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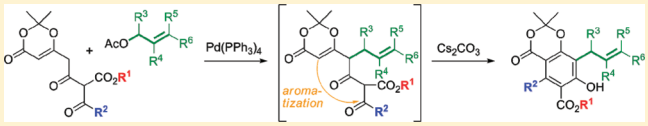
Palladium(0)-Catalyzed Allylic Alkylation of Diketoester−Dioxinones with Allyl Acetates under Neutral Conditions: Synthesis of Hexasubstituted Benzene Derivatives

Jens Cordes, Sylvain Laclef, Andrew J. P. White, and Anthony G. M. Barrett*

Department of Chemistry, Imperial College, London SW7 2AZ, England

Supporting Information

ABSTRACT: Intermolecular palladium(0)-catalyzed allylic alkylation of diketoester−dioxinones was performed under neutral conditions with 2-alkenyl and 2-cycloalkenyl acetates. Subsequent aromatization using cesium carbonate gave rise to isopropylidene-protected hexasubstituted resorcylates.



INTRODUCTION

The construction of new C−C bonds by palladium-catalyzed reactions of allylic compounds via the formation of π-allyl palladium complexes is a powerful synthetic method that is widely used in organic chemistry.[1] Soft carbon-centered nucleophiles[2] such as the carbanions derived from malonates and acetoacetates as well as enamines can react in such Tsuji−Trost reactions with Pd(0) complexes, which are accessible from various allylic precursors.

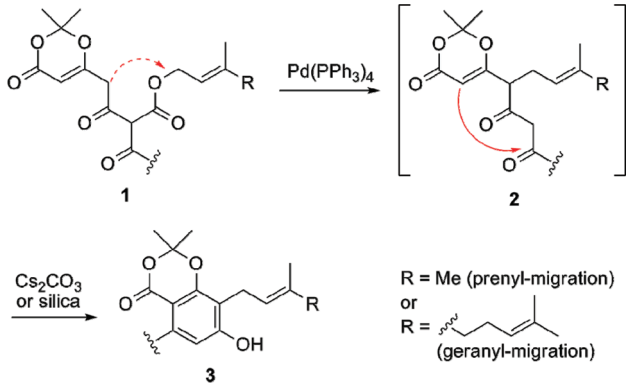
The reaction of allyl acetates, which are most widely used, usually requires a strong base in order to generate the required stabilized carbanion intermediates and to neutralize the acetic acid formed during the reaction. Generally, sodium hydride, alkali metal alkoxides, or hydroxides are used, and these may cause problems when base-labile functionalities are present. The first allylation of β-ketoesters using allylic acetates under neutral conditions was described by Giambastiani and Poli demonstrating that the acetate anion can deprotonate substrates of suitable pK_a.[3]

We recently reported palladium-catalyzed decarboxylative prenyl or geranyl migration and aromatization reactions (Scheme 1),[4] which were successfully employed in the total synthesis of the terpenoid resorcylates angelicoin A (**4**),[5,6] hericenone J (**5**),[6] hericenol A (**6**),[6] and amorfrutin A (**7**)[7] (Figure 1). Such resorcylate natural products display interesting biological activities, for example, as antitumor, antimicrobial, or immunosuppressant agents.[8]

Herein, we report an extension of this chemistry for the concise and practically simple synthesis of hexasubstituted resorcylates, which should be useful to generate novel diverse pharmacophores.

Such hexafunctionalized arenes are usually tedious to synthesize[9] via long sequences using transition-metal-mediated cyclizations of appropriately functionalized enynes[10] and Diels−Alder cycloadditions of furans.[11] We considered that hexasubstituted benzenes like **8** (Scheme 2) should be available from diketoester−dioxinone **10** via **9** by selective C-3 allylation using π-allyl palladium chemistry and in situ aromatization.[12] The diketoester−dioxinone **10** should be readily accessed by two sequential acylations of dioxinone **13** with acyl chlorides **12** and **14**.

Scheme 1. Palladium-Catalyzed Migratory Allylation and Aromatization Sequences[5−7]



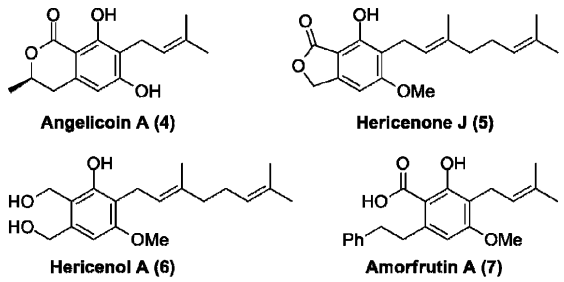


Figure 1. Resorcylate natural products that are accessible via the transformation of dioxinones **1** to resorcylates **3**.

RESULTS AND DISCUSSION

Deprotonation of dioxinone **13** with lithium hexamethyldisilazide and Claisen condensation reaction with the commercially

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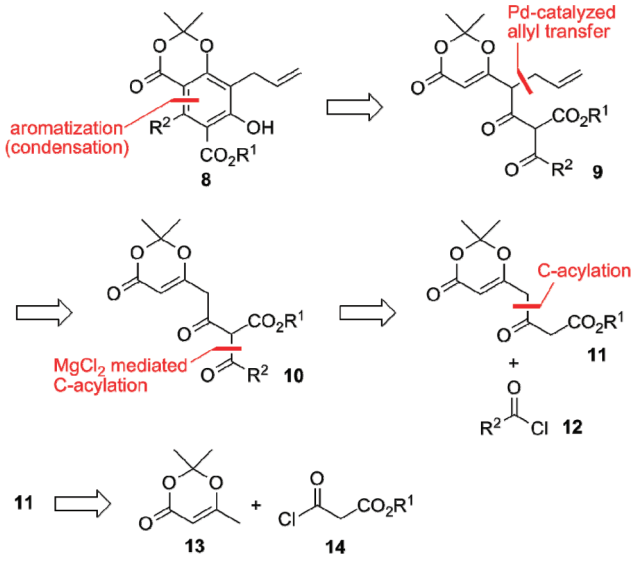
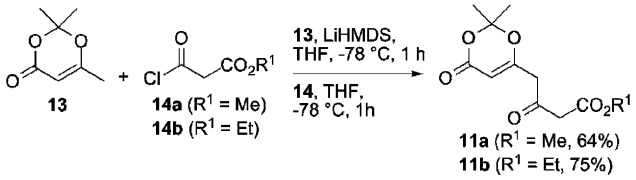
Scheme 2. Retrosynthetic Analysis of the Hexasubstituted Resorcylate 8



available acyl chlorides **14a** or **14b** gave ketoester–dioxinones **11a** and **11b** (64–75%, Scheme 3). Although only methyl and ethyl esters were prepared during this study, this reaction should be of general utility for various esters, as the necessary acid chlorides **14** can be prepared from the corresponding alcohol (R^1OH) and Meldrum's acid in two steps.[6]

Scheme 3. Synthesis of the β-Ketoesters 11a and 11b

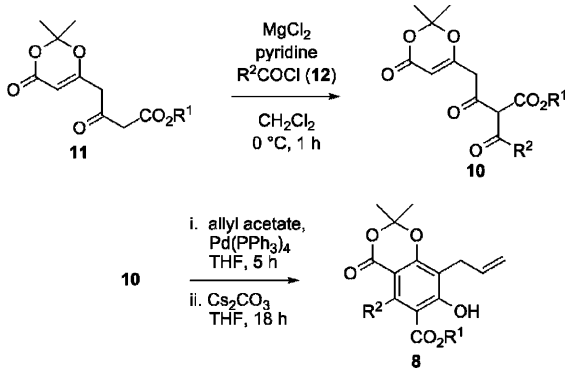


The second Claisen condensation reaction was carried out regioselectively in the presence of magnesium chloride and pyridine. By varying the acid chloride **12**, a series of eight different diketoesters **10a–h** was prepared from β-ketoesters **11a** and **11b** (42–80%, Table 1). The resultant diketoesters **10a–h** were subsequently allowed to react with allyl acetate catalyzed by $Pd(PPh_3)_4$ to afford the allyl-substituted diketoesters **9**, which were smoothly aromatized with cesium carbonate, providing the isopropylidene-protected resorcylates **8a–h** (Table 1). The regioselectivity of the allylation step was unambiguously proven in the case of **8c** (Table 1, entry 3) by a single-crystal X-ray structure determination.[13]

