Tetrahedron 72 (2016) 3454–3467

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Formation of substituted 1-naphthols and related products via dimerization of alkyl 3-(*o*-halo(het)aryl)-oxopropanoates based on a CuI-catalyzed domino *C*-arylation/condensation/aromatization process

Heike Weischedel [a], Kavitha Sudheendran [a], Alevtina Mikhael [a], Jürgen Conrad [a], Wolfgang Frey [b], Uwe Beifuss [a,*]

[a] Bioorganische Chemie, Institut für Chemie, Universität Hohenheim, Garbenstraße 30, D-70599 Stuttgart, Germany
[b] Institut für Organische Chemie, Universität Stuttgart, Pfaffenwaldring 55, D-70569 Stuttgart, Germany

ARTICLE INFO

Article history:
Received 15 March 2016
Received in revised form 21 April 2016
Accepted 22 April 2016
Available online 25 April 2016

Keywords:
C-Arylation
Copper
Cross-coupling
Dimerization
Domino reaction

ABSTRACT

Substrates bearing both a β-ketoester moiety and a (het)aryl halide structure element were dimerized to 1-naphthols and related products in the presence of catalytic amounts of CuI in isopropanol. The reaction starts with an intermolecular *C*-arylation, which is followed by an intramolecular condensation. The final aromatization delivers the highly substituted products with yields up to 81%.

1. Introduction

The *C*-arylation of active methylene compounds ranks among the most important copper-catalyzed cross-coupling reactions.[1] This transformation has been introduced by Hurtley in 1929 who reacted 2-bromobenzoic acid with several β-dicarbonyls, such as acetyl acetone, ethyl acetoacetate and diethyl malonate, using copper bronze or copper acetate as the catalyst and sodium ethoxide as the base in boiling anhydrous ethanol.[2] The scope of the classical Hurtley reaction is narrow since it is limited to 2-halobenzoic acids and similar activated substrates. For many decades, reactions with non activated substrates such as aryl halides could only be carried out with success by employing strong bases, high loads of the copper-source and harsh reaction conditions.[3] Only over the last decade, we have witnessed remarkable progress in the development of mild reaction conditions for the copper-catalyzed *C*-arylation of CH acidic compounds with non activated aryl halides.[4] The achievements made can be primarily attributed to the use of additives with complex forming abilities, such as diamines, amino acids and carboxylic acids.[5] Nowadays, aryl iodides and aryl bromides are routinely employed as *C*-arylation reagents in Hurtley type reactions. Acyclic and cyclic β-diketones, acyclic β-ketoesters, malonic esters, cyanoacetic esters and malononitriles are particular suitable as CH acidic compounds. In addition to intermolecular reactions the intramolecular version of the Hurtley reaction has also been addressed and exploited for the construction of different carbo- and heterocycles, such as 3,4-dihydronaphthalen-2(1*H*)-ones[6a] and oxindoles.[6b] The synthetic value of the Hurtley reaction for the preparation of carbo- and heterocycles can be broadened significantly by its combination with other transformations to new domino reactions.[7,8] Typical examples include the copper-catalyzed reactions between 1,2-dihaloarenes and β-dicarbonyls for the synthesis of benzofurans[9a] and dibenzofurans,[9b] the transformations of *o*-halophenols with β-dicarbonyls to benzofuran-2(3*H*)ones[10] and the reactions of both unprotected and protected *o*-haloanilines with β-dicarbonyls for the preparation of indoles.[11] Other substrates for domino reactions including copper-catalyzed *C*-arylations are *o*-halobenzylamines for the synthesis of isoquinolines,[12] *o*-halobenzamides for the preparation of isoquinolin-1(2*H*)-ones[13a] and benzimidazo[1,2-*b*]*iso*-quinolin-ones,[13b] and *o*-halobenzyl halides for the construction of either naphthalenes[14a,b] or 4*H*-chromenes.[14b]

This work focuses on an aspect of copper-catalyzed arylations that has not yet been addressed: the dimerization of substrates

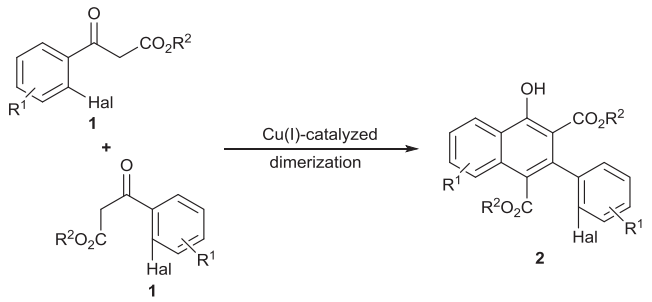
* Corresponding author. Tel.: +49 711 459 22171; fax: +49 711 459 22951; e-mail address: ubeifuss@uni-hohenheim.de (U. Beifuss).

http://dx.doi.org/10.1016/j.tet.2016.04.067
0040-4020/

containing both a β-ketoester moiety and a (het)aryl halide structural element. Here, we report on the conversion of two alkyl 3-(*o*-halo(het)aryl)-3-oxopropanoates into substituted 3-aryl-1-naphthols and related products. The copper-catalyzed process is based on a domino *C*-arylation/condensation/aromatization.

2. Results and discussion

We wondered whether it is possible to achieve the dimerization of alkyl 3-(*o*-haloaryl)-3-oxopropanoates **1** under the conditions of a Cu(I)-catalyzed cross-coupling to deliver 3-aryl-1-naphthols **2** as outlined in Scheme 1.



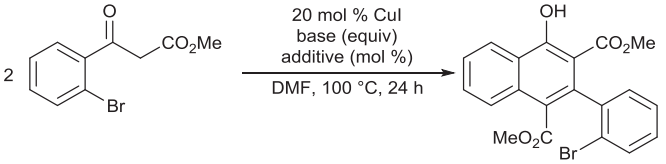
Scheme 1. Proposed dimerization of two 3-(*o*-haloaryl)-3-oxopropanoates **1**.

A report on the formation of traces of such dimerization products upon reaction between an alkyl 3-(*o*-haloaryl)-3-oxopropanoate and a β-dicarbonyl[15] confirmed our assumption concerning the feasibility of the transformation envisaged. The conversion of two molecules of methyl 3-(2′-bromophenyl)-3-oxopropanoate (**1a**) into the 3-aryl-1-naphthol **2a** was chosen as the model reaction.

To achieve the dimerization, 1 mmol of **1a** was reacted with 2 mmol of Cs_2CO_3 as the base and 20 mol % of CuI as the catalyst in DMF under argon at 100 °C for 24 h (Table 1, entry 1). Fortunately, the exclusive formation of the 3-aryl-1-naphthol **2a** was observed, albeit in low yield (26%). For optimizing the model reaction, the effect of different bases, additives, catalysts and solvents on the outcome of the transformation was studied. To start with, the role of the base and the additive was addressed (Table 1). When the amount of Cs_2CO_3 was decreased from 2.0 to 1.5 equiv, the yield of **2a** increased to 34% (Table 1, entry 3). Control experiments that were run under air demonstrated that it is advantageous to perform the transformations under argon (Table 1, entries 2 and 4). Then, it was studied whether Cs_2CO_3 can be replaced with other bases, such as K_2CO_3, K_3PO_4, DABCO and $NaHCO_3$ (Table 1, entries 5–8). K_2CO_3 turned out to give the best yields. With 1.5 equiv K_2CO_3, 40% of the product could be isolated (Table 1, entry 5). Interestingly, the 3-aryl-1-naphthol **2a** could be isolated in 37% yield when the amount of K_2CO_3 was further decreased to 1.0 equiv (Table 1, entry 9).

Next, the effect of different additives on the yield of the model reaction was evaluated. For this purpose, β-ketoester **1a** was reacted under the conditions of Table 1, entry 5 in the presence of 30 mol % of a number of additives, which have proven their value in numerous Cu(I)-catalyzed reactions. However, 1,10-phenanthroline, DMEDA as well as L-proline were found not suitable to improve the yield of **2a** (Table 1, entries 10–12). Fortunately, it turned out that acidic additives, such as acetic acid, propionic acid, pivalic acid, isovaleric acid and picolinic acid are particularly useful to increase the yield of the model reaction (Table 1, entries 13–17). Best results were achieved with propionic acid and pivalic acid which allowed the isolation of **2a** in 49 and 50%, resp. (Table 1, entries 14 and 15). The yield of **2a** could be slightly improved when the transformation was run in the presence of 50 mol % propionic acid (Table 1, entry 18). A further increase of the amount of the acidic additive to 80 and 120 mol %, resp., had no positive effect on the yield (Table 1, entries 19 and 20). Interestingly, the yield of **2a** could be improved slightly when molecular sieves 4 Å were added to the reaction mixture (Table 1, entry 21). Since propionic acid is cheaper than pivalic acid, all further optimizations were run in the presence of this carboxylic acid.

Table 1
Impact of different bases and additives on the Cu(I)-catalyzed dimerization of **1a**[a]

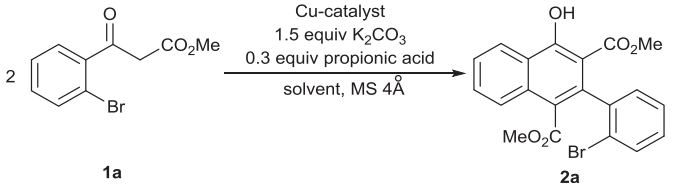


Entry	Base (equiv)	Additive (mol %)	Yield **2a** (%)
1	Cs_2CO_3 (2)	—	26
2	Cs_2CO_3 (2)	—	12[b]
3	Cs_2CO_3 (1.5)	—	34
4	Cs_2CO_3 (1.5)	—	17[b]
5	K_2CO_3 (1.5)	—	40
6	K_3PO_4 (1.5)	—	32
7	DABCO (1.5)	—	—
8	$NaHCO_3$ (1.5)	—	18
9	K_2CO_3 (1.0)	—	37
10	K_2CO_3 (1.5)	1.10-Phenanthroline (30)	2
11	K_2CO_3 (1.5)	DMEDA (30)	16
12	K_2CO_3 (1.5)	L-Proline (30)	30
13	K_2CO_3 (1.5)	Acetic acid (30)	44
14	K_2CO_3 (1.5)	Propionic acid (30)	49
15	K_2CO_3 (1.5)	Pivalic acid (30)	50
16	K_2CO_3 (1.5)	Isovaleric acid (30)	48
17	K_2CO_3 (1.5)	Picolinic acid (30)	38
18	K_2CO_3 (1.5)	Propionic acid (50)	52
19	K_2CO_3 (1.5)	Propionic acid (80)	44
20	K_2CO_3 (1.5)	Propionic acid (120)	43
21	K_2CO_3 (1.5)	Propionic acid (30)	54[c]

[a] All reactions were performed using 1 mmol of **1a** in 2 mL DMF in a sealed vial.
[b] The reactions were run under air.
[c] The reaction was run in the presence of molecular sieves 4 Å.

The influence of different Cu-sources and solvents was studied next (Table 2). Exploratory experiments were performed under the conditions of Table 1, entry 21. They clearly demonstrated that the formation of **2a** can not only be catalyzed by CuI, but also by a range of other Cu(I) compounds, such as CuBr, CuCl, Cu_2O and Cu(I)acetate (Table 2, entries 2–5), by elemental copper (Table 2, entry 8) and Cu(II) compounds such as Cu(II)acetate and $Cu(OTf)_2$ (Table 2, entries 6 and 7). Even in the absence of any copper-source the product **2a** was formed in 30% yield (Table 2, entry 11). However, it should be noted a) that with none of the other Cu-sources the yield obtained with 20 mol % CuI (Table 2, entry 1) could be improved and b) that with Cu-powder and Cu(II)acetate the yield was not higher than in the absence of any Cu-source (Table 2, entries 8, 6 and 11). It is also remarkable that the yield of **2a** was only slightly lower when the amount of CuI was decreased from 20 to 5 mol % (Table 2, entry 10) As a result, all further experiments were run with only 5 mol % CuI as the catalyst. Next, we focused on the effect of different solvents on the outcome of the model reaction. For this purpose, the transformation was run in a number of solvents which have been used successfully in Cu(I)-catalyzed cross couplings. The yield could not be improved by running the reaction in other polar aprotic solvents, such as acetonitrile, DMSO and DMA (Table 2, entries 12–14). It came as a surprise that the yield of **2a** could be increased considerably

Table 2
Influence of the Cu-source and the solvent on the Cu(I)-catalyzed dimerization of **1a**[a]

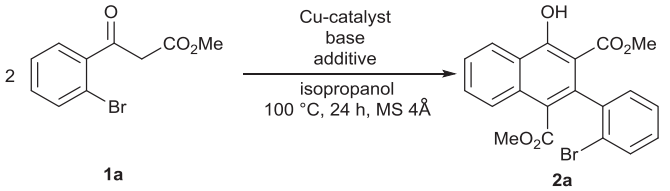


1a **2a**

Entry	Catalyst (mol %)	Solvent	*T* (°C)	Time (h)	Yield **2a** (%)
1	CuI (20)	DMF	100	24	54
2	CuBr (20)	DMF	100	24	46
3	CuCl (20)	DMF	100	24	47
4	Cu_2O (20)	DMF	100	24	36
5	Cu(I)acetate (20)	DMF	100	24	34
6	Cu(II)acetate (20)	DMF	100	24	30
7	$Cu(OTf)_2$ (20)	DMF	100	24	35
8	Cu-powder (20)	DMF	100	24	25
9	CuI (10)	DMF	100	24	37
10	Cu(I) (5)	DMF	100	24	45
11	—	DMF	100	24	30
12	Cu(I) (5)	Acetonitrile	100	24	42
13	Cu(I) (5)	DMSO	100	24	30
14	Cu(I) (5)	DMA	100	24	30
15	Cu(I) (5)	Isopropanol	100	24	82
16	Cu(I) (5)	Water	100	24	42
17	Cu(I) (5)	1,2-Dichlorobenzene	100	24	60
18	Cu(I) (5)	THF	100	24	64
19	Cu(I) (5)	Isopropanol	100	24	79[b]
20	Cu(I) (5)	Isopropanol	80	16	75
21	Cu(I) (5)	Isopropanol	85	24	67[c]
22	Cu(I) (5)	Ethanol	80	16	70
23	Cu(I) (5)	Methanol	80	16	61
24	Cu(I) (5)	Ethylene glycol	80	16	2

[a] The reactions were performed in a sealed vial with 1 mmol of **1a**, molecular sieves 4 Å in 2 mL solvent under argon.
[b] The reaction was performed with 1 equiv base.
[c] The reaction was performed in a flask equipped with reflux condenser and a balloon filled with argon.

Table 3
Influence of bases, additives and Cu-sources on the dimerization of **1a** with isopropanol as the solvent[a]



1a **2a**

Entry	Additive	Base	Catalyst	Yield **2a** (%)
1	Pivalic acid	K_2CO_3[b]	CuI	72
2	Acetic acid	K_2CO_3[b]	CuI	70
3	Isovaleric acid	K_2CO_3[b]	CuI	69
4	Propionic acid	K_2CO_3[b]	CuI	62[c]
5	Propionic acid	K_2CO_3[b]	CuI	64[c]
6	Propionic acid	Na_2CO_3	CuI	71
7	Propionic acid	$(NH_4)_2CO_3$	CuI	59
8	Propionic acid	K_3PO_4	CuI	76
9	Propionic acid	—	CuI	—
10	—	K_2CO_3[b]	CuI	55
11	Propionic acid	K_2CO_3[b]	CuBr	73
12	Propionic acid	K_2CO_3[b]	CuCl	56
13	Propionic acid	K_2CO_3[b]	Cu_2O	58
14	Propionic acid	K_2CO_3[b]	CuI	70[d]
15	Propionic acid	K_2CO_3[b]	—	34
16	Propionic acid	K_2CO_3[e]	—	4

[a] The reactions were performed in a sealed tube with 1 mmol of **1a**, 5 mol % catalyst, 30 mol % additive, 1.0 equiv base and molecular sieve 4 Å in 2 mL isopropanol under argon.
[b] The purity of the potassium carbonate was 99.0%.
[c] The reactions were performed with 15 mol % additive (entry 4) and 7.5 mol % additive (entry 5).
[d] The reaction was performed with 1 mol % catalyst.
[e] The purity of the potassium carbonate was 99.995%.

when the reaction was performed in either protic solvents such as water and isopropanol (Table 2, entries 15 and 16) or in less polar solvents such as 1,2-dichlorbenzene and THF (Table 2, entries 17 and 18). With isopropanol as the solvent, the yield of **2a** amounted to 82% (Table 2, entry 15). Further experiments with isopropanol as the solvent revealed that a reduction of the amount of K_2CO_3 from 1.5 to 1.0 equiv (Table 2, entry 19) as well as a decrease of the reaction temperature from 100 to 80 °C (Table 2, entry 20) had only minor effects on the yield. It should also be mentioned that the reaction can also be performed under standard reflux conditions (Table 2, entry 21). The successful use of isopropanol prompted us to evaluate other alcohols as the reaction medium. It was found that ethanol as well as methanol can be used as solvents at 80 °C; however, the yields did not exceed the yield obtained with isopropanol (Table 2, entries 22 and 23). With ethylene glycol as the solvent only traces of **2a** were formed (Table 2, entry 24). This might be due to the chelating properties of this diol.

