Catalyst-Controlled Regio- and Stereoselective Synthesis of Diverse 12H-6,12-Methanodibenzo[d,g][1,3]dioxocines

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Catalyst-Controlled Regio- and Stereoselective Synthesis of Diverse 12*H*-6,12-Methanodibenzo[*d*,*g*][1,3]dioxocines

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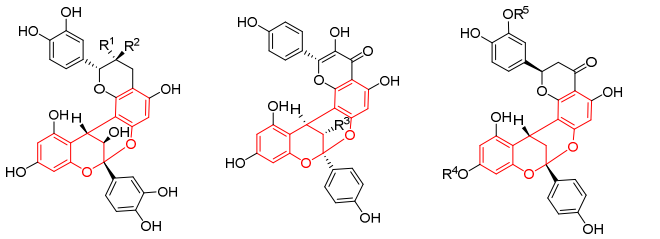
We describe an efficient one-pot regio- and stereoselective method for synthesizing diverse 1-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocines and 3-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocines using ethylenediammonium diacetate (EDDA) or *p*-toluenesulfonic acid (PTSA) catalyzed reactions between various resorcinols and a number of 2-hydroxychalcones. These reactions involve a catalyst-controlled cascade Michael-type reaction/double cyclization process. Importantly, these reactions provide a rapid synthetic route to the production of biologically interesting complex molecules that are generally prepared using multi-steps reactions.

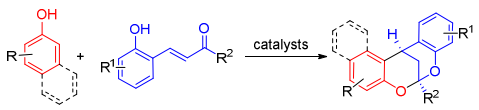
The biological activities and structural complexities of natural products have stimulated organic chemists to design novel and efficient strategies for assembling challenging structures.[1] In particular, the synthesis of complex molecules from simple starting materials in a minimum number of steps represents one of the most challenging goals in organic synthesis.[2] Organocatalyzed cascade reactions have become powerful tools for the construction of functionalized polycyclic molecules.[3] Molecules bearing a 12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine moiety are widely found in nature (Figure 1) and have been shown to possess a number of important and potent biological and pharmacological activities. For example, the flavonoids proanthocyanidin A1 (**1**) and A2 (**2**) isolated from the skins of mature peanuts (*Arachis hypogaes* L.),[4a-c] *Ecdysanthera* utilis,[4d] and cacao beans (*Theobroma cacao* L., Sterculiaceae)[4e] exhibit a range of biological and pharmacological properties, including antioxidant,[5a] intestinal disaccharidase inhibitory,[5a] anti-diabetic,[5b] anti-inflammatory,[5c] antiangiogenic,[5d] anti-wrinkle,[5e] antimicrobial,[5f] antiviral,[5g] and anti-HIV-1 activities.[5h] In addition, proanthocyanidin A2 (**2**) exhibit higher selective inhibition of viral RNA synthesis in canine distemper virus (CDV) infection than ribavirin; therefore **2** has potential usefulness as an anti-CDV compound inhibiting viral replication.[5i] Both ephedrannin A (**3**) and B (**4**) were isolated from *Ephedra sinica*[6a,b] and *Daphniphyllum angustifolium Hutch*[6c] and found to effectively suppress the transcription of tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β). They also showed potent anti-inflammatory effects on LPS-stimulated macrophages by suppressing the translocation of nuclear factor-kappa B (NF-κB) and the phosphorylation of p38 mitogen-activated protein (MAP) kinase.[6a] Diinsininol (**5**) and diinsinin (**6**) were isolated from the rhizomes of *Sarcophyte piriei,* and exhibited inhibition in a prostaglandin synthesis assay with IC_{50} values of 9.20 μM and 13.14 μM, respectively.[7] They also showed inhibition in a platelet-activating-factor (PAF)-induced exocytosis assay with IC_{50} values of 49 μM and 39 μM, respectively, which were more potent than that shown by the known PAF antagonist ginkgolide BN 52021 isolated from the tree *Ginkgo biloba* (IC_{50} 80 μM).[7]



Proanthocyanidin A1 (**1**) R^1= H, R^2= OH Ephedrannin A (**3**) R^3= OH Diinsininol (**5**) R^4= β-D-glucose, R^5 = OH
Proanthocyanidin A2 (**2**) R^1= OH, R^2= H Ephedrannin B (**4**) R^3= H Diinsinin (**6**) R^4= β-D-glucose, R^5 = H

Figure 1. Selected biogically interesting natural products bearing a methanodibenzodioxocine moiety

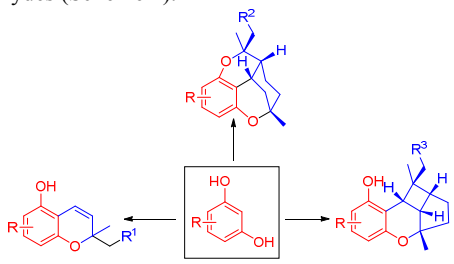
Given the importances of these biological and pharmacological activities, several synthetic methods have been devised for 12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocines, including 2,8-dioxabicyclo[3.3.1]nonanes.[8] Of these methods, sequential Michael addition/bicyclization was recently developed for the synthesis of 2,8-dioxabicyclo[3.3.1]nonanes.[8a,d] In addition, the $Pd(PhCN)_2Cl_2$/(*R*)-3,5-xylyl-BINAP catalyzed reaction was developed for the asymmetric synthesis of chiral 12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocines from 2-hydroxyphenylboronic acids and 2-hydroxychalcones.[8b] Recently, other general methods of producing 12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocines have been developed by reacting phenols or naphthols with 2-hydroxychalcones in the presence of catalytic amounts of AgOTf[8c] or 10-camphorsulfonic



Scheme 1. Reported general method for 12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocines

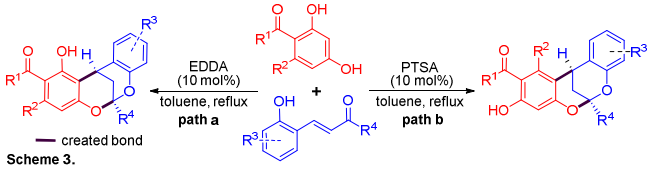
acid[8q] (Scheme 1). Although several methods have been described for the synthesis of 12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocines from phenols or naphthols, no method employing substituted resorcinols and 2-hydroxychalcones has been previously reported.

Recently, based on substituted resorcinols, a number of important methods for synthesizing biologically interesting and active heterocycles bearing benzopyrans[9] and benzoxazoles[10] have been devised, and we have also reported new methods of preparing a variety of benzopyrans[11] and polycycles bearing citran[12a-c] or cyclol nuclei[12d] using organocatalytic domino reactions between resorcinols and various α,β-unsaturated aldehydes (Scheme 2).



Scheme 2. Our reported methodologies of for the synthesis of benzopyrans and polycycles starting from substituted resorcinols

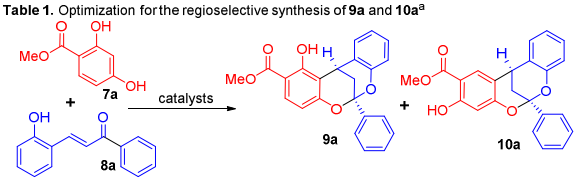
As part of our ongoing studies on new methods of synthesizing biologically interesting heterocycles, we examined novel cascade reactions between resorcinols and 2-hydroxychalcones in the presence of several organocatalysts. Herein, we report the straightforward, efficient one-pot synthesis of diverse 1-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine derivatives (path a) and 3-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine derivatives (path b) using catalyst-controlled regio- and stereoselective cascade reactions between resorcinols and 2-hydroxychalcones (Scheme 3).



Scheme 3.

To synthesize 12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine derivatives, we first examined reactions between methyl 2,4-dihydroxybenzoate (**7a**) and (*E*)-3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one (**8a**) in the presence of several Lewis acids, Brønsted acids or Brønsted acids/bases. The results obtained are depicted in Table 1. In the absence of catalyst, no products were formed (entry 1). With $MgBr_2$ or $FeCl_3$ as Lewis acid catalyst in refluxing toluene for 24 h, trace amounts of **9a** and **10a** were produced (entries 2 and 3). When 10 mol% of other Lewis acid catalysts, namely, $InCl_3$, $In(OTf)_3$, $Yb(OTf)_3$, or AgOTf were used in refluxing toluene for 12 h, product **9a** was produced in 10-65% yield as a major component with a trace of **10a** (entries 4-7). Interestingly, using 10 mol % of iodine, products **9a** and **10a** were formed in 42 and 15% yield, respectively (entry 8). When *p*-toluenesulfonic acid (PTSA, 10 mol %) was used as a Brønsted acid, **10a** was produced in 82% yield with excellent regioselectivity (entry 9). As bifunctional catalysts of Brønsted acids and bases, further reactions utilizing several other organocatalysts, such as, pyridine hydrochloride (Pyr·HCl), pyridinium *p*-toluenesulfonate (PPTS), L-proline, or ethylenediammonium diacetate (EDDA) were attempted. Treatment of **7a** with **8a** in the presence of 10 mol% of pyridinium *p*-toluenesulfonate (PPTS) in refluxing toluene for 12 h provided **9a** and **10a** in 15 and 33% yield, whereas reaction in the presence of Pyr·HCl (10 mol%) afforded compounds **9a** (40%) and **10a** (15%), respectively (entries 10 and 11). Interestingly, using L-proline or EDDA as bifunctional catalysts, **9a** was exclusively formed in 62 and 85% yield, respectively (entries 12 and 13). Further screening of solvents and reaction temperatures indicated that non-polar aromatic solvents and high reaction temperature generally favor this reaction (entries 14-17).[13] In view of these results, we found that products **9a** and **10a** could be regioselectively synthesized depending on the used catalysts. Compounds **9a** and **10a** were assigned based on analyses of their spectral data. In the ^{1}H NMR spectrum of **9a**, two characteristic aromatic protons on the benzene ring derived from a resorcinol ring produced doublets at δ 7.62 (d, J = 9.0 Hz) and 6.57 (d, J = 9.0 Hz) ppm, whereas in **10a**, the two singlet protons produced peaks at 7.66 and 6.53 ppm (Figure 2). The stereochemistry of **9a** was confirmed by X-ray crystallographic analysis of the structurally related compound **9n** and the stereochemistry of **10a** was confirmed directly by X-ray crystallographic analysis.[14]

Table 1. Optimization for the regioselective synthesis of **9a** and **10a**[a]



Entry	Catalysts	Solvent	Temp.	Time (h)	Yield [%][b] 9a	10a
1	-	Toluene	Reflux	15	NR	NR
2	$MgBr_2$	Toluene	Reflux	15	Trace	Trace
3	$FeCl_3$	Toluene	Reflux	15	Trace	Trace
4	$InCl_3$	Toluene	Reflux	12	20	Trace
5	$In(OTf)_3$	Toluene	Reflux	12	61	Trace
6	$Yb(OTf)_3$	Toluene	Reflux	12	10	Trace
7	AgOTf	Toluene	Reflux	12	65	Trace
8	Iodine	Toluene	Reflux	12	42	15
9	**PTSA**	**Toluene**	**Reflux**	**6**	**Trace**	**82**
10	PPTS	Toluene	Reflux	12	15	33
11	Pyr•HCl	Toluene	Reflux	12	40	15
12	L-Proline	Toluene	Reflux	12	62	Trace
13	**EDDA**	**Toluene**	**Reflux**	**8**	**85**	**Trace**
14	EDDA	*p*-xylene	Reflux	12	70	Trace
15	EDDA	1,4-Dioxane	Reflux	12	74	Trace
16	EDDA	MeCN	Reflux	12	40	Trace
17	EDDA	Ethanol	Reflux	12	10	Trace

[a] Reaction conditions: **7a** (1.0 mmol) and **8a** (1.1 mmol), catalyst (10 mol%), and solvent (5 mL) under a nitrogen atmosphere.
[b] Isolated yields.