The best results were obtained by using initial Pd(0)-catalyzed allylation in the absence of base, indicating that substrates containing a diketoester–dioxinone unit are sufficiently acidic to be deprotonated by the acetate anion generated as part of the palladium catalytic cycle. After allylation, cesium carbonate was added to catalyze aromatization providing the corresponding isopropylidene-protected isophthalate esters **8**. For sterically hindered substituents on position R^2, the cyclization did not proceed upon addition of cesium carbonate but could be accomplished by subsequent reaction with silica (Table 1, entries 5 and 6). The yields for α-branched ketones (R^2 = isopropyl, cyclopropyl, phenyl, or furan-2-yl), however, were considerably lower (42–59%, Table 1, entries 5–8) than in the case of less substituted moieties like methyl, ethyl, and 2-phenethyl (83–90%, Table 1, entries 1–4).

The diketoester–dioxinones **10a–c** were also allowed to react with more functionalized 2-alkenyl and 2-cycloalkenyl

Table 1. Synthesis of Allyl-Substituted Resorcylates 8a–h



entry	keto-ester	R^1	R^2	diketo-ester	yield (%)[a]	allyl-phenol	yield (%)[a]
1	**11a**	Me	Me	**10a**	71	**8a**	84
2	**11b**	Et	Me	**10b**	76	**8b**	90
3	**11b**	Et	$Ph(CH_2)_2$	**10c**	78	**8c**	84
4	**11b**	Et	Et	**10d**	71	**8d**	83
5	**11b**	Et	^{i}Pr	**10e**	42	**8e**	43[b]
6	**11b**	Et		**10f**	80	**8f**	59[b]
7	**11b**	Et	Ph	**10g**	73	**8g**	53
8	**11a**	Me		**10h**	69	**8h**	42

[a]Isolated yield. [b]Silica was used for cyclization.

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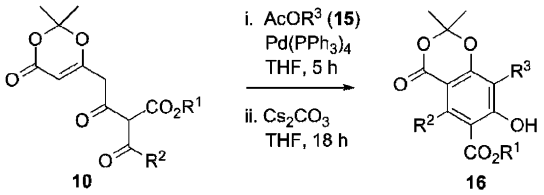
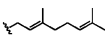
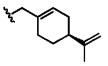
Table 2. Synthesis of Hexasubstituted Resorcylates 16a−o with Substituted Allyl Side Chains



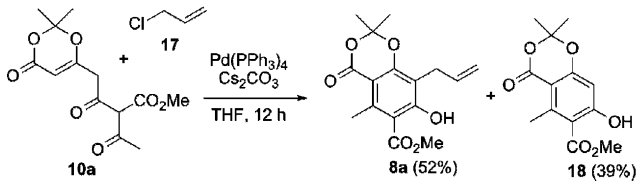
entry	diketo-ester	R^1	R^2	R^3	allyl-phenol	yield (%)[a]
1	**10a**	Me	Me		**16a**	63
2	**10b**	Et	Me		**16b**	76
3	**10c**	Et	$Ph(CH_2)_2$		**16c**	58
4	**10a**	Me	Me		**16d**	68
5	**10c**	Et	$Ph(CH_2)_2$		**16e**	62
6	**10a**	Me	Me		**16f**	74
7	**10c**	Et	$Ph(CH_2)_2$		**16g**	78
8	**10a**	Me	Me		**16h**	73
9	**10c**	Et	$Ph(CH_2)_2$		**16i**	71
10	**10b**	Et	Me		**16j**	52[b]
11	**10c**	Et	$Ph(CH_2)_2$		**16k**	47[b]
12	**10b**	Et	Me		**16l**	67
13	**10c**	Et	$Ph(CH_2)_2$		**16m**	64
14	**10b**	Et	Me		**16n**	70
15	**10c**	Et	$Ph(CH_2)_2$		**16o**	68

[a]Isolated yield. [b]Longer reaction time (24 h) required for (i).

acetates (Table 2). Although the yields of arenes were generally lower, the reaction proceeded in all cases, and it is noteworthy that the substitution on the allyl moiety has less impact on the efficiency of the synthesis of the isophthalates **16** than substitutions on the diketoester−dioxinone (R^2). Substitution at C-1 of the allyl donor resulted in slightly lower yields (58−76%; Table 2, entries 1−5), although it is clear that the method proceeds easily for allyl acetates with up to two substituents on different positions of the allyl core. The reaction of geranyl acetate required longer reaction times and proceeded in lower yield (47−52%, Table 2, entries 10 and 11), probably due to steric hindrance, but resulted only in the formation of the linear and not the branched geranyl isophthalate. In all cases that could result in product mixtures (Table 2, entries 8−15), only linear allylated arenes were isolated. This indicates a mechanism occurring through an attack of the enol or enolate of diketoester **10** on a π-allyl palladium complex at C-1 of the allyl ligand. Indeed, cinnamylations using cinnamyl acetate are known to provide excellent linear to branched ratios,[3,14] and since the resorcylates **16h** and **16i** were isolated without any branched side products, a mechanism proceeding via an *O*-allylation followed by a subsequent Claisen rearrangement to form the observed C−C bonds is unlikely to have occurred.

Furthermore, direct C-allylation catalyzed by acetate anion was supported by the fact that allyl chloride **17**, which produces the less basic chloride anion, did not react with diketoester−dioxinone **10a** in the presence of $Pd(PPh_3)_4$. Nevertheless, when the same reaction was carried out using cesium carbonate as base, both isophthalate **8a** and resorcylate **18**, resulting from the cyclization of the starting diketoester−dioxinone **10a**, were produced (Scheme 4). The same reaction carried out in the absence of $Pd(PPh_3)_4$ did not provide the arene **8a**.

Scheme 4. Synthesis of Resorcylates by Using Allyl Chloride



CONCLUSION

In conclusion, we describe Pd(0)-catalyzed allylic alkylations of diketoester−dioxinones using allylic acetates under neutral conditions and subsequent aromatization to produce diverse tetrasubstituted isophthalates in four steps with good overall yields. The reaction, which is suitable for delicate substrates, is currently being applied in total synthesis and medicinal chemistry.

EXPERIMENTAL SECTION

General Methods. All reactions were carried out in oven-dried glassware under Ar using commercially supplied solvents and reagents unless otherwise stated. THF was redistilled from Na−Ph_2CO. Hexanes refers to petroleum spirits 40−60 °C. Column chromatography was carried out on silica gel using flash techniques (eluents are given in parentheses). Analytical TLC was performed on precoated silica gel F_{254} aluminum plates with visualization under UV light or by staining with acidic vanillin, anisaldehyde, or ninhydrin spray reagents. ^1H and ^{13}C NMR spectra were respectively recorded at 400 and 100 MHz with chemical shifts (δ) quoted in ppm. Data are reported as follows: s = singlet, d = duplet, t = triplet, q = quartet, m_c = symmetric multiplet (center is given), m = unsymmetric multiplet (shift range is given).

