, 2H), 6.56 (dt, J = 15.6, 7.8 Hz, 1H), 5.97 (d, J = 15.6 Hz, 1H), 5.24 (s, 1H), 4.81 (t, J = 6.1 Hz, 1H), 2.64–2.56 (m, 2H), 2.31 (br s, 1H), 1.70 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 162.8, 162.0, 142.5, 137.3, 131.7, 127.4, 125.3, 121.7, 106.4, 94.0, 72.6, 42.3, 25.0. MS (ESI) *m/z*: 355 $[M(^{81}Br) + H]^+$, 353 $[M(^{79}Br) + H]^+$. HR-MS (ESI) *m/z* calcd for $C_{16}H_{18}BrO_4$: 353.0388 $[M + H]^+$; found: 353.0389. Anal. calcd for $C_{16}H_{17}BrO_4$: C 54.41, H 4.85; found: C 54.25, H 4.73.

***(E)-6-(4-(4-Chlorophenyl)-4-hydroxybut-1-enyl)-2,2-dimethyl-4H-1,3-dioxin-4-one* (15c)**

According to general procedure A, reaction of alcohol **14c** (183 mg, 1 mmol) and dioxinone **10** (308 mg, 2 mmol) with catalyst **12** (63 mg, 0.1 mmol) for 18 h and chromatography (hexanes–Et_2O, 3:2 to 2:3) gave dioxinone **15c** (271 mg, 88%) as a brown solid; mp 76–80 °C (Et_2O–pentane). IR (thin film, cm^{-1}): 3457, 1690, 1652, 1591, 1394, 1376, 1279, 1203, 1087, 1021, 971, 830. ^1H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.36–7.26 (m, 4H), 6.55 (dt, J = 15.7, 7.8 Hz, 1H), 5.97 (d, J = 15.6 Hz, 1H), 5.24 (s, 1H), 4.85–4.77 (m, 1H), 2.66–2.56 (m, 2H), 2.14 (d, J = 3.4 Hz, 1H), 1.70 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 162.7, 161.9, 141.9, 137.2, 133.6, 128.8, 127.0, 125.4, 106.4, 94.1, 72.6, 42.4, 25.0. MS (ESI) *m/z*: 311 $[M(^{37}Cl) + H]^+$, 309 $[M(^{35}Cl) + H]^+$. HR-MS (ESI) *m/z* calcd for $C_{16}H_{18}ClO_4$: 309.0894 $[M + H]^+$; found: 309.0887. Anal. calcd for $C_{16}H_{17}ClO_4$: C 62.24, H 5.55; found: C 62.18, H 5.43.

***(E)-6-(4-(4-Fluorophenyl)-4-hydroxybut-1-enyl)-2,2-dimethyl-4H-1,3-dioxin-4-one* (15d)**

According to general procedure A, reaction of alcohol **14d** (166 mg, 1 mmol) and dioxinone **10** (308 mg, 2 mmol) with catalyst **12** (63 mg, 0.1 mmol) for 18 h and chromatography (hexanes–Et_2O, 3:2 to 2:3) gave dioxinone **15d** (244 mg, 84%) as a brown gum. IR (thin film, cm^{-1}): 3429, 1701, 1650, 1603, 1508, 1390, 1375, 1274, 1202, 1156, 1018, 835. ^1H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.35–7.30 (m, 2H), 7.08–7.03 (m, 2H), 6.56 (dt, J = 15.2, 7.8 Hz, 1H), 5.98 (d, J = 15.6 Hz, 1H), 5.25 (s, 1H), 4.83 (dd, J = 7.8, 4.9 Hz, 1H), 2.70–2.55 (m, 2H), 2.21 (br s, 1H), 1.70 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 162.8, 162.0, 162.3 (d, J = 245.7 Hz), 139.3, 137.5, 127.3 (d, J = 8 Hz), 125.2, 115.4 (d, J = 22.5 Hz), 106.4, 94.0, 72.6, 42.4, 25.0. MS (ESI) *m/z*: 293 $[M + H]^+$. HR-MS (ESI) *m/z* calcd for $C_{16}H_{18}FO_4$: 293.1189 $[M + H]^+$; found: 293.1177. Anal. calcd for $C_{16}H_{17}FO_4$: C 65.74, H 5.86; found: C 65.90, H 5.90.

***(E)-6-(4-Hydroxy-4-(4-methoxyphenyl)but-1-enyl)-2,2-dimethyl-4H-1,3-dioxin-4-one* (15e)**

According to general procedure A, reaction of alcohol **14e** (120 mg, 0.67 mmol) and dioxinone **10** (156 mg, 1.01 mmol) with catalyst **12** (21 mg, 0.034 mmol) for 18 h and chromatography (hexanes–Et_2O, 3:2 to 2:3) gave dioxinone **15e** (158 mg, 78%) as a brown oil. IR (thin film, cm^{-1}): 3424, 1702, 1650, 1512, 1389, 1374, 1245, 1018, 831. ^1H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.30–7.27 (m, 2H), 6.92–6.89 (m, 2H), 6.59 (dt, J = 15.7, 7.8 Hz, 1H), 5.99 (d, J = 15.6 Hz, 1H), 5.26 (s, 1H), 4.79 (dd, J = 7.8, 4.9 Hz, 1H), 3.82 (s, 3H), 2.73–2.54 (m, 2H), 1.90 (br s, 1H), 1.71 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 162.9, 162.0, 159.3, 138.0, 135.6, 126.9, 125.0, 114.0, 106.4, 93.9, 73.0, 55.3, 42.3, 25.0. MS (ESI) *m/z*: 305 $[M + H]^+$. HR-MS (ESI) *m/z* calcd for $C_{17}H_{21}O_5$: 305.1389 $[M + H]^+$; found: 305.1382. Anal. calcd for $C_{17}H_{20}O_5$: C 67.09, H 6.62; found: C 66.96, H 6.55.