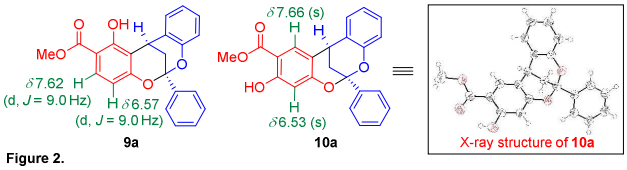
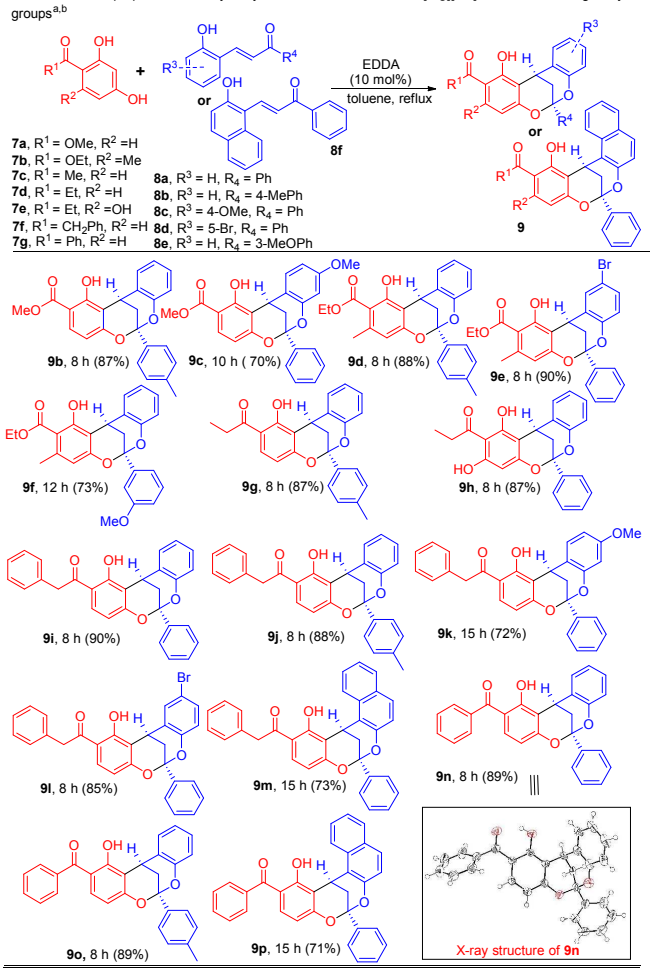


Figure 2.

To prepare a variety of 1-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocines **9** bearing aryl groups at C-6, further reactions between various resorcinols and a number of 2-hydroxychalcones were examined under the optimized reaction conditions. As shown in Table 2, resorcinols **7a-7g** with ester and ketone substituents reacted with 2-hydroxychalcones **8a-8e** to afford corresponding 1-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocines **9b-9p** in 70-90% yield with

Table 2. Further preparation of 1-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocines bearing 6-aryl groups[a,b]

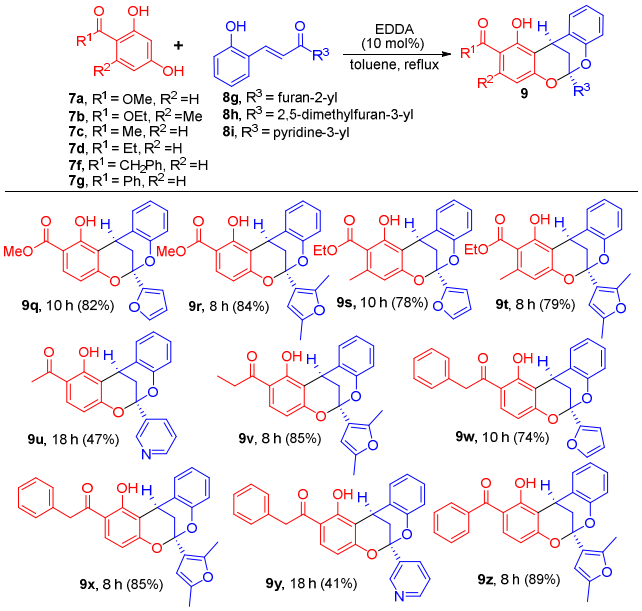


[a] Reaction conditions: **7** (1.0 mmol), **8a-e** (1.1 mmol), EDDA (10 mmol%), and toluene (5.0 mL) under a nitrogen atmosphere.
[b] Isolated yields.

excellent regioselectivity. Molecules bearing an electron-donating or -withdrawing group on the 3-(2-hydroxy phenyl) ring of 2-hydroxychalcones provided the desired products. For example, reaction of **7a** with **8c** in the presence of 10 mol% of EDDA in refluxing toluene for 10 h provided **9c** in 70% yield, whereas treatment of **7b** with **8d** for 8 h gave the desired product **9e** in 90% yield. Similarly, reactions between **7f** and **8c** or **8d** provided the desired products **9k** and **9l** in 72 and 85% yield, respectively. Furthermore, reactions between resorcinols **7a**, **7b**, **7d**, **7f**, or **7g** and 2- hydroxychalcones **8b** or **8e** bearing an electron-donating group, such as, a methyl or a methoxy group, gave the desired products **9b**, **9d**, **9f**, **9g**, **9j**, and **9o** in 73-89% yield. Importantly, reaction between **7e** and **8a** provided polyphenol-substituted 1-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine **9h** in 87% yield. In addition, the biologically interesting naphthalene-fused 1-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocines **9m** and **9p** were synthesized by reacting **7f** or **7g** with **8f** in 73 and 71% yield, respectively. These reactions provide rapid synthetic routes to a variety of 1-hydroxymethanodibenzo[*d*,*g*][1,3]dioxocine derivatives bearing aryl groups on C-6.

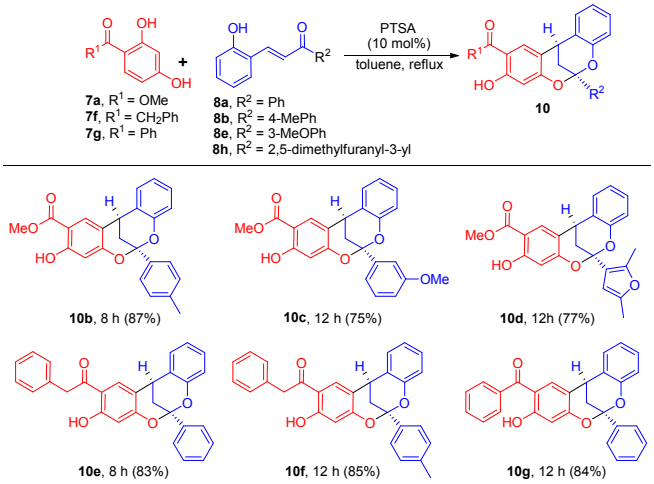
Using optimized conditions, we further explored the generality of this cascade reaction for the synthesis of 1-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine derivatives **9** bearing heterocycles at C-6, by using resorcinols and heterocyclic 2-hydroxychalcones. Results are summarized in Table 3. Reactions between **7a**, **7b**, or **7f** and **8g** bearing a 1-(furan-2-yl) ring in the presence of 10 mol % of EDDA in refluxing toluene for 10 h afforded the desired products **9q**, **9s**, and **9w** in 82, 78, and 74% yield, respectively. Also, cascade reactions of **7a**, **7b**, **7d**, **7f** or **7g** with **8h** bearing a 1-(2,5-dimethylfuran-3-yl) ring provided the desired products **9r**, **9t**, **9v**, **9x** and **9z** in the range of 79-89% yield. Furthermore, treatment of **7c** or **7f** with **8i** containing a 1-(pyridine-3-yl) ring provided the products **9u** and **9y** in 47 and 41% yield, respectively. These reactions provided diverse 1-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine derivatives with heterocycles on the C-6.

Table 3. Further reactions for preparation of 2-substituted 1-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocines bearing 6-heterocycles[a,b]

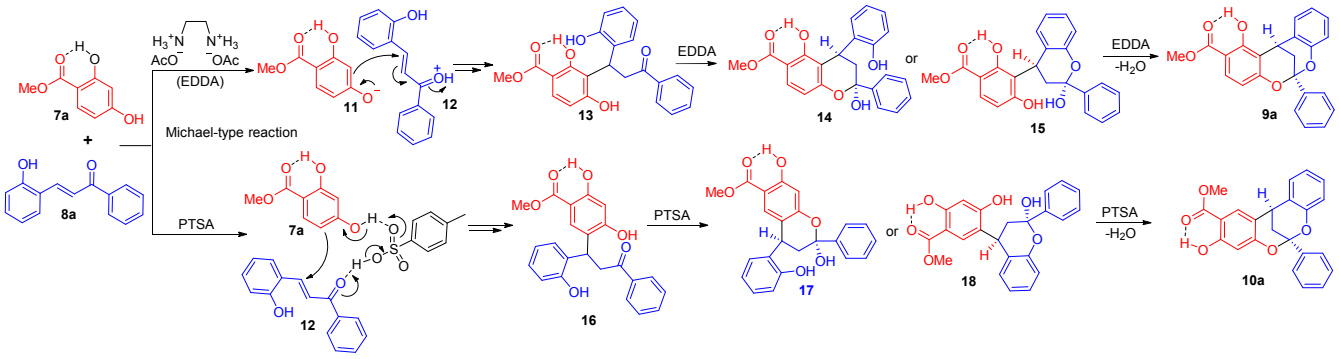


[a] Reaction conditions: **7** (1.0 mmol), **8g-i** (1.1 mmol), EDDA (10 mmol%), and toluene (5.0 mL) under a nitrogen atmosphere.
[b] Isolated yields.

Table 4. Regioselective synthesis of 3-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocines **10**[a,b]



[a] Reaction conditions: **7** (1.0 mmol), **8** (1.1 mmol), PTSA (10 mmol%), and toluene (5.0 mL) under a nitrogen atmosphere.
[b] Isolated yields.