General Procedure for the Synthesis of β-Ketoester−Dioxinones 11a,b. *n*-BuLi (2.5 M in hexanes; 50.5 mL, 126 mmol,

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3.6 equiv) was added with stirring to $(Me_3Si)_2NH$ (26.3 mL, 105 mmol, 3.6 equiv) in THF (200 mL) at −78 °C. After 1 h, dioxinone **13** (14.9 g, 105 mmol, 3.0 equiv) in THF (45 mL) and, after an additional 1 h, acyl chloride **14a,b** (35.1 mmol, 1.0 equiv) in THF (20 mL) were each added dropwise. After a further 1 h at −78 °C, the reaction was quenched at this temperature by the addition of saturated aqueous NH_4Cl (150 mL), and the mixture was allowed to warm to room temperature. The aqueous layer was acidified to pH 3 with 1 M HCl and was extracted with EtOAc (3 × 250 mL). The combined organic extracts were washed with brine (25 mL), dried ($MgSO_4$), rotary evaporated, and chromatographed (hexanes/EtOAc 100:1, 10:1, 5:1, 4:1, 3:2) to give β-keto ester dioxinones **11a,b**.

*Methyl 4-(2,2-dimethyl-4-oxo-4H-1,3-dioxin-6-yl)-3-oxobutanoate (**11a**):* yellow oil; 64%; R_f 0.36 (hexanes/EtOAc 1:1); IR 1724, 1637, 1438, 1391, 1332, 1273, 1204 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz,) δ 5.37 (s, 1H), 3.76 (s, 3H), 3.53 (s, 2H), 3.49 (s, 2H), 1.71 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 166.7, 163.4, 160.4, 107.4, 97.1, 52.6, 48.8, 46.9, 24.9 (2C); MS (ES) *m*/*z* 243 (M + H^+); HRMS (ES) calcd for $C_{11}H_{15}O_6$ (M + H^+) 243.0863, found 243.0869. Anal. Calcd for $C_{11}H_{14}O_6$: C, 54.54; H, 5.83. Found: C, 54.65; H, 5.75.

*Ethyl 4-(2,2-dimethyl-4-oxo-4H-1,3-dioxin-6-yl)-3-oxobutanoate (**11b**):* white solid; 75%; mp 42−45 °C (hexanes); R_f 0.48 (hexanes/EtOAc 1:1); IR 1746, 1717, 1393, 1377, 1336, 1275, 1263, 1202, 1028, 1015 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.33 (s, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 3.48 (s, 4H), 1.68 (s, 6H), 1.25 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.7, 166.3, 163.5, 160.4, 107.2, 97.0, 61.7, 49.0, 46.9, 24.9 (2C), 14.0; HRMS-ESI (*m*/*z*) calcd for $C_{12}H_{17}O_6$ (M + H^+) 257.1020, found 257.1020. Anal. Calcd for $C_{12}H_{16}O_6$: C, 56.24; H, 6.29. Found: C, 56.24; H, 6.35.

General Procedure for the Synthesis of Diketoester−Dioxinones 10a−h. Ketoester dioxinone **11a,b** (3.4 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was added with stirring to $MgCl_2$ (640 mg, 6.7 mmol, 2.0 equiv) and pyridine (0.8 mL, 9.2 mmol, 2.7 equiv) in CH_2Cl_2 (100 mL) at 0 °C. After 30 min, acyl chloride **12a−h** (4.1 mmol, 1.2 equiv) was added. After the mixture was stirred for 1 h at 0 °C, the reaction was quenched with brine (100 mL) and the mixture extracted with EtOAc (2 × 200 mL). The combined organic layers were dried ($MgSO_4$) and rotary evaporated, and the residue was chromatographed (Et_2O/hexanes 1:4 to 100% Et_2O) to afford diketoester−dioxinone **10a−h**.

*Methyl 2-acetyl-4-(2,2-dimethyl-4-oxo-4H-1,3-dioxin-6-yl)-3-oxobutanoate (**10a**):* colorless oil; 71%; R_f 0.48 (AcOEt/hexanes 3:7); IR 1714, 1637, 1564, 1436, 1390, 1374, 1270, 1251, 1200, 1081, 1013, 959, 901 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.31 (s, 1H), 3.79 (s, 3H), 3.71 (s, 2H), 2.40 (s, 3H), 1.67 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 196.0, 193.8, 166.6, 165.1, 160.7, 108.1, 107.1, 96.3, 51.8, 43.2, 25.5, 24.8 (2C); HRMS-ESI (*m*/*z*) calcd for $C_{13}H_{17}O_7$ (M + H^+) 285.0969, found 285.0964.

*Ethyl 2-acetyl-4-(2,2-dimethyl-4-oxo-4H-1,3-dioxin-6-yl)-3-oxobutanoate (**10b**):* colorless oil; 76%; R_f 0.54 (AcOEt/hexanes 3:7); IR 1725, 1637, 1565, 1373, 1271, 1251, 1201, 1078, 1013, 901 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.31 (s, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.71 (s, 2H), 2.40 (s, 3H), 1.67 (s, 6H), 1.32 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.8, 193.5, 166.2, 165.2, 160.7, 108.4, 107.1, 96.3, 61.0, 43.1, 25.5, 24.8 (2C), 14.1; HRMS-ESI (*m*/*z*) calcd for $C_{14}H_{19}O_7$ (M + H^+) 299.1131, found 299.1137.

*Ethyl 2-(2-(2,2-dimethyl-4-oxo-4H-1,3-dioxin-6-yl)acetyl)-3-oxo-5-phenylpentanoate (**10c**):* colorless oil; 78%; R_f 0.54 (AcOEt/hexanes 2:8); IR 1726, 1710, 1637, 1560, 1389, 1374, 1271, 1250, 1201, 1071, 1014 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.19−7.31 (m, 5H), 5.34 (s, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.69 (s, 2H), 3.05 (m, 2H), 2.97 (m, 2H), 1.69 (s, 6H), 1.32 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 197.5, 192.4, 166.1, 165.0, 160.7, 140.2, 128.5 (2C), 128.2 (2C), 126.3, 108.6, 107.1, 96.4, 61.2, 42.8, 39.2, 31.6, 24.9 (2C), 14.1; HRMS-ESI (*m*/*z*) calcd for $C_{21}H_{25}O_7$ (M + H^+) 389.1600, found 389.1602.

*Ethyl 2-(2-(2,2-dimethyl-4-oxo-4H-1,3-dioxin-6-yl)acetyl)-3-oxopentanoate (**10d**):* colorless oil; 71%; R_f 0.42 (Et_2O/hexanes 1:1); IR 1725, 1390, 1373, 1271, 1251, 1202, 1071, 1015 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.31 (s, 1H), 4.25 (q, 2H, *J* = 7.1 Hz), 3.66 (s, 2H), 2.71 (q, 2H, *J* = 7.4 Hz), 1.66 (s, 6H), 1.32 (t, 3H, *J* = 7.2 Hz), 1.16 (t, 3H, *J* = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.7, 191.9, 166.3, 165.2, 160.6, 108.2, 107.1, 96.2, 61.1, 42.5, 31.1, 24.8 (2C), 14.1, 9.6; HRMS-ESI (*m*/*z*) calcd for $C_{15}H_{21}O_7$ (M + H^+) 313.1287, found 313.1283.

*Ethyl 2-(2-(2,2-dimethyl-4-oxo-4H-1,3-dioxin-6-yl)acetyl)-4-methyl-3-oxopentanoate (**10e**):* colorless oil; 42%; R_f 0.42 (Et_2O/hexanes 1:1); IR 1713, 1373, 1271, 1249, 1201, 1092, 1063 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.34 (s, 1H), 4.27 (q, 2H, *J* = 7.1 Hz), 3.64 (s, 2H), 3.20 (sept., 1H, *J* = 6.8 Hz), 1.69 (s, 6H), 1.34 (t, 3H, *J* = 7.2 Hz), 1.18 (d, 6H, *J* = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.7, 192.3, 166.6, 165.0, 160.7, 107.9, 107.2, 96.4, 61.3, 42.6, 34.5, 24.9 (2C), 19.4 (2C), 14.1; HRMS-ESI (*m*/*z*) calcd for $C_{16}H_{23}O_7$ (M + H^+) 327.1444, found 327.1446.

