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Note

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Self-Condensation of Enaminodiones as a Method for the Benzene Ring Construction: Synthesis of Diacyl-Substituted Phenols and Catechols

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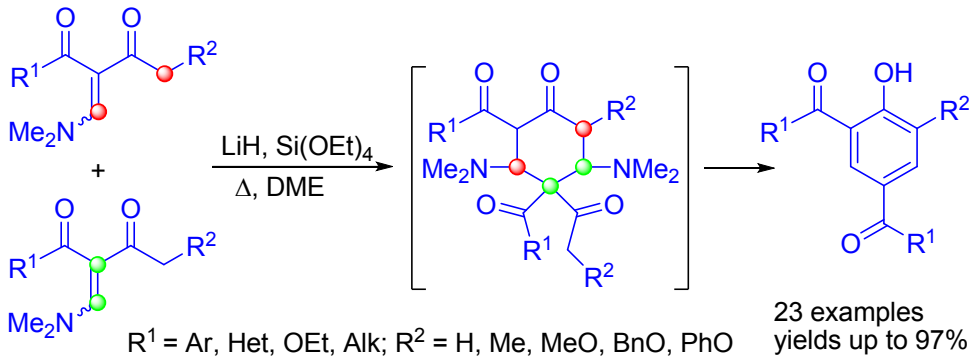
Supporting Information Placeholder



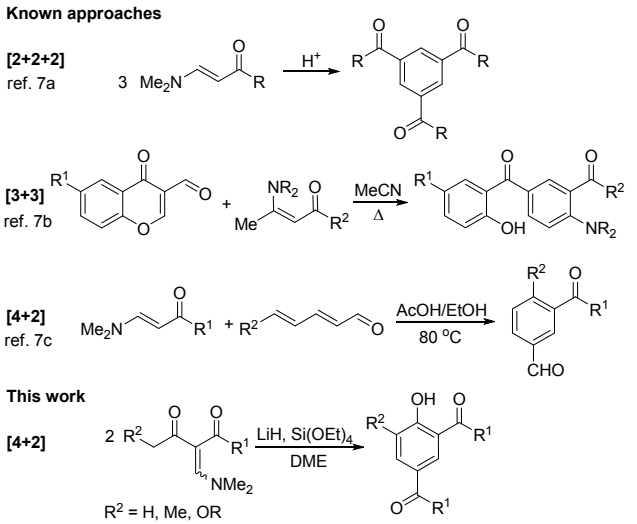
ABSTRACT: A novel transition metal-free approach for the construction of the benzene core has been developed through self-condensation of available enaminodiones. Functionalized acyl-substituted phenols and catechols were obtained in 29–97% yields and with high chemoselectivity under mild conditions. This base-promoted formal [4+2] annulation proceeds *via* cyclohexanone formation and involves the cascade transformation based on double Michael addition and aromatization (retro-Claisen cleavage, amine elimination).

Benzene derivatives are an important class of molecules that are widely used in human life, including bioactive compounds[1a–c] and modern materials.[1d,e] Therefore, efficient methods for the preparation of polysubstituted benzenes have always been paid a lot of attention. The most popular and convenient methods include CH-functionalization[2] of preexisting arenes, such as electrophilic (Friedel-Crafts reaction[2a,b]) and nucleophilic substitution transformations, as well as interactions with organometallic reagents.[2c,d] However, there are often difficulties related to the selectivity because of substituent influence, as a result, the use of multistage sequential manipulation of functional groups is necessary. Therefore, straightforward and efficient *de novo* syntheses of highly functionalized benzenes on the basis of easily accessible precursors are highly attractive, moreover, these approaches are also important for sustainable chemistry.[3] The well-explored strategies include Reppe trimerization of alkynes, Diels−Alder reaction, Bergman cyclization, Danheiser annulation, ring-closing metathesis, Dötz [3+2+1] reaction and Wulff [5+1] *ortho*-benzannulation.[4] In recent time, selective transformations for the construction of substituted benzenes have been developed on the basis of diketones and enones,[5] which are usually used as valuable building blocks, including multicomponent,[5f] carbene-catalyzed,[5g,h] and transition metal-free[5i] reactions. Since enaminones can be related to enones and hidden diketones, this structural feature allows to consider them as convenient intermediates for the synthesis of arenes.[6] There are several transition metal-free approaches in the literature (Scheme 1) based on enaminones, such as the acid-promoted [2+2+2] trimerization,[7a] the catalyst-free [3+3] reaction with 3-formylchromones,[7b] and the acid-promoted formal [4+2] cycloaddition with dienals.[7c] Besides, Rh- and In-catalyzed benzannulations have also been actively developed with the use of enaminones.[8]

We envisaged to introduce an additional nucleophilic center into the enaminone structure, which could be used for designing a domino transformation to obtain cyclohexanones based on the double Michael addition.[9] Subsequent aromatization including dimethylamine elimination and retro-Claisen reaction[10] should lead to the formation of acyl-substituted phenols and catechols (R^2 = OR). This transformation will open access to an important class of compounds, such as hydroxy-substituted benzophenones,

which are used as UV filters,[11a,b] biologically active compounds,[11c–e] and intermediates for organic synthesis.[11f] Although *de novo* approaches for the construction of phenols have been described in the literature,[5a] methods for the preparation of catechols derivatives are a little-studied area. In addition, such self-condensation is of interest because it allows to develop a convenient method for the synthesis of asymmetric benzene derivatives.

Scheme 1. Transition Metal-Free Reactions of Benzene Ring Formation Based on Enaminones

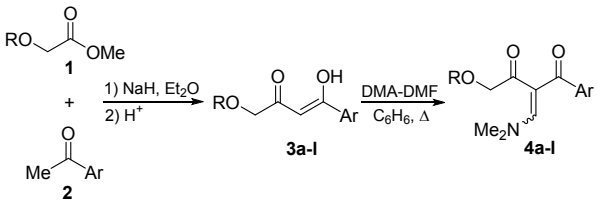


On the other hand, enaminodiones have been described to be multifunctional building blocks for organic synthesis and are usually used as 1,3-bielectrophiles for the preparation of pyrazoles,[12a,b] isoxazoles,[12c] and 2-pyridones.[12d] The application of enaminodiones as 1,4-ambiphiles has been actively developed in recent times to obtain highly reactive 3-acyl-4-pyrones.[13] To the best of our knowledge, in the chemistry of enaminodiones there is only one fact of the benzene formation as a by-product based on ethyl 2-((dimethylamino)methylene)-3-oxobutanoate.[14]

It should also be noted that aminomethylidene derivatives of 4-hydroxyacetoacetic esters are the starting molecules for the preparation of modern HIV integrase inhibitors, such as dolutegravir and bictegravir.[15] On this point, we were especially interested in RO-substituted enaminodiones, which may be the core structure for introducing the moiety of diketobutanoic acid into various compounds. Here, we describe a transition metal-free and general approach for the synthesis of acyl-substituted phenols and catechols with the use of the base-promoted self-condensation of easily accessible enaminodiones.

We started this study with the synthesis of alkoxy- and phenoxy-substituted enaminodiones **4** because this class of compounds has not been previously reported in the literature, excepting aminomethylidene derivatives of 4-hydroxyacetoacetic ester. 4-Alkoxy- and 4-phenoxy-substituted 1,3-diketones **3a–l** were obtained in 54–85% by the Claisen condensation of acetates **1** with various acetophenones **2** in the presence of NaH in Et_2O at 0 °C (Scheme 2, see SI, Table S1). With obtained 1,3-diketones **3**, the enamination reaction was performed with DMA-DMF. The transformation proceeded at only one methylene group, and previously unknown enaminodiones **4a–l** were obtained in 40–95% yields.[16]

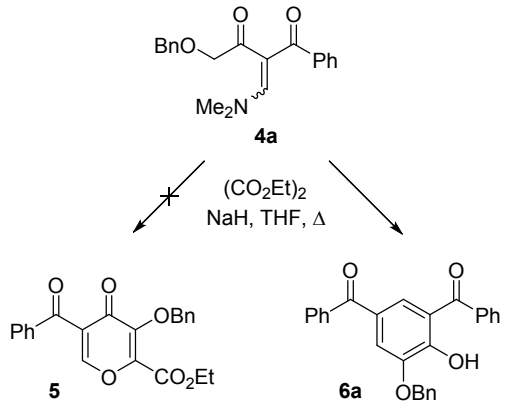
Scheme 2. Synthesis of RO-Substituted Enaminodiones 4