Scheme 4. Possible mechanism for formation of **9a** and **10a**.

The regioselective synthesis of 3-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine derivatives **10** were carried out in the presence of 10 mol% of PTSA as catalyst (Table 4). Reactions between **7a** and **8b**, **8e**, or **8h** in the presence of 10 mol% PTSA in refluxing toluene for 8-12 h afforded products **10b**-**10d** in 87, 75, and 77% yield, respectively. Similarly, reaction between **7f** and **8a** or **8b** in refluxing toluene for 8 h or 12 h provided the desired products **10e** and **10f** in 83 and 85% yield, respectively, whereas reaction between **7g** and **8a** for 12 h gave **10g** in 84% yield. These reactions provided a rapid means of synthesizing a variety of novel 3-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine derivatives in good yields.

A proposed mechanism for the catalyst-controlled regioselective synthesis of **9a** and **10a** using the Michael-type addition/double cyclization processes[8a-d,q] is depicted in Scheme 4. We propose that the 2-hydroxychalcone (**8a**) is protonated by EDDA to give intermediate **12**, which facilitates a regioselective Michael-type reaction at the C-3 position of **11,** derived from catalytic reaction between **7a** and the ⁻OAc of EDDA, to give intermediate **13** via isomerization and tautomerism. Next, in the presence of EDDA, intermediate **13** undergoes intramolecular cyclization to give two possible hemiketal intermediates (**14** or **15**). The regioselectivity for formation of **9a** can be rationalized by regioselective intramolecular cyclization of more reactive 4-hydroxy group of intermediate **13** or **15**, probably due to intramolecular hydrogen bonding between carbonyl and adjacent 2-hydroxy group. This kind of regioselective nucleophilic attack of **7a** at C-3 agrees well with our previous observation of EDDA catalyzed reactions.[11d,e,15] Further intramolecular cyclization followed by dehydration of **14** or **15** gives final product **9a**. In addition, the usage of various metal salts as catalysts provides the same product **9a** as EDDA. In the presence of metal salts, the reaction mechanism for **9a** can be explained through the coordination of metal salts to β-hydroxycarbonyl unit of **7a**[16] followed by double cyclization on more reactive 4-hydroxy group. On the other hand, the PTSA catalyzed regioselective Michael-type addition reaction of **7a** to **12** at C-5 with less steric hindrance followed by tautomerization gives intermediate **16** through a double activation of the catalyst, which can play a role as a Brønsted acid and base to the carbonyl group of **12** and the 4-hydroxy group of **7a** by hydrogen bondings.[17] This similar regioselectivity was also observed for orthophosphoric acid catalyzed reactions between 2′,4′-dihydroxyacetophenones and isoprene or 3-buten-2-ol to give 7-hydroxychromans.[18] Intermediate **16** would then undergo further intramolecular cyclization to give intermediate **17** or **18**, which by cyclization and dehydration gives **10a**.

Conclusions

In summary, the efficient regio- and stereoselective one-step synthesis of 1-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine or 3-hydroxy-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine derivatives was achieved using EDDA or PTSA-catalyzed cascade reactions between resorcinols and 2-hydroxychalcones. Using this methodology, a variety of novel 12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine derivatives were synthesized. The described methodology has the advantages of utilizing mild reaction conditions, inexpensive non-metal catalysts, and of being straightforward. In particular, this reaction solves the problems posed by the need for multi-step reactions to synthesize complex 12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine derivatives.

Acknowledgments

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Experimental section

General Experimental Details

All experiments were conducted in a nitrogen atmosphere. Merck precoated silica gel plates (Art. 5554) containing a fluorescent indicator were used for analytical TLC, and flash column chromatography was performed using silica gel (Merck, Kieselgel60, 230-400 mesh, Art. 9385). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker ARX-300 MHz spectrometer (at 300 and 75 MHz, respectively) or Varian VNS-600 MHz spectrometer (at 600 and 150 MHz, respectively) in $CDCl_3$ as the solvent. IR spectra were recorded on a Jasco FTIR 5300 spectrophotometer. HRMS was carried out at the Korean Basic Science Institute.

General Procedure for the Synthesis of methanodibenzo[*d*,*g*][1,3]dioxocine derivatives: 9-10. To a solution of resorcinols **7** (1.0 mmol) in toluene (4 mL) was added 2-hydroxychalcones (1.1 mmol) and ethylenediamine diacetate (EDDA, 18 mg, 0.1 mmol) or *p*-toluenesulfonic acid (PTSA, 17 mg 10 mol%) at room temperature. The reaction mixture was refluxed for 6-12 h. After completion of the reaction as indicated by TLC (hexane/EtOAc, 10:1, v/v), the solvent was evaporated,

and the residue was purified by flash column chromatography on silica gel using hexane/EtOAc (15:1, v/v) to give 12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine derivatives **9-10**.

Methyl 1-hydroxy-6-phenyl-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine-2-carboxylate (9a). Yellow solid; yield 318 mg; 85%; m.p. 124-125 °C; IR (KBr): 3067, 2952, 1666, 1623, 1488, 1442, 1262, 1166, 1131, 1078, 1018, 900, 796, 758, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.33 (s, 1H), 7.75-7.72 (m, 2H), 7.62 (d, J = 9.0 Hz, 1H), 7.53-7.48 (m, 1H), 7.46-7.41 (m, 3H), 7.15 (dd, J = 8.1, 7.2 Hz, 1H), 7.02 (d, J = 8.1 Hz, 1H), 6.93 (dd, J = 7.5, 7.2 Hz, 1H), 6.57 (d, J = 9.0 Hz, 1H), 4.61 (t, J = 3.0 Hz, 1H), 3.89 (s, 3H), 2.35 (dq, J = 13.2, 3.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.59, 159.45, 157.62, 151.95, 140.84, 128.97, 128.92, 128.36, 128.09, 127.90, 126.09, 125.68, 121.42, 116.34, 114.07, 108.61, 105.75, 98.87, 52.06, 32.65, 26.34. HRMS: *m/z* [M$^+$] calcd. for $C_{23}H_{18}O_5$ 374.1154; found: 374.1153.

Methyl 1-hydroxy-6-(*p*-tolyl)-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine-2-carboxylate (9b). Yellow solid; yield 338 mg; 87%; m.p. 176-177 °C; IR (KBr): 3091, 2953, 1667, 1625, 1489, 1441, 1346, 1262, 1131, 1079, 1020, 901, 797, 759 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.33 (s, 1H), 7.64-7.60 (m, 3H), 7.52 (dd, J = 7.5, 1.5 Hz, 1H), 7.27 (d, J = 8.1 Hz, 2H), 7.15 (dd, J = 8.1, 7.2 Hz, 1H), 7.02 (d, J = 7.2 Hz, 1H), 6.93 (dd, J = 7.5, 7.2 Hz, 1H), 6.56 (d, J = 9.0 Hz, 1H), 4.61 (t, J = 3.0 Hz, 1H), 3.89 (s, 3H), 2.41 (s, 3H), 2.34 (dq, J = 13.2, 3.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.58, 159.45, 157.71, 152.01, 138.73, 138.03, 129.00, 128.92, 128.06, 127.84, 126.09, 125.56, 121.34, 116.34, 114.10, 108.62, 105.69, 98.91, 52.00, 32.62, 26.39, 21.16. HRMS: *m/z* [M$^+$] calcd. for $C_{24}H_{20}O_5$ 388.1311; found: 388.1308.

Methyl 1-hydroxy-9-methoxy-6-phenyl-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine-2-carboxylate (9c). Yellow solid; yield 283 mg; 70%; m.p. 172-173 °C; IR (KBr): 2956, 1666, 1494, 1445, 1261, 1138, 897 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.30 (s, 1H), 7.72-7.70 (m, 2H), 7.61 (d, J = 9.0 Hz, 1H), 7.46-7.43 (m, 2H), 7.41-7.39 (m, 1H), 7.05 (d, J = 3.0 Hz, 1H), 6.33 (d, J = 9.6 Hz, 1H), 6.69 (dd, J = 9.0, 3.0 Hz, 1H), 6.55 (d, J = 9.0 Hz, 1H), 4.54 (t, J = 3.0 Hz, 1H), 3.89 (s, 3H), 3.76 (s, 3H), 2.32 (dq, J = 13.8, 3.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.63, 159.45, 157.90, 154.04, 145.83, 141.01, 129.05, 128.89, 128.36, 126.63, 125.70, 116.94, 113.99, 113.76, 112.69, 108.65, 105.75, 98.88, 55.75, 52.06, 32.70, 26.72. HRMS: *m/z* [M$^+$] calcd. for $C_{24}H_{20}O_6$ 404.1260; found: 404.1259.

Ethyl 1-hydroxy-3-methyl-6-(*p*-tolyl)-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine-2-carboxylate (9d). Yellow solid; yield 366 mg; 88%; m.p. 133-134 °C; IR (KBr): 3041, 2970, 1641, 1585, 1452, 1262, 1159, 1113, 1025, 907, 812, 750 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.27 (s, 1H), 7.65 (d, J = 8.1 Hz, 2H), 7.55 (d, J = 7.5 Hz, 1H), 7.28 (d, J = 8.1 Hz, 2H), 7.16 (dd, J = 8.1, 7.5 Hz, 1H), 7.03 (d, J = 8.1 Hz, 1H), 6.94 (dd, J = 7.5, 7.2 Hz, 1H), 6.45 (s, 1H), 4.59 (t, J = 3.0 Hz, 1H), 4.40 (q, J = 7.2 Hz, 2H), 2.49 (s, 3H), 2.43 (s, 3H), 2.34 (dq, J = 13.2, 3.0 Hz, 2H), 1.41 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.94, 161.10, 156.06, 152.01, 140.93, 138.62, 138.17, 128.96, 127.99, 127.68, 126.40, 125.55, 121.24, 116.25, 111.99, 111.68, 105.61, 98.88, 61.24, 32.90, 26.43, 24.21, 21.15, 14.17. HRMS: *m/z* [M$^+$] calcd. for $C_{26}H_{24}O_5$ 416.1624; found: 416.1625.

Ethyl 10-bromo-1-hydroxy-3-methyl-6-phenyl-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine-2-carboxylate (9e). Yellow solid; yield 432 mg; 90%; m.p. 137-138 °C; IR (KBr): 3057, 2976, 2931, 2358, 1643, 1583, 1474, 1413, 1321, 1259, 1161, 1124, 1020, 910, 813, 737, 495 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.22 (s, 1H), 7.69 (d, J = 7.8 Hz, 2H), 7.62 (d, J = 1.8 Hz, 1H), 7.45 (t, J = 7.2 Hz, 2H), 7.41 (t, J = 7.2 Hz, 1H), 7.21 (dd, J = 7.8, 2.4 Hz, 1H), 6.87 (d, J = 9.0 Hz, 1H), 6.42 (s, 1H), 4.52 (t, J = 3.0 Hz, 1H), 4.42-4.37 (m, 2H), 2.47 (s, 3H), 2.30 (dq, J = 13.8, 3.0 Hz, 2H), 1.40 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.86, 161.01, 155.79, 151.21, 141.38, 140.61, 130.57, 130.53, 129.00, 128.47, 128.39, 125.60, 118.06, 113.45, 111.65, 111.32, 105.95, 98.93, 61.38, 32.59, 26.32, 24.21, 14.23. HRMS: *m/z* [M$^+$] calcd. for $C_{25}H_{21}BrO_5$ 480.0572; found: 480.0571.