*Ethyl 2-(cyclopropanecarbonyl)-4-(2,2-dimethyl-4-oxo-4H-1,3-dioxin-6-yl)-3-oxobutanoate (**10f**):* colorless oil; 80%; R_f 0.43 (Et_2O/hexanes 1:1); IR 1726, 1708, 1637, 1390, 1374, 1272, 1252, 1203, 1098, 1064, 1015 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.35 (s, 1H), 4.30 (q, 2H, *J* = 7.2 Hz), 3.65 (s, 2H), 2.50 (tt, 1H, *J* = 7.9, 4.6 Hz), 1.68 (s, 6H), 1.35 (t, 3H, *J* = 7.1 Hz), 1.30 (m_c, 2H), 1.08 (m_c, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.3, 189.9, 166.8, 165.4, 160.8, 108.8, 107.1, 96.2, 61.1, 42.2, 24.9 (2C), 16.6, 14.2, 12.9 (2C); HRMS-ESI (*m*/*z*) calcd for $C_{16}H_{21}O_7$ (M + H^+) 325.1287, found 325.1281.

*Ethyl 2-benzoyl-4-(2,2-dimethyl-4-oxo-4H-1,3-dioxin-6-yl)-3-oxobutanoate (**10g**):* colorless oil; 73%; R_f 0.23 (Et_2O:hexanes 1:1); IR 1728, 1640, 1601, 1391, 1376, 1273, 1245, 1204, 1015 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) *mixture of several keto−enol tautomers, two sets of signals are dominating this mixture: keto−enol tautomer 1 (ca. 40%)* δ 7.58−7.40 (m, 5H), 5.40 (s, 1H), 3.94 (q, 2H, *J* = 7.1 Hz), 3.75 (s, 2H), 1.70 (s, 6H), 0.84 (t, 3H, *J* = 7.2 Hz); *keto−enol tautomer 2 (ca. 30%):* δ 13.28 (s, 1H), 7.79−7.77 (m, 2H), 7.58−7.40 (m, 3H), 5.37 (s, 1H), 4.11 (q, 2H, *J* = 7.2 Hz), 3.33 (s, 2H), 1.60 (s, 6H), 0.96 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) *keto−enol tautomer 1:* δ 191.0, 173.7, 167.2, 164.8, 160.7, 136.2, 132.0, 128.3 (2C), 127.5 (2C), 108.6, 107.2, 96.5, 61.2, 41.6, 24.9 (2C), 13.3; *keto−enol tautomer 2:* δ 190.2, 170.9, 167.2, 165.1, 160.5, 138.6, 133.2, 128.8 (2C), 128.4 (2C), 107.3, 107.1, 95.8, 61.5, 37.2, 24.8 (2C), 13.5; HRMS-ESI (*m*/*z*) calcd for $C_{19}H_{21}O_7$ (M + H^+) 361.1287, found 361.1284.

*Methyl 4-(2,2-dimethyl-4-oxo-4H-1,3-dioxin-6-yl)-2-(furan-2-carbonyl)-3-oxobutanoate (**10h**):* yellow oil; 69%; R_f 0.21 (Et_2O/hexanes 1:1); IR 1721, 1391, 1376, 1273, 1248, 1200, 1013, 903, 859, 766, 728 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) *mixture of several keto−enol tautomers, two sets of signals are dominating this mixture: keto−enol tautomer 1 (ca. 45%):* δ 7.58−7.49 (m, 1H), 7.22 (d, 1H, *J* = 3.4 Hz), 6.59−6.51 (m, 1H), 5.35 (s, 1H), 3.75 (s, 3H), 3.54 (s, 2H), 1.64 (s, 6H); *keto−enol tautomer 2 (ca. 30%):* δ 13.05 (s, 1H), 7.58−7.49 (m, 1H), 7.13 (d, 1H, *J* = 3.5 Hz), 6.59−6.51 (m, 1H), 5.32 (s, 1H), 3.69 (s, 3H), 3.27 (s, 2H), 1.55 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) *keto−enol tautomer 1:* δ 188.9, 173.4, 164.5, 160.5, 147.8, 147.1, 119.1, 112.7, 107.1, 106.9, 96.4, 52.3, 40.9, 24.7 (2C); *keto−enol tautomer 2:* δ 193.3, 174.1, 167.1, 164.8, 148.4, 146.9, 118.9, 112.6, 106.7, 106.4, 95.7, 53.2, 36.9, 24.6 (2C); HRMS-ESI (*m*/*z*) calcd for $C_{16}H_{17}O_8$ (M + H^+) 337.0923, found 337.0929.

General Procedure for the Synthesis of Resorcylates 8a−h and 16a−o. Diketoester-dioxinone **10a−h** (0.30 mmol, 1.0 equiv) and allyl acetate **15** (0.33 mmol, 1.1 equiv) in THF (0.5 mL) were added with stirring to $Pd(PPh_3)_4$ (8.7 mg, 0.008 mmol, 2.5 mol %) in THF (1 mL). After 5 h (24 h in the case of geranyl acetate) at 25 °C, Cs_2CO_3 (294 mg, 0.90 mmol, 3.0 equiv) was added, and the resulting mixture was stirred for 12 h at 25 °C. Reaction was quenched by addition of brine (20 mL) and the mixture acidified to pH 3 with 1 M HCl and extracted with EtOAc (2 × 50 mL). The organic extracts were combined, dried ($MgSO_4$), filtered, rotary evaporated, and (unless noted otherwise) chromatographed (hexanes/EtOAc 9:1) to provide resorcylate **8a−h** (R^3 = allyl) or **16a−o** (R^3 = 2-alkenyl or 2-cycloalkenyl).

*Methyl 8-allyl-7-hydroxy-2,2,5-trimethyl-4-oxo-4H-benzo[d][1,3]-dioxine-6-carboxylate (**8a**):* white solid; 84%; mp 59−60 °C (hexanes); R_f 0.69 (EtOAc/hexanes 1:9); IR 1730, 1657, 1583,

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1436, 1377, 1330, 1265, 1234, 1208, 1139, 1029, 992, 977, 914 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.86 (s, 1H), 5.88 (m, 1H), 5.02−4.97 (m, 2H), 3.99 (s, 3H), 3.37 (d, J = 6.2 Hz, 2H), 2.88 (s, 2H), 1.69 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.0, 164.7, 160.1, 158.4, 147.3, 135.0, 115.0, 113.5, 110.4, 106.5, 104.7, 52.7, 26.8, 25.7 (2C), 20.2; HRMS-ESI (m/z) calcd for $C_{16}H_{19}O_6$ (M + H^+) 307.1176, found 307.1175. Anal. Calcd for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.84; H, 6.01.

*Ethyl 8-allyl-7-hydroxy-2,2,5-trimethyl-4-oxo-4H-benzo[d][1,3]-dioxine-6-carboxylate (**8b**):* colorless oil; 90%; R_f 0.71 (EtOAc/hexanes 1:9); IR 1725, 1637, 1565, 1373, 1271, 1251, 1201, 1078, 1013, 901 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.93 (s, 1H), 5.87 (m, 1H), 5.00−4.95 (m, 2H), 4.45 (q, J = 7.2 Hz, 2H), 3.35 (d, J = 6.2 Hz, 2H), 2.88 (s, 3H), 1.68 (s, 6H), 1.42 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.4, 164.7, 160.1, 158.3, 147.2, 135.0, 115.0, 113.5, 110.5, 106.4, 104.7, 62.3, 26.7, 25.7 (2C), 20.3, 14.1; HRMS-ESI (m/z) calcd for $C_{17}H_{21}O_6$ (M + H^+) 321.1338, found 321.1349.