Having a number of enaminodiones **4** in our hands, we tried to carry out the condensation of enaminodione **4a** with diethyl oxalate to prepare 5-acyl-3-hydroxy-4-pyrone **5** according to the known methods (Table 1).[13] To our surprise, diaroylbenzene **6a** as a self-condensation product was obtained in the presence of NaH or LiH in 15% and 55%, respectively (entries 1 and 2). Interestingly, when we decided to carry out this transformation without diethyl oxalate using LiH as the base of choice in various solvents (entries 3–5), product **6a** was obtained in extremely low yields. Thus, the presence of diethyl oxalate is important for increasing the outcome of the reaction, and this fact can be probably connected with the formation of the ethoxide anion. Next, we added EtOH and *t*-BuOH to prepare *in situ* LiOEt and LiO*t*-Bu, respectively, but benzophenone **6a** was obtained in low yields (15–20%, entries 6 and 7). When $Ti(O\textit{i}\text{-}Bu)_4$ (0.5 equiv.) was used as an additive with LiH in THF, the reaction gave the desired product in only 22% yield (entry 8). To our delight, the reaction in the presence of $Si(OEt)_4$ (0.5 equiv.) and LiH (1.2 equiv.) in THF led to compound **6a** in 59% yield (entry 9).

Although changing amounts of $Si(OEt)_4$ (entries 10 and 11) did not allow to improve the reaction outcome, solvent screening with the use of $Si(OEt)_4$ as the additive of choice (0.5 equiv.) made it possible to achieve a higher yield of **6a** (entries 12 and 13). Thus, refluxing of enaminodione **4a** in glyme for 5 h in the presence of $Si(OEt)_4$ (0.5 equiv.) with LiH (1.2 equiv.) turned out to be the best conditions for the self-condensation resulting in benzophenone **6a** in 71% yield. When $Si(OMe)_4$ was used as an additive, benzophenone **6a** was obtained in a lower yield (63%, entry 14). Enaminodione **4a** did not give the product in the absence of a base (entry 15) and was recovered without changing. Our attempts to use CaH_2 as a base (entry 16) or acid catalysts did not lead to the formation of compound **6a** (entry 17, Table 1).

Table 1. Optimization of the Reaction Conditions for the Self-Condensation of Enaminodione **4a**[a]

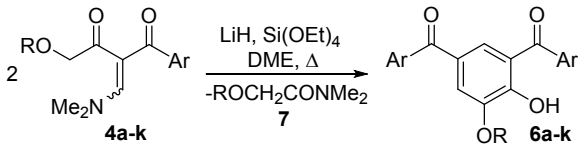


Entry	Base (equiv.)	Solvent	Time, h, Δ	Additive (equiv.)	Yield **6a**, %
1	NaH (1.2)	THF	4	$(CO_2Et)_2$ (1.2)	15
2	LiH (1.2)	THF	8	$(CO_2Et)_2$ (1.2)	55
3	NaH (1.2)	THF	1	–	9
4	LiH (1.2)	THF	12	–	5
5	LiH (1.2)	dioxane	2	–	10
6	LiH (1.2)	THF	8	EtOH (4.0)	15
7	LiH (1.2)	glyme	5	*t*-BuOH (1.0)	13
8	LiH (1.2)	THF	8	$Ti(Oi\text{-}Bu)_4$ (0.5)	22
9	LiH (1.2)	THF	8	$Si(OEt)_4$ (0.5)	59
10	LiH (1.2)	THF	8	$Si(OEt)_4$ (1.0)	50
11	LiH (1.2)	THF	2	$Si(OEt)_4$ (0.25)	22
12	LiH (1.2)	dioxane	8	$Si(OEt)_4$ (0.5)	48
13	**LiH (1.2)**	**glyme**	**5**	**$Si(OEt)_4$ (0.5)**	**71**
14	LiH (1.2)	glyme	5	$Si(OMe)_4$ (0.5)	63
15	–	glyme	–	$Si(OEt)_4$ (0.5)	–
16	CaH_2	glyme	5	$Si(OEt)_4$ (0.5)	–
17	–	EtOAc	1	LiCl (0.5), HCl	–

[a] Enaminodione **4a** (196 mg, 0.607 mmol) was refluxed in a solvent (1 mL).

The optimized conditions were extended to a variety of RO-substituted enaminodiones **4** (Table 2). As a result, self-condensation products **6a–k** were obtained in 29–73% yields. In the case of benzyloxy derivatives, the nature of the aromatic substituent has almost no effect on this transformation, and benzenes **6a**–**h** were prepared in 49–73% yields, but 3-methoxyphenyl substituted enaminodione **4l** did not give the desired product leading to a mixture of unidentified aromatic compounds. The nature of the RO-substituent has a strong influence on the formation of compounds **6**. Thus, phenoxy substituted benzophenones **6i,j** were obtained in 46–52% yields, while in the case of methoxy derivative **4k**, the outcome decreased to 29% because of the formation of a complex mixture of products. This fact can be connected with demethylation process, which proceeds more readily than debenzylation.

Table 2. Synthesis of Catechols **6** Based on Self-Condensation of Enaminodiones **4**[a]



Catechol 6	R	Ar	Yield, %
a	Bn	Ph	71
b	Bn	4-$MeOC_6H_4$	56
c	Bn	4-MeC_6H_4	66
d	Bn	4-PhC_6H_4	63
e	Bn	4-ClC_6H_4	52
f	Bn	2-Naphthyl	63
g	Bn	1-Naphthyl	49
h	Bn	2-Thienyl	73
i	Ph	Ph	46
j	Ph	2-Thienyl	52
k	Me	Ph	29

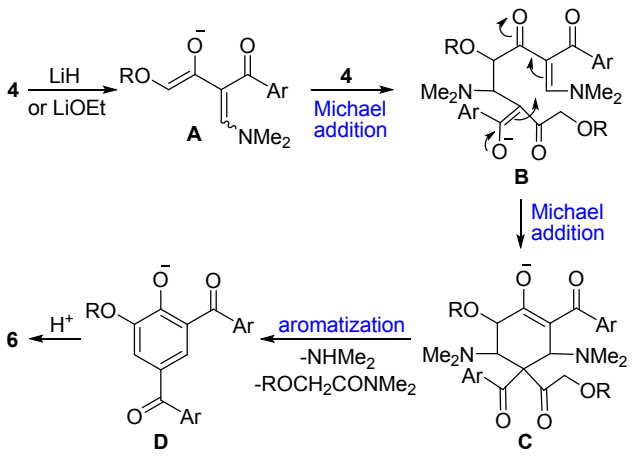
[a] Unless otherwise noted, enaminodione **4** (0.607 mmol), $Si(OEt)_4$ (63.1 mg, 0.303 mmol), and LiH (5.8 mg, 0.729 mmol) were refluxed in glyme (1 mL) for 5 h.

Products **6** were isolated without using column chromatography by simple recrystallization from ethanol, which is a convenient solvent to separate products **6** from dimethylacetamides **7** and plausible by-products, 1,3-diketones **3**. The latter could be generated during incomplete conversion of enaminodiones **4** or their reaction with water. For benzyloxy derivatives, we could observe the second product, dimethylamide of benzyloxyacetic acid (**7a**), by NMR spectroscopy in the filtrate after the recrystallization of products **6** from ethanol (see SI).

The structure of the products **6** was assigned on the basis of ^1H and ^{13}C NMR spectra, and the data of elemental analysis. In the ^1H NMR spectra of benzophenones **6** in $CDCl_3$, a characteristic downfield doublet of the H-2 proton of the benzene ring was observed at δ 7.68–8.42 ppm with J = 1.6–2.0 Hz, and the OH group appeared at δ 12.19–12.74 ppm as the result of the formation of the intramolecular hydrogen bond.

A possible mechanism (Scheme 3) of this transformation includes deprotonation (anion **A**), Michael addition (intermediate **B**) followed by cyclization to cyclohexadienone **C**. This transformation including the double Michael addition can be considered as Rauhut − Currier reaction.[9] The aromatization of cyclohexadienone **C** gives more stable intermediate **D** as the result of the elimination of $NHMe_2$ and the retro-Claisen reaction leading to the cleavage of dimethylacetamide **7**. Our attempts to isolate or detect any cyclohexane intermediates by NMR spectroscopy were unsuccessful. In the ^1H NMR spectra of the reaction mixture, only the starting compounds, corresponding dimethylacetamide **7**, and phenolate **D** were observed. Apparently, upon heating the aromatization proceeds much faster than the double Michael reaction. An important feature of the aromatization is selectivity of the retro-Claisen reaction (intermediate **C**). The cleavage occurs only at the RO-acetyl moiety, which is confirmed by the formation of only one benzophenone **6**, while the other possible benzophenone was not even detected. The explanation of this selectivity is associated with a higher reactivity of the carbonyl group of the acetyl moiety compared to the aroyl moiety.