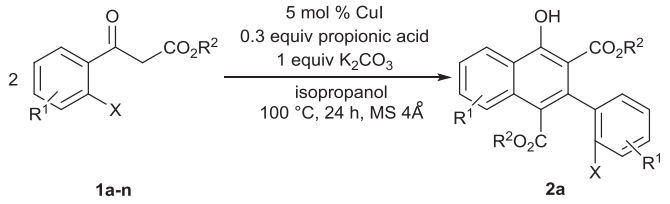
As the optimal solvent was identified only during the final stage of the optimization process it was decided to reoptimize the transformation in isopropanol with regard to additives, bases and Cu-sources. For this purpose, **1a** was reacted with 30 mol % of an acidic additive, 1.0 equiv of a base and 5 mol % of a catalyst in isopropanol at 100 °C for 24 h (Table 3). Reactions with different acidic additives using K_2CO_3 as base and CuI as Cu-source were performed with pivalic acid, acetic acid and isovaleric acid; however, the yields of **2a** did not exceed 72% (Table 3, entries 1–3). Reactions with different bases established that the formation of **2a** could also be achieved using Na_2CO_3, $(NH_4)_2CO_3$ and K_3PO_4 as the base, albeit in lower yields than with K_2CO_3 (Table 3, entries 6–8). A control experiment confirmed the assumption that product formation takes place only under basic conditions (Table 3, entry 9). Experiments with CuBr, CuCl and Cu_2O demonstrated that with none of these Cu-sources the yield observed with CuI could be improved (Table 3, entries 11–13). Lowering the amount of CuI from 5 to 1 mol % caused a decrease of the yield of **2a** from 79 to 70% (Table 3, entry 14). The fact that even in the absence of any Cu-source the yield of **2a** amounted to 34% (Table 3, entry 15) suggested the assumption that a S_NAr reaction mechanism may be operative in this transformation. On the other hand, the purity of the K_2CO_3 employed did not exceed 99%. So, it could not be excluded that the transformation is catalyzed by trace amounts of Cu present in the base. This is why the reaction was repeated under copper-free conditions using 99.995% pure K_2CO_3. Using this protocol, **2a** was isolated in only 4% (Table 3, entry 16). The result of this control experiment emphasizes the role of the Cu-catalyst for this transformation. The finding also corroborates the assumption of a copper-catalyzed transformation. In our opinion a S_NAr reaction mechanism can be ruled out. It was also found that a reduction of the amount of propionic acid is not advisable, since the yield of **2a** in the presence of 15 and 7.5 mol % propionic acid, respectively, amounted only to 62 and 64%, respectively (Table 3, entries 4 and 5). Interestingly, even in the absence of any acidic additive **2a** could be isolated in 55% yield (Table 3, entry 10).

To summarize the results of the optimization, the highest yield of **2a** was obtained when the dimerization of **1a** was carried out with 5 mol % CuI as catalyst, 0.3 equiv of propionic acid as additive and 1 equiv of K_2CO_3 as base in isopropanol at 100 °C for 24 h in a sealed tube in the presence of molecular sieves 4 Å.

With the optimized reaction conditions in hand, the substrate scope of the new CuI-catalyzed dimerization was studied. The required bisfunctionalized substrates **1** were easily accessible via standard methods from readily available starting materials. The

alkyl 3-(*o*-haloaryl)-3-oxopropanoates **1a**–**k** were synthesized by Claisen condensation between an alkyl 2-halobenzoate and an alkyl acetate with yields up to 81% (for details, see Experimental Section).[16,17] Substrates **1l** and **1m** were prepared in two steps: Reformatsky reaction between 2-bromobenzaldehyde and bromoacetic esters delivered the corresponding 3-(*o*-haloaryl)-3-hydroxypropanoates, which were oxidized to give the 3-(*o*-haloaryl)-3-oxopropanoates **1l** and **1m** (for details, see Experimental Section).[18]

Table 4
CuI-catalyzed dimerizations of alkyl 3-(*o*-haloaryl)-3-oxopropanoates **1a**–**m** to the corresponding dialkyl 2-(*o*-haloaryl)-4-hydroxynaphthalene-1,3-dicarboxylates **2a**–**m**[a]



1a-n **2a**

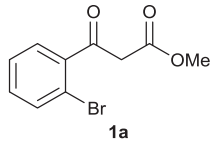
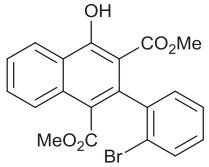
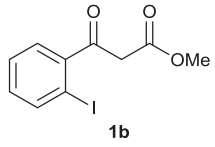
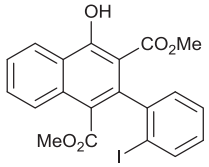
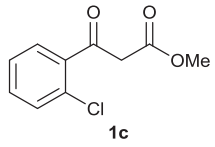
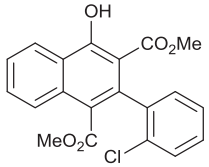
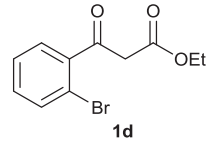
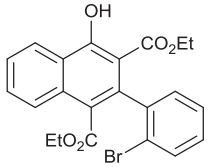
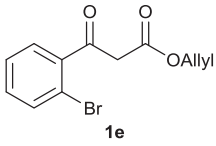
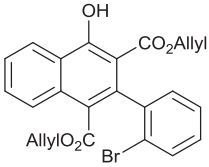
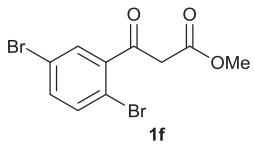
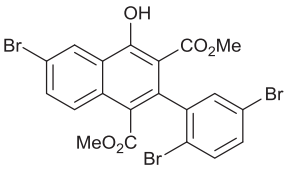
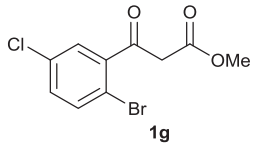
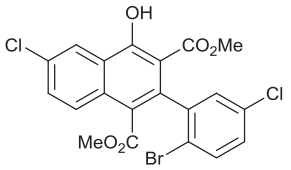
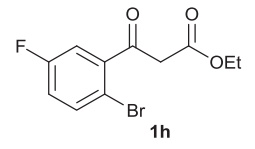
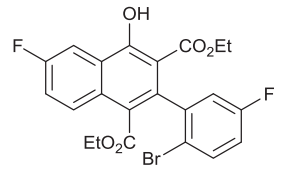
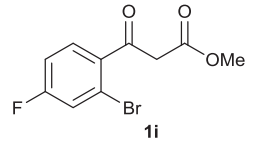
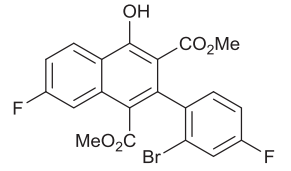
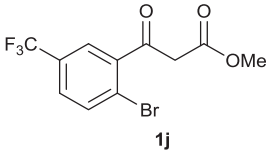
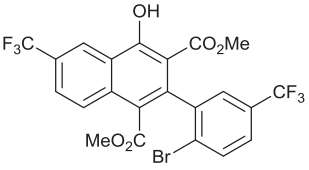
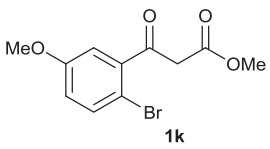
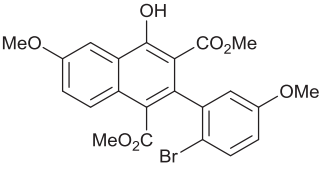
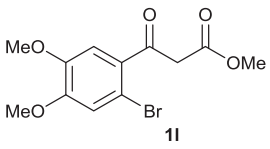
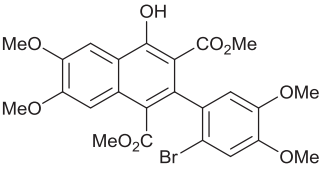
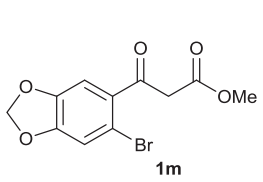
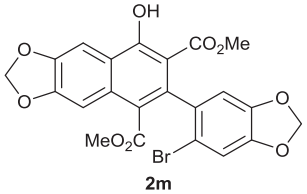
Entry	1	2 Yield (%)
1	 **1a**	 **2a** 79%
2	 **1b**	 **2b** 60%
3	 **1c**	 **2c** 48%
4	 **1d**	 **2d** 71%
5	 **1e**	 **2e** 81%

Table 4 (*continued*)

Entry	1	2 Yield (%)
6	 **1f**	 **2f** 67%
7	 **1g**	 **2g** 65%
8	 **1h**	 **2h** 66%
9	 **1i**	 **2i** 23%
10	 **1j**	 **2j** 69%
11	 **1k**	 **2k** 63%
12	 **1l**	 **2l** 61%

(*continued on next page*)

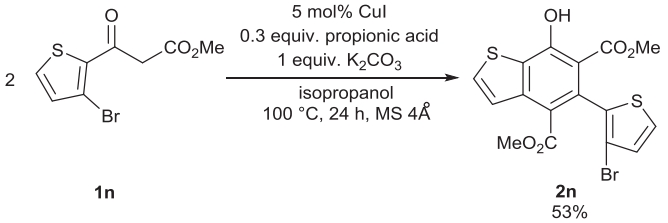
Table 4 (*continued*)

Entry	1	2 Yield (%)
13	 **1m**	 **2m** 67%

[a] The reactions were performed in a sealed tube with 1 mmol of alkyl 3-(*o*-haloaryl)-3-oxopropanoate **1** in 2 mL isopropanol.

After the successful preparation of the substrates **1a**–**m**, they were subjected to the dimerization using the optimized conditions of Table 2, entry 19. In order to study the influence of the *o*-halogen substituent on the outcome of the transformation, the 3-(2′-iodophenyl)-3-oxopropanoate **1b** and the 3-(2′-chlorophenyl)-3-oxopropanoate **1c** were reacted. It was found that in addition to the bromo derivative **1a** the iodo as well as the chloro compound could serve as substrates for the dimerization (Table 4, entries 2 and 3). The observation that the highest yield was obtained with the 3-(2′-bromophenyl)-3-oxopropanoate **1b** is in accordance with results obtained earlier.[14,19–21]

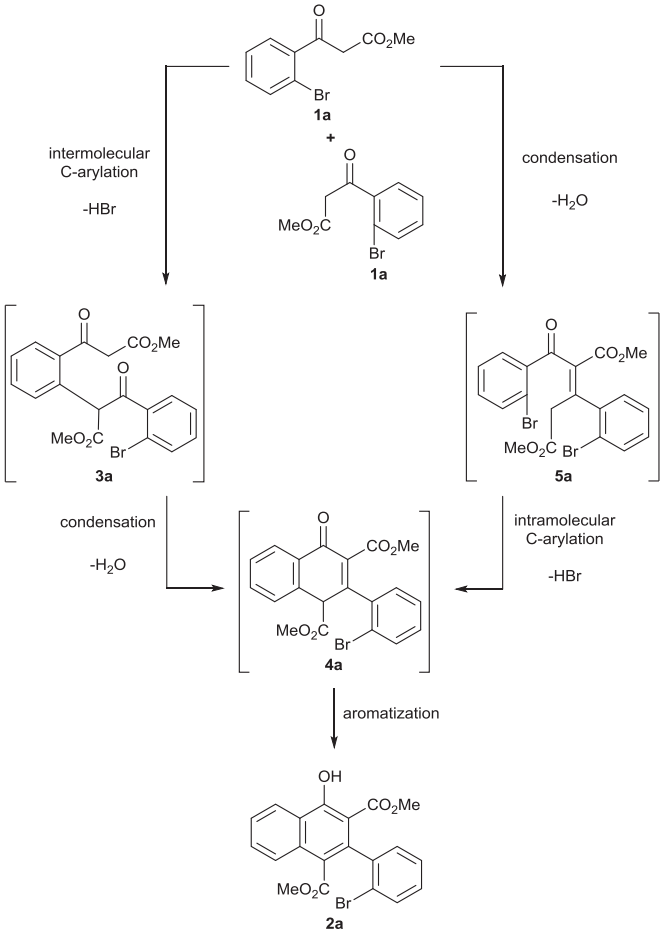
Next, we turned our attention to different ester functionalities. It was demonstrated that the dimerization was also successful with the ethyl ester **1d** and the allyl ester **1e** (Table 4, entries 4 and 5). Notably, the best result was observed with the allyl ester **1e** as substrate. Further experiments revealed that the transformation could also be achieved with substituted 3-(*o*-bromoaryl)-3-oxopropanoates carrying one or more additional substituents on the aryl ring. It turned out that the reaction tolerates a number of substituents, including halogens at C-5′ and C-4′ (fluorine), a CF_3 group at C-5′, and a methoxy group at C-5′. It seems that the position of the additional substituent has an influence on the yield. With electron withdrawing substituents in 5′-position the yields of the 1-naphthols are in the range between 63 and 69% (Table 4, entries 6, 7, 8, 10 and 11). An electron withdrawing group in *para* position to the ketoester moiety seems to lower the yield as exemplified by the reaction of **1i** (Table 4, entry 9). Finally, it was demonstrated that the transformation can also be achieved with substituted 3-(*o*-bromoaryl)-3-oxopropanoates carrying two additional substituents on the aryl ring. With the tetrasubstituted substrates **1l** and **1m**, the products **2l** and **2m** were isolated with 61 and 67% yield, respectively (Table 4, entries 12 and 13).



Scheme 2. CuI-catalyzed dimerization of methyl 3-(3′-bromothien-2-yl)-3-oxopropanoate (**1n**) to dimethyl 2-hydroxy-4-(3″-bromothien-2-ylbenzo[*b*]thiophene-3,5-dicarboxylate (**2n**).

To demonstrate that the new transformation is not restricted to 3-(*o*-haloaryl)-3-oxopropanoates, but can also be performed with 3-(*o*-halohetaryl)-3-oxopropanoates, methyl 3-(3′-bromothien-2-yl)-3-oxopropanoate (**1n**) was chosen as substrate. The thiophene derivative was obtained by reaction of 2-acetyl-3-bromothiophene with dimethylcarbonate in 69% yield. Reaction of **1n** under standard conditions delivered the corresponding benzo[*b*]thiophene **2n** in 53% yield (Scheme 2).

In summary, it was demonstrated that in addition to the model compound **1a** several alkyl 3-(*o*-halo(het)aryl)-3-oxopropanoates **1b**–**n** can serve as substrates for the new dimerization. The transformations afforded the substituted 1-naphthols and related compounds **2a**–**n** exclusively with yields up to 81%.



Scheme 3. Plausible reaction mechanism for the dimerization of **1a** to **2a**.

It is plausible to suppose that the first step of the domino process is an intermolecular Cu(I)-catalyzed *C*-arylation of two molecules of *β*-ketoester **1a** which is followed by an intramolecular condensation of **3a** to **4a** and aromatization to deliver the 3-aryl-1-naphthol **2a** (Scheme 3). However, it cannot be excluded that the sequence of reactions starts with an intermolecular condensation to give **5a** as an intermediate. Intramolecular *C*-arylation leads to the central intermediate **4a** which in turn aromatizes to the corresponding 1-naphthol **2a**. In the presence of a Cu-catalyst, none of the intermediates could be isolated, regardless of the reaction conditions. This is why we turned our attention to the reaction of **1a** under copper-free conditions. As already mentioned, the reaction of **1a** under basic conditions at 100 °C using K_2CO_3 of 99% purity delivered **2a** exclusively in 34% yield (Table 3, entry 15). We hoped that decreasing the reaction temperature would result in the formation of any of the intermediates as side products. This is why the transformation was performed at 80 °C, 50 °C and at room temperature. Unfortunately, this hope was not fulfilled: At 80 °C and 50 °C only the product **2a** was isolated with 28% and 12% yield, respectively. At room temperature no reaction took place at all and the substrate **1a** was recovered.

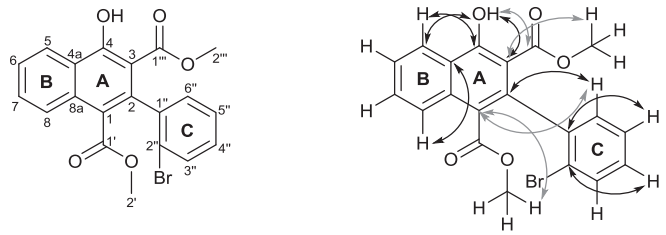


Fig. 1. ^{1}H spin systems and important gHMBC correlations (black arrows) and super long-range D-HSQHMBC correlations (gray arrows) for compound **2a**.

All compounds presented were characterized by UV, IR and NMR spectroscopy as well as by mass spectrometry. The full assignment of the ^{1}H and ^{13}C chemical shifts and the unambiguous structure elucidation are demonstrated for compound **2a**. 1-Naphthol **2a** contains five ^{1}H spin systems I-V (Fig. 1): spin system I consists of the OH-group attached to carbon C-4, spin system II is made up of the four protons attached to C-5, C-6, C-7 and C-8 of ring B. Spin system III contains the four protons attached to C-3″, C-4″, C-5″ and C-6″ of ring C, whereas the fourth and fifth spin system are made up of 3 protons each of the two ester functionalities at C-1 and C-3. The sequences of the protons and their directly attached carbons in spin systems II and III (rings B and C) were evaluated by analysis of the DQFCOSY and gHSQC spectrum. By $^{3}J_{CH}$ correlations in the standard ^{1}H–^{13}C gHMBC spectrum (optimized for J_{CH}=8 Hz) between the protons O-H, 5-H, 8-H, 4″-H and 6″-H and the corresponding carbon atoms the assignment of the quaternary carbons C-2, C-3, C-4, C-4a, C-8a and C-2″ (black arrows) could be achieved. To fix the positions of the two ester functionalities of the fourth and fifth spin systems the standard gHMBC providing mainly $^{2}J_{CH}$ and $^{3}J_{CH}$ correlations was not sufficient, so super long-range D-bsgHMBC[22] was used. Thus, the observed $^{4}J_{CH}$ correlations (grey arrows) allow unequivocally the assignment of the positions C-1, C-2 and C-1″.