*Ethyl 8-allyl-7-hydroxy-2,2-dimethyl-4-oxo-5-phenethyl-4H-benzo[d][1,3]dioxine-6-carboxylate (**8c**):* white solid; 84%; mp 63−65 °C (hexanes); R_f 0.78 (EtOAc/hexanes 1:9); IR 1730, 1647, 1595, 1580, 1377, 1274, 1263, 1233, 1214, 1137, 1046, 1015, 914 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.89 (s, 1H), 7.32−7.22 (m, 4H), 7.16 (m, 1H), 5.87 (m, 1H), 4.98 (m, 2H), 4.46 (q, J = 7.2 Hz, 2H), 3.76 (m, 2H), 3.35 (d, J = 6.2 Hz, 2H), 2.88 (m, 2H), 1.63 (s, 6H), 1.38 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.2, 164.8, 159.7, 158.6, 150.2, 141.9, 134.9, 128.4 (2C), 128.3 (2C), 125.9, 115.1, 114.1, 110.2, 105.7, 104.5, 62.5, 37.0, 33.1, 26.8, 25.7 (2C), 14.2; HRMS-ESI (m/z) calcd for $C_{24}H_{27}O_6$ (M + H^+) 411.1802, found 411.1790. Anal. Calcd for $C_{24}H_{26}O_6$: C, 70.23; H, 6.38. Found: C, 70.32; H, 6.28.

*Ethyl 8-allyl-5-ethyl-7-hydroxy-2,2-dimethyl-4-oxo-4H-benzo[d]-[1,3]dioxine-6-carboxylate (**8d**):* white solid; 83%; mp 82−84 °C (CH_2Cl_2); R_f 0.68 (Et_2O/hexanes 1:3); IR 1732, 1654, 1582, 1264, 1214, 1182, 1038 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.91 (s, 1H), 5.88 (ddt, 1H, J = 16.3, 10.0, 6.3 Hz), 5.03 − 4.96 (m, 2H), 4.46 (q, 2H, J = 7.1 Hz), 3.45 (q, 2H, J = 7.2 Hz), 3.36 (dt, 2H, J = 6.3, 1.4 Hz), 1.67 (s, 6H), 1.44 (t, 3H, J = 7.2 Hz), 1.26 (t, 3H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.4, 164.8, 159.5, 158.6, 153.0, 135.0, 115.1, 113.8, 109.9, 105.5, 104.4, 62.3, 26.8, 25.7, 24.9 (2C), 15.4, 13.9.; HRMS-ESI (m/z) calcd for $C_{18}H_{23}O_6$ (M + H^+) 335.1495, found 335.1487.

*Ethyl 8-Allyl-7-hydroxy-5-isopropyl-2,2-dimethyl-4-oxo-4H-benzo[d][1,3]dioxine-6-carboxylate (**8e**).* After the aqueous workup, the resultant oil was dissolved in Et_2O (10 mL), and silica (1 g) was added. After the mixture was stirred at 20 °C for 18 h, the solvent was evaporated and the product was isolated by chromatography: white solid; 43%; mp 95−96 °C (CH_2Cl_2); R_f 0.68 (Et_2O/hexanes 1:3); IR 1732, 1578, 1376, 1298, 1265, 1211, 1183, 1134, 1048, 1019 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.93 (s, 1H), 5.87 (ddt, 1H, J = 16.5, 10.1, 6.3 Hz), 5.06 − 4.99 (m, 2H), 4.44 (q, 2H, J = 7.2 Hz), 4.03 (sept., 1H, J = 7.1 Hz), 3.36 (dt, 2H, J = 6.3, 1.3 Hz), 1.67 (s, 6H), 1.44 (t, J = 7.2 Hz, 3H), 1.41 (d, 6H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.1, 161.5, 159.6, 158.0, 154.9, 135.0, 115.4, 113.7, 113.1, 106.9, 104.3, 62.4, 31.8, 27.1, 25.6 (2C), 21.2 (2C), 13.9; HRMS-ESI (m/z) calcd for $C_{19}H_{25}O_6$ (M + H^+) 349.1646, found 349.1645.

*Ethyl 8-Allyl-5-cyclopropyl-7-hydroxy-2,2-dimethyl-4-oxo-4H-benzo[d][1,3]dioxine-6-carboxylate (**8f**).* After the aqueous workup, the resultant oil was dissolved in Et_2O (10 mL), and silica (1 g) was added. After the mixture was stirred at 20 °C for 18 h, the solvent was evaporated and the product was isolated by chromatography: white solid; 59%; mp 130−132 °C (CH_2Cl_2); R_f 0.48 (Et_2O/hexanes 1:3); IR 1740, 1659, 1581, 1266, 1236, 1209, 1019 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.03 (s, 1H), 5.84 (ddt, 1H, J = 16.5, 10.0, 6.3 Hz), 5.01 − 4.94 (m, 2H), 4.41 (q, 2H, J = 7.1 Hz), 3.33 (d, 2H, J = 6.3), 2.49 (tt, 1H, J = 8.6, 6.0 Hz), 1.66 (s, 6H), 1.39 (t, 3H, J = 7.0 Hz), 1.07 (m_c, 2H), 0.30 (m_c, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.0, 162.6, 158.9, 157.5, 151.5, 134.9, 115.1, 113.8, 112.8, 109.0, 104.9, 62.1, 26.8, 25.6 (2C), 16.9, 13.9, 10.0 (2C); HRMS-ESI (m/z) calcd for $C_{19}H_{23}O_6$ (M + H^+): 347.1495, found: 347.1498.

*Ethyl 8-allyl-7-hydroxy-2,2-dimethyl-4-oxo-5-phenyl-4H-benzo-[d][1,3]dioxine-6-carboxylate (**8g**):* white solid; 53%; mp 84−86 °C (CH_2Cl_2); R_f 0.33 (Et_2O/hexanes 1:3); IR 1739, 1268, 1237, 1205, 1189, 1172, 1009, 921, 742 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.88 (s, 1H), 7.37−7.33 (m, 3H), 7.15−7.10 (m, 2H), 5.94 (ddt, 1H, J = 16.3, 10.0, 6.3 Hz), 5.08 (dq, 1H, J = 17.1, 1.8 Hz), 5.04 (dq, 1H, J = 10.0, 1.6 Hz), 3.88 (q, 2H, J = 7.1 Hz), 3.45 (dt, 2H, J = 6.3, 1.4 Hz), 1.73 (s, 6H), 1.73 (t, 3H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 164.3, 158.4, 158.2, 147.7, 140.0, 134.7, 127.7 (2C), 127.4 (2C), 127.0, 115.3, 115.0, 109.9, 104.9, 61.4, 26.8, 25.8 (2C), 12.8; HRMS-ESI (m/z) calcd for $C_{22}H_{23}O_6$ (M + H^+) 383.1495, found 383.1494.

*Methyl 8-allyl-5-(furan-2-yl)-7-hydroxy-2,2-dimethyl-4-oxo-4H-benzo[d][1,3]dioxine-6-carboxylate (**8h**):* white solid; 42%; mp 78−80 °C ($CHCl_3$); R_f 0.27 (Et_2O/hexanes 1:3); IR 1746, 1666, 1581, 1432, 1380, 1335, 1268, 1243, 1204, 1146, 997, 916 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.51 (s, 1H), 7.54 (d, 1H, J = 2.1 Hz), 6.49 (dd, 1H, J = 1.9, 3.3 Hz), 6.26 (d, 1H, J = 3.6 Hz), 5.08 − 5.01 (m, 2H), 5.91 (ddt, 1H, J = 16.3, 10.0, 6.2 Hz), 3.63 (s, 3H), 3.44 (dt, 2H, J = 6.1, 1.4 Hz), 1.74 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 163.8, 158.2, 158.1, 148.9, 142.0, 134.9, 134.4, 116.6, 115.5, 111.1, 110.5, 108.9, 106.8, 105.3, 53.0, 26.9 (2C), 25.8; HRMS-ESI (m/z) calcd for $C_{19}H_{19}O_7$ (M + H^+) 359.1131, found 359.1122.