***(E)-6-(4-(Furan-2-yl)-4-hydroxybut-1-enyl)-2,2-dimethyl-4H-1,3-dioxin-4-one* (15f)**

According to general procedure A, reaction of alcohol **14f** (138 mg, 1 mmol) and dioxinone **10** (308 mg, 2 mmol) with catalyst **12** (63 mg, 0.1 mmol) for 18 h and chromatography (hexanes–Et_2O, 3:2 to 1:1) gave dioxinone **15f** (228 mg, 86%) as a brown gum. IR (thin film, cm^{-1}): 3400, 1689, 1654, 1590, 1379, 1280, 1197, 1017, 1003, 973, 728, 596. ^1H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.41–7.38 (m, 1H), 6.58 (dt, J = 16.1, 7.8 Hz, 1H), 6.36 (dd, J = 2.9, 2.0 Hz, 1H), 6.27 (d, J = 3.4 Hz, 1H), 6.02 (d, J = 15.6 Hz, 1H), 5.27 (s, 1H), 4.89–4.80 (m, 1H), 2.80–2.72 (m, 2H), 2.19 (d, J = 4.4 Hz, 1H), 1.70 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 162.8, 162.0, 155.5, 142.2, 137.0, 125.2, 110.3, 106.4, 106.3, 94.0, 66.6, 38.8, 25.0. MS (ESI) *m/z*: 265 $[M + H]^+$. HR-MS (ESI) *m/z* calcd for $C_{14}H_{17}O_5$: 265.1076 $[M + H]^+$; found: 265.1075. Anal. calcd for $C_{14}H_{16}O_5$: C 63.63, H 6.10; found: C 63.53, H 6.05.

***(E)-6-(4-Hydroxypent-1-enyl)-2,2-dimethyl-4H-1,3-dioxin-4-one* (15g)**

According to general procedure A, reaction of alcohol **14g** (103 μL, 1.00 mmol) and dioxinone **10** (308 mg, 2.00 mmol) with catalyst **12** (63 mg, 0.10 mmol) for 18 h and chromatography (pentane–Et_2O, 55:45 to 1:3) gave dioxinone **15g** (173 mg, 82%) as a brown oil. IR (thin film, cm^{-1}): 3435, 1702, 1650, 1590, 1389, 1374, 1273, 1253, 1201, 1123, 1017, 971, 903, 816, 796, 603. ^1H NMR (400 MHz, $CDCl_3$, ppm) δ: 6.60 (dt, J = 15.4, 7.5 Hz, 1H), 6.01 (dt, J = 15.6, 1.0 Hz, 1H), 5.28 (s, 1H), 3.99 (m, 1H), 2.35–2.42 (m, 2H), 1.72–1.75 (m, 7H), 1.26 (d, J = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 163.0, 162.1, 138.2, 124.9, 106.4, 93.8, 67.0, 42.3, 25.1, 25.0, 23.4. MS (ESI) *m/z*: 213 $[M + H]^+$. HR-MS (ESI) *m/z* calcd for $C_{11}H_{17}O_4$: 213.1127 $[M + H]^+$; found: 213.1123. Anal. calcd for $C_{11}H_{16}O_4$: C 62.25, H 7.60; found: C 62.12, H 7.48.

***(E)-6-(4-Hydroxyhex-1-enyl)-2,2-dimethyl-4H-1,3-dioxin-4-one* (15h)**

According to general procedure A, reaction of alcohol **14h** (300 mg, 3.00 mmol) and dioxinone **10** (693 mg, 4.80 mmol) with catalyst **12** (94 mg, 0.15 mmol) for 18 h and chromatography (hexanes–Et_2O, 1:1 to 2:3) gave dioxinone **15h** (372 mg, 55%) as a brown oil. IR (thin film, cm^{-1}): 3427,

1707, 1650, 1591, 1340, 1375, 1274, 1254, 1203, 1019, 971, 904, 801, 603. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 6.60 (dt, J = 15.4, 7.5 Hz, 1H), 5.99 (dt, J = 15.7, 1.5 Hz, 1H), 5.26 (s, 1H), 3.63–3.74 (m, 1H), 2.37–2.47 (m, 1H), 2.28–2.37 (m, 1H), 1.70 (s, 7H), 1.45–1.57 (m, 2H), 0.97 (t, J = 7.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 162.9, 162.0, 138.5, 124.7, 106.3, 93.7, 72.1, 40.1, 30.0, 25.0, 9.8. MS (ESI) *m/z*: 227 $[M + H]^+$. HR-MS (ESI) *m/z* calcd for $C_{12}H_{19}O_4$: 227.1283 $[M + H]^+$; found: 227.1283. Anal. calcd for $C_{12}H_{18}O_4$: C 63.70, H 8.02; found: C 63.75, H 8.13.