Ethyl 1-hydroxy-6-(3-methoxyphenyl)-3-methyl-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocine-2-carboxylate (9f). Yellow solid; yield 315 mg; 73%; m.p. 123-124 °C; IR (KBr): 3065, 2961, 1634, 1458, 1266, 1115, 1034, 897, 807 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.19 (s, 1H), 7.50 (dd, J = 7.8, 1.2 Hz, 1H), 7.36 (t, J = 7.8 Hz, 1H), 7.29 (d, J = 8.4 Hz, 2H), 7.12 (dd, J = 7.8, 7.2 Hz, 1H), 7.00 (d, J = 7.8 Hz, 1H), 6.94 (dd, J = 7.2, 1.2 Hz, 1H), 6.91 (dd, J = 7.8, 6.6 Hz, 1H), 6.42 (s, 1H), 4.56 (t, J = 3.0 Hz, 1H), 4.38 (q, J = 7.2 Hz, 2H), 3.85 (s, 3H), 2.45 (s, 3H), 2.32 (dq, J = 13.8, 3.0 Hz, 2H), 1.38 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.96, 161.10, 159.62, 155.98, 151.95, 142.63, 141.02, 129.44, 128.03, 127.75, 126.42, 121.36, 118.06, 116.31, 114.18, 112.04, 111.73, 111.71, 105.78, 98.77, 61.29, 55.36, 32.93, 26.42, 24.21, 14.22. HRMS: *m/z* [M$^+$] calcd. for $C_{26}H_{24}O_6$ 432.1573; found: 432.1573.

1-(1-Hydroxy-6-(*p*-tolyl)-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocin-2-yl)propan-1-one (9g). Yellow solid; yield 336 mg; 87%; m.p. 126-127 °C; IR (KBr): 3039, 2975, 1626, 1488, 1456, 1239, 1164, 1110, 1032, 897, 813, 755 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.22 (s, 1H), 7.64 (d, J = 8.4 Hz, 2H), 7.55-7.52 (m, 2H), 7.28 (d, J = 7.8 Hz, 2H), 7.16 (dd, J = 8.7, 8.4 Hz, 1H), 7.03 (d, J = 8.1 Hz, 1H), 6.94 (t, J = 7.2 Hz, 1H), 6.56 (d, J = 9.0 Hz, 1H), 4.62 (t, J = 3.0 Hz, 1H), 2.95-2.88 (m, 2H), 2.42 (s, 3H), 2.35 (dq, J = 13.5, 3.0 Hz, 2H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.72, 160.80, 158.03, 151.92, 138.78, 137.89, 129.23, 129.01, 128.10, 127.85, 126.04, 125.53, 121.39, 116.30, 114.44, 113.44, 108.33, 99.01, 32.57, 31.16, 26.10, 21.17, 8.55. HRMS: *m/z* [M$^+$] calcd. for $C_{25}H_{22}O_4$ 386.1518; found: 386.1518.

1-(1,3-Dihydroxy-6-phenyl-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocin-2-yl)propan-1-one (9h). Yellow solid; yield 338 mg; 87%; m.p. 201-202 °C; IR (KBr): 2974, 1616, 1434, 1235, 1131, 1028, 893, 753 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 7.2 Hz, 1H), 7.32 (t, J = 7.8 Hz, 2H), 7.29-7.27 (m, 1H), 7.02 (dd, J = 7.8, 7.2 Hz, 1H), 6.90 (d, J = 7.8 Hz, 1H), 6.81 (dd, J = 7.8, 7.2 Hz, 2H), 5.78 (s, 1H), 4.38 (t, J = 3.0 Hz, 1H), 2.96-2.87 (m, 2H), 2.19 (dq, J = 13.8, 3.0 Hz, 2H), 1.15 (dd, J = 7.8, 7.2 Hz, 1H), 1.03 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.39, 162.39, 158.40, 157.79, 151.65, 140.74, 128.90, 128.32, 127.97, 127.74, 126.70, 125.60, 121.54, 116.12, 106.81, 105.05, 99.29, 95.16, 37.23, 33.10, 25.89, 8.66. HRMS: *m/z* [M$^+$] calcd. for $C_{24}H_{20}O_5$ 388.1311; found: 388.1309.

1-(1-Hydroxy-6-phenyl-12*H*-6,12-

methanodibenzo[*d,g*][1,3]dioxocin-2-yl)-2-phenylethan-1-one (9i). Yellow solid; yield 391 mg; 90%; m.p. 182-183 °C; IR (KBr): 3034, 2943, 2359, 1624, 1489, 1451, 1420, 1351, 1237, 1102, 1028, 897, 756, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 13.17 (s, 1H), 7.80-7.77 (m, 2H), 7.66 (d, J = 9.0 Hz, 1H), 7.57 (d, J = 7.5 Hz, 1H), 7.52-7.47 (m, 3H), 7.40-7.34 (m, 2H), 7.32-7.28 (m, 3H), 7.23-7.17 (m, 1H), 7.08 (d, J = 8.1 Hz, 1H), 6.98 (dd, J = 7.5, 7.2 Hz, 1H), 6.61 (d, J = 8.7 Hz, 1H), 4.65 (t, J = 3.0 Hz, 1H), 4.21 (s, 2H), 2.33 (dq, J = 13.5, 3.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.31, 161.35, 158.29, 151.78, 140.60, 134.22, 129.91, 129.26, 128.94, 128.67, 128.34, 128.11, 127.92, 127.01, 125.87, 125.60, 121.49, 116.28, 114.51, 113.31, 108.55, 99.00, 44.74, 32.51, 26.00. HRMS: *m/z* [M^+] calcd. for $C_{29}H_{22}O_4$ 434.1518; found: 434.1517.

1-(1-Hydroxy-6-(*p*-tolyl)-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-2-yl)-2-phenylethan-1-one (9j). Yellow solid; yield 394 mg; 88%; m.p. 205-206 °C; IR (KBr): 3034, 2947, 1624, 1489, 1352, 1237, 1173, 1103, 1031, 897, 813, 737 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 13.09 (s, 1H), 7.66-7.61 (m, 3H), 7.51 (dd, J = 7.5, 1.5 Hz, 1H), 7.33-7.24 (m, 7H), 7.15 (dd, J = 8.1, 7.2 Hz, 1H), 7.02 (d, J = 7.2 Hz, 1H), 6.93 (dd, J = 7.5, 7.2 Hz, 1H), 6.56 (d, J = 9.0 Hz, 1H), 4.60 (t, J = 3.3 Hz, 1H), 4.19 (s, 2H), 2.41 (s, 3H), 2.34 (dq, J = 13.5, 3.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.31, 161.40, 158.44, 151.86, 138.83, 137.79, 134.28, 129.91, 129.28, 129.03, 128.71, 128.12, 127.90, 127.05, 125.90, 125.52, 121.44, 116.33, 114.57, 113.30, 108.62, 99.07, 44.80, 32.53, 26.06, 21.18. HRMS: *m/z* [M^+] calcd. for $C_{30}H_{24}O_4$ 448.1675; found: 448.1672.

1-(1-Hydroxy-9-methoxy-6-phenyl-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-2-yl)-2-phenylethan-1-one (9k). Yellow solid; yield 408 mg; 88%; m.p. 80-81 °C; IR (KBr): 3052, 2943, 2345, 1619, 1493, 1233, 1100, 1036, 893, 807, 737 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 13.07 (s, 1H), 7.71-7.69 (m, 2H), 7.64 (d, J = 9.0 Hz, 1H), 7.46-7.43 (m, 2H), 7.42-7.39 (m, 1H), 7.33-7.31 (m, 2H), 7.26-7.24 (m, 3H), 7.04 (d, J = 3.0 Hz, 1H), 6.93 (d, J = 9.0 Hz, 1H), 6.69 (dd, J = 9.0, 3.0 Hz, 1H), 6.55 (d, J = 9.0 Hz, 1H), 4.54 (t, J = 3.0 Hz, 1H), 4.18 (d, J = 2.4 Hz, 2H), 3.75 (s, 3H), 2.32 (dq, J = 13.8, 3.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 202.35, 161.43, 158.65, 154.10, 145.68, 140.80, 134.33, 130.02, 129.33, 128.96, 128.75, 128.39, 127.10, 126.46, 125.67, 116.97, 114.51, 113.93, 113.39, 112.61, 108.65, 99.07, 55.73, 44.87, 32.63, 26.43. HRMS: *m/z* [M^+] calcd. for $C_{30}H_{24}O_5$ 464.1624; found: 464.1622.

1-(10-Bromo-1-hydroxy-6-phenyl-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-2-yl)-2-phenylethan-1-one (9l). Yellow solid; yield 435 mg; 85%; m.p. 195-196 °C; IR (KBr): 3065, 3032, 2980, 1625, 1484, 1422, 1353, 1241, 1102, 1045, 898, 810, 739, 701, 601, 516 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 13.01 (s, 1H), 7.66 (d, J = 7.2 Hz, 2H), 7.57 (d, J = 9.0 Hz, 1H), 7.53 (d, J = 2.4 Hz, 1H), 7.38-7.34 (m, 3H), 7.24 (dd, J = 8.4, 7.2 Hz, 2H), 7.18-7.17 (m, 3H), 7.14 (dd, J = 8.4, 1.8 Hz, 1H), 6.80 (d, J = 9.0 Hz, 1H), 6.47 (d, J = 9.0 Hz, 1H), 4.47 (t, J = 3.0 Hz, 1H), 4.10 (d, J = 3.6 Hz, 2H), 2.23 (dq, J = 13.8, 3.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 202.36, 161.33, 158.11, 151.06, 140.24, 134.23, 130.79, 130.65, 130.22, 129.29, 129.13, 128.75, 128.45, 127.96, 127.10, 125.57, 118.12, 113.92, 113.63, 113.50, 108.55, 99.09, 44.88, 32.22, 25.94. HRMS: *m/z* [M^+] calcd. for $C_{29}H_{21}BrO_4$ 512.0623; found: 512.0626.