*Methyl 8-(cyclohex-2-enyl)-7-hydroxy-2,2,5-trimethyl-4-oxo-4H-benzo[d][1,3]dioxine-6-carboxylate (**16a**):* white solid; 63%; mp 76−78 °C (hexanes); R_f 0.74 (EtOAc/hexanes 1:9); IR 1731, 1720, 1656, 1573, 1436, 1375, 1360, 1302, 1262, 1229, 1217, 1118, 1025, 962 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 11.21 (s, 1H), 5.80 (m, 1H), 5.54 (bd, J = 10.0 Hz, 1H), 3.97 (s, 1H), 2.81 (s, 3H), 2.09 (bs, 2H), 1.90−1.75 (m, 4H), 1.69 (s, 3H), 1.65 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.5, 163.8, 160.2, 158.4, 146.0, 130.0, 126.9, 118.5, 111.9, 106.7, 104.5, 52.6, 32.1, 27.4, 26.0, 25.1, 24.7, 22.9, 20.0; HRMS-ESI (m/z) calcd for $C_{19}H_{23}O_6$ (M + H^+) 347.1489, found 347.1486. Anal. Calcd for $C_{19}H_{22}O_6$: C, 65.88; H, 6.40. Found: C, 65.79; H, 6.47.

*Ethyl 8-(cyclohex-2-enyl)-7-hydroxy-2,2,5-trimethyl-4-oxo-4H-benzo[d][1,3]dioxine-6-carboxylate (**16b**):* white solid; 76%; mp 39−41 °C (hexanes); R_f 0.68 (EtOAc/hexanes 1:9); IR 1728, 1647, 1561, 1445, 1378, 1301, 1266, 1232, 1218, 1185, 1029, 913 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.75 (m, 1H), 5.50 (bd, J = 10.0 Hz, 1H), 4.42 (q, J = 7.2 Hz, 2H), 3.94 (bs, 1H), 2.80 (s, 3H), 2.05 (m, 2H), 1.86−1.74 (m, 4H), 1.66 (s, 3H), 1.63 (s, 3H), 1.39 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.0, 163.9, 160.1, 158.3, 146.0, 129.9, 126.6, 118.5, 111.7, 106.6, 104.3, 62.1, 31.9, 27.2, 25.9, 24.9, 24.6, 22.8, 20.0, 14.0; HRMS-ESI (m/z) calcd for $C_{20}H_{25}O_6$ (M + H^+) 361.1646, found 361.1639. Anal. Calcd for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.71; H, 6.86.

*Ethyl 8-(cyclohex-2-enyl)-7-hydroxy-2,2-dimethyl-4-oxo-5-phenethyl-4H-benzo[d][1,3]dioxine-6-carboxylate (**16c**):* colorless oil; 58%; R_f 0.72 (EtOAc/hexanes 1:9); IR 1730, 1653, 1577, 1388, 1377, 1299, 1265, 1230, 1220, 1044, 1021, 916 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 10.95 (s, 1H), 7.35−7.28 (m, 4H), 7.19 (m, 1H), 5.85 (m, 1H), 5.59 (m, 1H), 4.48 (q, J = 7.2 Hz, 2H), 3.99 (m, 1H), 3.64 (m, 2H), 2.92 (s, 2H), 2.11 (m, 2H), 1.92−1.81 (m, 4H), 1.68 (s, 3H), 1.64 (s, 3H), 1.41 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 163.5, 159.8, 158.5, 148.6, 142.0, 129.8, 128.5 (2C), 128.3 (3C), 127.5, 125.9, 118.9, 105.8, 104.3, 62.4, 37.0, 33.5, 32.1, 27.4, 26.0, 25.1, 24.7, 22.8, 14.3; HRMS-ESI (m/z) calcd for $C_{27}H_{31}O_6$ (M + H^+) 451.2115, found 451.2111.

*(E)-Methyl 7-hydroxy-2,2,5-trimethyl-4-oxo-8-(pent-3-en-2-yl)-4H-benzo[d][1,3]dioxine-6-carboxylate (**16d**):* white solid; 68%; mp 48−50 °C (hexanes); R_f 0.73 (EtOAc/hexanes 1:9); IR 1726, 1656, 1573, 1441, 1378, 1310, 1267, 1234, 1032, 1074, 1017, 967, 924 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.73 (s, 1H), 5.81 (ddd, J = 15.2, 7.2, 1.5 Hz, 1H), 5.50 (dqd, J = 15.2, 6.5, 1.5 Hz, 1H), 4.06 (quint, J = 7.2 Hz, 1H), 4.00 (s, 3H), 2.85 (s, 3H), 1.72 (s, 3H), 1.71 (s, 3H), 1.35 (d, J = 6.5 Hz, 3H), 1.65 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.0, 164.1, 160.2, 158.1, 146.5, 133.8, 124.2, 119.4, 111.0, 106.8, 104.4, 52.6, 32.2, 25.8, 25.5, 20.2, 18.5, 17.8; HRMS-ESI (m/z) calcd for $C_{18}H_{23}O_6$ (M + H^+) 335.1495, found 335.1498. Anal. Calcd for $C_{18}H_{22}O_6$: C, 64.66; H, 6.63. Found: C, 64.75; H, 6.56.

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*(E)-Ethyl 7-hydroxy-2,2-dimethyl-4-oxo-8-(pent-3-en-2-yl)-5-phenethyl-4H-benzo[d][1,3]dioxine-6-carboxylate (**16e**):* colorless oil; 62%; R_f 0.76 (EtOAc/hexanes 1:9); IR 1729, 1653, 1575, 1496, 1452, 1416, 1389, 1376, 1264, 1226, 1046, 1013, 966, 927 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.65 (s, 1H), 7.36−7.28 (m, 4H), 7.19 (m, 1H), 5.82 (ddd, J = 15.2, 7.2, 1.5 Hz, 1H), 5.50 (dqd, J = 15.2, 6.5, 1.5 Hz, 1H), 4.49 (q, J = 7.2 Hz, 2H), 4.06 (quint, J = 7.2 Hz, 1H), 3.71 (m, 2H), 2.91 (m, 2H), 1.68 (d, J = 6.5 Hz, 3H), 1.67 (s, 6H), 1.41 (t, J = 7.2 Hz, 3H), 1.35 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.2, 164.1, 159.8, 158.3, 149.4, 142.0, 133.8, 128.5 (2C), 128.3 (2C), 125.9, 124.3, 119.9, 111.0, 106.1, 104.2, 62.5, 37.0, 33.3, 32.3, 25.8, 25.5, 18.5, 17.9, 14.3; HRMS-ESI (m/z) calcd for $C_{26}H_{31}O_6$ (M + H^+) 439.2115, found 439.2124.

*Methyl 7-hydroxy-2,2,5-trimethyl-8-(2-methylallyl)-4-oxo-4H-benzo[d][1,3]dioxine-6-carboxylate (**16f**):* white solid; 74%; mp = 42−43 °C (hexanes); R_f 0.76 (EtOAc/hexanes 1:9); IR 1730, 1656, 1583, 1437, 1377, 1328, 1307, 1265, 1232, 1207, 1174, 1126, 1028, 979, 913, 889 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.83 (s, 1H), 4.71 (bs, 1H), 4.51 (bs, 1H), 3.98 (s, 3H), 3.30 (s, 2H), 2.87 (s, 3H), 1.76 (s, 3H), 1.67 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.9, 164.9, 160.2, 158.7, 147.2, 143.2, 113.5, 110.4 (2C), 110.2, 104.7, 52.6, 30.4, 25.6 (2C), 22.7, 20.2; HRMS-ESI (m/z) calcd for $C_{17}H_{21}O_6$ (M + H^+) 321.1338, found 321.1342. Anal. Calcd for $C_{17}H_{20}O_6$: C, 63.74; H, 6.29. Found: C, 63.65; H, 6.27.