(E)-6-(4-Hydroxy-6-methylhept-1-enyl)-2,2-dimethyl-4H-1,3-dioxin-4-one (15i)

According to general procedure A, reaction of alcohol **14i** (128 mg, 1.00 mmol) and dioxinone **10** (308 mg, 2.00 mmol) with catalyst **12** (63 mg, 0.10 mmol) for 18 h and chromatography (hexanes–Et_2O, 55:45 to 45:55) gave dioxinone **15i** (185 mg, 73%) as a brown gum. IR (thin film, cm^{-1}): 3421, 1703,1650, 1590, 1389, 1374, 1273, 1253, 1202, 1017, 969, 903. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 6.63 (dt, J = 15.4, 7.5 Hz, 1H), 6.01 (dt, J = 15.6, 1.5 Hz, 1H), 5.28 (s, 1H), 3.81–3.91 (m, 1H), 2.38–2.48 (m, 1H), 2.26–2.37 (m, 1H), 1.77–1.84 (m, 1H), 1.73 (s, 6H), 1.65 (d, J = 4.4 Hz, 1H), 1.43–1.50 (m, 1H), 1.24–1.32 (m, 1H), 0.93–0.97 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 163.0, 162.0, 138.5, 124.9, 106.4, 93.8, 68.8, 46.5, 41.2, 25.1, 25.0, 24.6, 23.4, 22.0. MS (ESI) *m/z*: 277 $[M + Na]^+$, 255 $[M + H]^+$. Anal. calcd for $C_{14}H_{22}O_4$: C 66.12, H 8.72; found: C 66.10, H 8.65.

(E)-6-(4-Hydroxy-4-mesitylbut-1-enyl)-2,2-dimethyl-4H-1,3-dioxin-4-one (15j)

According to general procedure A, reaction of alcohol **14j** (350 mg, 1.84 mmol) and dioxinone **10** (426 mg, 2.76 mmol) with catalyst **12** (58 mg, 0.09 mmol) for 16 h and chromatography (hexanes–Et_2O, 4:1 to 1:1) gave dioxinone **15j** (377 mg, 65%) as a brown gum. IR (thin film, cm^{-1}): 3442, 2951, 1702, 1650, 1591, 1389, 1373, 1273, 1202, 1017, 967, 851, 801. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 6.84 (s, 2H), 6.64 (dt, J = 15.7, 7.8 Hz, 1H), 6.02 (d, J = 15.6 Hz, 1H), 5.29–5.22 (m, 2H), 2.97–2.85 (m, 1H), 2.63–2.49 (m, 1H), 2.41 (s, 6H), 2.26 (s, 3H), 2.00 (d, J = 2.4 Hz, 1H), 1.71 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 163.0, 162.0, 138.8, 137.0, 135.8, 135.6, 130.3, 124.6, 106.3, 93.8, 70.5, 39.0, 25.0, 24.9, 20.7. MS (ESI) *m/z*: 317 $[M + H]^+$. HR-MS (ESI) *m/z* calcd for $C_{19}H_{25}O_4$: 317.1753 $[M + H]^+$; found: 317.1753. Anal. calcd for $C_{19}H_{24}O_4$: C 72.13, H 7.65; found: C 71.97, H 7.59.

(E)-2,2-Dimethyl-6-(4-oxo-4-phenylbut-1-enyl)-4H-1,3-dioxin-4-one (16a)

According to general procedure B, oxidation of dioxinone **15a** (329 mg, 1.21 mmol) for 3.5 h and chromatography (hexanes–Et_2O, 7:3 to 1:1) gave enone–dioxinone **16a** (255 mg, 77%) as a yellow solid; mp 58–61 °C (Et_2O–pentane). IR (thin film, cm^{-1}): 1714, 1687, 1655, 1597, 1392, 1369, 1278, 1204, 1019, 991, 905, 816. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.04–7.91 (m, 2H), 7.74–7.56 (m, 1H), 7.56–7.36 (m, 2H), 6.85 (dt, J = 15.7, 7.1 Hz, 1H), 6.08 (d, J = 15.6 Hz, 1H), 5.31 (s, 1H), 3.93 (dd, J = 7.1, 1.2 Hz, 2H), 1.73 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 196.3, 162.4, 161.6, 136.2, 133.7, 133.7, 128.8, 128.2, 125.7, 106.6, 94.6, 41.7, 25.0. MS (ESI) *m/z*: 273 $[M + H]^+$. HR-MS (EI) *m/z* calcd for $C_{16}H_{17}O_4$: 273.1127 $[M + H]^+$; found: 273.1121. Anal. calcd for $C_{16}H_{16}O_4$: C 70.58, H 5.92; found: C 70.53, H 5.85.