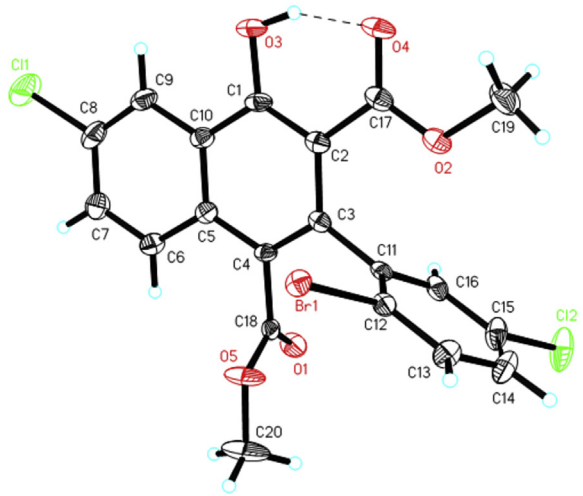


Fig. 2. Structure of dimethyl 2-(2″-bromo-5″-chlorophenyl)-6-chloro-4-hydroxynaphthalene-1,3-dicarboxylate (**2h**), derived from X-ray crystal structure analysis.

Unequivocal evidence for the structure of 1-naphthol **2h** was provided by single crystal X-ray diffraction. Fig. 2 illustrates the planar structure of the naphthalene moiety carrying a hydroxyl group at C-1, ester functions at C-2 and C-4, an aryl group at C-3 and a chlorine atom at C-8.[†] It is interesting to see that the ester function attached to C-2 is nearly coplanar to the naphthalene core, while the ester moiety at C-4 is not in plane. The interplanar angle for the C-2 ester moiety and the naphthalene core is 4.1(3)°. The short distance of 2.542(2) Å between O-3 and O-4 is a hint for an intramolecular hydrogen bond between O-3–H-3 as donor and O-4 as acceptor. The H-3–O-4 distance is 1.71(3) Å and the relevant angle is 153(3)°. In contrast to the planar arrangement of the ester function at C-2 the haloaryl moiety attached to C-3 is nearly perpendicular to the planar naphthalene core. The interplanar angles are 86.0(1)° and 84.07(4)°. It is also interesting to see that the distance between Br-1 and O-1 is really short, 2.981(2)°, respectively.

[†] CCDC 1406374 (**2g**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

3. Conclusions

In summary, it has been demonstrated that the dimerization of alkyl 3-(o-halo(het)aryl)-3-oxopropanoates, i.e., compounds bearing both a β-ketoester and a (het)aryl halide moiety, can be achieved by means of a copper-catalyzed domino process. The CuI-catalyzed reactions of the easily available alkyl 3-(o-halo(het)aryl)-3-oxopropanoates deliver the substituted 3-aryl-1-naphthols and related products as the result of a domino intermolecular *C*-arylation/intramolecular Knoevenagel type condensation/aromatization process with yields up to 81%. The method provides an efficient and selective access to interesting organic building blocks in one-pot. Due to their high functional density, including a 3-haloaryl moiety, they are predestinated for further modification.

4. Experimental section

4.1. General

All commercially available reagents were used without further purification. Glassware was dried for 24 h at 120 °C in an oven. Solvents used in reactions were distilled over appropriate drying agents prior to use. Solvents used for extraction and purification were distilled prior to use. Reaction temperatures are reported as bath temperatures. Thin-layer chromatography (TLC) was performed on precoated aluminum plates (silica gel Merck 60 F_{254}) and visualized by UV light (254 nm) and/or by immersion in an ethanolic vanillin solution or by immersion in a $KMnO_4$ solution followed by heating. Products were purified by flash chromatography on silica gel (MN 60, 0.04–0.063 mm; Marcherey & Nagel).

Melting points were determined on a Büchi Melting Point apparatus B-545 and are uncorrected. IR spectra were measured on a Bruker Alpha FT-IR spectrometer. UV/Vis spectra were recorded on a Cary 4E spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded at 300 (75) MHz and 500 (100) MHz on Varian Unity Inova spectrometers using $CDCl_3$ as solvent. The ^{1}H and ^{13}C chemical shifts were referenced to residual solvent signals at δ H/C 7.26/77.00 ($CDCl_3$) relative to TMS as internal standard. DQFCOSY, HSQC-, gHMBC-, and D-bsgHMBC-spectra were recorded on an NMR spectrometer at 300 MHz or 500 MHz. Coupling constants *J* [Hz] were directly taken from the spectra and are not averaged. Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), m (multiplet), and ov (overlapped). 1D and 2D homonuclear NMR spectra were measured with standard pulse sequences. Low-resolution electron impact mass spectra [MS (EI)] and exact mass electron impact mass spectra [HRMS (EI)] were obtained at 70 eV using a double focusing sector field mass spectrometer Finnigan MAT 95, for the measurement of exact mass electrospray ionization mass spectra [ESI (HRMS)] a Bruker Daltonik spectrometer micrOTOF-Q was used. Intensities are reported as percentages relative to the base peak (I=100%).

4.2. Synthesis and characterization of starting materials 1a–n

*4.2.1. General procedures I for the synthesis of starting materials **1a–n**.* Compounds **1a–g**, **i–n** were synthesized according to general procedures I. Compound **1h** was commercially available.

Method A:[16,17] A two-necked round-bottomed flask equipped with a reflux condenser and a magnetic stir bar was charged with the 2-bromobenzoic acid (20 mmol) and freshly distilled methanol (25 mL). The solution was heated in a hot water bath, conc. H_2SO_4 (8 mmol) was added slowly and the reaction mixture was refluxed for 24 h. After cooling to room temperature around half of the amount of the solvent was removed in vacuo and the residue was partitioned between water (50 mL) and diethyl ether (70 mL). The organic layer was separated and washed with saturated $NaHCO_3$ (2×50 mL), water (50 mL) and brine (50 mL), dried over anhydrous $MgSO_4$ and the volatiles were removed under reduced pressure. The crude product thus obtained was purified by flash chromatography on silica gel to afford the alkyl-2-halobenzoate.

In a two-necked round-bottomed flask equipped with a reflux condenser and a magnetic stir bar the alkyl 2-halobenzoate (22.5 mmol) was dissolved in freshly distilled dry THF (30 mL) under argon. The solution was cooled to 0 °C using an ice bath and NaH (60% in mineral oil, 15 mmol) was added portionwise. After stirring for 15 min a solution of the alkyl acetate (15 mmol) in dry THF (30 mL) was added dropwise to the reaction mixture at 0 °C. The mixture was warmed up, stirred at room temperature for 2 h and heated under reflux for 24 h. After cooling to room temperature around half of the amount of the solvent was removed in vacuo and the reaction mixture was diluted with toluene (50 mL). The resulting mixture was washed with 2N HCl (50 mL), saturated NH_4Cl (50 mL), dried over anhydrous $MgSO_4$ and the volatiles were removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel to afford the alkyl 3-(2′-halophenyl)-3-oxo-propanoate **1**.

Method B:[18] A two-necked round-bottomed flask equipped with a reflux condenser and a magnetic stir bar was charged with the 2-bromobenzaldehyde (10 mmol) and freshly distilled toluene (50 mL). Zn powder (15 mmol) and methyl bromoacetate (15 mmol) were added slowly under argon and the reaction mixture was heated at 100 °C for 2 h. After completion, the reaction mixture was poured into saturated NH_4Cl (50 mL) and extracted with dichloromethane (3×30 mL). The combined organic layers were washed with brine (50 mL), dried over anhydrous $MgSO_4$ and concentrated in vacuo.

The crude methyl 3-(2′-bromophenyl)-3-hydroxypropanoate thus obtained (ca. 7 mmol) was dissolved in dichloromethane (100 mL) and pyridinium chlorochromate (PCC) (14 mmol) was added portionwise. After stirring for 8 h at room temperature Celite was added and the reaction mixture was stirred for another 10 min at room temperature. The reaction mixture was filtered and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel to afford the corresponding alkyl 3-(2′-halophenyl)-3-oxopropanoate **1**.

*4.2.2. Methyl 3-(2′-bromophenyl)-3-oxopropanoate (**1a**).* According to general procedure I, method A, methyl 2-bromobenzoate (21.8 g, 101 mmol), methyl acetate (5 g, 68 mmol) and NaH (60% in mineral oil, 2.7 g, 67.5 mmol) were reacted in THF at 70 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) gave methyl 3-(2′-bromophenyl)-3-oxopropanoate (**1a**) as a yellow oil in 64% yield (11.01 g, 43.02 mmol); R_f 0.48 (petroleum ether:EtOAc=9:1); IR (ATR) ν 1742 (CO ester), 1700 (CO ketone), 1626 (OCC enol), 1586, 1562, 1510, 1432, 1387, 1322, 1269, 1245, 1201, 1175, 1059, 1020, 757 cm^{-1}; UV (MeCN) λ_{max} (log ε) 207 (4.39), 244 (3.93) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.73 (s, 3H, 1″-H, ketone), 3.80 (s, 3H, 1″-H, enol), 4.03 (s, 2H, 2-H, ketone), 5.46 (s, 1H, 2-H, enol), 7.26 (ddd, ^3J(3′-H, 4′-H)=7.6 Hz, ^3J(5′-H, 4′-H)=7.7 Hz, ^4J(6′-H, 4′-H)=1.8 Hz, 2H, 4′-H, ketone and enol), 7.33 (ddd, ^3J(4′-H, enol, 5′-H, enol)=7.3 Hz, ^3J(6′-H, enol, 5′-H, enol)=7.8 Hz, ^4J(3′-H, enol, 5′-H, enol)=1.7 Hz, 1H, 5′-H, enol), 7.39 (ddd, ^3J(4′-H, ketone, 5′-H, ketone)=7.4 Hz, ^3J(6′-H, ketone, 5′-H, ketone)=7.6 Hz, ^4J(3′-H, ketone, 5′-H, ketone)=1.2 Hz, 1H, 5′-H, ketone), 7.50 (ddd, ^3J(5′-H, ketone, 6′-H, ketone)=7.8 Hz, ^3J(5′-H, enol, 6′-H, enol)=8.4 Hz, ^4J(4′-H, 6′-H)=1.8 Hz, 2H, 6′-H, ketone and enol), 7.62 (dd, ^3J(4′-H, 3′-H)=7.8 Hz, ^4J(5′-H, 3′-H)=1 Hz, 2H, 3′-H, ketone and enol), 12.33 (s, 1H, OH, enol); ^{13}C NMR (75 MHz, $CDCl_3$) δ 48.49 (C-2, ketone), 51.51 (C-1″, enol), 52.38 (C-1″, ketone), 92.85 (C-2, enol), 119.15 (C-2′, ketone), 120.93 (C-2′, enol), 127.30 (C-5′, enol), 127.53 (C-5′, ketone), 129.49 (C-6′, ketone), 130.19 (C-6′, enol), 131.19 (C-4′, enol), 132.37 (C-4′, ketone), 133.74 (C-3′, enol), 133.93 (C-3′, ketone), 135.66 (C-1′, enol), 139.89 (C-1′, ketone), 167.20 (C-1, ketone), 171.94 (C-3, enol), 172.82 (C-1, enol) and 195.43 (C-3, ketone); MS (EI, 70 eV) *m/z* (%) 256 (6) $[M]^+$, 185 (92), 177 (100), 89 (18), 76 (34), 69 (22), 50 (18); HRMS (EI, M^+) calculated for $C_{10}H_9BrO_3$ 255.9735 found 255.9758.

*4.2.3. Methyl 3-(2′-iodophenyl)-3-oxopropanoate (**1b**).* According to general procedure I, method A, methyl 2-iodobenzoate (8.0 g, 30 mmol), methyl acetate (1.5 g, 20 mmol) and NaH (60% in mineral oil, 0.8 g, 20 mmol) were reacted in THF at 70 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) gave methyl 3-(2′-iodophenyl)-3-oxopropanoate (**1b**) as a yellow oil in 51% yield (3.2 g, 11 mmol); R_f 0.42 (petroleum ether:EtOAc=9:1); IR (ATR) ν 1739 (CO ester), 1696 (CO ketone), 1630 (OCC enol), 1579, 1560, 1434, 1386, 1320, 1243, 1200, 1149, 1055, 1010, 756 cm^{-1}; UV (MeCN) λ_{max} (log ε) 222 (4.16) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.74 (s, 3H, 1″-H, ketone), 3.8 (s, 3H, 1″-H, enol), 3.99 (s, 2H, 2-H, ketone), 5.35 (s, 1H, 2-H, enol), 7.06–7.12 (m, 1H, 4′-H, enol), 7.16 (ddd, ^3J(3′-H, ketone, 4′-H, ketone)=7.8 Hz, ^3J(5′-H, ketone, 4′-H, ketone)=7.7 Hz, ^4J(6′-H, ketone, 4′-H, ketone)=1.8 Hz, 1H, 4′-H, ketone), 7.40 (ddd, ^3J(5′-H, ketone, 6′-H, ketone)=8.5 Hz, ^3J(5′-H, enol, 6′-H, enol)=8.6 Hz, ^4J(4′-H, 6′-H)=1.1 Hz, 2H, 6′-H, ketone and enol), 7.48 (ddd, ^3J(6′-H, 5′-H)=8.6 Hz, ^3J(4′-H, 5′-H)=7.8 Hz, ^4J(3′-H, 5′-H)=1.9 Hz, 2H, 5′-H, ketone and enol), 7.91 (d, ^3J(4′-H, enol, 3′-H, enol)=7.9 Hz, 1H, 3′-H, enol), 7.95 (dd, ^3J(4′-H, ketone, 3′-H, ketone)=7.9 Hz, ^4J(5′-H, ketone, 3′-H, ketone)=1 Hz, 1H, 3′-H, ketone), 12.27 (s, 1H, OH, enol); ^{13}C NMR (75 MHz, $CDCl_3$) δ 47.84 (C-2, ketone), 51.56 (C-1″, enol), 52.50 (C-1″, ketone), 91.40 (C-2′, ketone), 92.58 (C-2, enol), 94.33(C-2′, enol), 128.02 (C-5′, enol), 128.11 (C-5′, ketone), 128.78 (C-6′, ketone), 129.53 (C-6′, enol), 131.16 (C-4′, enol), 132.35 (C-4′, ketone), 139.70 (C-1′, enol), 140.25 (C-3′, enol), 141.08 (C-3′, ketone), 142.41 (C-1′, ketone), 167.13 (C-1, ketone), 172.73 (C-1, enol), 174.11 (C-3, enol), 195.69 (C-3, ketone); MS (EI, 70 eV) *m/z* (%) 304 (22) $[M]^+$, 272 (25), 231 (98), 177 (100), 146 (19), 135 (38), 121 (25), 105 (38), 89 (46), 77 (56), 69 (43), 50 (74); HRMS (EI, M^+) calculated for $C_{10}H_9IO_3$ 303.9596 found 303.9591.

*4.2.4. Methyl 3-(2′-chlorophenyl)-3-oxopropanoate (**1c**).* According to general procedure I, method A, methyl 2-chlorobenzoate (5.2 g, 30 mmol), methyl acetate (1.5 g, 20 mmol) and NaH (60% in mineral oil, 0.8 g, 20 mmol) were reacted in THF at 70 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) gave methyl 3-(2′-chlorophenyl)-3-oxopropanoate (**1c**) as a yellow oil in 41% yield (1.8 g, 8 mmol); R_f 0.57 (petroleum ether:EtOAc=9:1); IR (ATR) ν 1743 (CO ester), 1698 (CO ketone), 1625 (OCC enol), 1589, 1566, 1470, 1434, 1387, 1323, 1272, 1245, 1200, 1150, 1069, 1008, 760 cm^{-1}; UV (MeCN) λ_{max} (log ε) 209 (4.30), 243 (3.82) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.74 (s, 3H, 1″-H, ketone), 3.81 (s, 3H, 1″-H, enol), 4.06 (s, 2H, 2-H, ketone), 5.57 (s, 1H, 2-H, enol), 7.32 (ov, 2H, 5′-H, ketone and enol), 7.35 (ov, 2H, 3′-H, ketone and enol), 7.43 (dd-like, 2H, 4′-H, ketone and enol), 7.56 (dd, ^3J(5′-H, enol, 6′-H, enol)=6.8 Hz, ^4J(4′-H, enol, 6′-H, enol)=2.7 Hz, 1H, 6′-H, enol), 7.61

(dd, ^3J(5′-H, ketone, 6′-H, ketone)=7.3 Hz, ^4J(4′-H, ketone, 6′-H, ketone)=1 Hz, 1H, 6′-H, ketone), 12.38 (s, 1H, OH, enol); ^{13}C NMR (75 MHz, $CDCl_3$) δ 48.92 (C-2, ketone), 51.56 (C-1″, enol), 52.45 (C-1″, ketone), 93.02 (C-2, enol), 126.81 (C-5′, enol), 127.10 (C-5′, ketone), 130.06 (C-6′, ketone), 130.13 (C-6′, enol), 130.61 (C-3′, enol), 130.76 (C-4′, enol), 131.12 (C-3′, ketone), 131.56 (C-2′, enol), 132.16 (C-2′, ketone), 132.68 (C-4′, ketone), 133.49 (C-1′, enol), 167.42 (C-1, ketone), 170.50 (C-3, enol), 173.00 (C-1, enol), 194.56 (C-3, ketone); MS (EI, 70 eV) *m/z* (%) 212 (8) $[M]^+$, 181 (12), 177 (89), 139 (100), 111 (55), 89 (27), 75 (51), 69 (29), 50 (21); HRMS (EI, M^+) calculated for $C_{10}H_9ClO_3$ 212.0240 found 212.0246.