1-(1-Hydroxy-6-phenyl-14*H*-6,14-methanobenzo[*d*]naphtho[1,2-*g*][1,3]dioxocin-2-yl)-2-phenylethan-1-one (9m). Yellow solid; yield 353 mg; 73%; m.p. 107-108 °C; IR (KBr): 2358, 1625, 1492, 1232, 1101, 904, 815, 748 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 13.42 (s, 1H), 8.90 (d, J = 8.4 Hz, 1H), 7.75-7.73 (m, 3H), 7.66 (dd, J = 13.2, 12.0 Hz, 2H), 7.55 (dd, J = 8.4, 7.2 Hz, 1H), 7.47 (dd, J = 7.8, 7.2 Hz, 2H), 7.44-7.42 (m, 1H), 7.36 (dd, J = 7.8, 6.6 Hz, 1H), 7.29 (dd, J = 7.8, 7.2 Hz, 2H), 7.24 (dd, J = 5.4, 3.6 Hz, 2H), 7.23-7.21 (m, 2H), 6.58 (d, J = 8.4 Hz, 1H), 5.27 (t, J = 3.0 Hz, 1H), 4.16 (s, 2H), 2.43 (dq, J = 13.8, 3.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 202.36, 161.68, 159.59, 149.82, 140.50, 134.30, 131.49, 130.29, 129.74, 129.29, 129.05, 128.78, 128.72, 128.45, 128.02, 127.07, 126.46, 125.67, 124.45, 123.93, 118.29, 118.19, 114.59, 113.47, 108.68, 98.60, 44.86, 33.33, 22.47. HRMS: *m/z* [M^+] calcd. for $C_{33}H_{24}O_4$ 484.1675; found: 484.1676.

(1-Hydroxy-6-phenyl-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-2-yl)(phenyl)methanone (9n). Yellow solid; yield 374 mg; 89%; m.p. 209-210 °C; IR (KBr): 3055, 2923, 1611, 1486, 1344, 1261, 1175, 1085, 1025, 896, 755 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 12.97 (s, 1H), 7.64 (d, J = 8.1 Hz, 2H), 7.50-7.47 (m, 3H), 7.41 (d, J = 7.2 Hz, 1H), 7.37-7.34 (m, 5H), 7.27 (d, J = 8.7 Hz, 1H), 7.11-7.04 (m, 1H), 6.94 (d, J = 7.5 Hz, 1H), 6.86 (dd, J = 7.5, 7.2 Hz, 1H), 6.43 (d, J = 9.0 Hz, 1H), 4.58 (t, J = 3.0 Hz, 1H), 2.27 (dq, J = 13.5, 3.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.35, 161.86, 158.37, 151.89, 140.65, 138.12, 133.16, 131.43, 128.97, 128.78, 128.37, 128.24, 128.15, 127.98, 125.98, 125.63, 121.54, 116.35, 114.56, 113.36, 108.25, 99.10, 32.61, 26.19. HRMS: *m/z* [M^+] calcd. for $C_{28}H_{20}O_4$ 420.1362; found: 420.1362. Structure confirmed by X-ray crystallography: CCDC 981010.

(1-Hydroxy-6-(*p*-tolyl)-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-2-yl)(phenyl)methanone (9o). Yellow solid; yield 386 mg; 89%; m.p. 186-187 °C; IR (KBr): 3057, 2945, 1612, 1485, 1344, 1261, 1177, 1084, 1028, 895, 812, 755 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 13.05 (s, 1H), 7.65-7.52 (m, 6H), 7.49-7.46 (m, 2H), 7.38 (d, J = 8.7 Hz, 1H), 7.27 (d, J = 7.8 Hz, 2H), 7.17 (dd, J = 8.4, 6.9 Hz, 1H), 7.04 (d, J = 7.5 Hz, 1H), 6.97 (dd, J = 7.5, 7.2 Hz, 1H), 6.53 (d, J = 9.0 Hz, 1H), 4.68 (t, J = 2.7 Hz, 1H), 2.41 (s, 3H), 2.38 (dq, J = 13.2, 2.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.37, 161.87, 158.49, 151.96, 138.85, 138.17, 137.84, 133.16, 131.43, 129.05, 128.78, 128.26, 128.15, 127.95, 126.02, 125.54, 121.49, 116.38, 114.59, 113.33, 108.29, 99.16, 26.23. HRMS: *m/z* [M^+] calcd. for $C_{29}H_{22}O_4$ 434.1518; found: 434.1518.

(1-Hydroxy-6-phenyl-14*H*-6,14-methanobenzo[*d*]naphtho[1,2-*g*][1,3]dioxocin-2-yl)(phenyl)methanone (9p). Yellow solid; yield 334 mg; 71%; m.p. 141-142 °C; IR (KBr): 3059, 2358, 1613, 1483, 1345, 1263, 1088, 1023, 902, 813, 749, 699 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 13.37 (s, 1H), 8.97 (d, J = 7.2 Hz, 1H), 7.77-7.75 (m, 3H), 7.70 (d, J = 9.0 Hz, 1H), 7.61 (dd, J = 8.4, 7.8 Hz, 1H), 7.56-7.54 (m, 2H), 7.52 (dd, J = 7.8, 7.2 Hz, 1H), 7.48 (d, J = 6.6 Hz, 1H), 7.46 (d, J = 6.0 Hz, 1H), 7.44-7.43 (m, 3H), 7.39 (d, J = 9.0 Hz, 2H), 7.27(d, J = 9.0 Hz, 1H), 6.56 (d, J = 9.0 Hz, 1H), 5.35 (t, J = 3.0 Hz, 1H), 2.48 (dq, J = 13.8, 3.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.46, 162.05, 159.59, 149.86, 140.48, 138.16, 133.57, 131.51, 131.45, 129.75, 129.06, 128.81, 128.46, 128.27, 128.07, 126.56, 125.69, 124.46,

123.99, 118.34, 118.25, 114.55, 113.48, 108.33, 98.65, 33.35, 22.55. HRMS: *m/z* [M^+] calcd. for $C_{32}H_{22}O_4$ 470.1518; found: 470.1519.

Methyl 6-(furan-2-yl)-1-hydroxy-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-2-carboxylate (9q). Yellow solid; yield 299 mg; 82%; m.p. 80-81 °C; IR (KBr): 3155, 2957, 1666, 1485, 1342, 1260, 1153, 1019, 896, 749 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 11.30 (s, 1H), 7.59 (d, *J* = 9.0 Hz, 1H), 7.49-7.47 (m, 2H), 7.11 (dd, *J* = 8.4, 7.2 Hz, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 6.91 (t, *J* = 7.2 Hz, 1H), 6.72 (d, *J* = 3.6 Hz, 1H), 6.51 (d, *J* = 9.0 Hz, 1H), 6.45-6.44 (m, 1H), 4.61 (t, *J* = 3.0 Hz, 1H), 3.88 (s, 3H), 2.49 (dq, *J* = 12.6, 3.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.58, 159.40, 156.97, 151.34, 142.93, 128.99, 128.13, 127.93, 125.93, 121.60, 116.39, 114.03, 110.45, 108.59, 107.63, 105.92, 95.47, 52.05, 29.26, 25.52. HRMS: *m/z* [M^+] calcd. for $C_{21}H_{16}O_6$ 364.0947; found: 364.0948.

Methyl 6-(2,5-dimethylfuran-3-yl)-1-hydroxy-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-2-carboxylate (9r). Yellow solid; yield 329 mg; 84%; m.p. 150-151 °C; IR (KBr): 3056, 2976, 2936, 2359, 1626, 1488, 1419, 1373, 1239, 1109, 1076, 1020, 890, 802, 754 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 11.29 (s, 1H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.48 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.11 (dd, *J* = 9.0, 6.6 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 6.90 (dd, *J* = 7.8, 6.6 Hz, 1H), 6.48 (d, *J* = 9.0 Hz, 1H), 6.05 (s, 1H), 4.56 (t, *J* = 3.0 Hz, 1H), 3.78 (s, 3H), 2.42 (s, 3H), 2.31 (dq, *J* = 13.2, 3.0 Hz, 2H), 2.25 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.60, 159.46, 157.42, 151.68, 149.50, 147.60, 128.94, 128.13, 127.84, 126.06, 121.35, 121.01, 116.20, 114.08, 108.45, 105.67, 105.49, 97.45, 52.04, 31.55, 26.10, 13.38, 13.31. HRMS: *m/z* [M^+] calcd. for $C_{23}H_{20}O_6$ 392.1260; found: 392.1262.

Ethyl 6-(Furan-2-yl)-1-hydroxy-3-methyl-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-2-carboxylate (9s). Yellow solid; yield 306 mg; 78%; m.p. 57-58 °C; IR (KBr): 3074, 2980, 1643, 1585, 1483, 1457, 1413, 1320, 1266, 1160, 1024, 909, 813, 749 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 12.20 (s, 1H), 7.49 (d, *J* = 7.2 Hz, 1H), 7.47 (d, *J* = 1.2 Hz, 1H), 7.10 (dd, *J* = 8.4, 7.2 Hz, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 6.90 (dd, *J* = 7.8, 7.2 Hz, 1H), 6.72 (d, *J* = 3.0 Hz, 1H), 6.45-6.44 (m, 1H), 6.38 (s, 1H), 4.58 (t, *J* = 3.0 Hz, 1H), 4.37 (d, *J* = 7.2 Hz, 2H), 2.48 (dq, *J* = 13.2, 3.0 Hz, 2H), 2.45 (s, 3H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.93, 161.03, 155.33, 152.27, 151.36, 142.86, 141.03, 128.06, 127.76, 126.25, 121.50, 116.31, 111.93, 111.64, 110.41, 107.52, 105.89, 95.47, 61.28, 29.54, 25.58, 24.17, 14.19. HRMS: *m/z* [M^+] calcd. for $C_{23}H_{20}O_6$ 392.1260; found: 392.1260.

Ethyl 6-(2,5-dimethylfuran-3-yl)-1-hydroxy-3-methyl-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-2-carboxylate (9t). Yellow solid; yield 332 mg; 79%; m.p. 119-120 °C; IR (KBr): 3043, 2978, 1642, 1584, 1482, 1456, 1399, 1320, 1277, 1159, 1110, 1020, 905, 810, 753 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 12.20 (s, 1H), 7.49 (dd, *J* = 6.6, 1.2 Hz, 1H), 7.10 (dd, *J* = 8.4, 7.8 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 6.90 (dd, *J* = 7.8, 7.2 Hz, 1H), 6.36 (s, 1H), 6.06 (s, 1H), 4.53 (t, *J* = 3.0 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 2.44 (s, 3H), 2.43 (s, 3H), 2.33 (dq, *J* = 13.2, 3.0 Hz, 2H), 2.26 (s, 3H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.94, 161.07, 155.77, 151.68, 149.42, 147.52, 140.95, 128.04, 127.67, 126.36, 121.24, 121.12, 116.11, 111.97, 111.50, 105.62, 105.49, 97.42, 61.25, 31.81, 26.14, 24.20, 14.19, 13.35, 13.29. HRMS: *m/z* [M^+] calcd. for $C_{25}H_{24}O_6$ 420.1573; found: 420.1575.