(E)-6-(4-(4-Bromophenyl)-4-oxobut-1-enyl)-2,2-dimethyl-4H-1,3-dioxin-4-one (16b)

According to general procedure B, oxidation of dioxinone **15b** (23 mg, 0.065 mmol) for 2 h and chromatography (hexanes–Et_2O, 1:1) gave enone–dioxinone **16b** (19 mg, 83%) as a yellow solid; mp 68–72 °C (Et_2O–pentane). IR (thin film, cm^{-1}): 1713, 1693, 1659, 1586, 1391, 1374, 1273, 1199, 1011, 991, 970, 800. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.85–7.80 (m, 2H), 7.67–7.62 (m, 2H), 6.81 (dt, J = 15.5, 6.9 Hz, 1H), 6.07 (d, J = 15.6 Hz, 1H), 5.30 (s, 1H), 3.89 (dd, J = 7.1, 1.2 Hz, 2H), 1.72 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 187.9, 160.9, 141.9, 134.9, 133.5, 132.2, 132.0, 130.2, 129.1, 128.1, 128.0, 107.2, 100.8, 25.1. MS (CI) *m/z*: 370 $[M(^{81}Br) + H_2O]^+$, 368 $[M (^{79}Br) + H_2O]^+$. Anal. calcd for $C_{16}H_{15}BrO_4$: C 54.72, H 4.31; found: C 54.63, H 4.21.

(E)-6-(4-(4-Chlorophenyl)-4-oxobut-1-enyl)-2,2-dimethyl-4H-1,3-dioxin-4-one (16c)

According to general procedure B, oxidation of dioxinone **15c** (82 mg, 0.266 mmol) for 2 h and chromatography (hexanes–Et_2O, 7:3 to 1:1) gave enone–dioxinone **16c** (63 mg, 77%) as an orange oil. IR (thin film, cm^{-1}): 1711, 1689, 1587, 1376, 1391, 1270, 1200, 1089, 1022, 985, 839, 784. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.93–7.88 (m, 2H), 7.50–7.45 (m, 2H), 6.81 (dt, J = 15.7, 7.1 Hz, 1H), 6.07 (dt, J = 15.7, 1.5 Hz, 1H), 5.31 (s, 1H), 3.90 (dd, J = 6.8, 1.5 Hz, 2H), 1.72 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 195.0, 162.3, 161.7, 140.2, 134.4, 133.2, 129.6, 129.2, 125.9, 106.6, 94.7, 41.6, 25.0. MS (ESI) *m/z*: 309 $[M(^{37}Cl) + H]^+$, 307 $[M(^{35}Cl) + H]^+$. HR-MS (ESI) *m/z* calcd for $C_{16}H_{16}ClO_4$: 307.0737 $[M + H]^+$; found: 307.0732. Anal. calcd for $C_{16}H_{15}ClO_4$: C 62.65, H 4.93; found: C 62.77, H 4.84.

(E)-6-(4-(4-Fluorophenyl)-4-oxobut-1-enyl)-2,2-dimethyl-4H-1,3-dioxin-4-one (16d)

According to general procedure B, oxidation of dioxinone **15d** (226 mg, 0.774 mmol) for 3 h and chromatography (hexanes–Et_2O, 7:3 to 1:1) gave enone–dioxinone **16d** (143 mg, 67%) as an orange oil. IR (thin film, cm^{-1}): 1710, 1692, 1597, 1379, 1275, 1200, 1158, 1021, 846, 793. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 8.02–7.97 (m, 2H), 7.20–7.14 (m, 2H), 6.82 (dt, J = 15.5, 6.9 Hz, 1H), 6.07 (d, J = 16.1 Hz, 1H), 5.30 (s, 1H), 3.90 (dd, J = 1.2, 7.1 Hz, 2H), 1.72 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 194.7, 167.3, 163.5 (d, J = 239.3 Hz), 161.7, 133.4, 132.5, 130.9 (d, J = 9.6 Hz), 125.8, 116.0 (d, J = 20.9 Hz), 106.6, 94.6, 41.6, 25.0. HR-MS (CI) *m/z* calcd for $C_{16}H_{19}NO_4F$: 308.1298 $[M + NH_4]^+$; found: 308.1301. Anal. calcd for $C_{16}H_{15}FO_4$: C 66.20, H 5.21; found: C 66.15, H 5.14.

(E)-6-(4-(4-Methoxyphenyl)-4-oxobut-1-enyl)-2,2-dimethyl-4H-1,3-dioxin-4-one (16e)

According to general procedure B, oxidation of dioxinone **15e** (150 mg, 0.493 mmol) for 0.75 h and chromatography (hexanes–Et_2O, 7:3 to 3.5:10) gave enone–dioxinone **16e** (98 mg, 66%) as a yellow solid; mp 89–92 °C (Et_2O–pentane). IR (thin film, cm^{-1}): 1710, 1674, 1655, 1573, 1374, 1255, 1204, 1182, 1020, 984, 967, 844, 790, 597. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.97–7.92 (m, 2H), 6.99–6.94 (m,

2H), 6.84 (dt, J = 15.4, 7.0 Hz, 1H), 6.06 (d, J = 15.7 Hz, 1H), 5.30 (s, 1H), 3.89 (s, 3H), 3.87 (dd, J = 7.3, 1.5 Hz, 2H), 1.72 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 194.8, 163.9, 162.5, 161.8, 134.3, 130.6, 129.2, 125.5, 114.0, 106.5, 94.4, 55.5, 41.5, 25.0. MS (ESI) *m/z*: 303 $[M + H]^+$. HR-MS (ESI) *m/z* calcd for $C_{17}H_{19}O_5$: 303.1232 $[M + H]^+$; found: 303.1226. Anal. calcd for $C_{17}H_{18}O_5$: C 67.54, H 6.00; found: C 67.43, H 6.05.