*4.2.5. Ethyl 3-(2′-bromophenyl)-3-oxopropanoate (**1d**).* According to general procedure I, method A, methyl 2-bromobenzoate (3.7 g, 17 mmol), ethyl acetate (1.0 g, 11 mmol) and NaH (60% in mineral oil, 0.45 g, 11 mmol) were reacted in THF at 70 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) gave ethyl 3-(2′-bromophenyl)-3-oxopropanoate (**1d**) as a yellow oil in 71% yield (2.2 g, 8 mmol); R_f 0.57 (petroleum ether:EtOAc=9:1); IR (ATR) ν 1738 (CO ester), 1701 (CO ketone), 1627 (OCC enol), 1586, 1563, 1467, 1406, 1382, 1318, 1268, 1243, 1192, 1149, 1087, 1024, 757 cm^{-1}; UV (MeCN) λ_{max} (log ε) 208 (4.22) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (t, ^3J(1″-H, ketone, 2″-H, ketone)=7.2 Hz, 3H, 2″-H, ketone), 1.33 (t, ^3J(1″-H, enol, 2″-H, enol)=7.2 Hz, 3H, 2″-H, enol), 4.01 (s, 2H, 2-H, ketone), 4.18 (q, ^3J(2″-H, ketone, 1″-H, ketone)=7.2 Hz, 2H, 1″-H, ketone), 4.27 (q, ^3J(2″-H, enol, 1″-H, enol)=7.2 Hz, 2H, 1″-H, enol), 5.45 (s, 1H, 2-H, enol), 7.26 (ddd, ^3J(3′-H, 4′-H)=7.8 Hz, ^3J(5′-H, 4′-H)=7.6 Hz, ^4J(6′-H, 4′-H)=1.8 Hz, 2H, 4′-H, ketone and enol), 7.33 (ddd, ^3J(4′-H, enol, 5′-H, enol)=7.6 Hz, ^3J(6′-H, enol, 5′-H, enol)=7.4 Hz, ^4J(3′-H, enol, 5′-H, enol)=2.1 Hz, 1H, 5′-H, enol), 7.38 (ddd, ^3J(4′-H, ketone, 5′-H, ketone)=7.6 Hz, ^3J(6′-H, ketone, 5′-H, ketone)=7.4 Hz, ^4J(3′-H, ketone, 5′-H, ketone)=1.2 Hz, 1H, 5′-H, ketone), 7.50 (ddd, ^3J(5′-H, enol, 6′-H, enol)=7.8 Hz, ^3J(5′-H, ketone, 6′-H, ketone)=7.9 Hz, ^4J(4′-H, 6′-H)=1.8 Hz, 2H, 6′-H, ketone and enol), 7.63 (dd, ^3J(4′-H, 3′-H)=7.8 Hz, ^4J(5′-H, 3′-H)=1 Hz, 2H, 3′-H, ketone and enol), 12.43 (s, 1H, OH, enol); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.16 (C-2′, ketone), 14.38 (C-2′, enol), 48.89 (C-2, ketone), 60.69 (C-1″, enol), 61.62 (C-1″, ketone), 93.35 (C-2, enol), 119.34 (C-2′, ketone), 121.08 (C-2′, enol), 127.45 (C-5′, enol), 127.64 (C-5′, ketone), 129.66 (C-6′, ketone), 130.36 (C-6′, enol), 131.29 (C-4′, enol), 132.46 (C-4′, ketone), 133.89 (C-3′, ketone), 134.04 (C-3′, enol), 135.94 (C-1′, enol), 140.14 (C-1′, ketone), 166.90 (C-1, ketone), 172.05 (C-3, enol), 172.69 (C-1, enol), 195.73 (C-3, ketone); MS (EI, 70 eV) *m/z* (%) 270 (7) $[M]^+$, 191 (100), 183 (21), 163 (66), 89 (17), 76 (22), 69 (18), 50 (12); HRMS (EI, M^+) calculated for $C_{11}H_{11}BrO_3$ 269.9892 found 269.9885.

*4.2.6. Allyl 3-(2′-bromophenyl)-3-oxopropanoate (**1e**).* According to general procedure I, method A, methyl 2-bromobenzoate (4.8 g, 22 mmol), allyl acetate (1.5 g, 15 mmol) and NaH (60% in mineral oil, 0.6 g, 15 mmol) were reacted in THF at 70 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) gave allyl 3-(2′-bromophenyl)-3-oxopropanoate (**1e**) as a yellow oil in 35% yield (1.5 g, 5 mmol); R_f 0.43 (petroleum ether:EtOAc=9:1); IR (ATR) ν 3689 (w; OH), 1738 (CO ester), 1701 (CO ketone), 1627 (OCC enol), 1586, 1562, 1467, 1429, 1399, 1269, 1241, 1186, 108, 982, 930, 757 cm^{-1}; UV (MeCN) λ_{max} (log ε) 209 (4.17), 245 (3.64) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.06 (s, 2H, 2-H, ketone), 4.62 (ov, 1H, 1″-H_a, enol), 4.64 (ov, 1H, 1″-H_a, ketone), 4.72 (dt-like, ^3J(2″-H, enol, 1″-H_b, enol)=5.7 Hz, 1H, 1″-H_b, enol), 4.81 (dt-like, ^3J(2″-H, ketone, 1″-H_b, ketone)=5.7 Hz, 1H, 1″-H_b, ketone), 5.22 (dd-like, ^3J(2″-H, enol, 3″-$H_{(Z)}$, enol)=10.0 Hz, 1H, 3″-$H_{(Z)}$, enol), 5.33 (dd-like, ^3J(2″-H, ketone, 3″-$H_{(Z)}$, ketone)=10.9 Hz, 1H, 3″-$H_{(Z)}$, ketone), 5.42 (dd-like, ^3J(2″-H, enol, 3″-$H_{(E)}$, enol)=17.1 Hz, 1H, 3″-$H_{(E)}$, enol), 5.49 (dd-like, ^3J(2″-H, ketone, 3″-$H_{(E)}$, ketone)=17.2 Hz, 1H, 3″-$H_{(E)}$, ketone), 5.50 (s, 1H, 2-H, enol), 5.88 (m, 1H, 2″-H, enol), 6.02 (m, 1H, 2″-H, ketone), 7.33 (ddd, ^3J(4′-H, enol, 5′-H, enol)=7.6 Hz, ^3J(6′-H, enol, 5′-H, enol)=7.7 Hz, ^4J(3′-H, enol, 5′-H, enol)=1.8 Hz, 1H, 5′-H, enol), 7.39 (ddd, ^3J(4′-H, ketone, 5′-H, ketone)=7.3 Hz, ^3J(6′-H, ketone, 5′-H, ketone)=7.4 Hz, ^4J(3′-H, ketone, 5′-H, ketone)=1.3 Hz, 1H, 5′-H, ketone), 7.44 (ddd, ^3J(3′-H, 4′-H)=7.6 Hz, ^3J(5′-H, 4′-H)=7.7 Hz, ^4J(6′-H, 4′-H)=1.8 Hz, 2H, 4′-H, ketone and enol), 7.51 (ddd, ^3J(5′-H, enol, 6′-H, enol)=7.5 Hz, ^3J(5′-H, ketone, 6′-H, ketone)=7.4 Hz, ^4J(4′-H, 6′-H)=1.8 Hz, 2H, 6′-H, ketone and enol), 7.65 (ddd, ^3J(4′-H, ketone, 3′-H, ketone)=7.3 Hz, ^3J(4′-H, enol, 3′-H, enol)=7.8 Hz, ^4J(5′-H, 3′-H)=2.3 Hz, 2H, 3′-H, ketone and enol), 12.32 (s, 1H, OH, enol); ^{13}C NMR (75 MHz, $CDCl_3$) δ 48.66 (C-2, ketone), 65.12 (C-1″, enol), 65.43 (C-1″, ketone), 92.99 (C-2, enol), 118.06 (C-3″, ketone), 118.80 (C-3″, enol), 119.19 (C-2′, ketone), 120.37 (C-2′, enol), 127.31 (C-5′, enol), 127.53 (C-5′, ketone), 129.54 (C-6′, ketone), 130.21 (C-6′, enol), 132.37 (C-2″, enol), 132.53 (C-2″, ketone), 133.36 (C-4′, ketone), 133.77 (C-4′, enol), 133.92 (C-3′, ketone), 134.32 (C-3′, enol), 135.68 (C-1′, enol), 139.94 (C-1′, ketone), 166.62 (C-1, ketone), 172.15 (C-3, enol), 172.24 (C-1, enol), 195.36 (C-3, ketone); MS (EI, 70 eV) *m/z* (%) 284 (3) $[M]^+$, 203 (100), 183 (97), 161 (38), 155 (27), 120 (31), 89 (11), 76 (17), 69 (12); HRMS (EI, M^+) calculated for $C_{12}H_{11}BrO_3$ 281.9892 found 281.9886.

*4.2.7. Methyl 3-(2′,5′-dibromophenyl)-3-oxopropanoate (**1f**).* According to general procedure I, method A, methyl 2,5-dibromobenzoate (4.0 g, 14 mmol), methyl acetate (0.7 g, 9 mmol) and NaH (60% in mineral oil, 0.4 g, 10 mmol) were reacted in THF at 70 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) gave methyl 3-(2′,5′-dibromophenyl)-3-oxopropanoate (**1f**) as a white solid in 55% yield (1.7 g, 5 mmol): mp 62–63 °C; R_f 0.60 (petroleum ether:EtOAc=9:1); IR (ATR) ν 3069 (w; OH), 1735 (CO ketone), 1623 (OCC enol), 1574, 1550, 1441, 1382, 1274, 1223, 1199, 1081, 1026, 1007, 801, 732 cm^{-1}; UV (MeCN) λ_{max} (log ε) 240 (3.60), 218 (3.87) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.75 (s, 3H, 1″-H, ketone), 3.82 (s, 3H, 1″-H, enol), 4.02 (s, 2H, 2-H, ketone), 5.48 (s, 1H, 2-H, enol), 7.39 (dd, ^3J(3′-H, enol, 4′-H, enol)=8.4 Hz, ^4J(6′-H, enol 4′-H, enol)=2.2 Hz, 1H, 4′-H, enol), 7.44 (dd, ^3J(3′-H, ketone, 4′-H, ketone)=8.4 Hz, ^4J(6′-H, ketone 4′-H, ketone)=2.1 Hz, 1H, 4′-H, ketone), 7.50 (d, ^3J(4′-H, 3′-H)=8.3 Hz, 2H, 3′-H, ketone and enol), 7.62 (d, ^3J(4′-H, ketone, 6′-H, ketone)=2.3 Hz, 1H, 6′-H, ketone), 7.64 (d, ^3J(4′-H, enol, 6′-H, enol)=2.4 Hz, 1H, 6′-H, enol), 12.31 (s, 1H, OH, enol); ^{13}C NMR (75 MHz, $CDCl_3$) δ 48.32 (C-2, ketone), 51.69 (C-1″, enol), 52.57 (C-1″, ketone), 93.39 (C-2, enol), 117.67 (C-5′, ketone), 119.66 (C-5′, enol), 121.21 (C-2′, enol), 121.60 (C-2′, ketone), 132.28 (C-6′, ketone), 133.10 (C-6′, enol), 134.10 (C-4′, enol), 135.14 (C-4′, ketone), 135.23 (C-3′, enol), 135.26 (C-3′, ketone), 137.25 (C-1′, enol), 141.49 (C-1′, ketone), 166.86 (C-1, ketone), 170.25 (C-3, enol), 172.65 (C-1, enol), 194.20 (C-3, ketone) ppm; MS (EI, 70 eV) *m/z* (%) 336 (2) $[M]^+$, 263 (69), 255 (100), 235 (15), 213 (2), 156 (6), 89 (4), 75 (11); HRMS (ESI, $[M+H]^+$) calculated for $C_{10}H_8Br_2O_3$ 338.8874 found 338.8850.

*4.2.8. Methyl 3-(2′-bromo-5′-chlorophenyl)-3-oxopropanoate (**1g**).* According to general procedure I, method A, methyl 2-bromo-5-chlorobenzoate (7.6 g, 30 mmol), methyl acetate (1.5 g, 20 mmol) and NaH (60% in mineral oil, 0.8 g, 20 mmol) were reacted in THF at 70 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) gave methyl 3-(2′-bromo-5′-chlorophenyl)-3-oxopropanoate (**1g**) as a white solid in 49% yield (2.9 g, 10 mmol): mp 58–59 °C; R_f 0.61 (petroleum ether:EtOAc=9:1); IR (ATR) ν 3088 (w; OH), 1707 (CO ketone), 1621 (OCC enol), 1579, 1438, 1383, 1338, 1276, 1226, 1198, 1099, 1086, 1012, 878, 785 cm^{-1}; UV (MeCN) λ_{max} (log ε) 216 (4.29) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.76 (s, 3H, 1″-H, ketone), 3.82 (s, 3H, 1″-H, enol), 4.03 (s, 2H, 2-H, ketone), 5.49 (s, 1H, 2-H, enol), 7.24 (dd, ^3J(3′-H, 4′-H)=8.5 Hz, ^4J(6′-H, 4′-H)=2.6 Hz, 2H, 4′-H, ketone and enol),

7.50 (d, ^4J(4′-H, 6′-H)=2.6 Hz, 2H, 6′-H, ketone and enol), 7.55 (d, ^3J(4′-H, 3′-H)=8.6 Hz, 2H, 3′-H, ketone and enol), 12.32 (s, 1H, OH, enol); ^{13}C NMR (75 MHz, $CDCl_3$) δ 48.31 (C-2, ketone), 51.67 (C-1″, enol), 52.55 (C-1″, ketone), 93.35 (C-2, enol), 116.90 (C-2′, ketone), 118.85 (C-2′, enol), 129.43 (C-6′, ketone), 130.15 (C-6′, enol), 131.14 (C-4′, enol), 132.30 (C-4′, ketone), 133.54 (C-5′, enol), 133.95 (C-5′, ketone), 134.88 (C-3′, enol), 134.99 (C-3′, ketone), 136.92 (C-1′, enol), 141.19 (C-1′, ketone), 166.85 (C-1, ketone), 170.31 (C-3, enol), 172.64 (C-1, enol), 194.22 (C-3, ketone); MS (EI, 70 eV) *m/z* (%) 292 (6) $[M]^+$, 211 (100), 189 (17), 169 (12), 89 (8), 75 (17), 69 (24); HRMS (EI, M^+) calculated for $C_{10}H_8BrClO_3$ 289.9345 found 289.9336.

*4.2.9. Methyl 3-(2′-bromo-4′-fluorophenyl)-3-oxopropanoate (**1i**).* According to general procedure I, method A, methyl 2-bromo-4-fluorobenzoate (3.7 g, 16 mmol), methyl acetate (0.8 g, 11 mmol) and NaH (60% in mineral oil, 0.4 g, 11 mmol) were reacted in THF at 70 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) gave methyl 3-(2′-bromo-4′-fluorophenyl)-3-oxopropanoate (**1i**) as a yellow solid in 47% yield (1.4 g, 5 mmol): mp 49–50 °C; R_f 0.54 (petroleum ether:EtOAc=9:1); IR (ATR) ν 1722 (CO ketone), 1596, 1492, 1431, 1256, 1230, 1184, 1112, 1027, 861, 767 cm^{-1}; UV (MeCN) λ_{max} (log ε) 212 (4.41), 254 (4.07) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.81 (s, 3H, 1″-H, ketone), 3.86 (s, 3H, 1″-H, enol), 4.01 (s, 2H, 2-H, ketone), 5.44 (s, 1H, 2-H, enol), 7.04 (ddd-like, ^3J(6′-H, enol, 5′-H, enol)=8.5 Hz, ^3J(4′-F, enol, 5′-H, enol)=11.0 Hz, ^4J(3′-H, enol, 5′-H, enol)=2.5 Hz, 1H, 5′-H, enol), 7.10 (ddd-like, ^3J(6′-H, ketone, 5′-H, ketone)=8.1 Hz, ^3J(4′-F, ketone, 5′-H, ketone)=10.4 Hz, ^4J(3′-H, ketone, 5′-H, ketone)=2.4 Hz, 1H, 5′-H, ketone), 7.35 (dd-like, ^3J(4′-F, 3′-H)=8.9 Hz, ^4J(5′-H, 3′-H)=2.5 Hz, 2H, 3′-H, ketone and 3′-H, enol), 7.48 (dd, ^3J(5′-H, enol, 6′-H, enol)=8.6 Hz, ^4J(4′-F, enol, 6′-H, enol)=5.9 Hz, 1H, 6′-H, enol), 7.58 (dd, ^3J(5′-H, ketone, 6′-H, ketone)=8.8 Hz, ^4J(4′-F, ketone, 6′-H, ketone)=5.9 Hz, 1H, 6′-H, ketone), 12.32 (s, 1H, OH, enol); ^{13}C NMR (75 MHz, $CDCl_3$) δ 48.28 (C-2, ketone), 52.03 (C-1″, enol), 55.59 (C-1″, ketone), 92.94 (C-2, enol), 112.92 (C-2′, enol), 114.62 (d, ^2J(F-4′, enol, C-5′, enol)=21 Hz, C-5′, enol), 114.86 (d, ^2J(F-4′, ketone, C-5′, ketone)=21 Hz, C-5′, ketone), 119.74 (C-2′, ketone), 121.05 (d, ^2J(F-4′, enol, C-3′, enol)=25 Hz, C-3′, enol), 121.46 (d, ^2J(F-4′, ketone, C-3′, ketone)=25 Hz, C-3′, ketone), 131.52 (d, ^3J(F-4′, enol, C-6′, enol)=9 Hz, C-6′, enol), 131.69 (d, ^3J(F-4′, ketone, C-6′, ketone)=9 Hz, C-6′, ketone), 131.89 (d, ^4J(F-4′, enol, C-1′, enol)=4 Hz, C-1′, enol), 135.70 (d, ^4J(F-4′, ketone, C-1′, ketone)=4 Hz, C-1′, ketone), 163.60 (d, ^1J(F-4′, enol, C-4′, enol)=250 Hz, C-4′, enol), 164.00 (d, ^1J(F-4′, ketone, C-4′, ketone)=250 Hz, C-4′, ketone), 167.10 (C-1, ketone), 170.82 (C-3, enol), 172.68 (C-1, enol), 193.76 (C-3, ketone); MS (EI, 70 eV) *m/z* (%) 276 (1) $[M]^+$, 244 (36), 215 (100), 195 (49), 170 (8), 78 (9), 63 (20); HRMS (EI, M^+) calculated for $C_{10}H_8BrFO_3$ 273.9641 found 273.9643.