1-(1-Hydroxy-6-(pyridin-3-yl)-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-2-yl)ethan-1-one (9u). Yellow solid; yield 169 mg; 47%; m.p. 210-211 °C; IR (KBr): 3074, 2925, 1626, 1488, 1424, 1370, 1257, 1114, 1077, 1026, 901, 804, 758 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 13.09 (s, 1H), 8.97 (s, 1H), 8.68 (d, *J* = 4.2 Hz, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.52 (d, *J* = 9.0 Hz, 1H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.40 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.15 (dd, *J* = 8.4, 7.8 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.94 (dd, *J* = 7.8, 7.2 Hz, 1H), 6.56 (d, *J* = 9.0 Hz, 1H), 4.63 (t, *J* = 2.4 Hz, 1H), 2.52 (s, 3H), 2.35 (dq, *J* = 13.2, 2.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 203.02, 160.80, 157.69, 151.47, 150.11, 147.51, 136.53, 133.65, 130.27, 128.22, 128.11, 125.73, 123.19, 121.87, 116.31, 114.37, 114.25, 108.32, 98.05, 32.52, 26.26, 25.89. HRMS: *m/z* [M^+] calcd. for $C_{22}H_{17}NO_4$ 359.1158; found: 359.1155.

1-(6-(2,5-Dimethylfuran-3-yl)-1-hydroxy-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-2-yl)propan-1-one (9v). Yellow solid; yield 332 mg; 85%; m.p. 155-156 °C; IR (KBr): 2962, 2359, 1764, 1667, 1441, 1244, 1064, 890, 800 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 13.17 (s, 1H), 7.51-7.48 (m, 2H), 7.11 (dd, *J* = 8.4, 7.8 Hz, 1H), 6.94 (d, *J* = 7.8 Hz, 1H), 6.90 (dd, *J* = 7.8, 6.6 Hz, 1H), 6.48 (d, *J* = 9.0 Hz, 1H), 6.06 (s, 1H), 4.57 (t, *J* = 3.0 Hz, 1H), 2.92-2.87 (m, 2H), 2.42 (s, 3H), 2.32 (dq, *J* = 13.8, 3.0 Hz, 2H), 2.26 (s, 3H), 1.19 (dd, *J* = 7.8, 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 205.71, 160.82, 157.77, 151.60, 149.52, 147.60, 129.24, 128.17, 127.84, 126.03, 121.40, 120.92, 116.16, 114.44, 113.43, 108.15, 105.45, 97.57, 31.53, 31.17, 25.83, 13.36, 13.30, 8.57. HRMS: *m/z* [M^+] calcd. for $C_{24}H_{22}O_5$ 390.1467; found: 390.1465.

1-(6-(Furan-2-yl)-1-hydroxy-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-2-yl)-2-phenylethan-1-one (9w). Yellow solid; yield 314 mg; 74%; m.p. 68-69 °C; IR (KBr): 3086, 2364, 1626, 1490, 1352, 1237, 1104, 900, 804, 743 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 12.99 (s, 1H), 7.55 (d, *J* = 9.6 Hz, 1H), 7.42-7.41 (m, 2H), 7.24 (t, *J* = 7.8 Hz, 2H), 7.19-7.16 (m, 3H), 7.05 (dd, *J* = 8.4, 7.8 Hz, 1H), 6.89 (d, *J* = 7.8 Hz, 1H), 6.84 (t, *J* = 7.2 Hz, 1H), 6.66 (d, *J* = 2.4 Hz, 1H), 6.45 (d, *J* = 8.4 Hz, 1H), 6.39-6.38 (m, 1H), 4.55 (t, *J* = 3.0 Hz, 1H), 4.10 (d, *J* = 3.6 Hz, 2H), 2.42 (dq, *J* = 13.8, 3.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 202.39, 161.36, 157.70, 151.93, 151.21, 142.99, 134.26, 129.94, 129.31, 128.74, 128.20, 127.99, 127.08, 125.77, 121.70, 116.39, 114.55, 113.50, 110.47, 108.57, 107.70, 95.61, 44.85, 29.21, 25.23. HRMS: *m/z* [M^+] calcd. for $C_{27}H_{20}O_5$ 424.1311; found: 424.1311.

1-(6-(2,5-Dimethylfuran-3-yl)-1-hydroxy-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-2-yl)-2-phenylethan-1-one (9x). Yellow solid; yield 384 mg; 85%; m.p. 169-170 °C; IR (KBr): 3032, 2927, 2359, 1736, 1625, 1419, 1353, 1240, 1165, 1101, 1038, 891, 802, 755 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 12.99 (s, 1H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.24 (dd, *J* = 7.8, 7.2 Hz, 2H), 7.18-7.15 (m, 3H), 7.04 (dd, *J* = 8.4, 6.6 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 6.83 (t, *J* = 7.2 Hz, 1H), 6.41 (d, *J* = 9.0 Hz, 1H), 5.97 (s, 1H), 4.49 (t, *J* = 3.0 Hz, 1H), 4.09 (d, *J* = 4.8 Hz, 2H), 2.34 (s, 3H), 2.22 (dq, *J* = 13.2, 3.0 Hz, 2H), 2.18 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 202.29, 161.41, 158.15, 151.54, 149.54, 147.61, 134.30, 129.92, 129.27, 128.72, 128.18, 127.89, 127.05, 125.89, 121.44, 120.84, 116.16,

114.55, 113.29, 108.43, 105.42, 97.62, 44.81, 31.48, 25.79, 13.35, 13.29. HRMS: *m/z* [M^+] calcd. for $C_{29}H_{24}O_5$ 452.1624; found: 452.1622.

1-(1-Hydroxy-6-(pyridin-3-yl)-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-2-yl)-2-phenylethan-1-one (9y). Yellow solid; yield 178 mg; 41%; m.p. 168-169 °C; IR (KBr): 3036, 2925, 1625, 1489, 1421, 1351, 1237, 1102, 1027, 901, 803, 754 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 13.07 (s, 1H), 8.97 (s, 1H), 8.67 (d, *J* = 3.6 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.51 (d, *J* = 6.0 Hz, 1H), 7.41 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.31 (dd, *J* = 7.8, 7.2 Hz, 2H), 7.24 (dd, *J* = 8.4, 7.2 Hz, 3H), 7.15 (dd, *J* = 7.8, 7.2 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 6.94 (dd, *J* = 7.8, 7.2 Hz, 1H), 6.58 (d, *J* = 9.0 Hz, 1H), 4.62 (t, *J* = 3.0 Hz, 1H), 4.18 (s, 2H), 2.34 (dq, *J* = 13.8, 3.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 202.46, 161.39, 157.76, 151.41, 149.95, 147.35, 136.62, 134.19, 133.83, 130.11, 129.29, 128.81, 128.24, 128.14, 127.12, 125.63, 123.29, 121.91, 116.31, 114.45, 113.64, 108.48, 98.03, 44.90, 32.50, 25.87. HRMS: *m/z* [M^+] calcd. for $C_{28}H_{21}NO_4$ 435.1471; found: 435.1474.

(6-(2,5-Dimethylfuran-3-yl)-1-hydroxy-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-2-yl)(phenyl)methanone (9z). Yellow solid; yield 390 mg; 89%; m.p. 189-190 °C; IR (KBr): 3058, 2925, 1611, 1485, 1415, 1344, 1263, 1171, 1082, 1020, 888, 806, 754 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 13.04 (s, 1H), 7.58 (d, *J* = 6.6 Hz, 2H), 7.56-7.52 (m, 2H), 7.46 (dd, *J* = 7.8, 7.2 Hz, 2H), 7.36 (d, *J* = 9.0 Hz, 1H), 7.15 (dd, *J* = 8.4, 7.8 Hz, 1H), 6.98-6.94 (m, 2H), 6.47 (d, *J* = 9.0 Hz, 1H), 6.08 (s, 1H), 4.56 (t, *J* = 3.0 Hz, 1H), 2.44 (s, 3H), 2.37 (dq, *J* = 13.8, 3.0 Hz, 2H), 2.27 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.41, 161.91, 158.24, 151.66, 149.61, 147.68, 138.20, 133.22, 131.49, 128.83, 128.31, 128.26, 127.99, 126.03, 121.53, 120.91, 116.26, 114.58, 113.34, 108.15, 105.49, 97.75, 31.58, 25.98, 13.41, 13.37. HRMS: *m/z* [M^+] calcd. for $C_{28}H_{22}O_5$ 438.1467; found: 438.1466.

Methyl 3-hydroxy-6-phenyl-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-2-carboxylate (10a). Yellow solid; yield 307 mg; 82%; m.p. 172-173 °C; IR (KBr): 3704, 2953, 1672, 1597, 1482, 1451, 1351, 1276, 1229, 1139, 1020, 903, 751 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 10.65 (s, 1H), 7.66 (s, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.89 (t, *J* = 7.2 Hz, 2H), 7.35 (d, *J* = 7.2, 6.6 Hz, 1H), 7.18 (dd, *J* = 7.8, 4.2 Hz, 1H), 7.09 (dd, *J* = 7.8, 7.2 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.86 (dd, *J* = 7.8, 7.2 Hz, 1H), 6.53 (s, 1H), 3.98 (t, *J* = 1.2 Hz, 1H), 3.85 (s, 3H), 2.32 (dq, *J* = 13.2, 1.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.03, 162.13, 158.07, 151.38, 140.73, 128.98, 128.55, 128.41, 128.31, 127.18, 126.07, 125.64, 121.80, 118.95, 116.94, 106.45, 104.57, 98.98, 52.05, 33.45, 33.37. HRMS: *m/z* [M^+] calcd. for $C_{23}H_{18}O_5$ 374.1154; found: 374.1151. Structure confirmed by X-ray crystallography: CCDC 991036.

Methyl 3-hydroxy-6-(*p*-tolyl)-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-2-carboxylate (10b). Yellow solid; yield 338 mg; 87%; m.p. 197-198 °C; IR (KBr): 2950, 1671, 1592, 1484, 1442, 1346, 1274, 1144, 1026, 901, 756 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 10.73 (s, 1H), 7.73 (s, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.27-7.24 (m, 3H), 7.16 (dd, *J* = 8.4, 7.8 Hz, 1H), 7.02 (d, *J* = 7.8 Hz, 1H), 6.93 (dd, *J* = 7.8, 6.6 Hz, 1H), 6.60 (s, 1H), 4.04 (t, *J* = 3.0 Hz, 1H), 3.92 (s, 3H), 2.40 (s, 3H), 2.38 (dq, *J* = 13.8, 3.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.02, 162.08, 158.13, 151.41, 138.82, 137.88, 129.03, 128.51, 128.23, 127.15, 126.08, 125.51, 121.70, 118.98, 116.91, 106.35, 104.51, 99.01, 52.01, 33.46, 33.29, 21.16. HRMS: *m/z* [M^+] calcd. for $C_{24}H_{20}O_5$ 388.1311; found: 388.1312.