***(E)-6-(4-(Furan-2-yl)-4-oxobut-1-enyl)-2,2-dimethyl-4H-1,3-dioxin-4-one* (16f)**

According to general procedure B, oxidation of dioxinone **15f** (94 mg, 0.356 mmol) for 2 h and chromatography (hexanes–Et_2O, 7:3 to 1:1) gave enone–dioxinone **16f** (35 mg, 38%) as a yellow oil. IR (thin film, cm^{-1}): 1721, 1675, 1655, 1466, 1392, 1376, 1275, 1204, 1019. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.63 (d, J = 1.0 Hz, 1H), 7.28–7.25 (m, 1H), 6.76 (dt, J = 15.6, 7.3 Hz, 1H), 6.58 (dd, J = 3.4, 1.5 Hz, 1H), 6.12–6.04 (m, 1H), 5.30 (s, 1H), 3.78 (dd, J = 7.3, 1.5 Hz, 2H), 1.71 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 185.1, 162.4, 161.8, 152.0, 146.9, 132.9, 125.9, 117.9, 112.6, 106.6, 94.6, 41.6, 25.0. MS (ESI) *m/z*: 263 $[M + H]^+$. HR-MS (ESI) *m/z* calcd for $C_{14}H_{15}O_5$: 263.0919 [M + H]; found: 263.0912. Anal. calcd for $C_{14}H_{14}O_5$: C 64.12, H 5.38; found: C 60.65, H 5.34.

***(E)-2,2-Dimethyl-6-(4-oxopent-1-enyl)-4H-1,3-dioxin-4-one* (16g)**

According to general procedure B, oxidation of dioxinone **15g** (145 mg, 0.684 mmol) for 1.25 h and chromatography (pentane–Et_2O, 1:1 to 2:3) gave enone–dioxinone **16g** (78 mg, 54%) as a yellow oil. IR (thin film, cm^{-1}): 1711, 1654, 1593, 1390, 1274, 1273, 1251, 1200, 1158, 1016, 968, 903, 859, 808. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 6.67 (dt, J = 15.7, 7.3 Hz, 1H), 6.00 (dt, J = 15.6, 1.5 Hz, 1H), 5.32 (s, 1H), 3.39 (dd, J = 7.3, 1.0 Hz, 2H), 2.24 (s, 3H), 1.74 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 204.5, 162.4, 161.8, 132.9, 125.8, 106.6, 94.7, 46.7, 30.1, 25.0. MS (ESI) *m/z*: 233 $[M + Na]^+$, 211 $[M + H]^+$. HR-MS (ESI) *m/z* calcd for $C_{11}H_{15}O_4$: 211.0965 $[M + H]^+$; found: 211.0966.

***(E)-2,2-Dimethyl-6-(4-oxohex-1-enyl)-4H-1,3-dioxin-4-one* (16h)**

According to general procedure B, oxidation of dioxinone **15h** (60 mg, 0.265 mmol) for 0.75 h and chromatography (hexanes–Et_2O, 1:1) gave enone–dioxinone **16h** (47 mg, 79%) as a yellow oil. IR (thin film, cm^{-1}): 1711, 1630, 1586, 1460, 1391, 1376, 1276, 1252, 1200, 1096, 1017, 973, 903, 812. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 6.66 (dt, J = 15.6, 6.8 Hz, 1H), 5.98 (dt, J = 15.7, 1.5 Hz, 1H), 5.29 (s, 1H), 3.34 (dd, J = 7.3, 1.5 Hz, 2H), 2.50 (q, J = 7.3 Hz, 2H), 1.71 (s, 6H), 1.08 (t, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 207.3, 162.4, 161.7, 133.3, 125.6, 106.5, 94.5, 45.5, 36.1, 25.0, 7.6. MS (ESI) *m/z*: 247 $[M + Na]^+$, 225 $[M + H]^+$.

***(E)-2,2-Dimethyl-6-(6-methyl-4-oxohept-1-enyl)-4H-1,3-dioxin-4-one* (16i)**

According to general procedure B, oxidation dioxinone **15i** (151 mg, 0.594 mmol) for 1.25 h and chromatography (pentane–Et_2O, 7:3 to 1:1) gave enone–dioxinone **16i** (101 mg, 67%) as a yellow oil. IR (thin film, cm^{-1}): 1707, 1655, 1594, 1451, 1392, 1373, 1277, 1204, 1105, 1019, 979, 906, 864, 849, 812. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 6.68 (dt, J = 15.7, 7.3 Hz, 1H), 6.00 (dt, J = 15.7, 1.5 Hz, 1H), 5.31 (s, 1H), 3.34 (dd, J = 7.3, 1.0 Hz, 2H), 2.37 (d, J = 7.3 Hz, 2H), 2.10–2.25 (m, 1H), 1.74 (s, 6H), 0.96 (d, J = 6.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 206.6, 162.4, 161.8, 133.3, 125.6, 106.5, 94.5, 51.9, 46.3, 25.0, 24.5, 22.5. MS (ESI) *m/z*: 275 $[M + Na]^+$, 253 $[M + H]^+$. Anal. calcd for $C_{14}H_{20}O_4$: C 66.65, H 7.99; found: C 66.74, H 7.90.