*4.2.10. Methyl 3-(2′-bromo-5′-trifluoromethylphenyl)-3-oxopropanoate (**1j**).* According to general procedure I, method A, methyl 2-bromo-5-trifluoromethylbenzoate (4 g, 14 mmol), methyl acetate (0.7 g, 9 mmol) and NaH (60% in mineral oil, 0.4 g, 9 mmol) were reacted in THF at 70 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) gave methyl 3-(2′-bromo-5′-trifluoromethylphenyl)-3-oxopropanoate (**1j**) as a yellow solid in 61% yield (1.9 g, 6 mmol): mp 51–52 °C; R_f 0.63 (petroleum ether:EtOAc=9:1); IR (ATR) ν 1729 (CO ketone), 1695, 1606 (OCC enol), 1440, 1322, 1290, 1245, 1201, 1110, 1083, 1015, 986, 827 cm^{-1}; UV (MeCN) λ_{max} (log ε) 208 (4.04) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.75 (s, 3H, 1″-H, ketone), 3.83 (s, 3H, 1″-H, enol), 4.06 (s, 2H, 2-H, ketone), 5.51 (s, 1H, 2-H, enol), 7.51 (dd, ^3J(3′-H, enol, 4′-H, enol)=8.3 Hz, ^4J(6′-H, enol, 4′-H, enol)=2 Hz, 1H, 4′-H, enol), 7.58 (dd, ^3J(3′-H, ketone, 4′-H, ketone)=8.4 Hz, ^4J(6′-H, ketone, 4′-H, ketone)=2 Hz, 1H, 4′-H, ketone), 7.75 (d-like, 2H, 6′-H, ketone and enol), 7.79 (s, 2H, 3′-H, ketone and enol), 12.36 (s, 1H, OH, enol); ^{13}C NMR (75 MHz, $CDCl_3$) δ 48.26 (C-2, ketone), 51.72 (C-1″, enol), 52.52 (C-1″, ketone), 93.55 (C-2, enol), 122.97 (C-2′, ketone), 123.19 (d, ^1J(F, ketone, C-1‴ ketone)=250 Hz, C-1‴, ketone), 123.36 (d, ^1J(F, enol, C-1‴ enol)=250 Hz, C-1‴, enol), 125.17 (C-2′, enol), 126.38 (q-like, ^3J(F, ketone, C-6′, ketone)=7 Hz, C-6′, ketone), 127.12 (q-like, ^3J(F, enol, C-6′, enol)=7 Hz, C-6′, enol), 127.60 (q-like, ^3J(F, enol, C-4′, enol)=7 Hz, C-4′, enol), 128.68 (q-like, ^3J(F, ketone, C-4′, ketone)=7 Hz, C-4′, ketone), 130.02 (q-like, ^2J(F, enol, C-5′, enol)=33 Hz, C-5′, enol), 130.29 (q-like, ^2J(F, ketone, C-5′, ketone)=33 Hz, C-5′, ketone), 134.47 (C-3′, enol), 134.55 (C-3′, ketone), 136.40 (C-1′, enol), 140.69 (C-1′, ketone), 166.73 (C-1, ketone), 170.18 (C-3, enol), 172.56 (C-1, enol), 194.40 (C-3, ketone); MS (EI, 70 eV) *m/z* (%) 324 (3) $[M]^+$, 293 (7), 251 (33), 246 (44), 223 (49), 203 (10), 144 (100), 125 (25), 69 (24); HRMS (EI, M^+) calculated for $C_{11}H_8BrF_3O_3$ 323.9609 found 323.9605.

*4.2.11. Methyl 3-(2′-bromo-5′-methoxyphenyl)-3-oxopro-panoate (**1k**).* According to general procedure I, method A, methyl 2-bromo-5-methoxybenzoate (7.5 g, 30 mmol), methyl acetate (1.5 g, 20 mmol) and NaH (60% in mineral oil, 0.8 g, 20 mmol) were reacted in THF at 70 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) gave methyl 3-(2′-bromo-5′-methoxyphenyl)-3-oxopropanoate (**1k**) as a yellow oil in 60% yield (3.4 g, 12 mmol); R_f 0.46 (petroleum ether:EtOAc=9:1); IR (ATR): ν 1742 (CO ester), 1702 (CO ketone), 1630 (OCC enol), 1590, 1567, 1465, 1440, 1392, 1287, 1224, 1195, 1150, 1089, 1015, 810 cm^{-1}; UV (MeCN) λ_{max} (log ε) 222 (4.24) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.73 (s, 3H, 1″-H, ketone), 3.786 (s, 6H, 1‴-H, ketone and 1‴-H, enol), 3.794 (s, 3H, 1″-H, enol), 4.03 (s, 2H, 2-H, ketone), 5.48 (s, 1H, 2-H, enol), 6.81 (dd, ^3J(3′-H, ketone, 4′-H, ketone)=8.8 Hz, ^4J(6′-H, ketone, 4′-H, ketone)=3 Hz, 1H, 4′-H, ketone), 6.86 (dd, ^3J(3′-H, enol, 4′-H, enol)=8.8 Hz, ^4J(6′-H, enol, 4′-H, enol)=3 Hz, 1H, 4′-H, enol), 7.02 (d, ^4J(4′-H, 6′-H)=3 Hz, 2H, 6′-H, ketone and enol), 7.47 (d, ^3J(4′-H, ketone, 3′-H, ketone)=8.9 Hz, 1H, 3′-H, ketone), 7.48 (d, ^3J(4′-H, enol, 3′-H, enol)=8.9 Hz, 1H, 3′-H, enol), 12.32 (s, 1H, OH, enol); ^{13}C NMR (75 MHz, $CDCl_3$) δ 48.33 (C-2, ketone), 51.50 (C-1″, enol), 52.37 (C-1″, ketone), 55.52 (C-1‴, enol), 55.61 (C-1‴, ketone), 92.83 (C-2, enol), 109.21 (C-2′, ketone), 111.07 (C-2′, enol), 114.66 (C-6′, ketone), 115.35 (C-6′, enol), 117.36 (C-4′, enol), 118.55 (C-4′, ketone), 134.46 (C-3′, enol), 134.60 (C-3′, ketone), 136.17 (C-1′, enol), 140.57 (C-1′, ketone), 158.67 (C-5′, enol), 158.82 (C-5′, ketone), 167.17 (C-1, ketone), 171.62 (C-3, enol), 172.78 (C-1, enol), 195.36 (C-3, ketone); MS (EI, 70 eV) *m/z* (%) 286 (8) $[M]^+$, 213 (18), 207 (100), 185 (45), 170 (25), 150 (37), 91 (10), 78 (40), 63 (80); HRMS (EI, M^+) calculated for $C_{11}H_{11}BrO_4$ 285.9841 found 285.9840.

*4.2.12. Methyl 3-(2′-bromo-4′,5′-dimethoxyphenyl)-3-oxopro-panoate (**1l**).* According to general procedure I, method B, 6-bromoveratraldehyde (2.5 g, 10 mmol), Zn powder (1 g, 15 mmol) and methyl bromoacetate (2.3 g, 15 mmol) were reacted in toluene at 100 °C for 2 h. The crude methyl 3-(2′-bromo-4′,5′-dimethoxyphenyl)-3-hydroxypropanoate and PCC (2 equiv) were reacted in dichloromethane at room temperature for 8 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) gave methyl 3-(2′-bromo-4′,5′-dimethoxyphenyl)-3-oxopro-panoate (**1l**) as a yellow oil in 43% yield (over 2 steps) (1.4 g, 4 mmol); R_f 0.15 (petroleum ether:EtOAc=9:1); IR (ATR) ν 1738 (CO ester), 1687 (CO ketone), 1590, 1563, 1505, 1437, 1372, 1333, 1255, 1198, 1166, 1058, 1019, 787 cm^{-1}; UV(MeCN) λ_{max} (log ε) 234 (4.29), 277 (3.88) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.75 (s, 3H, 1″-H, ketone), 3.81 (s, 3H, 1″-H, enol), 3.88 (s, 3H, 1‴′-H, enol), 3.90 (s, 3H, 1‴′-H, ketone), 3.92 (2, 6H, 1‴-H, ketone and enol), 4.11 (s, 2H, 2-H, ketone), 5.57 (s, 1H, 2-H, enol), 7.05 (s, 1H, 3′-H, ketone), 7.06 (s, 1H, 3′-H, enol), 7.22 (s, 2H, 6′-H, ketone and enol), 12.41 (s, 1H, OH, enol); ^{13}C NMR (75 MHz, $CDCl_3$) δ 48.45 (C-2, ketone), 51.44 (C-1″, ketone), 52.32 (C-1″, enol), 56.09 (C-1‴′, ketone and enol), 56.29 (C-1‴, ketone and enol), 92.32 (C-2, enol), 111.64 (C-2′, enol), 112.13 (C-2′, ketone), 112.39 (C-3′, enol), 113.04 (C-6′, ketone and enol), 116.43 (C-3′,

ketone), 127.31 (C-1′, enol), 130.94 (C-1′, ketone), 148.11 (C-5′, enol), 148.17 (C-5′, ketone), 150.51 (C-4′, enol), 152.12 (C-4′, ketone), 167.63 (C-1, ketone), 171.32 (C-3, enol), 172.93 (C-1, enol), 193.37 (C-3, ketone); MS (EI, 70 eV) *m/z* (%) 316 (14) $[M]^+$, 284 (7), 244 (12), 138 (29), 222 (9), 180 (12), 157 (6), 108 (8), 93 (8); HRMS (EI, M^+) calculated for $C_{12}H_{13}BrO_5$ 315.9946 found 315.9973.

*4.2.13. Methyl 3-(6′-bromobenzo[d][1′,3′]dioxol-5′-yl)-3-oxo-propanoate (**1m**).* According to general procedure I, method B, 6-bromopiperonal (2.3 g, 10 mmol), Zn powder (1 g, 15 mmol) and methyl bromoacetate (2.3 g, 15 mmol) were reacted in toluene at 100 °C for 2 h. The crude methyl 3-(6′-bromobenzo[*d*][1′,3′]dioxol-5′-yl)-3-hydroxypropanoate and PCC (2 equiv) were reacted in dichloromethane at room temperature for 8 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) gave methyl 3-(6′-bromobenzo[*d*][1′,3′]dioxol-5′-yl)-3-oxo-propanoate (**1m**) as a yellow solid in 37% yield (over 2 steps) (1.2 g, 4 mmol): mp 62–63 °C; R_f 0.23 (petroleum ether:EtOAc=9:1); IR (ATR) ν 3056 (w; OH), 1724 (CO ketone), 1689, 1612 (OCC enol), 1500, 1480, 1439, 1385, 1316, 1273, 1236, 1192, 1111, 1024, 998, 924, 885 cm^{-1}; UV (MeCN) λ_{max} (log ε) 232 (4.15), 281 (3.58) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 3.74 (s, 3H, 1″-H, ketone), 3.80 (s, 3H, 1″-H, enol), 4.02 (s, 2H, 2-H, ketone), 5.46 (s, 1H, 2-H, enol), 6.02 (s, 2H, 2′-H, enol), 6.05 (s, 2H, 2′-H, ketone), 6.98 (s, 1H, 4′-H, enol), 7.05 (s, 1H, 7′-H, enol), 7.06 (s, 1H, 7′-H, ketone), 7.08 (s, 1H, 4′-H, ketone), 12.34 (s, 1H, OH, enol); ^{13}C NMR (75 MHz, $CDCl_3$) δ 48.37 (C-2, ketone), 51.48 (C-1″, enol), 52.38 (C-1″, ketone), 92.66 (C-2, enol), 102.24 (C-2′, enol), 102.57 (C-2′, ketone), 109.72 (C-4′, ketone and enol), 112.47 (C-6′, enol), 113.67 (C-6′, ketone), 113.91 (C-7′, ketone and enol), 128.79 (C-5′, enol), 132.71 (C-5′, ketone), 147.29 (C-3a′, enol), 147.48 (C-3a′, ketone), 149.57 (C-7a′, enol), 150.88 (C-7a′, ketone), 167.41 (C-1, ketone), 171.46 (C-3, enol), 172.85 (C-1, enol), 193.57 (C-3, ketone); MS (EI, 70 eV) *m/z* (%) 300 (9) $[M]^+$, 227 (100), 221 (95), 199 (15), 111 (11), 62 (7); HRMS (EI, M^+) calculated for $C_{11}H_9BrO_5$ 299.9633 found 299.9643.

*4.2.14. Methyl 3-(3′-bromothien-2-yl)-3-oxopropanoate (**1n**).* According to general procedure I, method A, 2-acetyl-3-bromothiophene (2.0 g, 10 mmol), dimethylcarbonate (4.7 g, 53 mmol) and NaH (60% in mineral oil, 0.8 g, 20 mmol) were reacted in THF at 70 °C for 8 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) gave methyl 3-(3′-bromothien-2-yl)-3-oxopropanoate (**1n**) as a yellow oil in 69% yield (1.8 g, 7 mmol); R_f 0.36 (petroleum ether:EtOAc=9:1); IR (ATR) ν 1737 (CO ester), 1653 (CO ketone), 1614 (OCC enol), 1490, 1436, 1400, 1325, 1268, 1236, 1198, 1144, 1017, 1015, 873, 730 cm^{-1}; UV (MeCN) λ_{max} (log ε) 278 (4.10) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 3.77 (s, 3H, 1″-H, ketone), 3.81 (s, 3H, 1″-H, enol), 4.12 (s, 2H, 2-H, ketone), 6.20 (s, 1H, 2-H, enol), 7.07 (d-like, ^3J(5′-H, enol, 4′-H, enol)=5.3 Hz, 1H, 4′-H, enol), 7.16 (d-like, ^3J(5′-H, ketone, 4′-H, ketone)=5.2 Hz, 1H, 4′-H, ketone), 7.43 (d-like, ^3J(4′-H, enol, 5′-H, enol)=5.2 Hz, 1H, 5′-H, enol), 7.59 (d-like, ^3J(4′-H, ketone, 5′-H, ketone)=5.2 Hz, 1H, 5′-H, ketone), 12.56 (s, 1H, OH, enol); ^{13}C NMR (75 MHz, $CDCl_3$) δ 47.59 (C-2, ketone), 51.64 (C-1″, enol), 52.49 (C-1″, ketone), 89.04 (C-2, enol), 111.02 (C-3′, enol), 115.08 (C-3′, ketone), 128.69 (C-4′, enol), 132.93 (C-5′, enol), 133.51 (C-4′, ketone), 133.70 (C-5′, ketone), 138.09 (C-2′, enol), 138.14 (C-2′, ketone), 164.26 (C-3, enol), 167.29 (C-1, ketone), 173.36 (C-1, enol) 184.75 (C-3, ketone); MS (EI, 70 eV) *m/z* (%) 264 (4) $[M]^+$, 191 (72), 183 (100), 163 (2), 117 (2), 83 (10), 69 (5); HRMS (ESI, $[M+Na]^+$) calculated for $C_8H_7BrO_3S$ M+Na 286.9171 found 286.9172.

4.3. Synthesis and characterization of 2a–n

*4.3.1. General procedure II for the CuI-catalyzed synthesis of **2a–n**.* An oven-dried 10 mL vial equipped with a magnetic stir bar was charged with CuI (0.05 mmol, 10 mg) and K_2CO_3 (1 mmol, 138 mg). The sealed tube was evacuated and backfilled with argon (two times). Then, the methyl 3-(2′-bromophenyl)-3-oxopropanoate **1** (1 mmol), propionic acid (22 mg, 0.3 mmol) and freshly distilled isopropanol (2 mL) were added and the reaction mixture was stirred at 100 °C for 24 h. After cooling to room temperature, the reaction mixture was diluted with water (15 mL) and extracted with EtOAc (3×20 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and the solvents were evaporated in vacuo. The crude product was purified by flash column chromatography on silica gel to afford the 1-naphthol **2** in analytically pure form.