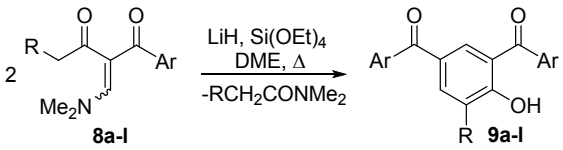
Scheme 3. Possible Mechanism of Enaminodione Self-Condensation



In the literature the application of $Si(OR)_4$/CsF mixture has been previously described as the catalyst and the source of alkoxide anions for the reaction of ketones with aldehydes or Michael acceptors.[17] The use of $Si(OEt)_4$ as an additive in our transformation can probably have several functions: (*a*) activation of LiH, which has low solubility in organic solvents, as the result of formation of LiOEt or hydroethoxysilicates;[17] (*b*) coordination with the enaminodione molecules and the formation of intermediate triethoxysilylenolates,[18a] which make it possible to bring together two molecules and to promote the Michael addition;[18b,c] (*c*) fixation of small amounts of water, which may be present in reactants and initiates side-processes, such as destruction and hydrolysis.

Next, we decided to extend this transformation to the simplest enaminodiones (without the RO group) for the synthesis of 2,4-diacylsubstituted phenols (Table 3). We thought that enaminodiones **8** should be deprotonated under more severe conditions due to their lower CH acidity. However, it was observed that the reaction under the same conditions (in glyme or dioxane) led to the substituted phenols **9a–i** in 51–97% yields. Although in most cases, glyme was a convenient solvent for this transformation, in the case of compounds **9e,f,h**, the use of higher boiling dioxane as a solvent allowed to increase the outcome by 16–38%. For compounds **8j,k** bearing the propionyl moiety, the transformation was carried out in dioxane and the yield decreased to 36–37%, which is in good agreement with the steric and electron-donating effects of the methyl group, which lowers the CH acidity of the enaminodiones. It should be noted that diacyl-substituted phenols **9a–k** are hard-to-reach compounds because of low selectivity of the direct double acylation of phenols, and in the literature, only benzophenone **9a** has been described.[19] Interestingly, this reaction was also extended to the carboethoxy derivative **8l**, which led to diethyl 4-hydroxyisophthalate (**9l**, 92% yield), an important intermediate for the preparation of natural compounds.[20]

Table 3. Synthesis of Phenols **9** Based on Self-Condensation of Enaminodiones **8**[a]



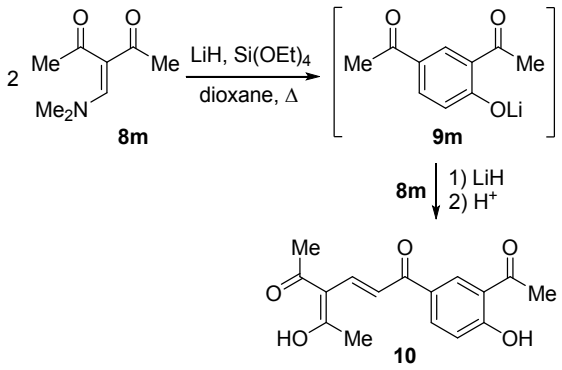
Phenol **9**	R	Ar	Yield, %
a	H	Ph	62
b	H	4-$MeOC_6H_4$	91
c	H	3-$MeOC_6H_4$	94
d	H	2-$MeOC_6H_4$	82
e	H	4-MeC_6H_4	80[b]
f	H	4-ClC_6H_4	51[b]
g	H	4-$NO_2C_6H_4$	53
h	H	2-Naphthyl	97[b]
i	H	2-Thienyl	53
j	Me	Ph	37[b]
k	Me	2-Thienyl	36[b]
l	H	OEt	92

[a] Unless otherwise noted, enaminodione **1a** (1.214 mmol), $Si(OEt)_4$ (126.2 mg, 0.606 mmol), and LiH (11.6 mg, 1.458 mmol) were refluxed in glyme (2 mL) for 5 h.
[b] Refluxing in dioxane for 8 h.

In the case of enaminodione **8m**, which was obtained from acetylacetone and bears two reactive methyl groups, the self-condensation was observed to proceed with the participation

of three molecules, as a result, compound **10** was formed in 32% yield (Scheme 4). A possible mechanism involves the formation of 2,4-diacetylphenolate **9m**, which then reacts with another molecule of enaminodione **8m**.

Scheme 4. Self-condensation of enaminodione 8m



In summary, we have developed a selective *de novo* synthesis of diverse acyl-substituted phenols and catechols based on enaminodione self-condensation, which exhibits both the broad substrate scope and a good functional group tolerance. This cascade transformation includes the double Michael addition followed by the subsequent aromatization as the result of $NHMe_2$ elimination and retro-Claisen reaction. The obtained benzophenones are of further interest as bioactive compounds and UV filters.

EXPERIMENTAL SECTION

^{1}H NMR spectra were recorded on 400 and 500 MHz instruments, ^{13}C NMR spectra were recorded on 100 and 126 MHz instruments in DMSO-d_6 or $CDCl_3$. Chemical shifts are reported relative to TMS, $CHCl_3$ (δ = 7.26 ppm, ^{1}H NMR), DMSO-d_6 (δ = 2.50 ppm, ^{1}H NMR), $CDCl_3$ (δ = 77.16 ppm, ^{13}C NMR) and DMSO-d_6 (δ = 39.52 ppm, ^{13}C NMR). IR spectra were recorded on a FTIR spectrometer with ATR accessory. High-resolution mass spectra (HRMS) were carried out at a instrument for HRMS-ESI-QTOF. All solvents used were dried and distilled by standard procedures. Methyl 2-(benzyloxy)acetate, methyl 2-methoxyacetate, and methyl 2-phenoxyacetate were prepared based on the reported procedures.[21a,b] Enaminodiones **8a,b,e–i,l,m** were prepared according to the literature procedure.[13]

General method for the preparation of 4-benzyloxy-1,3-diketones 3a–h,l and 4-methoxy-1,3-diketone 3i.

In cooled in a ice bath a 50 mL-flask with a reflux condenser equipped with a calcium chloride drying tube, NaH (60%-suspension in oil) (1.11 g, 27.7 mmol) was slowly added to a stirred solution of acetophenone (23.1 mmol) and methyl 2-(benzyloxy)acetate (5.00 g, 27.7 mmol) or methyl 2-methoxyacetate (2.88 g, 27.7 mmol) in dry Et_2O (15 mL) (in the case of **3i**, the reaction mixture was heated for initiating the condensation). The reaction temperature was allowed to rise to ambient temperature, and the reaction mixture was stirred overnight. Then the resulting mixture was treated wth AcOH (4 mL) and H_2O (4 mL) at 0 ºC and stirred for 30 min. The product was extracted with EtOAc (3 × 10 mL). The combined extracts were washed with saturated sodium bicarbonate solution (10 mL), water (10 mL), and brine (10 mL). The organic phase was dried with anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was boiled in *n*-hexane, and after cooling *n*-hexane was decanted if the product is liquid. For solid products, the product was isolated by filtration.

4-(Benzyloxy)-1-phenylbutane-1,3-dione (3a).

Yield 72% (4.46 g), yellow liquid. IR (ATR): 3064, 3032, 2864, 1602, 1573, 1266, 1108, 696 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 4.18 (s, 2H, CH_2), 4.22 (s, 2H, CH_2), 6.57 (s, 1H, =CH), 7.24–7.40 (m, 5H, Bn), 7.49 (t, J = 7.5 Hz, 2H, H-3, H-5 Ph), 7.57 (tt, J = 7.2 Hz, J = 1.2 Hz, 1H, H-4 Ph), 7.90 (d, J = 8.0 Hz, 2H, H-2, H-6 Ph), 15.95 (s, 1H, OH). The analytical data are in accordance with those reported in the literature.[22]

4-(Benzyloxy)-1-(4-methoxyphenyl)butane-1,3-dione (3b).