*Ethyl 7-hydroxy-2,2-dimethyl-8-(2-methylallyl)-4-oxo-5-phenethyl-4H-benzo[d][1,3]dioxine-6-carboxylate (**16g**):* white solid; 78%; mp = 61−63 °C (hexanes); R_f 0.74 (EtOAc/hexanes 1:9); IR 1718, 1660, 1583, 1373, 1303, 1271, 1226, 1207, 1164, 1118, 1050, 1017, 1007, 912, 890 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.85 (s, 1H), 7.34−7.27 (m, 4H), 7.19 (m, 1H), 4.74 (bs, 1H), 4.53 (bs, 1H), 4.49 (q, J = 7.2 Hz, 2H), 3.81 (m, 2H), 3.33 (s, 2H), 2.92 (m, 2H), 1.79 (s, 3H), 1.65 (s, 6H), 1.42 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.2, 165.0, 159.8, 158.9, 150.3, 143.2, 141.9, 128.5 (2C), 128.3 (2C), 125.9, 114.2, 110.2 (2C), 105.7, 104.5, 62.5, 37.1, 33.1, 30.5, 25.6 (2C), 22.8, 14.3; HRMS-ESI (m/z) calcd for $C_{25}H_{29}O_6$ (M + H^+) 425.1964, found 425.1982. Anal. Calcd for $C_{25}H_{28}O_6$: C, 70.74; H, 6.65. Found: C, 70.84; H, 6.56.

*Methyl 8-cinnamyl-7-hydroxy-2,2,5-trimethyl-4-oxo-4H-benzo-[d][1,3]dioxine-6-carboxylate (**16h**):* colorless oil; 73%; R_f 0.71 (EtOAc/hexanes 1:9); IR 1729, 1656, 1584, 1437, 1377, 1328, 1309, 1265, 1233, 1208, 1125, 1029, 966, 915 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.92 (s, 1H), 7.31−7.24 (m, 4H), 7.16 (m, 1H), 6.39 (d, J = 15.6 Hz, 1H), 6.25 (dt, J = 15.6, 6.5 Hz, 1H), 3.99 (s, 2H), 3.52 (d, J = 6.5 Hz, 2H), 2.89 (s, 3H), 1.70 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.0, 164.7, 160.1, 158.4, 147.3, 137.4, 130.6, 128.4 (2C), 127.0, 126.8, 125.9 (2C), 113.6, 110.4, 106.5, 104.8, 52.7, 26.0, 25.8 (2C), 20.2; HRMS-ESI (m/z) calcd for $C_{22}H_{23}O_6$ (M + H^+) 383.1489, found 383.1479.

*Ethyl 8-cinnamyl-7-hydroxy-2,2-dimethyl-4-oxo-5-phenethyl-4H-benzo[d][1,3]dioxine-6-carboxylate (**16i**):* colorless oil; 71%; R_f 0.72 (EtOAc/hexanes 1:9); IR 1728, 1654, 1581, 1495, 1452, 1417, 1377, 1265, 1229, 1208, 1181, 1046, 1017, 964 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.98 (s, 1H), 7.23−7.35 (m, 8H), 7.19 (m, 2H), 6.41 (d, J = 15.8 Hz, 1H), 6.26 (dt, J = 15.7, 6.6 Hz, 1H), 4.49 (q, J = 7.2 Hz, 2H), 3.80 (m, 2H), 3.53 (d, J = 6.6 Hz, 2H), 2.92 (m, 2H), 1.67 (s, 6H), 1.41 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.2, 164.8, 159.6, 158.6, 150.3, 141.9, 137.4, 130.6, 128.4 (5C), 128.3 (2C), 127.0, 126.7, 125.9 (2C), 114.3, 110.2, 105.8, 104.5, 62.5, 37.0, 33.2, 26.1, 25.7 (2C), 14.2; HRMS-ESI (m/z) calcd for $C_{30}H_{31}O_6$ (M + H^+) 487.2115, found 487.2111.

*(E)-Ethyl 8-(3,7-dimethylocta-2,6-dienyl)-7-hydroxy-2,2,5-trimethyl-4-oxo-4H-benzo[d][1,3]dioxine-6-carboxylate (**16j**):* colorless oil; 52%; R_f 0.22 (hexanes/Et_2O 9:1); IR 1732, 1654, 1583, 1377, 1298, 1264, 1233, 1223, 1185, 1028 cm^{-1}; ^1H NMR ($CHCl_3$, 400 MHz) δ 11.86 (s, 1H), 5.13 (m, 1H), 5.04 (m, 1H), 4.44 (q, 2H, J = 7.1 Hz), 3.30 (d, 2H, J = 7.3 Hz), 2.87 (s, 3H), 2.09−1.93 (m, 4H), 1.75 (s, 3H), 1.68 (s, 6H), 1.62 (s, 3H), 1.55 (s, 3H), 1.42 (t, 3H, J = 7.1 Hz); ^{13}C NMR ($CHCl_3$, 100 MHz) δ 171.5, 164.6, 160.2, 158.0, 146.6, 135.7, 131.3, 124.1, 120.9, 115.4, 110.6, 106.4, 104.5, 62.2, 39.7, 26.6, 25.7 (2C), 25.6, 21.7, 20.2, 17.6, 16.1, 14.1; HRMS (ESI) m/z calcd for $C_{24}H_{33}O_6$ (M + H^+) 417.2277, found 417.2271.

*(E)-Ethyl 8-(3,7-dimethylocta-2,6-dienyl)-7-hydroxy-2,2-dimethyl-4-oxo-5-phenethyl-4H-benzo[d][1,3]dioxine-6-carboxylate (**16k**):* colorless oil; 47%; R_f 0.80 (EtOAc/hexanes 1:8); IR 1733, 1655, 1584, 1454, 1377, 1300, 1267, 1235, 1048, 1020, 916 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.80 (s, 1H), 7.35−7.27 (m, 4H), 7.19 (m, 1H), 5.16 (m, 1H), 5.06 (m, 1H), 4.49 (q, J = 7.2 Hz, 2H), 3.76 (m, 2H), 3.33 (d, J = 7.2 Hz, 2H), 2.91 (m, 2H), 2.04 (m, 2H), 1.97 (m, 2H), 1.77 (s, 3H), 1.67 (s, 6H), 1.64 (s, 3H), 1.57 (s, 3H), 1.41 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.3, 164.7, 159.8, 158.4, 149.7, 142.0, 136.0, 131.4, 128.5 (2C), 128.3 (2C), 125.9, 124.1, 120.8, 116.1, 110.4, 105.7, 104.4, 62.5, 39.7, 37.1, 33.2, 26.6, 25.7 (2C), 25.6, 21.9, 17.7, 16.2, 14.3; HRMS-ESI (m/z) calcd for $C_{31}H_{39}O_6$ (M + H^+) 507.2741, found 507.2747.