***(E)-6-(4-Mesityl-4-oxobut-1-enyl)-2,2-dimethyl-4H-1,3-dioxin-4-one* (16j)**

2-Iodoxybenzoic acid (842 mg, 2.94 mmol) was added with stirring to dioxinone **15j** (310 mg, 0.981 mmol) in EtOAc (7 mL) open to the air at 80 °C for 2 h. The mixture was filtered through Celite and rotary evaporated. Chromatography (hexanes–Et_2O, 4:1 to 1:1) of the residue gave enone–dioxinone **16j** as a 2:1 mixture of the β,δ-enone: α,β-enone (207 mg, 67%) as a yellow oil. IR (thin film, cm^{-1}): 1713, 1698, 1603, 1373, 1268, 1200, 1148, 1017, 978, 852, 802, 602. β,δ-Enone: ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 6.87 (s, 2H), 6.78 (dt, J = 15.6, 7.8 Hz, 1H), 6.04 (d, J = 15.7 Hz, 1H), 5.31 (s, 1H), 3.63 (dd, J = 7.1, 1.2 Hz, 2H), 2.30 (s, 3H), 2.21 (s, 6H), 1.73 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 206.5, 162.4, 161.8, 138.7, 133.8, 132.8, 132.5, 128.6, 125.8, 106.6, 94.7, 47.8, 25.0, 21.1, 19.2. α,β-Enone: ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 6.87 (s, 2H), 6.47–6.29 (m, 2H), 5.22 (s, 1H), 3.16 (d, J = 6.4 Hz, 2H), 2.30 (s, 3H) 2.14 (s, 6H), 1.66 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 206.5, 162.4, 161.8, 141.6, 138.7, 136.1, 133.8, 132.5, 128.4, 106.6, 94.5, 36.3 25.0, 21.1, 19.2. MS (CI) *m/z*: 332 $[M + H_2O]^+$, 315 $[M + H]^+$. Anal. calcd for $C_{19}H_{22}O_4$: C 72.59, H 7.05; found: C 72.44, H 6.95.

***Isopropyl 3-hydroxybiphenyl-2-carboxylate* (17a)**

According to general procedure C, aromatization of enone–dioxinone **16a** (50 mg, 0.184 mmol) and chromatography (hexanes–Et_2O, 100:0 to 19:1) gave salicylate **17a** (26 mg, 55%) as a colorless solid; mp 53–55 °C (Et_2O–pentane). IR (thin film, cm^{-1}): 1650, 1606, 1597, 1441, 1370, 1278, 1225, 1178, 1097, 922, 897, 814. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 10.96 (s, 1H), 7.48–7.30 (m, 4H), 7.30–7.12 (m, 2H), 7.01 (dd, J = 8.3, 1.0 Hz, 1H), 6.78 (dd, J = 7.3, 1.0 Hz, 1H), 5.05–4.85 (m, 1H), 0.86 (d, J = 6.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 170.4, 161.5, 145.0, 143.2, 133.3, 128.3, 127.6, 126.6, 122.4, 116.6, 112.6, 69.1, 20.9. HR-MS (EI) *m/z* calcd for $C_{16}H_{17}O_3$: 257.1178 $[M + H]^+$; found: 257.1168. Anal. calcd for $C_{16}H_{16}O_3$: C 74.98, H 6.29; found: C 74.90, H 6.37.

***Isopropyl 4′-bromo-3-hydroxybiphenyl-2-carboxylate* (17b)**

According to general procedure C, aromatization of enone–dioxinone **16b** (100 mg, 0.29 mmol) and chromatography (hexanes–Et_2O, 100:0 to 9:1) gave salicylate **17b** (43 mg, 45%) as a colorless solid; mp 79–83 °C (Et_2O–pentane). IR (thin film, cm^{-1}): 1663, 1600, 1575, 1492, 1444, 1363, 1314, 1273, 1209, 1173, 1100, 1066, 918, 807. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 11.04 (s, 1H), 7.54–7.46 (m, 2H), 7.40 (t, J = 8.1 Hz, 1H), 7.14–7.06 (m, 2H), 7.02 (dd, J = 8.3, 1.0 Hz, 1H), 6.73 (dd, J = 7.3, 1.0 Hz, 1H), 4.98 (spt, J = 6.2 Hz, 1H), 0.91 (d, J = 6.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 170.1, 161.8, 143.6, 142.2, 133.5, 130.6, 130.0, 122.2, 120.7, 117.1, 112.2, 69.5, 21.0. MS (CI) *m/z*: 354 $[M(^{81}Br) + H_2O]^+$, 352 $[M(^{79}Br) + H_2O]^+$, 337 $[M(^{81}Br) + H]^+$, 335

[M(^{79}Br) + H]$^+$. HR-MS (CI) *m/z* calcd for $C_{16}H_{16}BrO_3$: 335.0283 [M + H]$^+$; found: 335.0274. Anal. calcd for $C_{16}H_{15}BrO_3$: C 57.33, H 4.51; found: C 57.25, H 4.56.