Yield 55% (3.79 g), orange liquid. IR (ATR): 3031, 2934, 2840, 1601, 1509, 1256, 1173, 1107, 788, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 3.87 (s, 3H, Me), 4.17 (s, 2H, CH_2), 4.65 (s, 2H, CH_2), 6.48 (s, 1H, =CH), 6.94 (d, J = 9.0 Hz, 2H, H-3, H-5 Ar), 7.25–7.40 (m, 5H, Bn), 7.89 (d, J = 9.0 Hz, 2H, H-2, H-6 Ar), 16.11 (s, 1H, OH); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 55.5, 71.5, 73.5, 92.7, 114.0, 127.1, 127.9, 128.0, 128.6, 129.4, 137.8, 163.4, 183.9, 192.4; HRMS (ESI/Q-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{18}NaO_4$ 321.1103; Found 321.1113.

4-(Benzyloxy)-1-*p*-tolylbutane-1,3-dione (3c).

Yield 75% (4.89 g), yellow powder, mp 34–35 °C. IR (ATR): 3029, 2913, 2863, 1727, 1607, 1104, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 2.41 (s, 3H, Me), 4.17 (s, 2H, CH_2), 4.65 (s, 2H, CH_2), 6.52 (s, 1H, =CH), 7.26 (d, J = 8.1 Hz, 2H, H-3, H-5 Ar), 7.27–7.42 (m, 5H, Bn), 7.81 (d, J = 8.1 Hz, 2H, H-2, H-6 Ar), 15.99 (s, 1H, OH); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 21.7, 71.7, 73.5, 93.2, 127.3, 128.0, 128.1, 128.6, 129.4, 131.8, 137.4, 143.5, 183.6, 193.9; HRMS (ESI/Q-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{18}NaO_3$ 305.1154; Found 305.1147.

4-(Benzyloxy)-1-(biphenyl-4-yl)butane-1,3-dione (3d).

Yield 85% (6.67 g), light-yellow powder, mp 81–83 °C. IR (ATR): 3060, 3035, 2863, 1605, 1433, 1119, 763 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 4.19 (s, 2H, CH_2), 4.66 (s, 2H, CH_2), 6.59 (s, 1H, =CH), 7.26–7.43 (m, 6H, Bn, Ph), 7.47 (t, J = 7.5 Hz, 2H, H-3, H-5 Ph), 7.63 (t, J = 8.1 Hz, 2H, Ph), 7.68 (d, J = 8.4 Hz, 2H, Ph), 7.98 (d, J = 8.4 Hz, 2H, Ph), 15.96 (s, 1H, OH); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 71.8, 73.5, 93.4, 127.2, 127.3, 127.7, 127.9, 128.0, 128.2, 128.6, 128.9, 133.2, 137.2, 139.9, 145.3, 182.6, 194.5. Anal.

Calcd for $C_{23}H_{20}O_3$: C, 80.21; H, 5.85. Found: C, 80.12; H, 5.81.

4-(Benzyloxy)-1-(4-chlorophenyl)butane-1,3-dione (3e).

Yield 76% (5.32 g), yellow crystals, mp 63–66 °C. IR (ATR): 3059, 3029, 2862, 1591, 1531, 1454, 1087, 778 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 4.17 (s, 2H, CH_2), 4.65 (s, 2H, CH_2), 6.51 (s, 1H, =CH), 7.28–7.40 (m, 5H, Bn), 7.43 (d, J = 8.6 Hz, 2H, H-3, H-5 Ar), 7.87 (d, J = 8.6 Hz, 2H, H-2, H-6 Ar), 15.88 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 71.8, 73.6, 93.5, 128.0, 128.2, 128.6, 128.7, 129.1, 133.1, 137.3, 138.9, 182.0, 194.6. Anal. Calcd for $C_{17}H_{15}ClO_3$: C, 67.44; H, 4.99. Found: C, 67.24; H, 4.96.

4-(Benzyloxy)-1-(naphthalen-2-yl)butane-1,3-dione (3f).

Yield 84% (6.18 g), yellow powder, mp 20–21 °C. IR (ATR): 3061, 3031, 2864, 1604, 1570, 1232, 1106, 736, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 4.22 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 6.69 (s, 1H, =CH), 7.30–7.45 (m, 5H, Bn), 7.54 (td, J = 7.0 Hz, J = 1.1 Hz, 1H, Naph), 7.58 (td, J = 7.0 Hz, J = 1.1 Hz, 1H, Naph), 7.85–7.92 (m, 3H, Naph), 7.95 (d, J = 8.0 Hz, 1H, H-3 Naph), 8.47 (d, J = 0.8 Hz, 1H, H-1 Naph), 15.99 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 71.8, 73.6, 93.9, 123.1, 126.8, 127.8, 128.0, 128.1, 128.2, 128.5, 128.6, 129.4, 131.7, 132.7, 135.4, 137.3, 182.9, 194.6 (1C was not observed); HRMS (ESI/Q-TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{18}NaO_3$ 341.1154; Found 341.1155.

4-(Benzyloxy)-1-(naphthalen-1-yl)butane-1,3-dione (3g).

Yield 54% (3.97 g), yellow powder, mp 37–39 °C. IR (ATR): 3061, 3032, 2864, 1728, 1601, 1105, 776, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 4.22 (s, 2H, CH_2), 4.65 (s, 2H, CH_2), 6.41 (s, 1H, =CH), 7.23–7.66 (m, 8H, Bn), 7.77 (d, J = 7.0 Hz, 1H, Naph), 7.90 (d, J = 7.0 Hz, 1H, Naph), 7.98 (d, J = 8.0 Hz, 1H, Naph), 8.49 (d, J = 8.3 Hz, 1H, Naph), 15.91 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 71.6, 73.6, 98.7, 124.9, 125.6, 126.5, 127.4, 127.5, 127.9, 128.1, 128.6, 130.2, 132.0, 137.3, 133.8, 133.9, 188.1, 193.1 (1C was not observed). Anal. Calcd for $C_{21}H_{18}O_3$: C, 79.22; H, 5.70. Found: C, 79.18; H, 5.86.

4-(Benzyloxy)-1-(thiophen-2-yl)butane-1,3-dione (3h).

Yield 75% (4.75 g), yellow liquid. IR (ATR): 3090, 2865, 1756, 1659, 1453, 1310, 1109, 726 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 4.16 (s, 2H, CH_2), 4.64 (s, 2H, CH_2), 6.38 (s, 1H, =CH), 7.14 (d, J = 5.0 Hz, J = 3.8 Hz,1H, H-4 Th), 7.27–7.42 (m, 5H, Bn), 7.62 (dd, J = 5.0 Hz, J = 1.1 Hz, 1H, H-5 Th), 7.73 (dd, J = 3.8 Hz, J = 1.1 Hz, 1H, H-3 Th), 15.50 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 70.4, 73.5, 93.8, 127.9, 128.1, 128.3, 128.6, 130.8, 132.8, 137.2, 141.2, 181.6, 187.6. Anal. Calcd for $C_{15}H_{14}O_3S$: C, 65.67; H, 5.14. Found: C, 65.27; H, 5.49.

4-Methoxy-1-phenylbutane-1,3-dione (3k).

Yield 63% (2.80 g), yellow liquid. IR (ATR): 2934, 2825, 1713, 1600, 1569, 1449, 1265, 1114, 772 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 3.49 (s, 3H, Me), 4.11 (s, 2H, CH_2), 6.49 (s, 1H, =CH), 7.46 (dd, J = 7.8 Hz, J = 7.3 Hz, 2H, H-3, H-5 Ph), 7.54 (tt, 1H, J = 7.3 Hz, J = 1.0 Hz, H-4 Ph), 7.97 (dd, J = 7.8 Hz, J = 1.0 Hz,2H, H-2, H-6 Ph), 15.87 (s, 1H, OH). The analytical data are in accordance with those reported in the literature.[22]

4-(Benzyloxy)-1-(3-methoxyphenyl)butane-1,3-dione (3l).