Methyl 3-hydroxy-6-(3-methoxyphenyl)-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-2-carboxylate (10c). Yellow solid; yield 303 mg; 75%; m.p. 77-78 °C; IR (KBr): 2953, 1673, 1593, 1486, 1446, 1277, 1234, 1142, 905, 757 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 10.70 (s, 1H), 7.72 (s, 1H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.28-7.25 (m, 3H), 7.15 (dd, *J* = 8.4, 7.8 Hz, 1H), 7.01 (d, *J* = 7.8 Hz, 1H), 6.95-6.91 (m, 2H), 6.59 (s, 1H), 4.04 (t, *J* = 3.0 Hz, 1H), 3.92 (s, 3H), 3.84 (s, 3H), 2.38 (dq, *J* = 13.2, 3.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.03, 162.12, 159.66, 158.02, 151.34, 142.30, 129.52, 128.54, 128.32, 127.18, 126.06, 121.82, 118.95, 117.99, 116.97, 114.32, 111.67, 106.47, 104.58, 98.87, 55.38, 52.07, 33.43, 33.29. HRMS: *m/z* [M^+] calcd. for $C_{24}H_{20}O_6$ 404.1260; found: 404.1257.

Methyl 6-(2,5-dimethylfuran-3-yl)-3-hydroxy-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocine-2-carboxylate (10d). Yellow solid; yield 302 mg; 77%; m.p. 73-74 °C; IR (KBr): 2924, 2358, 1673, 1486, 1446, 1274, 1227, 1140, 896, 755 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 10.69 (s, 1H), 7.69 (s, 1H), 7.22 (d, *J* = 6.6 Hz, 1H), 7.12 (dd, *J* = 7.8, 7.2 Hz, 1H), 6.94 (d, *J* = 7.8 Hz, 1H), 6.90 (dd, *J* = 7.8, 6.6 Hz, 1H), 6.51 (s, 1H), 6.03 (s, 1H), 4.01 (t, *J* = 3.0 Hz, 1H), 3.91 (s, 3H), 2.40 (s, 3H), 2.36 (dq, *J* = 13.2, 3.0 Hz, 2H), 2.24 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.03, 162.08, 157.85, 151.10, 149.56, 147.65, 128.55, 128.26, 127.21, 126.03, 121.71, 120.90, 118.98, 116.79, 106.36, 105.42, 104.37, 97.56, 52.05, 33.24, 32.22, 13.37, 13.30. HRMS: *m/z* [M^+] calcd. for $C_{23}H_{20}O_6$ 392.1260; found: 392.1262.

1-(3-Hydroxy-6-phenyl-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-2-yl)-2-phenylethan-1-one (10e). Yellow solid; yield 360 mg; 83%; m.p. 78-79 °C; IR (KBr): 3034, 2937, 2358, 1641, 1589, 1488, 1351, 1281, 1241, 1127, 1027, 900, 754, 698 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 12.39 (s, 1H), 7.73 (s, 1H), 7.72 (d, *J* = 7.2 Hz, 2H), 7.47 (dd, *J* = 7.8, 7.2 Hz, 2H), 7.44 (d, *J* = 7.2, 6.6 Hz, 1H), 7.36 (t, *J* = 7.2 Hz, 2H), 7.31-7.28 (m, 3H), 7.20-7.17 (m, 2H), 7.04 (d, *J* = 7.8 Hz, 1H), 6.96 (t, *J* = 7.2 Hz, 1H), 6.59 (s, 1H), 4.28 (s, 2H), 4.05 (t, *J* = 3.0 Hz, 1H), 2.41 (dq, *J* = 13.8, 3.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 201.83, 163.98, 158.72, 151.22, 140.48, 134.33, 129.34, 129.31, 129.03, 128.75, 128.40, 127.08, 127.02, 125.83, 125.57, 121.89, 118.83, 116.98, 114.01, 105.10, 99.09, 45.13, 33.55, 33.23. HRMS: *m/z* [M^+] calcd. for $C_{29}H_{22}O_4$ 434.1518; found: 434.1520.

1-(3-Hydroxy-6-(*p*-tolyl)-12*H*-6,12-methanodibenzo[*d,g*][1,3]dioxocin-2-yl)-2-phenylethan-1-one (10f). Yellow solid; yield 381 mg; 85%; m.p. 84-85 °C; IR (KBr): 3033, 2927, 2359, 1641, 1487, 1352, 1280, 1128, 1029, 900, 750 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 12.38 (s, 1H), 7.72 (s, 1H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.36 (dd, *J* = 7.8, 6.6 Hz, 2H), 7.30-7.27 (m, 4H), 7.19-7.16 (m, 3H), 7.03 (d, *J* = 7.8 Hz, 1H), 6.95 (dd, *J* = 8.4, 7.2 Hz, 1H), 6.58 (s, 1H), 4.25 (s, 2H), 4.04 (t, *J* = 3.0 Hz, 1H), 2.41 (s, 3H), 2.40 (dq, *J* = 13.2, 3.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 201.81, 163.99, 158.83, 151.30, 138.93, 137.65, 134.37, 129.32, 129.28, 129.07, 128.76, 128.37, 127.08, 127.01, 125.87, 125.47, 121.83, 118.89, 117.01, 113.97, 105.10, 99.14, 45.13, 33.62, 33.22, 21.17. HRMS: *m/z* [M^+] calcd. for $C_{30}H_{24}O_4$

448.1675; found: 448.1671.

(3-Hydroxy-6-phenyl-12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocin-2-yl)(phenyl)methanone (10g). Yellow solid; yield 353 mg; 84%; m.p. 97-98 °C; IR (KBr): 3060, 2938, 1634, 1592, 1484, 1345, 1277, 1232, 1151, 1111, 1025, 891, 753, 698 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 12.32 (s, 1H), 7.75 (d, J = 7.2 Hz, 2H), 7.66 (d, J = 7.2 Hz, 2H), 7.63 (dd, J = 7.8, 7.2 Hz, 1H), 7.55 (dd, J = 7.8, 7.2 Hz, 2H), 7.50 (s, 1H), 7.49 (t, J = 8.4 Hz, 2H), 7.46-7.43 (m, 1H), 7.18 (dd, J = 8.4, 6.6 Hz, 1H), 7.13 (dd, J = 7.8, 1.2 Hz, 1H), 7.06 (d, J = 7.8 Hz, 1H), 6.95 (dd, J = 7.8, 7.2 Hz, 1H), 6.69 (s, 1H), 3.99 (t, J = 3.0 Hz, 1H), 2.42 (dq, J = 13.2, 3.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.82, 164.32, 158.74, 151.20, 140.49, 138.19, 132.33, 131.64, 129.02, 128.92, 128.39, 128.33, 126.95, 125.91, 125.56, 121.87, 118.64, 116.98, 114.00, 105.04, 99.10, 33.32, 33.21. HRMS: m/z [M^+] calcd. for $C_{28}H_{20}O_4$ 420.1362; found: 420.1364.

Notes and references

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† Electronic Supplementary Information (ESI) available: Depiction of ^1H, ^{13}C NMR and HRMS spectra for all products **9-10**. CCDC 981010 (**9n**) and 991036 (**10a**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b000000x/

1 (a) B. Tan, N. R. Candeias and C. F. Barbas III, *Nat. Chem.*, 2011, **3**, 473-477; (b) T. Gaich and P. S. Baran, *J. Org. Chem.*, 2010, **75**, 4657-4673; (c) J. W. H. Li and J. C. Vederas, *Science*, 2009, **325**, 161-165; (d) K. C. Nicolaou, D. J. Edmonds and P. G. Bulger, *Angew. Chem., Int. Ed.*, 2006, **45**, 7134-7186; (e) K. C. Nicolaou and S. A. Snyder, *Proc. Natl. Acad. Sci. U. S. A.*, 2004, **101**, 11929-11936; (f) K. C. Nicolaou, D. Vourloumis, N. Winssinger and P. S. Baran, *Angew. Chem., Int. Ed.*, 2000, **39**, 44-122.

2 (a) T. J. J. Müeller, *Angew. Chem., Int. Ed.*, 2007, **46**, 2977-2978; (b) R. Breinbauer, *Synthesis*, 2007, 794; (c) R. A. Batey, *J. Am. Chem. Soc.*, 2007, **129**, 7476; (d) L. F. Tietze, *Chem. Rev.*, 1996, **96**, 115-136; (e) M. Malacria, *Chem. Rev.*, 1996, **96**, 289-306; (f) H. Henniges, F. E. Meyer, U. Schick, F. Funke, P. J. Parsons and M. A. de, *Tetrahedron*, 1996, **52**, 11545-11578; (g) K. H. Ang, S. Bräse, A. G. Steinig, F. E. Meyer, A. Llebaria, K. Voigt and M. A. de, *Tetrahedron*, 1996, **52**, 11503-11528; (h) P. A. Wender and B. L. Miller, *Org. Synth.: Theory Appl.*, 1993, **2**, 27-66.

3 (a) J. Alemán and S. Cabrera, *Chem. Soc. Rev.*, 2013, **42**, 774-793; (b) L.-Q. Lu, J.-R. Chen and W.-J. Xiao, *Acc. Chem. Res.*, 2012, **45**, 1278-1293; (c) F.-Z. Peng and Z.-H. Shao, *Curr. Org. Chem.*, 2011, **15**, 4144-4160; (d) B. Westermann, M. Ayaz and S. S. van Berkel, *Angew. Chem., Int. Ed.*, 2010, **49**, 846-849; (e) C. Grondal, M. Jeanty and D. Enders, *Nat. Chem.*, 2010, **2**, 167-178; (f) A.-N. Alba, X. Companyo, M. Viciano and R. Rios, *Curr. Org. Chem.*, 2009, **13**, 1432-1474; (g) X. Yu and W. Wang, *Org. Biomol. Chem.*, 2008, **6**, 2037-2046.

4 (a) H. Lou, Y. Yamazaki, T. Sasaki, M. Uchida, H. Tanaka and S. Oka, *Phytochemistry*, 1999, **51**, 297-308; (b) G. Nonaka, S. Morimoto, J. Kinjo, T. Nohara and I. Nishioka, *Chem. Pharm. Bull.*, 1987, **35**, 149-155; (c) J. J. Karchesy and R. W. Hemingway, *J. Agric. Food Chem.*, 1986, **34**, 966-970; (d) L.-C. Lin, Y.-C. Kuo and C.-J. Chou, *J. Nat. Prod.*, 2002, **65**, 505-508; (e)T. Hatano, H. Miyatake, M. Natsume, N. Osakabe, T. Takizawa, H. Ito and T. Yoshida, *Phytochemistry*, 2002, **59**, 749-758.