***Isopropyl 4′-chloro-3-hydroxybiphenyl-2-carboxylate* (17c)**

According to general procedure C, aromatization of enone-dioxinone **16c** (69 mg, 0.23 mmol) and chromatography (hexanes–Et_2O, 100:0 to 97:3) gave salicylate **17c** (32 mg, 49%) as a colorless solid; mp 73–76 °C ($CHCl_3$). IR (thin film, cm^{-1}): 1665, 1601, 1576, 1492, 1444, 1363, 1314, 1272, 1172, 1101, 807. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 11.04 (s, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.37–7.30 (m, 2H), 7.20–7.12 (m, 2H), 7.02 (dd, *J* = 8.6, 1.2 Hz, 1H), 6.73 (dd, *J* = 7.6, 1.2 Hz, 1H), 4.98 (spt, *J* = 6.3 Hz, 1H), 0.91 (d, *J* = 6.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 170.1, 161.8, 143.6, 141.7, 133.5, 132.7, 129.6, 127.7, 122.3, 117.1, 112.3, 69.4, 21.0. MS (CI) *m/z*: 310 [M(^{37}Cl) + H_2O]$^+$, 308 [M(^{35}Cl) + H_2O]$^+$, 293 [M(^{37}Cl) + H]$^+$, 291 [M(^{35}Cl) + H]$^+$. HR-MS (CI) *m/z* calcd for $C_{16}H_{16}ClO_3$: 291.0788 [M + H]$^+$; found: 291.0786. Anal. calcd for $C_{16}H_{15}ClO_3$: C 66.10, H 5.20; found: C 65.98, H 5.24.

***Isopropyl 4′-fluoro-3-hydroxybiphenyl-2-carboxylate* (17d)**

According to general procedure C, aromatization of enone–dioxinone **16d** (35 mg, 0.21 mmol) and chromatography (hexanes–Et_2O, 19:1) gave salicylate **17d** (17 mg, 51%) as a colorless solid; mp 85–87 °C (Et_2O–pentane). IR (thin film, cm^{-1}): 1650, 1606, 1513, 1445, 1367, 1280, 1227, 1213, 1177, 1093, 842, 815. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 11.01 (s, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.22–7.16 (m, 2H), 7.10–7.03 (m, 2H), 7.01 (dd, *J* = 8.3, 1.5 Hz, 1H), 6.74 (dd, *J* = 7.6, 1.2 Hz, 1H), 4.98 (spt, *J* = 6.3 Hz, 1H), 0.91 (d, *J* = 6.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 170.3, 161.7, 143.8, 139.2 133.4, 129.8, 122.5, 116.9, 114.5, 114.3, 112.5, 69.3, 21.0. MS (CI) *m/z*: 275 [M + H]$^+$. HR-MS (CI) *m/z* calcd for $C_{16}H_{16}FO_3$: 275.1083 [M + H]$^+$; found: 275.1081. Anal. calcd for $C_{16}H_{15}FO_3$: C 70.06, H 5.51; found: C 70.00, H 5.60.

***Isopropyl 3-hydroxy-4′-methoxybiphenyl-2-carboxylate* (17e)**

According to general procedure C, aromatization of enone–dioxinone **16e** (37 mg, 0.12 mmol) and chromatography (hexanes–Et_2O, 100:0 to 19:1) gave salicylate **17e** (17 mg, 48%) as a yellow solid; mp 42–45 °C (Et_2O). IR (thin film, cm^{-1}): 1655, 1602, 1515, 1446, 1369, 1271, 1243, 1218, 1175, 1094, 1034, 807. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 10.86 (s, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.18–7.11 (m, 2H), 6.98 (dd, *J* = 8.3, 1.0 Hz, 1H), 6.94–6.87 (m, 2H), 6.77 (dd, *J* = 7.3, 1.0 Hz, 1H), 4.97 (spt, *J* = 6.3 Hz, 1H), 3.86 (s, 3H), 0.91 (d, *J* = 6.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 170.5, 161.4, 158.7, 144.6, 135.7, 133.3, 129.4, 122.6, 116.3, 113.0, 112.8, 69.1, 55.4, 21.1. MS (CI) *m/z*: 304 [M + H_2O]$^+$, 287 [M + H]$^+$. HR-MS (CI) *m/z* calcd for $C_{17}H_{19}O_4$: 287.1283 [M + H]$^+$; found: 287.1275. Anal. calcd for $C_{17}H_{18}O_4$: C 71.31, H 6.34; found: C 68.02, H 6.55.