Yield 71% (4.89 g), yellow liquid. IR (ATR): 3031, 2936, 1729, 1578, 1455, 1273, 1108, 1041, 782, 736, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 3.86 (s, 3H, Me), 4.18 (s, 2H, CH_2), 4.65 (s, 2H, CH_2), 6.53 (s, 1H, =CH), 7.08 (ddd, J = 8.2 Hz, J = 2.6 Hz, J = 0.9 Hz, 1H, Ar), 7.27–7.41 (m, 6H, Bn, Ar), 7.44 (dd, J = 2.6 Hz, J = 1.6 Hz, 1H, H-2 Ar), 7.08 (ddd, J = 7.7 Hz, J = 1.5 Hz, J = 1.1 Hz, 1H, Ar), 15.88 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 55.4, 71.7, 73.5, 93.7, 111.9, 118.8, 119.7, 127.9, 128.1, 128.6, 129.7, 136.0, 137.3, 159.9, 183.2, 194.2; HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{18}H_{19}O_4$ 299.1283; Found 299.1297.

General method for the preparation of 4-phenoxy-1,3-diketones 3i,j

In cooled in a ice bath a 50 mL-flask with a reflux condenser equipped with a calcium chloride drying tube, NaH (60%-suspension in oil) (1.11 g, 27.7 mmol) was slowly added to a stirred solution of acetophenone (23.1 mmol) and methyl 2-(phenoxy)acetate (4.60 g, 27.7 mmol) in dry Et_2O (15 mL). The reaction temperature was allowed to rise to ambient temperature, and the reaction mixture was stirred overnight. Then a paticipate formed was filtered off and washed with toluene. To a suspension of the sodium salt in Et_2O (20 mL), a solution of hydrochloric acid (1 : 2) was added until the salt dissolved completely. The ether layer was separated, and additional quantity of Et_2O (10 mL) was used for extraction of the product. The combined extracts were washed with saturated sodium bicarbonate solution (10 mL), water (10 mL), and brine (10 mL). The organic phase was dried with anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was crystallized from *n*-heptane.

4-Phenoxy-1-phenylbutane-1,3-dione (3i).

Yield 62% (3.64 g), white powder, mp 69–71 °C. IR (ATR): 3064, 3032, 2864, 1602, 1573, 1266, 1108, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 4.69 (s, 2H, CH_2), 6.58 (s, 1H, =CH), 6.90–7.07 (m, 3H, Ph), 7.32 (t, J = 7.7 Hz, 2H, H-3, H-5 Ph), 7.45 (t, J = 7.5 Hz, 2H, H-3, H-5 Ph), 7.54 (t, J = 7.5 Hz, 1H, H-4 Ph), 7.89 (d, J = 8.0 Hz, 2H, H-2, H-6 Ph), 15.91 (s, 1H, OH). The analytical data are in accordance with those reported in the literature.[23]

4-Phenoxy-1-(thiophen-2-yl)butane-1,3-dione (3j).

Yield 58% (3.49 g), light yellow powder, mp 51–53 °C. IR (ATR): 3093, 2892, 2577, 1583, 1226, 1066, 780, 750, 687, 605 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 4.67 (s, 2H, CH_2), 6.41 (s, 1H, =CH), 6.90–7.06 (m, 3H, Ph), 7.13 (dd, J = 5.0 Hz, J = 3.9 Hz, 1H, H-4 Th), 7.27–7.36 (m, 2H, Ph), 7.62 (dd, J = 5.0 Hz, J = 1.1 Hz, 1H, H-5 Th), 7.72 (dd, J = 3.9 Hz, J = 1.1 Hz, 1H, H-3 Th), 15.56 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 64.8, 93.8, 114.8, 121.8, 128.4,

129.7, 131.0, 133.0, 133.0, 140.7, 157.9, 181.1, 187.0. Anal. Calcd for $C_{14}H_{12}O_3S$: C, 64.60; H, 4.65. Found: C, 64.67; H, 4.66.

General method for the preparation enaminodiones 4 and 8.

Dimethylformamide dimethyl acetal (1.55 g, 13.0 mmol) was added to the corresponding 1,3-diketone (10.0 mmol) in anhydrous benzene (4.6 mL), the reaction mixture was stirred for 24 h at room temperature and then refluxed for 1 h using a reflux condenser equipped with a calcium chloride drying tube. Then the solvent and an excess of DMF-DMA were removed at reduced pressure, the residue was diluted with *n*-hexane or Et_2O. The resulting mixture was maintained at –20 ºC for several hours (sometimes crystallization should be induced by rubbing the inside surface of the crystallization vessel), and the precipitate that formed was filtered off. Liquid product **4k** was isolated by decantation.

4-(Benzyloxy)-2-((dimethylamino)methylene)-1-phenylbutane-1,3-dione (4a).

Yield 88% (2.85 g), yellow powder, mp 85–87 °C. IR (ATR): 3032, 2925, 2882, 1651, 1573, 1085, 780 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.40 –3.40 (br m, 6H, 2Me), 4.01 (s, 2H, CH_2), 4.30 (s, 2H, CH_2), 7.16–7.32 (m, 5H, Bn), 7.40 (t, J = 7.5 Hz, 2H, H-3, H-5 Ph), 7.50 (t, J = 7.3 Hz, 1H, H-4 Ph), 7.73–7.83 (m, 3H, =CH, H-2, H-6 Ph); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 42.0, 47.3, 72.9, 74.6, 109.3, 127.5, 127.7, 128.2, 128.4, 129.0, 132.1, 137.5, 140.6, 157.1, 194.5, 195.4. Anal. Calcd for $C_{20}H_{21}NO_3$: C, 74.28; H, 6.55; N, 4.33. Found: C, 73.97; H, 6.78; N, 4.61.

4-(Benzyloxy)-2-((dimethylamino)methylene)-1-(4-methoxyphenyl)butane-1,3-dione (4b).

Yield 84% (2.97 g), yellow powder, mp 55–58 °C. IR (ATR): 3001, 2911, 2842, 1597, 1567, 1420, 1299, 1252, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.37–3.50 (br m, 6H, 2Me), 3.85 (s, 3H, MeO), 4.02 (s, 2H, CH_2), 4.33 (s, 2H, CH_2), 6.88 (d, J = 8.5 Hz, 2H, H-3, H-5 Ar), 7.16–7.30 (m, 5H, Bn), 7.70–7.81 (m, 3H, =CH, H-2, H-6 Ar); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 42.0, 47.2, 55.6, 73.1, 74.6, 109.4, 113.9, 127.6, 127.9, 128.4, 131.5, 133.6, 137.8, 156.2, 163.2, 193.9, 195.0. Anal. Calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.06; H, 6.57; N, 4.19.

4-(Benzyloxy)-2-((dimethylamino)methylene)-1-*p*-tolylbutane-1,3-dione (4c).

Yield 94% (3.17 g), light yellow powder, mp 65–67 °C. IR (ATR): 3060, 3028, 2923, 2834, 1659, 1557, 1370, 1112, 954, 736 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.88 (s, 3H, Me), 2.49–3.43 (br m, 6H, 2Me), 4.01 (s, 2H, CH_2), 4.31 (s, 2H, CH_2), 7.17–7.29 (m, 7H, Bn, Ar), 7.68 (d, J = 7.9 Hz, 2H, H-2, H-6 Ar), 7.74 (s, 1H, =CH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 21.6, 42.0, 47.4, 72.9, 74.5, 109.4, 127.5, 127.7, 128.2, 129.2, 137.5, 138.0, 143.0, 156.7, 194.4, 195.2. Anal. Calcd for $C_{21}H_{23}NO_3$: C, 74.75; H, 6.87; N, 4.15. Found: C, 74.54; H, 7.05; N, 4.31.

4-(Benzyloxy)-1-(biphenyl-4-yl)-2-((dimethylamino)methylene)butane-1,3-dione (4d).

Yield 78% (3.12 g), light yellow powder, mp 47–50 °C. IR (ATR): 3061, 3030, 2925, 1657, 1574, 1448, 1120, 747 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.49–3.45 (br m, 6H, 2Me), 4.05 (s, 2H, CH_2), 4.33 (s, 2H, CH_2), 7.12–7.29 (m, 5H, Bn), 7.39 (t, J = 7.3 Hz, 1H, H-4 Ph), 7.47 (t, J = 7.5 Hz, 2H, H-3, H-5 Ph), 7.58–7.67 (m, 4H, Ph), 7.77 (s, 1H, =CH), 7.85 (d, J = 8.1 Hz, 2H, H-2, H-6 Ph); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 42.1, 47.3, 72.9, 74.6, 109.4, 127.1, 127.2, 127.5, 127.7, 128.1, 128.2, 128.9, 129.6, 137.5, 139.3, 139.9, 144.8, 156.9, 194.1, 195.4. Anal. Calcd for $C_{26}H_{25}NO_3$: C, 78.17; H, 6.31; N, 3.51. Found: C, 78.22; H, 6.60; N, 3.75.