*4.3.2. Dimethyl 2-(2″-bromophenyl)-4-hydroxynaphthalene-1,3-dicarboxylate (**2a**).* According to general procedure II, methyl 3-(2′-bromophenyl)-3-oxopropanoate (**1a**) (257 mg, 1.0 mmol), CuI (10 mg, 5 mol%), K_2CO_3 (138 mg, 1.0 mmol), and propionic acid (22 mg, 0.3 mmol) were reacted in isopropanol (2 mL) at 100 °C for 24 h. Column chromatography on silica gel (petroleum ether: EtOAc=9:1) afforded dimethyl 2-(2″-bromophenyl)-4-hydroxy-naphthalene-1,3-dicarboxylate (**2a**) as a yellow solid in 79% yield (150 mg, 0.36 mmol): mp 108–109 °C; R_f 0.49 (petroleum ether: EtOAc=9:1); IR (ATR) ν_{max} 2948 (OH), 1722 (s; CO ester), 1648, 1621, 1575, 1444, 1403, 1342, 1239, 1212, 1162, 1101, 981, 771, 754, 731 cm^{-1}; UV (MeCN) λ_{max} (log ε) 224 (4.64), 258 (4.62), 344 (3.95) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 3.49 (s, 3H, 2′-H), 3.52 (s, 3H, 2‴-H), 7.20 (ddd, ^3J(5″-H, 4″-H)=7.2 Hz, ^3J(3″-H, 4″-H)=7.9 Hz, ^4J(6″-H, 4″-H)=2.0 Hz, 1H, 4″-H), 7.24 (d-like, 1H, 6-H″), 7.33 (ddd, ^3J(4″-H, 5″-H)=7.1 Hz, ^3J(6″-H, 5″-H)=7.5 Hz, ^4J(3″-H, 5″-H)=1.2 Hz, 1H, 5″-H), 7.600 (ddd, ^3J(4″-H, 3″-H)=7.8 Hz, ^4J(5″-H, 3″-H)=1.2 Hz, ^5J(6″-H, 3″-H)=0.4 Hz, 1H, 3″-H), 7.602 (ddd, ^3J(5-H, 6-H)=8.5 Hz, ^3J(7-H, 6-H)=6.8 Hz, ^4J(8-H, 6-H)=1.3 Hz, 1H, 6-H), 7.69 (ddd, ^3J(6-H, 7-H)=6.8 Hz, ^3J(8-H, 7-H)=6.8 Hz, ^4J(5-H, 7-H)=1.4 Hz, 1H, 7-H), 7.81 (ddd, ^3J(7-H, 8-H)=8.3 Hz, ^4J(6-H, 8-H)=1.3 Hz, ^5J(5-H, 8-H)=0.7 Hz, 1H, 8-H), 8.52 (ddd, ^3J(6-H, 5-H)=8.4 Hz, ^4J(7-H, 5-H)=1.4 Hz, ^5J(8-H, 5-H)=0.7 Hz, 1H, 5-H), 12.87 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.88 (C-2′), 52.30 (C-2‴), 104.97 (C-3), 123.95 (C-2″), 124.38 (C-5), 124.44 (C-4a), 124.45 (C-1), 125.00 (C-8), 126.50 (C-5″), 126.67 (C-6), 128.62 (C-4″), 130.10 (C-6″), 130.82 (C-7), 131.51 (C-3″), 132.40 (C-8a), 135.97 (C-2), 141.34 (C-1″), 162.59 (C-4), 168.62 (C-1′), 171.55 (C-1‴); MS (EI, 70 eV) *m/z* (%) 416 (20) $[M]^+$, 384 (23), 335 (22), 303 (100), 272 (17), 187 (10), 57 (3); HRMS (EI, M^+) calculated for $C_{20}H_{15}BrO_5$ 414.0103 found 414.0094.

*4.3.3. Dimethyl 2-(2″-iodophenyl)-4-hydroxynaphthalene-1,3-dicarboxylate (**2b**).* According to general procedure II, methyl 3-(2′-iodophenyl)-3-oxopropanoate (**1b**) (304 mg, 1.0 mmol), CuI (10 mg, 5 mol%), K_2CO_3 (138 mg, 1.0 mmol), and propionic acid (22 mg, 0.3 mmol) were reacted in isopropanol (2 mL) at 100 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) afforded dimethyl 2-(2″-iodophenyl)-4-hydroxynaphthalene-1,3-dicarboxylate (**2b**) as a yellow solid in 60% yield (140 mg, 0.31 mmol): mp 146–147 °C; R_f 0.62 (petroleum ether:EtOAc=9:1); IR (ATR) ν_{max} 2947 (OH), 1734 (s; CO ester), 1655, 1620, 1577, 1446, 1401, 1344, 1241, 1213, 1162, 1099, 989, 756 cm^{-1}; UV (MeCN) λ_{max} (log ε) 226 (4.59), 259 (4.58), 343 (3.82) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 3.49 (s, 3H, 2′-H), 3.51 (s, 3H, 2‴-H), 7.02 (ddd, ^3J(5″-H, 4″-H)=7.7 Hz, ^3J(3″-H, 4″-H)=7.8 Hz, ^4J(6″-H, 4″-H)=1.7 Hz, 1H, 4″-H), 7.24 (dd, ^3J(5″-H, 6″-H)=7.5 Hz, ^4J(4″-H, 6″-H)=1.5 Hz, 1H, 6-H″), 7.34 (ddd, ^3J(4″-H, 5″-H)=7.4 Hz, ^3J(6″-H, 5″-H)=7.5 Hz, ^4J(3″-H, 5″-H)=1.0 Hz, 1H, 5″-H), 7.60 (ddd, ^3J(5-H, 6-H)=7.0 Hz, ^3J(7-H, 6-H)=7.1 Hz, ^4J(8-H, 6-H)=1.0 Hz, 1H, 6-H), 7.69 (ddd, ^3J(6-H, 7-H)=6.8 Hz, ^3J(8-H, 7-H)=7.1 Hz, ^4J(5-H, 7-H)=1.2 Hz, 1H, 7-H), 7.80 (d, ^3J(7-H, 8-H)=8.4 Hz, 1H, 8-H), 7.87 (dd, ^3J(4″-H, 3″-H)=7.9 Hz, ^4J(5″-H, 3″-H)=1.2 Hz, 1H, 3″-H), 8.53 (d, ^3J(6-H, 5-H)=8.4 Hz, 1H, 5-H), 12.94 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.80 (C-2′), 52.31 (C-2‴), 99.78 (C-2″), 104.81 (C-3), 124.31 (C-4a), 124.35 (C-5), 124.42 (C-1), 125.72 (C-8), 126.66 (C-6), 127.22 (C-5″), 128.42 (C-4″), 129.25 (C-6″), 130.82 (C-7), 132.37 (C-8a), 137.85 (C-3″), 138.69 (C-2), 145.26 (C-1″), 162.63 (C-

4), 168.50 (C-1′), 171.40 (C-1‴); MS (EI, 70 eV) *m/z* (%) 462 (22) $[M]^+$, 430 (5), 335 (46), 303 (100), 275 (30), 247 (25), 232 (17), 204 (13), 187 (22), 176 (17), 151 (10), 94 (6); HRMS (EI, M^+) calculated for $C_{20}H_{15}IO_5$ 461.9964 found 461.9971.

*4.3.4. Dimethyl 2-(2″-chlorophenyl)-4-hydroxynaphthalene-1,3-dicarboxylate (**2c**).* According to general procedure II, methyl 3-(2′-chlorophenyl)-3-oxopropanoate (**1c**) (213 mg, 1.0 mmol), CuI (10 mg, 5 mol%), K_2CO_3 (138 mg, 1.0 mmol), and propionic acid (22 mg, 0.3 mmol) were reacted in isopropanol (2 mL) at 100 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) afforded dimethyl 2-(2″-chlorophenyl)-4-hydroxynaphthalene-1,3-dicarboxylate (**2c**) as a yellow oil in 48% yield (95 mg, 0.26 mmol); R_f 0.51 (petroleum ether:EtOAc=9:1); IR (ATR) ν 2950 (OH), 1724 (s; CO ester), 1651, 1620, 1575, 1443, 1401, 1340, 1215, 1160, 1101, 813, 753 cm^{-1}; UV (MeCN) λ_{max} (log ε) 214 (4.54), 258 (4.55), 343 (3.75) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 3.48 (s, 3H, 2′-H), 3.51 (s, 3H, 2‴-H), 7.25 (m, 1H, 3″-H), 7.27 (m, 1H, 6″-H), 7.28 (m, 1H, 4″-H), 7.40 (m, 1H, 5″-H), 7.59 (ddd, $^3J_{7\text{-H, 6-H}}$ 7.0 Hz, ^3J(5-H, 6-H)=7.0 Hz, ^4J(8-H, 6-H)=1.1 Hz, 1H, 6-H), 7.68 (ddd, ^3J(8-H, 7-H)=6.9 Hz, ^3J(6-H, 7-H)=7.0 Hz, ^4J(5-H, 7-H)=1.3 Hz, 1H, 7-H), 7.80 (d, ^3J(7-H, 8-H)=8.4 Hz, 1H, 8-H), 8.51 (d, ^3J(6-H, 5-H)=8.4 Hz, 1H, 5-H), 12.87 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.94 (C-2′), 52.32 (C-2‴), 104.98 (C-3), 124.42 (C-5), 124.47 (C-4a), 124.65 (C-1), 124.99 (C-8), 125.66 (C-3″), 126.70 (C-6), 128.37 (C-5″), 128.61 (C-4″), 130.11 (C-6″), 130.86 (C-7), 132.44 (C-8a), 133.75 (C-2″), 134.49 (C-2), 139.51 (C-1″), 162.64 (C-4), 168.72 (C-1′), 171.62 (C-1‴); MS (EI, 70 eV) *m/z* (%) 370 (10) $[M]^+$, 340 (6), 335 (11), 303 (84), 288 (15), 272 (9), 260 (6), 223 (8), 187 (13), 113 (5), 97 (7), 85 (15), 71 (21), 57 (29); HRMS (EI, M^+) calculated for $C_{20}H_{15}ClO_5$ 370.0608 found 370.0585.

*4.3.5. Diethyl 2-(2″-bromophenyl)-4-hydroxynaphthalene-1,3-dicarboxylate (**2d**).* According to general procedure II, ethyl 3-(2′-bromophenyl)-3-oxopropanoate (**1d**) (271 mg, 1.0 mmol), CuI (10 mg, 5 mol%), K_2CO_3 (138 mg, 1.0 mmol), and propionic acid (22 mg, 0.3 mmol) were reacted in isopropanol (2 mL) at 100 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) afforded diethyl 2-(2″-bromophenyl)-4-hydroxynaphthalene-1,3-dicarboxylate (**2d**) as a yellow oil in 71% yield (158 mg, 0.36 mmol); R_f 0.53 (petroleum ether:EtOAc=9:1); IR (ATR) ν 2981 (OH), 1722 (s; CO ester), 1649, 1620, 1576, 1443, 1402, 1238, 1216, 1100, 1017, 815, 751 cm^{-1}; UV (MeCN) λ_{max} (log ε) 258 (4.46), 343 (3.77) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 0.78 (t, 3H, 3′-H), 0.95 (t, 3H, 3‴-H), 3.98 (m, 2H, 2′-H), 4.16 (m, 2H, 2‴-H), 7.21 (ddd, ^3J(3″-H, 4″-H)=8.0 Hz, ^3J(5″-H, 4″-H)=7.7 Hz, ^4J(6″-H, 4″-H)=2.0 Hz, 1H, 4″-H), 7.27 (dd, ^3J(5″-H, 6″-H)=7.7 Hz, ^4J(4″-H, 6″-H)=2.3 Hz, 1H, 6″-H), 7.30 (ddd, ^3J(4″-H, 5″-H)=7.7 Hz, ^3J(6″-H, 5″-H)=7.3 Hz, ^4J(3″-H, 5″-H)=1.5 Hz, 1H, 5″-H), 7.58 (dd, ^3J(4″-H, 3″-H)=7.8 Hz, ^4J(5″-H, 3″-H)=1.0 Hz, 1H, 3″-H), 7.60 (ddd, ^3J(5-H, 6-H)=7.3 Hz, ^3J(7-H, 6-H)=7.0 Hz, ^4J(8-H, 6-H)=1.2 Hz, 1H, 7-H), 7.68 (ddd, ^3J(6-H, 7-H)=7.0 Hz, ^3J(8-H, 7-H)=6.9 Hz, ^4J(5-H, 7-H)=1.2 Hz, 1H, 7-H), 7.83 (d, ^3J(7-H, 8-H)=8.3 Hz, 1H, 8-H), 8.52 (d, ^3J(6-H, 5-H)=8.3 Hz, 1H, 5-H), 13.03 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.91 (C-3′), 13.61 (C-3‴), 61.12 (C-2′), 61.39 (C-2‴), 104.97 (C-3), 113.27 (C-2″), 120.04 (C-1), 124.33 (C-5), 124.51 (C-4a), 124.98 (C-8), 126.48 (C-5″), 126.59 (C-6), 128.61 (C-4″), 130.50 (C-6″), 130.73 (C-7), 131.53 (C-3″), 133.12 (C-8a), 135.69 (C-2), 141.63 (C-1″), 162.66 (C-4), 168.15 (C-1′), 171.22 (C-1‴); MS (EI, 70 eV) *m/z* (%) 442 (3) $[M]^+$, 382 (9), 349 (18), 317 (31), 303 (70), 288 (22), 272 (18), 233 (14), 187 (27), 176 (21), 151 (5), 88 (5), 69 (5); HRMS (EI, M^+) calculated for $C_{22}H_{19}BrO_5$ 442.0416 found 442.0415.

*4.3.6. Diallyl 2-(2″-bromophenyl)-4-hydroxynaphthalene-1,3-dicarboxylate (**2e**).* According to general procedure II, allyl 3-(2′-bromophenyl)-3-oxopropanoate (**1e**) (283 mg, 1.0 mmol), CuI (10 mg, 5 mol%), K_2CO_3 (138 mg, 1.0 mmol), and propionic acid (22 mg, 0.3 mmol) were reacted in isopropanol (2 mL) at 100 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) afforded diallyl 2-(2″-bromophenyl)-4-hydroxynaphthalene-1,3-dicarboxylate (**2e**) as a yellow oil in 81% yield (189 mg, 0.41 mmol); R_f 0.34 (petroleum ether:EtOAc=9:1); IR (ATR) ν 2950 (OH), 1724 (s; CO ester), 1649, 1620, 1577, 1444, 1402, 1340, 1238, 1163, 1100, 1016, 930, 751 cm^{-1}; UV (MeCN) λ_{max} (log ε) 259 (4.42), 343 (3.60) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 4.34 (m, 1H, 2′-H_a), 4.46 (m, 1H, 2‴-H_a), 4.63 (dt-like, ^3J(3′-H, 2′-H_b)=4.9 Hz, 1H, 2′-H_b), 4.81 (dt-like, ^3J(3‴-H, 2‴-H_b)=5.5 Hz, 1H, 2‴-H_b), 5.27 (dd-like, ^3J(3‴-H, 4‴-$H_{(Z)}$)=7.0 Hz, 1H, 4‴-$H_{(Z)}$), 5.29 (dd-like, ^3J(3′-H, 4′-$H_{(Z)}$)=7.1 Hz, 1H, 4′-$H_{(Z)}$), 5.42 (dd-like, ^3J(3‴-H, 4‴-$H_{(E)}$)=17.3 Hz, 1H, 4‴-$H_{(E)}$), 5.50 (dd-like, ^3J(3′-H, 4′-$H_{(E)}$)=17.3 Hz, 1H, 4′-$H_{(E)}$), 6.04 (m, 1H, 3‴-H), 6.07 (m, 1H, 3′-H), 7.19 (ddd, ^3J(3″-H, 4″-H)=7.3 Hz, ^3J(5″-H, 4″-H)=7.4 Hz, ^4J(6″-H, 4″-H)=2.2 Hz, 1H, 4″-H), 7.26 (ov, 1H, 6″-H), 7.30 (ov, 1H, 5″-H), 7.55 (dd-like, ^3J(4″-H, 3″-H)=8.2 Hz, 1H, 3″-H), 7.60 (ddd, ^3J(5-H, 6-H)=7.1 Hz, ^3J(7-H, 6-H)=7.0 Hz, ^4J(8-H, 6-H)=0.8 Hz, 1H, 6-H), 7.69 (ddd, ^3J(6-H, 7-H)=6.9 Hz, ^3J(8-H, 7-H)=7.3 Hz, ^4J(5-H, 7-H)=1.3 Hz, 1H, 7-H), 7.83 (dd, ^3J(7-H, 8-H)=7.7 Hz, ^4J(6-H, 8-H)=1.6 Hz, 1H, 8-H), 8.52 (d, ^3J(6-H, 5-H)=8.4 Hz, 1H, 5-H), 12.90 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 65.43 (C-2‴), 69.48 (C-2′), 105.08 (C-3), 113.57 (C-2″), 117.45 (C-4′), 118.06 (C-4‴), 120.38 (C-1), 124.37 (C-5), 124.46 (C-4a), 124.97 (C-8), 126.51 (C-5″), 126.66 (C-6), 128.65 (C-4″), 130.36 (C-6″), 130.84 (C-7), 131.74 (C-3″), 132.32 (C-3‴), 132.72 (C-3′), 133.36 (C-8a), 135.83 (C-2), 141.49 (C-1″), 162.74 (C-4), 167.84 (C-1′), 170.86 (C-1‴); MS (EI, 70 eV) *m/z* (%) 467 (1) $[M]^+$, 442 (4), 382 (7), 335 (7), 329 (15), 303 (46), 288 (11), 272 (8) 204 (4), 187 (8), 111 (4), 88 (3); HRMS (EI, M^+) calculated for $C_{24}H_{19}BrO_5$ 466.0416 found 466.0431.