5 (a) H. Zhang, Yerigui, Y. Yang and C. Ma, *J. Agric. Food Chem.*, 2013, **61**, 8814-8820; (b) Y. Tao, Z. Chen, Y. Zhang, Y. Wang and Y. Cheng, *J. Pharm. Biomed. Anal.*, 2013, **78-79**, 190-201; (c) M. C. Ignoato, R. M. Fabrão, I. T. A. Schuquel, M. F. P. Botelhoe, S. M. de O. Santin, L. L. M. de Arruda, C. A. Bersani-Amado and M. C. de Souza, *Quím. Nova*, 2012, **35**, 2241-2244; (d) M. S. Pesca, P. F. Dal, R. Sanogo, A. Vassallo, d. A. M. Bruzual, A. Rapisarda, M. P. Germanò, G. Certo, F. S. De, T. N. De and A. Braca, *J. Nat. Prod.*, 2013, **76**, 29-35; (e) S. Togni, G. Maramaldi, A. Mazzetti, M. Meschiari and A. Sparavigna, *Cosmet. Technol.,* 2012, **15**, 11-15; (f) V. J. Cheng, A. E.-D. A. Bekhit, M. McConnell, S. Mros and J. Zhao, *Food Chem.*, 2012, **134**, 474-482; (g) X. Xu, H. Xie, Y. Wang and X. Wei, *J. Agric. Food Chem.*, 2010, **58**, 11667-11672; (h) A. Suedee, S. Tewtrakul and P. Panichayupakaranant, *Pharm. Biol.,* 2013, **51**, 1256-1261; (i) L. Gallina, P. F. Dal, V. Galligioni, E. Bombardelli and A. Scagliarini, *Antiviral Res.*, 2011, **92**, 447-452.

6 (a) I.-S. Kim, Y.-J. Park, S.-J. Yoon and H.-B. Lee, *Int. Immunopharmacol.*, 2010, **10**, 1616-1625; (b) H. Tao, L. Wang, Z. Cui, D. Zhao and Y. Liu, *Planta Med.*, 2008, **74**, 1823-1825; (c) M.-F. Xu, L.-Q. Shen and K.-W. Wang, *Fitoterapia*, 2009, **80**, 461-464.

7 A. Ogundaini, M. Farah, P. Perera, G. Samuelsson and L. Bohlin, *J. Nat. Prod.*, 1996, **59**, 587-590.

8 (a) G. Yin, T. Ren, Y. Rao, Y. Zhou, Z. Li, W. Shu and A. Wu, *J. Org. Chem.*, 2013, **78**, 3132-3141; (b) F. Wang, F. Chen, M. Qu, T. Li, Y. Liu and M. Shi, *Chem. Commun.*, 2013, **49**, 3360-3362; (c) Y. Rao and G. Yin, *Org. Biomol. Chem.*, 2013, **11**, 6029-6035; (d) N. C. Ganguly, P. Mondal and S. Roy, *Tetrahedron Lett.*, 2013, **54**, 2386-2390; (e) C. T. Avetta, B. J. Shorthill, C. Ren and T. E. Glass, *J. Org. Chem.*, 2012, **77**, 851-857; (f) J. M. López-Valbuena, E. C. Escudero-Adan, J. Benet-Buchholz, Z. Freixa and P. W. N. M. van Leeuwen, *Dalton Trans.*, 2010, **39**, 8560-8574; (g) G. A. Kraus, Y. Yuan and A. Kempema, *Molecules*, 2009, **14**, 807-815; (h) I. Kim, S. G. Kim, J. Choi and G. H. Lee, *Tetrahedron*, 2007, **64**, 664-671; (i) C. Selenski and T. R. R. Pettus, *Tetrahedron*, 2006, **62**, 5298-5307; (j) B. J. Shorthill, C. T. Avetta and T. E. Glass, *J. Am. Chem. Soc.*, 2004, **126**, 12732-12733; (k) T. Rosenau, A. Potthast, A. Hofinger and P. Kosma, *Angew. Chem., Int. Ed.*, 2002, **41**, 1171-1173; (l) A. Banihashemi and A. Rahmatpour, *Tetrahedron*, 1999, **55**, 7271-7278; (m) K. Subburaj, R. Katoch, M. G. Murugesh and G. K. Trivedi, *Tetrahedron*, 1997, **53**, 12621-12628; (n) G. Nonaka, S. Morimoto, J. Kinjo, T. Nohara and I. Nishioka, *Chem. Pharm. Bull.*, 1987, **35**, 149-155; (o) L. Jurd, *J. Heterocycl. Chem.*, 1981, **18**, 429-430; (p) L. Jurd and B. J. Bergot, *Tetrahedron*, 1965, **21**, 3697-3705; (q) X. Jiang, Z. Song, C. Xu, Q. Yao and A. Zhang, *Eur. J. Org. Chem.*, 2014, **2014**, 418-425.

9 (a) H.-S. Yeom, H. Li, Y. Tang and R. P. Hsung, *Org. Lett.*, 2013, **15**, 3130-3133; (b) N. Tadigoppula, V. Korthikunta, S. Gupta, P. Kancharla, T. Khaliq, A. Soni, R. K. Srivastava, K. Srivastava, S. K. Puri, K. S. R. Raju, Wahajuddin, P. S. Sijwali, V. Kumar and I. S. Mohammad, *J. Med. Chem.*, 2013, **56**, 31-45; (c) C.-T. Yen, K. Nakagawa-Goto, T.-L. Hwang, S. L. Morris-Natschke, K. F. Bastow, Y.-C. Wu and K.-H. Lee, *Bioorg. Med. Chem. Lett.*, 2012, **22**, 4018-4022; (d) T. Zhou, Q. Shi and K. H. Lee, *Tetrahedron Lett.*, 2010, **51**, 4382-4386; (e) M. Mondal, V. G. Puranik and N. P. Argade, *J. Org. Chem.*, 2007, **72**, 2068-2076; (f) B. Lesch, J. Toräng, S. Vanderheiden and S. Bräse, *Adv. Synth. Catal.*, 2005, **347**, 555-562; (g) E. J. Tisdale, I. Slobodov and E. A. Theodorakis, *Proc. Natl. Acad. Sci. U. S. A.*, 2004, **101**, 12030-12035; (h) Y. Kang, Y. Mei, Y. Du and Z. Jin, *Org. Lett.*, 2003, **5**, 4481-4484; (i) V. Barragan-Montero, J.-Y. Winum, J.-P. Molès, E. Juan, C. Clavel and J.-L. Montero, *Eur. J. Med. Chem.*, 2005, **40**, 1022-1029.

10 Y. Omura, Y. Taruno, Y. Irisa, M. Morimoto, H. Saimoto and Y. Shigemasa, *Tetrahedron Lett.*, 2001, **42**, 7273-7275.

11 (a) R. P. Pandit and Y. R. Lee, *Synthesis*, 2012, **44**, 2910-2918; (b) B. H. Park, Y. R. Lee and W. S. Lyoo, *Synthesis*, 2009, 2146-2154; (c) Y. R. Lee, X. Li and J. H. Kim, *J. Org. Chem.*, 2008, **73**, 4313-4316; (d) Y. R. Lee and L. Xia, *Synthesis*, 2007, 3240-3246; (e) Y. R. Lee, J. H. Choi and S. H. Yoon, *Tetrahedron Lett.*, 2005, **46**, 7539-7543.

12 (a) X. Wang and Y. R. Lee, *Tetrahedron*, 2011, **67**, 9179-9184; (b) X. Wang and Y. R. Lee, *Tetrahedron*, 2009, **65**, 10125-10133; (c) Y. R. Lee and J. H. Kim, *Synlett*, 2007, 2232-2236; (d) X. Li and Y. R. Lee, *Org. Biomol. Chem.*, 2014, **12**, 1250-1257.

13 (a) Y. Sohtome, B. Shin, N. Horitsugi, K. Noguchi and K. Nagasawa, *Chem. - Asian J.*, 2011, **6**, 2463-2470; (b) H. Zhang, Y.-H. Liao, W.-C. Yuan and X.-M. Zhang, *Eur. J. Org. Chem.*, 2010, 3215-3218; (c) Y. Sohtome, B. Shin, N. Horitsugi, R. Takagi, K. Noguchi and K. Nagasawa, *Angew. Chem., Int. Ed.*, 2010, **49**, 7299-7303; (d) T.-Y.

Liu, H.-L. Cui, Q. Chai, J. Long, B.-J. Li, Y. Wu, L.-S. Ding and Y.-C. Chen, *Chem. Commun.*, 2007, 2228-2230.

14 Crystallographic data for compounds **9n** and **10a** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 981010 and 991036, respectively.

15 (a) Y. R. Lee and L. Xia, *Tetrahedron Lett.*, 2008, **49**, 3283-3287; (b) Y. R. Lee, Y. M. Kim and S. H. Kim, *Tetrahedron*, 2009, **65**, 101-108.

16 (a) K. Mariappan, P. N. Basa, V. Balasubramanian, S. Fuoss and A. G. Sykes, *Polyhedron*, 2013, **55**, 144-154; (b) B. Thati, A. Noble, R. Rowan, B. S. Creaven, M. Walsh, M. McCann, D. Egan and K. Kavanagh, *Toxicol. in Vitro*, 2007, **21**, 801-808; (c) S. France, M. H. Shah, A. Weatherwax, H. Wack, J. P. Roth and T. Lectka, *J. Am. Chem. Soc.*, 2005, **127**, 1206-1215; (d) M. Leschke, M. Melter and H. Lang, *Inorg. Chim. Acta*, 2003, **350**, 114-120; (e) N. K. Dutt and D. Majumdar, *J. Inorg. Nucl. Chem.*, 1972, **34**, 657-660.

17 J. Moreau, C. Hubert, J. Batany, L. Toupet, T. Roisnel, J.-P. Hurvois and J.-L. Renaud, *J. Org. Chem.*, 2009, **74**, 8963-8973.

18 (a) V. K. Ahluwalia, L. Nayal, S. Bala and S. Raghav, *Indian J. Chem., Sect. B*, 1988, **27B**, 629-632; (b) V. K. Ahluwalia, R. P. Singh and R. P. Tripathi, *Gazz. Chim. Ital.*, 1984, **114**, 359-361; (c) V. K. Ahluwalia, D. Singh and R. P. Singh, *Indian J. Chem., Sect. B*, 1984, **23B**, 883-884; (d) V. K. Ahluwalia and K. Mukherjee, *Indian J. Chem., Sect. B*, 1984, **23B**, 880-882.

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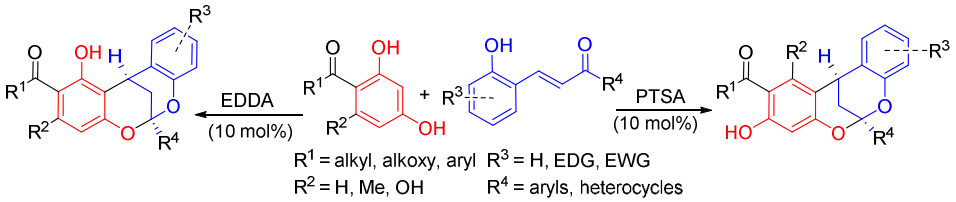
ARTICLE TYPE

Graphic Abstract

Catalyst-Controlled Regio- and Stereoselective Synthesis of Diverse 12*H*-6,12-Methanodibenzo[*d*,*g*][1,3]dioxocines

Likai Xia, Hongyun Cai, and Yong Rok Lee*



Regio- and stereoselective synthesis of 12*H*-6,12-methanodibenzo[*d*,*g*][1,3]dioxocines has been accomplished by the EDDA and PTSA-catalyzed cascade reactions of resorcinols and 2-hydroxychalcones.