4-(Benzyloxy)-1-(4-chlorophenyl)-2-((dimethylamino)methylene)butane-1,3-dione (4e).

Yield 95% (3.40 g), yellow powder, mp 71–74 °C. IR (ATR): 3056, 2961, 2882, 1649, 1575, 1087, 759 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.41–3.40 (br m, 6H, 2Me), 3.99 (s, 2H, CH_2), 4.30 (s, 2H, CH_2), 7.14–7.20 (m, 2H, Bn), 7.22–7.31 (m, 3H, Bn), 7.35 (d, J = 8.5 Hz, 2H, H-3, H-5 Ar), 7.69 (d, J = 8.5 Hz, 2H, H-2, H-6 Ph), 7.72 (s, 1H, =CH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 42.3, 47.5, 73.0, 74.7, 109.1, 127.7, 128.3, 128.7, 130.4, 137.3, 138.4, 139.0, 157.2, 193.1, 195.4 (1C was not observed). Anal. Calcd for $C_{20}H_{20}ClNO_3$: C, 67.13; H, 5.63; N, 3.91. Found: C, 66.96; H, 5.77; N, 3.77.

4-(Benzyloxy)-2-((dimethylamino)methylene)-1-(naphthalen-2-yl)butane-1,3-dione (4f).

Yellow 65% (2.43 g), light yellow powder, mp 74–75 °C. IR (ATR): 3055, 2924, 2838, 1630, 1557, 1310, 1099, 833 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.53–3.47 (br m, 6H, 2Me), 4.00 (s, 2H, CH_2), 4.26 (s, 2H, CH_2), 7.09–7.21 (m, 5H, Bn), 7.50–7.62 (m, 2H, Naph), 7.82 (s, 1H, =CH), 7.83–7.93 (m, 4H, Naph), 8.23 (s, 1H, H-1 Naph); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 41.8, 47.2, 73.0, 74.8, 109.6, 125.0, 126.8, 127.6, 127.8, 127.9, 128.2, 128.3, 128.7, 130.7, 132.6, 135.4, 137.5, 138.2, 157.1, 194.7, 195.8 (1C was not observed); HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{24}H_{24}NO_3$ 374.1756; Found 374.1765.

4-(Benzyloxy)-2-((dimethylamino)methylene)-1-(naphthalen-1-yl)butane-1,3-dione (4g).

Yield 80% (2.99 g), yellow powder, mp 72–75 °C. IR (ATR): 3029, 2841, 1653, 1567, 1305, 1091, 786 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.57–3.47 (br m, 6H, 2Me), 4.09 (s, 2H, CH_2), 4.29 (s, 2H, CH_2), 7.10–7.21 (m, 5H, Bn), 7.41 (dd, J = 8.1 Hz, J = 7.2 Hz, 1H, Naph), 7.43–7.54 (m, 2H, Naph), 7.57 (s, 1H, =CH), 7.61 (d, J = 6.9 Hz, 1H, Naph), 7.86 (d, J = 7.8 Hz, 1H, Naph), 7.91 (d, J = 8.2 Hz, 1H, Naph), 8.38 (d, J = 7.6 Hz, 1H, Naph); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 42.7, 48.1, 73.3, 75.5, 112.4, 124.6, 126.2, 126.6, 127.6, 127.7, 127.9, 128.1, 128.4, 130.8, 131.4, 134.1, 137.7, 138.9, 159.3, 194.9, 197.3 (1C was not observed); HRMS

(ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{24}H_{24}NO_3$ 374.1756; Found 374.1761.

4-(Benzyloxy)-2-((dimethylamino)methylene)-1-(thiophen-2-yl)butane-1,3-dione (4h).

Yield 84% (2.62 g), yellow powder, mp 73–77 °C. IR (ATR): 3106, 3093, 2927, 2839, 1652, 1601, 1563, 1422, 1106, 726 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.59–3.41 (br m, 6H, 2Me), 4.15 (s, 2H, CH_2), 4.39 (s, 2H, CH_2), 7.06 (dd, 1H, J = 4.9 Hz, J = 3.8 Hz, H-4 Th), 7.20–7.39 (m, 5H, Bn), 7.48 (dd, J = 3.8 Hz, J = 1.1 Hz, 1H, H-3 Th), 7.60 (dd, J = 4.9 Hz, J = 1.1 Hz, 1H, H-5 Th), 7.73 (s, 1H, =CH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 73.1, 74.3, 109.3, 127.5, 127.7, 127.9, 128.2, 128.6, 132.6, 133.4, 137.6, 147.5, 155.8, 186.7, 194.5. Anal. Calcd for $C_{18}H_{19}NO_3S$: C, 65.63; H, 5.81; N, 4.25. Found: C, 65.73; H, 6.09; N, 4.47.

2-((Dimethylamino)methylene)-4-phenoxy-1-phenylbutane-1,3-dione (4i).

Yield 85% (2.62 g), light yellow powder, mp 113–115 °C. IR (ATR): 3060, 2975, 2929, 1650, 1587, 1492, 1319, 1204, 983, 800, 689 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.66 (br s, 3H, Me), 3.24 (br s, 3H, Me), 4.55 (s, 2H, CH_2), 6.70 (d, J = 8.0 Hz, 2H, H-2, H-6 Ph), 6.89 (t, J = 7.5 Hz, 1H, H-4 Ph), 7.18 (t, J = 7.6 Hz, 2H, H-3, H-5 Ph), 7.39 (t, J = 7.6 Hz, 2H, H-3, H-5 Ph), 7.49 (t, J = 7.3 Hz, 1H, H-4 Ph), 7.72–7.81 (3H, m, Ph, =CH). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 42.3, 47.6, 71.8, 114.4, 121.1, 128.5, 129.0, 129.26, 129.3, 132.3, 140.6, 157.8, 193.7, 194.6 (1C was not observed); HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{20}NO_3$ 310.1443; Found 310.1447.

2-((Dimethylamino)methylene)-4-phenoxy-1-(thiophen-2-yl)butane-1,3-dione (4j).

Yield 83% (2.61 g), yellow crystals, mp 81–83 °C. IR (ATR): 3079, 2925, 1657, 1574, 1494, 1412, 1270, 1175, 944, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.71 (br s, 3H, Me), 3.22 (br s, 3H, Me), 4.68 (s, 2H, CH_2), 6.75 (dd, J = 8.7 Hz, J = 0.9 Hz, 2H, H-2, H-6 Ph), 6.90 (tt, J = 7.3 Hz, J = 0.9 Hz, 1H, H-4 Ph), 7.05 (dd, J = 4.9 Hz, J = 3.8 Hz, 1H, H-4 Th), 7.16–7.22 (m, 2H, H-3, H-5 Ph), 7.45 (dd, J = 3.8 Hz, J = 1.1 Hz, 1H, H-3 Th), 7.60 (dd, J = 4.9 Hz, J = 1.1 Hz, 1H, H-5 Th), 7.79 (s, 1H, =CH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 41.4, 47.8, 71.5, 108.9, 114.4, 121.0, 127.9, 129.3, 132.6, 133.6, 147.4, 156.3, 157.9, 186.7, 192.7. Anal. Calcd for $C_{17}H_{17}NO_3S$: C, 64.74; H, 5.43; N, 4.44. Found: C, 64.85; H, 5.40; N, 4.43.

2-((Dimethylamino)methylene)-4-methoxy-1-phenylbutane-1,3-dione (4k).

Yield 81% (2.00 g), yellow liquid. IR (ATR): 3060, 2972, 2821, 1658, 1568, 1369, 1116, 803 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.49–2.81 (br s, 3H, Me), 3.15 (s, 3H, MeO), 3.17–3.36 (br s, 3H, Me), 3.94 (s, 2H, CH_2), 7.44 (t, 2H, J = 7.5 Hz, H-3, H-5 Ph), 7.52 (tt, J = 7.4 Hz, J = 1.0 Hz, 1H, H-3, H-5 Ph), 7.76 (s, 1H, =CH), 7.79 (d, J = 7.4 Hz, H-2, H-6 Ph); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 42.0, 47.4, 58.6, 74.2, 109.1, 127.09, 128.5, 128.9, 132.2, 157.0, 194.5, 195.4; HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{14}H_{18}NO_3$ 248.1281; Found 248.1285.