*4.3.7. Dimethyl 2-(2″,5″-dibromophenyl)-6-bromo-4-hydroxynaphthalene-1,3-dicarboxylate (**2f**).* According to general procedure II, methyl 3-(2′,5′-dibromophenyl)-3-oxopropanoate (**1f**) (335 mg, 1.0 mmol), CuI (10 mg, 5 mol%), K_2CO_3 (138 mg, 1.0 mmol), and propionic acid (22 mg, 0.3 mmol) were reacted in isopropanol (2 mL) at 100 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) afforded dimethyl 2-(2″,5″-dibromophenyl)-6-bromo-4-hydroxynaphthalene-1,3-dicarboxylate (**2f**) as a white solid in 67% yield (190 mg, 0.33 mmol): mp 182–183 °C; R_f 0.52 (petroleum ether:EtOAc=9:1); IR (ATR) ν 2948 (OH), 1715 (s; CO ester), 1656, 1618, 1570, 1485, 1331, 1220, 1166, 1114, 993, 804, 778 cm^{-1}; UV (MeCN) λ_{max} (log ε) 233 (4.55), 267 (4.47), 361 (3.59) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 3.56 (s, 3H, 2′-H), 3.58 (s, 3H, 2‴-H), 7.35 (dd, ^3J(3″-H, 4″-H)=8.5 Hz, ^4J(6″-H, 4″-H)=2.4 Hz, 1H, 4″-H), 7.40 (d, ^4J(4″-H, 6″-H)=2.4 Hz, 1H, 6″-H), 7.46 (d, ^3J(4″-H, 3″H)=8.4 Hz, 1H, 3″-H), 7.69 (d, ^3J(7-H, 8-H)=8.9 Hz, 1H, 8-H), 7.76 (dd, ^3J(8-H, 7-H)=8.8 Hz, ^4J(5-H, 7-H)=2.1 Hz, 1H, 7-H), 8.67 (d, ^4J(7-H, 5-H)=2.2 Hz, 1H, 5-H), 12.86 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.15 (C-2′), 52.66 (C-2‴), 105.51 (C-3), 120.17 (C-5″), 121.34 (C-6), 122.71 (C-2″), 124.31 (C-1), 125.76 (C-4a), 126.87 (C-8), 126.88 (C-5), 130.86 (C-8a), 131.75 (C-4″), 132.64 (C-6″), 132.88 (C-3″), 134.20 (C-7), 135.02 (C-2), 142.97 (C-1″), 161.65 (C-4), 167.77 (C-1′), 170.98 (C-1‴); MS (EI, 70 eV) *m/z* (%) 572 (20) $[M]^+$, 540 (25), 493 (50), 461 (100), 446 (12), 402 (6), 365 (6), 295 (4), 267 (9), 230 (12), 187 (10), 84 (34); HRMS (ESI, $[M+Na]^+$) calculated for $C_{20}H_{13}Br_3O_5$ $[M+Na]$ 592.8205 found 592.8176.

*4.3.8. Dimethyl 2-(2″-bromo-5″-chlorophenyl)-6-chloro-4-hydroxynaphthalene-1,3-dicarboxylate (**2g**).* According to general procedure II, methyl 3-(2′-bromo-5′-chlorophenyl)-3-oxopropanoate (**1g**) (292 mg, 1.0 mmol), CuI (10 mg, 5 mol%), K_2CO_3 (138 mg, 1.0 mmol), and propionic acid (22 mg, 0.3 mmol) were reacted in isopropanol (2 mL) at 100 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) afforded dimethyl 2-(2″-bromo-5″-chlorophenyl)-6-chloro-4-hydroxynaphthalene-1,3-dicarboxylate (**2g**) as a white solid in 65% yield

(155 mg, 0.32 mmol): mp 198–199 °C; R_f 0.51 (petroleum ether: EtOAc=9:1); IR (ATR) ν 2950 (OH), 1715 (s; CO ester), 1656, 1621, 1574, 1463, 1334, 1220, 1166, 1116, 996, 805, 741 cm^{-1}; UV (MeCN) λ_{max} (log ε) 230 (4.62), 265 (4.50), 361 (3.63) nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.56 (s, 3H, 2′-H), 3.57 (s, 3H, 2‴-H), 7.21 (dd, ^3J(3″-H, 4″-H)=8.5 Hz, ^4J(6″-H, 4″-H)=2.5 Hz, 1H, 4″-H), 7.25 (d, ^4J(4″-H, 6″-H)=2.5 Hz, 1H, 6″-H), 7.53 (d, ^3J(4″-H, 3″H)=8.5 Hz, 1H, 3″-H), 7.63 (dd, ^3J(8-H, 7-H)=8.9 Hz, ^4J(5-H, 7-H)=2.2 Hz, 1H, 7-H), 7.77 (d, ^3J(7-H, 8-H)=8.9 Hz, 1H, 8-H), 8.49 (d, ^4J(7-H, 5-H)=2.2 Hz, 1H, 5-H), 12.86 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.13 (C-2′), 52.65 (C-2‴), 105.52 (C-3), 121.99 (C-2″), 123.59 (C-5), 124.21 (C-1), 125.46 (C-4a), 126.87 (C-8), 128.79 (C-4″), 129.87 (C-6″), 130.62 (C-8a), 131.65 (C-7), 132.57 (C-5″), 132.58 (C-3″), 133.25 (C-6), 134.98 (C-2), 142.68 (c-1″), 161.74 (C-4), 167.83 (C-1′), 171.02 (C-1‴); MS (EI, 70 eV) *m/z* (%) 482 (20) $[M]^+$, 450 (17), 402 (46), 371 (100), 353 (25), 252 (51), 166 (46), 111 (25), 69 (18); HRMS (EI, M^+) calculated for $C_{20}H_{15}Br\ OCl_2O_5$ 481.9323 found 481.9351.

*4.3.9. Diethyl 2-(2″-bromo-5″-fluorophenyl)-6-fluoro-4-hydroxy-naphthalene-1,3-dicarboxylate (**2h**).* According to general procedure II, methyl 3-(2′-bromo-5′-fluorophenyl)-3-oxopropanoate (**1h**) (289 mg, 1.0 mmol), CuI (10 mg, 5 mol %), K_2CO_3 (138 mg, 1.0 mmol), and propionic acid (22 mg, 0.3 mmol) were reacted in isopropanol (2 mL) at 100 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) afforded diethyl 2-(2″-bromo-5″-fluorophenyl)-6-fluoro-4-hydroxy-naphthalene-1,3-dicarboxylate (**2h**) as a white solid in 66% yield (159 mg, 0.33 mmol): mp 97–98 °C; R_f 0.69 (petroleum ether:EtOAc=9:1); IR (ATR) ν 2982 (OH), 1719 (s; CO ester), 1649, 1592, 1404, 1342, 1326, 1183, 1102, 979, 772 cm^{-1}; UV (MeCN) λ_{max} (log ε) 224 (4.55), 261 (4.49), 346 (3.63) nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.86 (t, 3H, 3′-H), 1.01 (t, 3H, 3‴-H), 4.05 (m, 2H, 2′-H), 4.13 (m, 2H, 2‴-H), 6.98 (ddd, ^3J(3″-H, 4″-H)=8.3 Hz, ^3J(5″-F, 4″-H)=8.4 Hz, ^4J(6″-H, 4″-H)=2.9 Hz, 1H, 4″-H), 7.03 (dd, ^3J(5″-F, 6″-H)=8.6 Hz, ^4J(4″-H, 6″-H)=2.8 Hz, 1H, 6″-H), 7.45 (ddd, ^3J(8-H, 7-H)=8.6 Hz, ^3J(6-F, 7-H)=8.8 Hz, ^4J(5-H, 7-H)=2.7 Hz, 1H, 7-H), 7.53 (dd, ^3J(4″-H, 3″H)=8.7 Hz, ^4J(5″-F, 3″-H)=5.3 Hz, 1H, 3″-H), 7.86 (dd, ^3J(7-H, 8-H)=9.2 Hz, ^4J(6-F, 8-H)=5.3 Hz, 1H, 8-H), 8.12 (dd, ^3J(6-F, 5-H)=9.6 Hz, ^4J(7-H, 5-H)=2.5 Hz, 1H, 5-H), 12.97 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.99 (C-3′), 13.64 (C-3‴), 61.40 (C-2′), 61.73 (C-2‴), 105.37 (C-3), 108.58 (d, ^2J(F, C-5)=23 Hz, C-5), 115.68 (d, ^2J(F, C-4″)=22 Hz, C-4″), 117.89 (d, ^2J(F, C-6″)=23 Hz, C-6″), 119.0 (d, ^4J(F, C-2″)=3 Hz, C-2″), 120.74 (d, ^2J(F, C-7)=25 Hz, C-7), 124.32 (C-1), 125.96 (d, ^3J(F, C-4a)=9 Hz, C-4a), 127.86 (d, ^3J(F, C-8)=9 Hz, C-8), 129.18 (d, ^4J(F, C-8a)=1 Hz, C-8a), 132.68 (d, ^3J(F, C-3″)=8 Hz, C-3″), 133.84 (C-2), 143.17 (d, ^3J(F, C-1″)=8 Hz, C-1″), 161.03 (d, ^1J(F, C-6)=50 Hz, C-6), 161.16 (d, ^1J(F, C-5″)=250 Hz, C-5″), 161.93 (C-4), 167.58 (C-1′), 170.77 (C-1‴); MS (EI, 70 eV) *m/z* (%) 478 (14) $[M]^+$, 431 (15), 398 (56), 353 (96), 325 (100), 235 (43), 203 (41), 167 (43), 149 (82), 111 (56), 77 (59), 57 (50); HRMS (EI, M^+) calculated for $C_{22}H_{17}BrF_2O_5$ 478.0227 found 478.0229.

*4.3.10. Dimethyl 2-(2″-bromo-4″-fluorophenyl)-7-fluoro-4-hydroxynaphthalene-1,3-dicarboxylate (**2i**).* According to general procedure II, methyl 3-(2′-bromo-4′-fluorophenyl)-3-oxopropanoate (**1i**) (275 mg, 1.0 mmol), CuI (10 mg, 5 mol %), K_2CO_3 (138 mg, 1.0 mmol), and propionic acid (22 mg, 0.3 mmol) were reacted in isopropanol (2 mL) at 100 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) afforded dimethyl 2-(2″-bromo-4″-fluorophenyl)-7-fluoro-4-hydroxynaphthalene-1,3-dicarboxylate (**2i**) as a white solid in 23% yield (53 mg, 0.12 mmol): mp 94–95 °C; R_f 0.56 (petroleum ether: EtOAc=9:1); IR (ATR) ν 2947 (OH), 1713 (s; CO ester), 1653, 1628, 1580, 1438, 1402, 1329, 1229, 1178, 1142, 1100, 876, 795, 743 cm^{-1}; UV (MeCN) λ_{max} (log ε) 214 (4.55), 259 (4.56) nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.54 (s, 3H, 2′-H), 3.56 (s, 3H, 2‴-H), 7.06 (ddd, ^3J(6″-H, 5″-H)=8.1 Hz, ^3J(4″-F, 5″-H)=8.0 Hz, ^4J(3″-H, 5″-H)=2.4 Hz, 1H, 5″-H), 7.20 (m, 1H, 6″-H), 7.35 (ddd, ^3J(5-H, 6-H)=8.2 Hz, ^3J(7-F, 6-H)=8.1 Hz, ^4J(8-H, 6-H)=2.4 Hz, 1H, 6-H), 7.37 (dd, ^3J(4″-F, 3″-H)=8.3 Hz, ^4J(5″-H, 3″-H)=2.5 Hz, 1H, 3″-H), 7.45 (dd, ^3J(7-F, 8-H)=10.3 Hz, ^4J(6-H, 8-H)=2.2 Hz, 1H, 8-H), 8.53 (dd, ^3J(6-H, 5-H)=9.1 Hz, ^4J(7-F, 5-H)=5.7 Hz, 1H, 5-H), 13.02 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.1 (C-2′), 52.52 (C-2‴), 104.61 (C-3), 109.45 (d, ^2J(F, C-8)=23 Hz, C-8), 113.67 (d, ^2J(F, C-5″)=21 Hz C-5″), 116.79 (d, ^2J(F, C-6)=25 Hz, C-6), 119.01 (d, ^2J(F, C-3″)=25 Hz, C-3″), 119.62 (C-2″), 121.41 (d, ^4J(F, C-4a)=2 Hz, C-4a), 124.05 (d, ^4J(F, C-1)=4 Hz, C-1), 127.59 (d, ^3J(F, C-5)=10 Hz, C-5), 130.76 (d, ^3J(F, C-6″)=8 Hz, C-6″), 134.12 (d, ^3J(F, C-8a)=10 Hz, C-8a), 137.26 (d, ^4J(F, C-1″)=4 Hz, C-1″), 161.52 (d, ^1J(F, C-4″)=250 Hz, C-4″), 162.71 (C-4), 164.04 (d, ^1J(F, C-7)=250 Hz, C-7), 168.08 (C-1′), 171.32 (C-1‴); MS (EI, 70 eV) *m/z* (%) 449 (8) $[M]^+$, 371 (33), 339 (100), 324 (17), 308 (12), 224 (8); HRMS (EI, M^+) calculated for $C_{20}H_{13}Br\ F_2O_5$ 449.9914 found 449.9903.

*4.3.11. Dimethyl 2-(2″-bromo-5″-trifluoromethylphenyl)-6-trifluoromethyl-4-hydroxynaphthalene-1,3-dicarboxylate (**2j**).* According to general procedure II, methyl 3-(2′-bromo-5′-trifluoromethylphenyl)-3-oxopropanoate (**1j**) (325 mg, 1.0 mmol), CuI (10 mg, 5 mol %), K_2CO_3 (138 mg, 1.0 mmol), and propionic acid (22 mg, 0.3 mmol) were reacted in isopropanol (2 mL) at 100 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) afforded dimethyl 2-(2″-bromo-5″-trifluoromethyl-phenyl)-6-trifluoromethyl-4-hydroxynaphthalene-1,3-dicarboxylate (**2j**) as a white solid in 69% yield (190 mg, 0.35 mmol): mp 169–170 °C; R_f 0.51 (petroleum ether:EtOAc=9:1); IR (ATR) ν 2947 (OH), 1719 (s; CO ester), 1654, 1422, 1390, 1317, 1240, 1114, 1080, 1025, 838, 826 cm^{-1}; UV (MeCN) λ_{max} (log ε) 226 (4.63), 259 (4.50) 339 (3.79) nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.54 (s, 3H, 2′-H), 3.55 (s, 3H, 2‴-H), 7.51 (dd, ^3J(3″-H, 4″-H)=8.2 Hz, ^4J(6″-H, 4″-H)=2.1 Hz, 1H, 4″-H), 7.54 (d-like, 1H, 6-H″), 7.76 (d, ^3J(4″-H, 3″-H)=8.2 Hz, 1H, 3″-H), 7.87 (dd, ^3J(8-H, 7-H)=8.9 Hz, ^4J(5-H, 7-H)=1.8 Hz, 1H, 7-H), 7.95 (d, ^3J(7-H, 8-H)=8.7 Hz, 1H, 8-H), 8.84 (s, 1H, 5-H), 13.03 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.14 (C-2′), 52.72 (C-2‴), 105.76 (C-3), 121.63 (d, ^1J(F, C-1‴′)=250 Hz, C-1‴′), 122.43 (q-like, ^3J(F, C-5)=9 Hz, C-5), 123.97 (C-1), 124.44 (C-4a), 125.55 (q-like, ^3J(F, C-4″)=8 Hz, C-4″), 125.93 (d, ^1J(F, C-1‴″)=250 Hz, C-1‴″), 126.38 (C-8), 126.65 (q-like, ^3J(F, C-7)=7 Hz, C-7), 126.73 (q-like, ^3J(F, C-6″)=7 Hz, C-6″), 127.8 (C-2″), 128.94 (q-like, ^2J(F, C-6)=33 Hz, C-6), 129.35 (q-like, ^2J(F, C-5″)=33 Hz, C-5″), 132.26 (C-3″), 133.87 (C-8a), 136.88 (C-2), 141.9 (C-1″), 163.08 (C-4), 167.51 (C-1′), 170.83 (C-1‴); MS (EI, 70 eV) *m/z* (%) 548 (9) $[M-1]^+$, 515 (10), 469 (24), 438 (100), 423 (14), 324 (8); HRMS (EI, M^+) calculated for $C_{22}H_{13}BrF_6O_5$ 549.9851 found 549.9872.

*4.3.12. Dimethyl 2-(2″-bromo-5″-methoxyphenyl)-4-hydroxy-6-methoxy-naphthalene-1,3-dicarboxylate (**2k**).* According to general procedure II, methyl 3-(2′-bromo-5′-methoxyphenyl)-3-oxopropanoate (**1k**) (287 mg, 1.0 mmol), CuI (10 mg, 5 mol %), K_2CO_3 (138 mg, 1.0 mmol), and propionic acid (22 mg, 0.3 mmol) were reacted in isopropanol (2 mL) at 100 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) afforded dimethyl 2-(2″-bromo-5″-methoxyphenyl)-4-hydroxy-6-methoxynaphthalene-1,3-dicarboxylate (**2k**) as a white solid in 63% yield (189 mg, 0.41 mmol): mp 122–123 °C; R_f 0.12 (petroleum ether:EtOAc=9:1); IR (ATR) ν 2944 (OH), 1720 (s; CO ester), 1650, 1623, 1573, 1434, 1408, 1330, 1239, 1180, 1002, 960, 781, 737 cm^{-1}; UV (MeCN) λ_{max} (log ε) 236 (4.56), 270 (4.51), 358 (3.46) nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.52 (s, 3H, 2′-H), 3.56 (s, 3H, 2‴-H), 3.78 (s, 3H, 1‴″-H), 3.98 (s, 3H, 1‴′-H), 6.75 (dd, ^3J(3″-H, 4″-H)=8.7 Hz, ^4J(6″-H, 4″-H)=3 Hz, 1H, 4″-H), 6.82 (d, ^4J(4″-H, 6″-H)=3 Hz, 1H, 6-H″), 7.32 (dd, ^3J(8-H, 7-H)=9.1 Hz, ^4J(5-H, 7-H)=2.6 Hz, 1H, 7-H), 7.45 (d, ^3J(4″-H, 3″-H)=8.8 Hz, 1H, 3″-H), 7.72 (d, ^3J(7-H, 8-H)=9.1 Hz, 1H, 8-H), 7.78 (d, ^4J(7-H, 5-H)=2.8 Hz, 1H, 5-H), 12.78 (s, 1H,

OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.96 (C-2′), 52.37 (C-2‴), 55.56 (C-1‴′ and C-1‴″), 102.57 (C-5), 105.35 (C-3), 114.65 (C-4″), 114.9 (C-2″), 115.67 (C-6″), 123.14 (C-7), 124.23 (C-1), 125.69 (C-4a), 126.68 (C-8), 127.53 (C-8a), 131.99 (C-3″), 133.49 (C-2), 142.24 (C-1″), 158.23 (C-5″), 158.36 (C-6), 161.21 (C-4), 168.76 (C-1′) and 171.68 (C-1‴); MS (EI, 70 eV) *m/z* (%) 474 (8) $[M]^+$, 395 (31), 363 (98), 335 (24), 292 (8), 182 (7); HRMS (EI, M^+) calculated for $C_{22}H_{19}BrO_7$ 474.0314 found 474.0319.