*Ethyl 8-(((1R,5S)-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)-methyl)-7-hydroxy-2,2,5-trimethyl-4-oxo-4H-benzo[d][1,3]dioxine-6-carboxylate (**16l**):* white solid; 67%; mp 84−86 °C (CH_2Cl_2); R_f 0.39 (Et_2O/hexanes 1:9); IR 1733, 1655, 1584, 1378, 1265, 1232, 1211, 1031 cm^{-1}; $[\alpha]^{25}_D$ −43.1 (c = 1.02, CH_2Cl_2); ^1H NMR ($CDCl_3$, 400 MHz) δ 11.78 (s, 1H), 4.89 (m, 1H), 4.45 (q, 2H, J = 7.1 Hz), 3.29 (dq, 1H, J = 15.5, 2.0 Hz), 3.16 (dq, 1H, J = 15.5, 2.0 Hz), 2.89 (s, 3H), 2.33 (dt, 1H, J = 8.5, 5.6 Hz), 2.19 (dq, 1H, J = 17.4, 2.0 Hz), 2.13 − 2.02 (m, 3H), 1.66 (s, 6H), 1.43 (t, 3H, J = 7.1 Hz), 1.24 (s, 3H), 1.14 (d, 1H, J = 8.6 Hz), 0.78 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.4, 164.9, 160.3, 158.5, 146.9, 145.2, 115.6, 113.1, 110.5, 106.2, 104.5, 62.2, 46.1, 40.9, 38.1, 31.5, 31.1, 29.4, 26.3, 25.8, 25.6, 20.8, 20.3, 14.1; HRMS-ESI (m/z) calcd for $C_{24}H_{31}O_6$ (M + H^+) 415.2121, found 415.2108.

*Ethyl 8-(((1R,5S)-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)-methyl)-7-hydroxy-2,2-dimethyl-4-oxo-5-phenethyl-4H-benzo[d]-[1,3]dioxine-6-carboxylate (**16m**):* white solid; 64%; mp 81−83 °C (CH_2Cl_2); R_f 0.41 (Et_2O/hexanes 1:9); IR 1726, 1666, 1583, 1275, 1228, 1050, 1021, 792, 752 cm^{-1}; $[\alpha]^{25}_D$ (c = 1.00, CH_2Cl_2) = −33.3; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.71 (s, 1H), 7.34−7.27 (m, 4H), 7.21−7.17 (m, 1H), 4.91 (m, 1H), 4.49 (q, 2H, J = 7.1 Hz), 3.82 (m, 2H), 3.32 (dq, 1H, J = 15.5, 2.0 Hz), 3.20 (dq, 1H, J = 15.5, 2.0 Hz), 2.92 (m, 2H), 2.89 (s, 3H), 2.36 (dt, 1H, J = 8.5, 5.6 Hz), 2.20 (dq, 1H, J = 17.4, 2.0 Hz), 2.16−2.05 (m, 3H), 1.65 (s, 3H), 1.64 (s, 3H), 1.42 (t, 3H, J = 7.1 Hz), 1.27 (s, 3H), 1.17 (d, 1H, J = 8.6 Hz), 0.81 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.4, 164.9, 160.3, 158.5, 146.9, 145.2, 115.6, 113.1, 110.5, 106.2, 104.5, 62.2, 46.1, 40.9, 38.1, 31.5, 31.1, 29.4, 26.3, 25.8, 25.6, 20.8, 20.3, 14.1; HRMS-ESI (m/z) calcd for $C_{31}H_{37}O_6$ (M + H^+) 505.2590, found: 505.2580.

*(S)-Ethyl 7-hydroxy-2,2,5-trimethyl-4-oxo-8-((4-(prop-1-en-2-yl)-cyclohex-1-enyl)methyl)-4H-benzo[d][1,3]dioxine-6-carboxylate (**16n**):* white solid; 70%; mp 73−75 °C (CH_2Cl_2); R_f 0.40 (Et_2O/hexanes 1: 9); IR 1734, 1655, 1584, 1377, 1304, 1266, 1233, 1214, 1031 cm^{-1}; $[\alpha]^{25}_D$ (c = 1.00, CH_2Cl_2) = −45.0; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.81 (s, 1H), 5.28 (s, 1H), 4.67 (d, 2H, J = 5.0 Hz), 4.45 (q, 2H, J = 7.2 Hz), 3.24 (s, 2H), 2.88 (s, 3H), 2.11−2.00 (m, 4H), 1.92−1.74 (m, 2H), 1.70 (s, 3H), 1.67 (s, 3H), 1.66 (s, 3H), 1.48−1.38 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.4, 164.8, 160.3, 158.6, 150.0, 146.9, 135.0, 120.7 (2C), 113.9, 110.6, 108.4, 106.4, 104.6, 62.2, 41.0, 30.7, 29.9, 29.1, 27.9, 25.7, 20.7, 20.3, 14.1; HRMS-ESI (m/z) calcd for $C_{24}H_{31}O_6$ (M + H^+) 415.2121, found 415.2109.

*(S)-Ethyl 7-hydroxy-2,2-dimethyl-4-oxo-5-phenethyl-8-((4-(prop-1-en-2-yl)cyclohex-1-enyl)methyl)-4H-benzo[d][1,3]dioxine-6-carboxylate (**16o**):* white solid; 68%; mp 82−84 °C (CH_2Cl_2); R_f 0.62 (Et_2O/hexanes 1:3); IR 1731, 1654, 1583, 1377, 1301, 1267, 1233, 1212 cm^{-1}; $[\alpha]^{25}_D$ (c = 1.00, CH_2Cl_2) = −36.0; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.75 (s, 1H), 7.34−7.27 (m, 4H), 7.21−7.17 (m, 1H), 5.30 (s, 1H), 4.70 (d, 2H, J = 5.0 Hz), 4.50 (q, 2H, J = 7.2 Hz), 3.80 (m, 2H), 3.28 (s, 2H), 2.93 (m, 2H), 2.88 (s, 3H), 2.13−2.06 (m, 4H), 1.96−1.78 (m, 2H), 1.72 (s, 3H), 1.64 (s, 6H), 1.51−1.41 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.2, 164.9, 159.8, 158.9, 149.9, 141.9, 135.0, 128.5 (2C), 128.3 (2C), 125.9, 120.8, 114.5, 110.3, 108.4, 105.7, 104.4, 62.5, 41.0, 37.1, 33.1, 30.7, 30.1, 29.1, 27.9, 25.7, 20.8, 14.2; HRMS-ESI (m/z) calcd for $C_{31}H_{37}O_6$ (M + H^+) 505.2590, found 505.2592.

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Synthesis of Resorcylates 8a and 18 Using Allyl Chloride. $Pd(PPh_3)_4$ (9.5 mg, 0.008 mmol, 2.5 mol %) and Cs_2CO_3 (323 mg, 0.99 mmol, 3.0 equiv) were stirred in THF (1 mL) for 10 min at 0 °C. A mixture of diketoester−dioxinone **10a** (94 mg, 0.33 mmol, 1.0 equiv) and allyl chloride **17** (28 mg, 0.36 mmol, 1.1 equiv) in THF (1 mL) was added with stirring, and after 12 h at 25 °C, reaction was quenched with brine (20 mL), acidified to pH 3 utilizing 1 M HCl, and extracted with EtOAc (2 × 50 mL). The organic extracts were combined, dried ($MgSO_4$), filtered, rotary evaporated, and chromatographed (hexanes/EtOAc 9:1) to give the isophthalate **8a** (53 mg, 52%) and resorcylate **18** (34 mg, 39%) as a colorless oil: R_f 0.62 (EtOAc/hexanes 1:9); IR 1718, 1663, 1582, 1435, 1310, 1269, 1210, 1176, 1154, 1032, 920 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 11.63 (s, 1H), 6.41 (s, 1H), 3.99 (s, 3H), 2.91 (s, 3H), 1.70 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.5, 167.1, 160.9, 159.7, 150.3, 110.8, 106.6, 104.9, 103.1, 52.7, 25.7 (2C), 20.3; HRMS-ESI (m/z) calcd for $C_{13}H_{15}O_6$ ($M + H^+$) 267.0869, found 267.0876.

■ ASSOCIATED CONTENT

Supporting Information

^1H and ^{13}C NMR spectra of compounds **8a−h**, **10a−h**, **11a,b**, **16a−o**, and **18**, as well as X-ray structural data for **8c**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: agm.barrett@imperial.ac.uk.

Notes

The authors declare no competing financial interest.

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