4-(Benzyloxy)-2-((dimethylamino)methylene)-1-(3-methoxyphenyl)butane-1,3-dione (4l).

Yield 40% (1.41 g), light yellow powder, mp 46–48 °C. IR (ATR): 3005, 2920, 1655, 1554, 1421, 1261, 1120, 767 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.55–2.80 (br s, 3H, Me), 3.11–3.36 (br s, 3H, Me), 3.75 (s, 3H, MeO), 4.02 (s, 2H, CH_2), 4.29 (s, 2H, CH_2), 7.04 (ddd, J = 7.7 Hz, J = 2.7 Hz, J = 1.5 Hz, 1H, Ph), 7.18–7.34 (m, 8H, Bn, Ar), 7.78 (s, 1H, =CH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 42.1, 47.6, 55.3, 72.9, 74.7, 109.5, 112.7, 119.0, 121.9, 127.5, 127.6, 128.2, 129.4, 137.6, 142.0, 157.0, 159.8, 194.3, 195.3. Anal. Calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.55; H, 6.72; N, 4.01.

2-((Dimethylamino)methylene)-1-(3-methoxyphenyl)butane-1,3-dione (8c).

Yield 90% (2.23 g), yellow powder, mp 57–59 °C. IR (ATR): 3030, 2973, 2930, 1647, 1584, 1480, 1281, 940, 868 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.04 (s, 3H, Me), 2.37–3.48 (br s, 6H, NMe_2), 3.86 (s, 3H, MeO), 7.09 (ddd, J = 8.0 Hz, J = 2.6 Hz, J = 1.5 Hz, 1H, Ar), 7.32–7.43 (m, 3H, Ar), 7.86 (s, 1H, =CH). Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 67.83; H, 6.91; N, 5.46.

2-((Dimethylamino)methylene)-1-(2-methoxyphenyl)butane-1,3-dione (8d).

Yield 86% (2.13 g), yellow powder, mp 70–72 °C. IR (ATR): 3067, 2927, 2840, 1643, 1581, 1387, 1107, 925, 747 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.10 (s, 3H, Me), 2.70–3.33 (br s, 6H, NMe_2), 3.84 (s, 3H, MeO), 6.94 (d, J = 8.4 Hz, 1H, H-3 Ar), 7.00 (td, J = 7.6 Hz, J = 0.7 Hz, 1H, H-5 Ar), 7.43 (ddd, J = 8.4 Hz, J = 7.6 Hz, J = 1.7 Hz, 1H, H-4 Ar), 7.49 (dd, J = 7.5 Hz, J = 1.7 Hz, 1H, H-6 Ar), 7.79 (s, 1H, =CH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 29.8, 44.9 (br s, $\underline{Me}_2N$), 55.7, 111.5, 115.0, 120.6, 130.2, 131.5, 132.1, 157.3, 158.3, 192.6, 197.1. Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 67.78; H, 6.95; N, 5.53.

2-((Dimethylamino)methylene)-1-phenylpentane-1,3-dione (8j).

Yield 88% (2.04 g), yellow powder, mp 82–83 °C. IR (ATR): 2924, 1648, 1575, 1369, 1122, 782 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 0.98 (t, J = 7.4 Hz, 3H, Me), 2.31 (q, J = 7.4 Hz, 2H, CH_2), 2.45–3.35 (br s, 6H, NMe_2), 7.45 (dd, J = 7.8 Hz, J = 7.2 Hz, 2H, H-3, H-5 Ph), 7.54 (tt, J = 7.4 Hz, J = 1.6 Hz, 1H, H-4 Ph), 7.83 (d, J = 7.8 Hz, 2H, H-2, H-6 Ph), 7.86 (s, 1H, =CH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 9.5, 34.2, 44.4 (br s, $\underline{Me}_2N$), 111.2, 128.6, 129.2, 132.4, 140.7, 155.6, 196.2, 198.7. Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.77; H, 7.34; N, 6.01.

2-((Dimethylamino)methylene)-1-(thiophen-2-yl)pentane-1,3-dione (8k).

Yield 77% (1.83 g), yellow powder, mp 59–60 °C. IR (ATR): 2973, 2923, 2807, 1634, 1571, 1516, 1406, 1350, 1189, 858 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 1.04 (t, J = 7.4 Hz, 3H, Me), 2.42 (q, J = 7.4 Hz, 2H, CH_2), 2.51–3.44 (br s, 6H, NMe_2), 7.11 (dd, J = 4.8 Hz, J = 3.8 Hz, 1H, H-4 Th), 7.54 (dd, J = 3.8 Hz, J = 0.8 Hz, 1H, H-3 Th), 7.66 (dd, J = 4.8 Hz, J = 0.8 Hz, 1H, H-5 Th), 7.75 (s, 1H, =CH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 9.6, 33.5, 42.4, 46.1, 110.9, 128.1, 133.2, 133.9, 147.7, 154.0, 188.6, 197.6. Anal. Calcd for $C_{12}H_{15}NO_2S$: C, 60.73; H, 6.37; N, 5.90. Found: C, 60.81; H, 6.39; N, 6.11.

General method for the preparation of diacyl-substituted catechols 6.

A mixture of the corresponding enaminodione **4** (0.607 mmol), $Si(OEt)_4$ (63.1 mg, 0.303 mmol), and LiH (5.8 mg, 0.729 mmol) was refluxed in 1,2-dimethoxyethane (1 mL) for 5 h using a reflux condenser equipped with a calcium chloride drying tube. After that, (in the case of enaminodiones **4b–e**) lithium salt of phenols **6b–e** formed as a solid, was filtered off, and washed with cold toluene. Then the salt was quenched with HCl (1 : 2) (2 mL) at 0 ºC and stirred for 30 min. The precipitate was filtered off and recrystallized from EtOH. In the case of enaminodiones **4a,f–k**, the reaction mixture was quenched with HCl (1 : 2) to pH = 2 at 0 ºC and stirred for 30 min. The reaction mixture was diluted with H_2O (3 mL), and the product was extracted with EtOAc (3 × 5 mL). The combined extracts were washed with water (5 mL) and brine (5 mL). The organic phase was dried with anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was diluted with EtOH (2 mL) and maintained at –20 ºC for 24 h. The precipitate that formed was filtered off.

(5-(Benzyloxy)-4-hydroxy-1,3-phenylene)bis(phenylmethanone) (6a).

Yield 71% (88 mg), yellow powder, mp 137–138 °C. IR (ATR): 3033, 1645, 1622, 1594, 1572, 1278, 713 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 5.27 (s, 2H, CH_2), 7.30–7.44 (m, 5H, Ph), 7.44–7.51 (m, 4H, Ph), 7.54 (tt, J = 7.5 Hz, J = 1.1 Hz, 1H, H-4 Ph), 7.57 (tt, J = 7.5 Hz, J = 1.1 Hz, 1H, H-4 Ph), 7.63–7.67 (м, 1H, H-6 Ar), 7.65 (dd, J = 8.7 Hz, J = 1.3 Hz, 2H, H-2, H-6 Ph), 7.70 (dd, J = 8.3 Hz, J = 1.3 Hz, 2H, H-2, H-6 Ph), 7.76 (d, J = 2.0 Hz, 1H, H-2 Ar), 12.68 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 71.5, 118.8, 120.0, 127.6, 127.7, 128.35, 128.39, 128.6, 128.9, 129.2, 129.4, 129.7, 132.3, 132.7, 136.3, 137.3, 137.5, 147.9, 158.0, 194.4, 201.4; HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{27}H_{21}O_4$ 409.1440; Found 409.1432.

(5-(Benzyloxy)-4-hydroxy-1,3-phenylene)bis((4-methoxyphenyl)methanone) (6b).