*4.3.13. Dimethyl 2-(2″-bromo-4″,5″-dimethoxyphenyl)-4-hydroxy-6,7-dimethoxy-naphthalene-1,3-dicarboxylate (**2l**).* According to general procedure II, methyl 3-(2′-bromo-4′,5′-dimethoxyphenyl)-3-oxopropanoate (**1l**) (317 mg, 1.0 mmol), CuI (10 mg, 5 mol %), K_2CO_3 (138 mg, 1.0 mmol), and propionic acid (22 mg, 0.3 mmol) were reacted in isopropanol (2 mL) at 100 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) afforded dimethyl 2-(2″-bromo-4″,5″-dimethoxyphenyl)-4-hydroxy-6,7-dimethoxy-naphthalene-1,3-dicarboxylate (**2l**) as a yellow solid in 61% yield (158 mg, 0.30 mmol): mp 176–177 °C; R_f 0.20 (petroleum ether:EtOAc=8:2); IR (ATR) ν 2949 (OH), 1720 (s; CO ester), 1651, 1503, 1438, 1241, 1206, 1168, 1015, 975, 836 cm^{-1}; UV (MeCN) λ_{max} (log ε) 204 (4.62), 242 (3.50), 267 (4.75), 358 (3.50) nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.54 (s, 3H, 2′-H), 3.57 (s, 3H, 2‴-H), 3.82 (s, 3H, 1‴‴′-H), 3.93 (s, 3H, 1‴″-H), 3.98 (s, 3H, 1‴″-H), 4.06 (s, 3H, 1‴′-H), 6.78 (s, 1H, 6″-H), 7.07 (s, 1H, 4-H″), 7.09 (s, 1H, 8-H), 7.76 (s, 1H, 5-H), 12.75 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.03 (C-2′), 52.42 (C-2‴), 55.96 (C-1‴″), 56.09 (C-1‴′), 56.15 (C-1‴″), 56.16 (C-1‴‴′), 103.04 (C-5), 103.94 (C-8), 104.27 (C-3), 113.37 (C-6″), 114.34 (C-3″), 114.45 (C-2″), 119.46 (C-4a), 123.32 (C-1), 128.77 (C-8a), 133.52 (C-1″), 134.70 (C-2), 147.51 (C-4″), 148.32 (C-5″), 149.75 (C-6), 153.12 (C-7), 160.94 (C-4), 169.25 (C-1′), 171.83 (C-1‴); MS (EI, 70 eV) *m/z* (%) 532 (11) $[M-2]^+$, 454 (84), 422 (81), 395 (84), 227 (13), 204 (10); HRMS (EI, M^+) calculated for $C_{24}H_{23}BrO_9$ 534.0525 found 534.0549.

*4.3.14. Dimethyl 6-(6′-bromobenzo[d][1′,3′]dioxol-5′-yl)-8-hydroxy-naphtho[2,3-d][1,3]dioxole-5,7-dicarboxylate (**2m**).* According to general procedure II, methyl 3-(6′-bromobenzo[*d*][1′,3′]dioxol-5′-yl)-3-oxo-propanoate (**1m**) (301 mg, 1.0 mmol), CuI (10 mg, 5 mol %), K_2CO_3 (138 mg, 1.0 mmol), and propionic acid (22 mg, 0.3 mmol) were reacted in isopropanol (2 mL) at 100 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) afforded dimethyl 6-(6′-bromobenzo[*d*][1′,3′]dioxol-5′-yl)-8-hydroxynaphtho[2,3-*d*][1,3]dioxole-5,7-dicarboxylate (**2m**) as a yellow solid in 67% yield (169 mg, 0.34 mmol): mp 151–152 °C; R_f 0.35 (petroleum ether:EtOAc=8:2); IR (ATR) ν 2950 (OH), 1709 (s; CO ester), 1655, 1617, 1477, 1458, 1429, 1210, 1176, 1032, 932, 862, 643 cm^{-1}; UV (MeCN) λ_{max} (log ε) 203 (4.53), 238 (4.32), 268 (4.63) nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.59 (s, 3H, 2‴-H), 3.60 (s, 1H, 2″-H), 6.02 (m, 2H, 2′-H) 6.10 (m 2H, 2-H), 6.73 (s, 1H, 4′-H), 7.05 (s, 1H, 7′-H), 7.07 (s, 1H, 4-H), 7.75 (s, 1H, 9-H), 12.65 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.03 (C-2″), 52.48 (C-2‴), 101.02 (C-9), 101.73 (C-2′), 101.85 (C-2), 101.97 (C-7′), 104.57 (C-7), 110.38 (C-4′), 111.84 (C-4), 114.81 (C-6′), 120.88 (C-8a), 124.06 (C-5), 130.3 (C-4a), 134.17 (C-5′), 134.64 (C-6), 146.43 (C-7a′), 147.29 (C-3a′), 148.11 (C-9a), 151.46 (C-3a), 161.14 (C-8), 168.77 (C-1″), 171.58 (C-1‴); MS (EI, 70 eV) *m/z* (%) 502 (9) $[M]^+$, 462 (9), 423 (100), 391 (95), 363 (78), 332 (11), 303 (36), 275 (13), 247 (10), 188 (14), 174 (9), 149 (7), 111 (5); HRMS (EI, M^+) calculated for $C_{22}H_{15}BrO_9$ 501.9899 found 501.9875.

*4.3.15. Dimethyl 2-hydroxy-4-(3″-bromothien-2″-yl)benzo[b]thiophene-3,5-dicarboxylate (**2n**).* According to general procedure II, methyl 3-(3′-bromothien-2-yl)-3-oxopropanoate (**1n**) (263 mg, 1.0 mmol), CuI (10 mg, 5 mol %), K_2CO_3 (138 mg, 1.0 mmol), and propionic acid (22 mg, 0.3 mmol) were reacted in isopropanol (2 mL) at 100 °C for 24 h. Column chromatography on silica gel (petroleum ether:EtOAc=9:1) afforded dimethyl 2-hydroxy-4-(3″-bromothien-2″-yl)benzo[*b*]thiophene-3,5-dicarboxylate (**2n**) as a white solid in 53% yield (108 mg, 0.25 mmol): mp 35–36 °C; R_f 0.46 (petroleum ether:EtOAc=9:1); IR (ATR) ν 2945 (OH), 1721 (s; CO ester), 1661, 1573, 1543, 1475, 1418, 1388, 1339, 1315, 1218, 1192, 1139, 1077, 881, 863, 704 cm^{-1}; UV (MeCN) λ_{max} (log ε) 248 (4.47), 336 (3.85) nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.64 (s, 3H, 2′-H), 3.67 (s, 3H, 2‴-H), 7.01 (d, ^3J(5″-H, 4″-H)=5.3 Hz, 1H, 4″-H), 7.34 (d, ^3J(5″-H, 4″-H)=5.3 Hz, 1H, 5″-H), 7.55 (d, ^3J(6-H, 7-H)=5.5 Hz, 1H, 6-H), 7.77 (d, ^3J(7-H, 6-H)=5.5 Hz, 1H, 7-H), 12.23 (s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.29 (C-2‴), 52.94 (C-2′), 106.84 (C-3), 111.16 (C-3″), 123.02 (C-5), 124.40 (C-6), 125.56 (C-5″), 129.40 (C-4″), 129.52 (C-1a), 131.09 (C-5a), 132.83 (C-7), 136.37 (C-4), 141.87 (C-2″), 159.28 (C-2), 167.49 (C-1‴), 171.12 (C-1′); MS (EI, 70 eV) *m/z* (%) 428 (5) $[M]^+$, 347 (85), 315 (100), 300 (29), 284 (10), 256 (4), 200 (5), 168 (9), 111 (14); HRMS (ESI, $[M+Na]^+$) calculated for $C_{16}H_{11}BrO_5S_2$ [M+Na] 448.9123 found 448.9152.

Acknowledgements

We thank Mr. Mario Wolf (Institut für Chemie, Universität Hohenheim) for recording NMR spectra and Dipl.-Ing. (FH) Joachim Trinkner (Institut für Organische Chemie, Universität Stuttgart) for recording ESI spectra.

Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2016.04.067.

References and notes

1. For reviews on copper-catalyzed *C*-arylations, see (a) Beletskaya, I. P.; Fedorov, A. Y. In *Copper-mediated Cross-coupling Reactions*; Evano, G., Blanchard, N., Eds.; Wiley & Sons: Hoboken, New Jersey, 2014; pp 283–311; (b) Lindley, J. *Tetrahedron* **1984**, *40*, 1433–1456; (c) Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337–2364; (d) Ma, D.; Cai, Q. *Acc. Chem. Res.* **2008**, *41*, 1450–1460; (e) Evano, G.; Blanchard, N.; Toumi, M. *Chem. Rev.* **2008**, *108*, 3054–3131; (f) Monnier, F.; Taillefer, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 6954–6971; (g) Johannson, C. C. C.; Colacot, T. J. *Angew. Chem., Int. Ed.* **2010**, *49*, 676–707; (h) Bellina, F.; Rossi, R. *Chem. Rev.* **2010**, *110*, 1082–1146; (i) Liu, Y.; Wan, J.-P. *Chem.—Asian. J.* **2012**, *7*, 1488–1501; (j) Sambiagio, C.; Marsden, S. P.; Blacker, A. J.; McGowen, P. C. *Chem. Soc. Rev.* **2014**, *43*, 3525–3550.
2. Hurtley, W. R. H. *J. Chem. Soc.* **1929**, 1870–1873.
3. For selected publications, see (a) Bruggink, A.; McKillop, A. *Tetrahedron* **1975**, *31*, 2607–2619; (b) Setsune, J.; Matsukawa, K.; Wakemoto, H.; Kitao, T. *Chem. Lett.* **1981**, 367–370; (c) Setsune, J.; Matsukawa, K.; Kitao, T. *Tetrahedron Lett.* **1982**, *23*, 663–666; (d) Suzuki, H.; Yi, Q.; Inoue, J.; Kusume, K.; Ogawa, T. *Chem. Lett.* **1987**, 887–890; (e) Pivsa-Art, S.; Fukui, Y.; Miura, M.; Nomura, M. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 2039–2042; (f) Bryson, T. A.; Stewart, J. J.; Gibson, J. M.; Thomas, P. S.; Berch, J. K. *Green Chem.* **2003**, *5*, 174–176.
4. For selected publications, see (a) Okuro, K.; Furuune, M.; Miura, M.; Nomura, M. *J. Org. Chem.* **1993**, *58*, 7606–7607; (b) Hennessy, E. J.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 269–272; (c) Cristau, H.-J.; Cellier, P. P.; Spindler, J.-F.; Taillefer, M. *Chem.—Eur. J.* **2004**, *10*, 5607–5622; (d) Jiang, Y.; Wu, N.; Wu, H.; He, M. *Synlett* **2005**, 2731–2734; (e) Yip, S. F.; Cheung, H. Y.; Zhou, Z.; Kwong, F. Y. *Org. Lett.* **2007**, *9*, 3469–3472; (f) Zeevart, Z. G.; Parkinson, C. J.; de Koning, C. B. *Tetrahedron Lett.* **2007**, *48*, 3289–3293; (g) Mino, T.; Yagishita, F.; Shibuya, M.; Kajiwara, K.; Shindo, H.; Sakamoto, M.; Fujita, T. *Synlett* **2009**, 2457–2460; (h) Kidwai, M.; Bhardwaj, S.; Poddar, R. *Beilstein J. Org. Chem.* **2010**, *6* (35); (i) Liu, J.; Zeng, R.; Zhou, C.; Zou, J. *Chin. J. Chem.* **2011**, *29*, 309–313.
5. For a review on ligands in copper-catalyzed reactions, see (a) Surry, D. S.; Buchwald, S. L. *Chem. Sci.* **2010**, *1*, 13–31 for selected publications, see; (b) Wang, Y. F.; Deng, W.; Liu, L.; Gao, Q. X. *Chin. Chem. Lett.* **2005**, *16*, 1197–1200; (c) Xie, X.; Cai, G.; Ma, D. *Org. Lett.* **2005**, *7*, 4693–4695; (d) Pei, L.; Qian, W. *Synlett* **2006**, 1719–1723.
6. (a) Fang, Y.; Li, C. *J. Org. Chem.* **2006**, *71*, 6427–6431; (b) Lu, B.; Ma, D. *Org. Lett.* **2006**, *8*, 6115–6118.
7. For a book on domino reactions, see:*Domino Reactions in Organic Synthesis*; Tietze, L. F., Brasche, G., Gericke, K. M., Eds.; Wiley-VCH: Weinheim, 2006.
8. For reviews on copper-catalyzed domino reactions for the synthesis of heterocycles, see (a) Liu, Y.; Wan, J.-P. *Org. Biomol. Chem.* **2011**, *9*, 6873–6894; (b)

Liu, T.; Fu, H. *Synthesis* **2012**, *44*, 2805–2824; (c) Gulevich, A. V.; Dudnik, A. S.; Chernyak, N.; Gevorgyan, V. *Chem. Rev.* **2013**, *113*, 3084–3213; (d) Ball, C. J.; Willis, M. C. *Eur. J. Org. Chem.* **2013**, 425–441; (e) Liao, Q.; Yang, X.; Xi, C. *J. Org. Chem.* **2014**, *79*, 8507–8515.

9. (a) Lu, B.; Wang, B.; Zhang, Y.; Ma, D. *J. Org. Chem.* **2007**, *72*, 5337–5341; (b) Aljaar, N.; Malakar, C. C.; Conrad, J.; Strobel, S.; Schleid, T.; Beifuss, U. *J. Org. Chem.* **2012**, *77*, 7793–7803.
10. For selected publications, see (a) Setsune, J.-I.; Ueda, T.; Shikata, K.; Matsukawa, K.; Iida, T.; Kitao, T. *Tetrahedron* **1986**, *42*, 2647–2656; (b) Konopelski, J. P.; Hottenroth, J. M.; Oltra, H. M.; Veliz, E. A.; Yang, Z.-C. *Synlett* **1996**, 609–611; (c) Hang, H. C.; Drotleff, E.; Elliott, G. I.; Ritsema, T. A.; Konopelski, J. P. *Synthesis* **1999**, *3*, 398–400.
11. For selected publications, see (a) Tanimori, S.; Ura, H.; Kirihata, M. *Eur. J. Org. Chem.* **2007**, 3977–3980; (b) Chen, Y.; Xie, X.; Ma, D. *J. Org. Chem.* **2007**, *72*, 9329–9334; (c) Chen, Y.; Wang, Y.; Sun, Z.; Ma, D. *Org. Lett.* **2008**, *10*, 625–628; (d) Yang, X.; Fu, H.; Qiao, R.; Jiang, Y.; Zhao, Y. *Adv. Synth. Catal.* **2010**, *352*, 1033–1038; (e) Kobayashi, K.; Komatsu, T.; Yokoi, Y.; Konishi, H. *Synthesis* **2011**, 764–768; (f) Ali, M. A.; Punniyamurthy, T. *Synlett* **2011**, 623–626.
12. Wang, B.; Lu, B.; Jiang, Y.; Zhang, Y.; Ma, D. *Org. Lett.* **2008**, *10*, 2761–2763.
13. For selected publications, see (a) Wang, F.; Liu, H.; Fu, H.; Jiang, Y.; Zhao, Y. *Org. Lett.* **2009**, *11*, 2469–2472; (b) Lu, J.; Gong, X.; Yang, H.; Fu, H. *Chem. Commun.* **2010**, 4172–4174.
14. (a) Sudheendran, K.; Malakar, C. C.; Conrad, J.; Beifuss, U. *Adv. Synth. Catal.* **2013**, *355*, 2400–2416; (b) Malakar, C. C.; Schmidt, D.; Conrad, J.; Beifuss, U. *Org. Lett.* **2011**, *13*, 1972–1975.
15. Xu, H.; Li, S.; Liu, H.; Fu, H.; Jiang, Y. *Chem. Commun.* **2010**, 7617–7619.
16. Hatano, B.; Miyoshi, K.; Sato, H.; Ito, T.; Ogata, T.; Kijimi, T. *Tetrahedron Lett.* **2010**, *51*, 5399–5401.
17. Tietze, L. F.; Redert, T.; Bell, H. P.; Hellkamp, S.; Levy, L. M. *Chem.—Eur. J.* **2008**, *14*, 2527–2535.
18. Jagdale, A. R.; Youn, S. W. *Eur. J. Org. Chem.* **2011**, 3904–3910.
19. Malakar, C. C.; Baskakova, A.; Conrad, J.; Beifuss, U. *Chem.—Eur. J.* **2012**, *18*, 8882–8885.
20. Sudheendran, K.; Malakar, C. C.; Conrad, J.; Beifuss, U. *J. Org. Chem.* **2012**, *77*, 10194–10210.
21. Aljaar, N.; Malakar, C. C.; Conrad, J.; Frey, W.; Beifuss, U. *J. Org. Chem.* **2013**, *78*, 154–166.
22. Abdel-Mohsen, H. T.; Conrad, J.; Beifuss, U. *J. Org. Chem.* **2013**, *78*, 7986–8003.