***Isopropyl 2-(furan-2-yl)-6-hydroxybenzoate* (17f)**

According to general procedure C, aromatization of enone–dioxinone **16f** (30 mg, 0.12 mmol) and chromatography (hexanes–Et_2O, 100:0 to 19:1) gave salicylate **17f** (13 mg, 46%) as a colorless oil. IR (thin film, cm^{-1}): 1664, 1606, 1572, 1453, 1374, 1275, 1222, 1178, 1103. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 10.67 (s, 1H), 7.47 (d, *J* = 1.0 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.03 (dd, *J* = 8.3, 1.0 Hz, 1H), 6.95 (dd, *J* = 7.3, 1.0 Hz, 1H), 6.47 (dd, *J* = 3.4, 2.0 Hz, 1H), 6.40 (d, *J* = 2.9 Hz, 1H), 5.13 (spt, *J* = 6.3 Hz, 1H), 1.12 (d, *J* = 6.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 170.0, 161.2, 154.2, 141.7, 133.5, 132.8, 122.3, 118.0, 112.7, 111.1, 107.1, 69.3, 21.5. MS (CI) *m/z*: 247 [M + H]$^+$. HR-MS (CI) *m/z* calcd for $C_{14}H_{15}O_4$: 247.0970 [M + H]$^+$; found: 247.0972.

***Isopropyl 2-hydroxy-6-methylbenzoate* (17g)**

According to general procedure C, aromatization of enone–dioxinone **16g** (73 mg, 0.348 mmol) and chromatography (pentane–Et_2O, 100:0 to 98:2) gave salicylate **17g** (45 mg, 67%) as a colorless oil. IR (thin film, cm^{-1}): 1727, 1650, 1606, 1580, 1459, 1439, 1365, 1291, 1251, 1212, 1165, 1100, 1078, 1034, 965, 911, 863, 806, 756, 702. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 11.43 (s, 1H), 7.27 (t, *J* = 7.8 Hz, 1H), 6.84 (d, *J* = 8.3 Hz, 1H), 6.71 (d, *J* = 7.3 Hz, 1H), 5.34 (spt, *J* = 6.2 Hz, 1H), 2.56 (s, 3H), 1.43 (d, *J* = 6.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 171.2, 162.8, 141.3, 133.9, 122.9, 115.6, 112.7, 69.7, 24.2, 22.0. MS (ESI) *m/z*: 212 [M + H_2O]$^+$, 195 [M + H]$^+$. Anal. calcd for $C_{11}H_{14}O_3$: C 68.02, H 7.27; found: C 67.87, H 7.21.

***Isopropyl 2-hydroxy-6-ethylbenzoate* (17h)**

According to general procedure C, aromatization of enone-dioxinone **16h** (76 mg, 0.339 mmol) and chromatography (pentane–Et_2O, 100:0 to 19:1) gave salicylate **17h** (41 mg, 58%) as a colorless oil. IR (thin film, cm^{-1}): 1727, 1654, 1606, 1577, 1447, 1363, 1308, 1295, 1245, 1207, 1167, 1102, 931, 908, 816. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 11.33 (s, 1H), 7.30 (t, *J* = 8.1 Hz, 1H), 6.85 (dd, *J* = 8.3, 1.5 Hz, 1H), 6.74 (d, *J* = 7.3 Hz, 1H), 5.36 (spt, *J* = 6.3 Hz, 1H), 2.96 (q, *J* = 7.3 Hz, 2H), 1.43 (d, *J* = 6.4 Hz, 6H), 1.23 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 171.0, 162.6, 147.4, 134.1, 121.7, 115.6, 112.2, 69.7, 29.6, 21.8, 16.5. MS (ESI) *m/z*: 231 [M + Na]$^+$, 209 [M + H]$^+$. Anal. calcd for $C_{12}H_{16}O_3$: C 69.21, H 7.74; found: C 69.18, H 7.64.

***Isopropyl 2-hydroxy-6-isobutylbenzoate* (17i)**

According to general procedure C, aromatization of enone–dioxinone **16i** (78 mg, 0.310 mmol) and chromatography (pentane–Et_2O, 100:0 to 19:1) gave salicylate **17i** (31 mg, 45%) as a colorless oil. IR (thin film, cm^{-1}): 1651, 1606, 1577, 1478, 1363, 1308, 1294, 1250, 1229, 1202, 1164, 1097, 1062, 911, 833, 803, 763, 709. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 11.35 (s, 1H), 7.28 (t, *J* = 7.8 Hz, 1H), 6.86 (dd, *J* = 8.3, 1.5 Hz, 1H), 6.66 (dd, *J* = 7.6, 1.2 Hz, 1H), 5.37 (spt, *J* = 6.3 Hz, 1H), 2.82 (d, *J* = 7.3 Hz, 2H), 1.76–1.91 (m, 1H), 1.43 (d, *J* = 6.4 Hz, 6H), 0.89 (d, *J* = 6.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, ppm) δ: 171.2, 162.8, 144.5, 133.5, 123.7, 115.8, 112.5, 69.6, 45.5, 30.0, 22.5, 21.8. MS (ESI) *m/z*: 259 [M + Na]$^+$, 237 [M + H]$^+$. Anal. calcd for $C_{14}H_{20}O_3$: C 71.16, H 8.53; found: C 71.08, H 8.45.

Supplementary data

Supplementary data are available with the article through the journal Web site http://nrcresearchpress.com/doi/suppl/10.1139/v2012-071.

Acknowledgements

We would like to thank GlaxoSmithKline for the generous endowment (to A.G.M.B.) and the Thorpe Bequest (Imperial

College) for studentship support (to P.S.B.). We also thank P.R. Haycock and R.N. Sheppard for NMR spectroscopy services and J. Barton for mass spectra.

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