Yield 56% (80 mg), yellow powder, mp 158–160 °C. IR (ATR): 3065, 3033, 2929, 2839, 1646, 1625, 1599, 1256, 1168, 847, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 3.88 (s, 6H, 2Me), 5.26 (s, 2H, CH_2), 6.90 (d, J = 8.9 Hz, 2H, H-3, H-5 Ar), 6.96 (d, J = 8.9 Hz, 2H, H-3, H-5 Ar), 7.31–7.37 (m, 1H, H-4 Bn), 7.40 (t, J = 7.5 Hz, 2H, H-3, H-5 Bn), 7.47 (d, J = 7.6 Hz, 2H, H-2, H-6 Bn), 7.57 (d, J = 1.8 Hz, 1H, H-6 Ar), 7.67 (d, J = 8.9 Hz, 2H, H-2, H-6 Ar), 7.74 (d, J = 8.9 Hz, 2H, H-2, H-6 Ar), 7.74–7.77 (m, 1H, H-2 Ar), 12.47 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6, ppm) δ 55.5, 55.6, 70.2, 113.8, 113.9, 116.3, 124.5, 125.3, 127.6, 127.9, 128.2, 128.4, 129.59, 129.62, 131.8, 131.9, 136.5, 146.6, 150.1, 162.5, 163.3, 192.4, 194.4; HRMS (ESI/Q-TOF) m/z: $[M+Na]^+$ Calcd for $C_{29}H_{24}NaO_6$ 491.1471; Found 491.1452.

(5-(Benzyloxy)-4-hydroxy-1,3-phenylene)bis(p-tolylmethanone) (6c).

Yield 66% (87 mg), light yellow powder, mp 175–176 °C. IR (ATR): 3066, 2923, 1649, 1626, 1604, 1498, 1275, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.43 (s, 6H, 2Me), 5.25 (s, 2H, CH_2), 7.22 (d, J = 7.9 Hz, 2H, H-3, H-5 Ar), 7.28 (d, J = 7.9 Hz, 2H, H-3, H-5 Ar), 7.32–7.43 (m, 3H, Bn), 7.47 (d, J = 7.1 Hz, 2H, H-2, H-6 Bn), 7.58 (d, J = 7.9 Hz, 2H, H-2, H-6 Ar), 7.60–7.62 (m, 1H, H-6 Ar), 7.63 (d, J = 7.9 Hz, 2H, H-2, H-6 Ar), 7.77 (d, J = 1.9 Hz, 1H, H-2 Ar), 12.64 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6, ppm) δ 21.1, 21.2, 70.2, 116.4, 124.9, 127.5, 127.6, 127.8, 127.9, 128.2, 128.4, 128.9, 129.2, 129.5, 134.3, 134.6, 136.5, 142.5, 143.7, 146.7, 150.7, 193.3, 195.7. Anal. Calcd for $C_{29}H_{24}O_4$: C, 79.80; H, 5.54. Found: C, 79.57; H, 5.51.

(5-(Benzyloxy)-4-hydroxy-1,3-phenylene)bis(biphenyl-4-ylmethanone) (6d).

Yield 63% (107 mg), light yellow powder, mp 193–195 °C. IR (ATR): 3056, 3031, 1649, 1618, 1602, 1302, 1277, 745, 694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 5.29 (s, 2H, CH_2), 7.32–7.52 (m, 11H, 3Ph), 7.58 (ddd, J = 7.8 Hz, J = 7.2 Hz, J = 1.1 Hz, 4H, H-3, H-5 2Ph), 7.64 (d, J = 8.3 Hz, 2H, H-3, H-5 Ar), 7.69 (d, J = 8.3 Hz, 2H, H-3, H-5 Ar), 7.70 (d, J = 1.8 Hz, 1H, H-6 Ar), 7.74 (d, J = 8.3 Hz, 2H, H-2, H-6 Ar), 7.80 (d, J = 8.3 Hz, 2H, H-2, H-6 Ar), 7.84 (d, J = 1.8 Hz, 1H, H-2 Ar), 12.55 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6, ppm) δ 70.4, 116.4, 124.8, 126.0, 126.8, 126.9, 127.0, 127.6, 127.7, 127.9, 128.4, 129.1, 130.07, 130.11, 135.8, 136.1, 136.5, 138.8, 138.9, 143.6, 144.6, 146.9, 151.1, 193.2, 195.7 (4C were not observed); HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{39}H_{29}O_4$ 561.2066; Found 561.2042.

(5-(Benzyloxy)-4-hydroxy-1,3-phenylene)bis((4-chlorophenyl)methanone) (6e).

Yield 57% (83 mg), yellow powder, mp 133–135 °C. IR (ATR): 3036, 2962, 1646, 1617, 1584, 1296, 840, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 5.26 (s, 2H, CH_2), 7.33–7.45 (m, 7H, Ph, Ar), 7.47 (d, J = 8.5 Hz, 2H, H-3, H-5 Ar), 7.54–7.56 (m, 1H, H-6 Ar), 7.56 (d, J = 8.6 Hz, 2H, H-2, H-6 Ar), 7.65 (d, J = 8.5 Hz, 2H, H-2, H-6 Ar), 7.68 (d, J = 1.9 Hz, 1H, H-2 Ar), 12.36 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6, ppm) δ 70.3, 116.5, 124.9, 125.1, 127.4, 127.6, 127.9, 128.4, 128.6, 128.7, 131.1, 131.2, 135.7, 136.0, 136.4, 137.1, 138.1, 146.9, 150.8, 192.6, 194.6; HRMS (ESI/Q-TOF)

m/z: $[M+H]^+$ Calcd for $C_{27}H_{19}Cl_2O_4$ 477.0660; Found 477.0670.

(5-(Benzyloxy)-4-hydroxy-1,3-phenylene)bis(naphthalen-2-ylmethanone) (6f).

Yield 63% (97 mg), yellow powder, mp 166–168 °C. IR (ATR): 3058, 2963, 1650, 1623, 1591, 1259, 1016, 793 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 5.29 (s, 2H, CH_2), 7.32–7.43 (m, 3H, Bn), 7.47–7.62 (m, 6H, Bn, Naph), 7.75–7.91 (m, 10H, Ar, Naph), 8.18 (d, J = 1.0 Hz, 1H, H-1 Naph), 8.22 (d, J = 1.0 Hz, 1H, H-1 Naph), 12.68 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 71.5, 119.0, 119.8, 125.2, 125.7, 127.0, 127.2, 127.7, 128.0, 128.2, 128.40, 128.43, 128.49, 128.7, 128.9, 129.1, 129.5, 131.0, 131.2, 132.27, 132.34, 134.6, 134.9, 135.2, 136.3, 148.2, 157.9, 194.7, 201.2 (3C were not observed). Anal. Calcd for $C_{35}H_{24}O_4$: C, 82.66; H, 4.76. Found: C, 82.87; H, 4.83.

(5-(Benzyloxy)-4-hydroxy-1,3-phenylene)bis(naphthalen-1-ylmethanone) (6g).

Yield 49% (76 mg), yellow powder, mp 104–106 °C. IR (ATR): 1629, 1578, 1456, 1280, 1027, 959 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 5.26 (s, 2H, CH_2), 7.32–7.43 (m, 21H, 2Naph, Ar, Bn), 13.22 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 71.4, 119.3, 119.5, 124.1, 125.1, 125.5, 126.4, 126.6, 127.05, 127.07, 127.3, 127.4, 127.6, 128.1, 128.3, 128.4, 128.5, 128.8, 130.2, 130.5, 130.7, 131.0, 131.6, 133.6, 134.3, 135.5, 136.0, 148.3, 158.9, 195.3, 203.4 (2C were not observed). Anal. Calcd for $C_{35}H_{24}O_4$: C, 82.66; H, 4.76. Found: C, 82.53; H, 4.61.

(5-(Benzyloxy)-4-hydroxy-1,3-phenylene)bis(thiophen-2-ylmethanone) (6h).

Yield 73% (103 mg), yellow powder, mp 133–135 °C. IR (ATR): 3100, 3080, 1615, 1585, 1408, 1301, 1251, 728 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 5.29 (s, 2H, CH_2), 7.09 (dd, J = 4.9 Hz, J = 3.8 Hz, 1H, H-4 Th), 7.19 (dd, J = 4.9 Hz, J = 3.8 Hz, 1H, H-4 Th), 7.32–7.44 (m, 4H, Bn, Th), 7.48 (d, J = 7.0 Hz, 2H, H-2, H-6 Bn), 7.66 (d, J = 1.9 Hz, 1H, H-6 Ar), 7.69 (dd, J = 4.9 Hz, J = 1.0 Hz, 1H, H-5 Th), 7.77 (dd, J = 4.9 Hz, J = 1.0 Hz, 1H, H-5 Th), 7.80 (dd, J = 3.8 Hz, J = 1.0 Hz, 1H, H-3 Th), 8.21 (d, J = 1.9 Hz, 1H, H-2 Ar), 12.19 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 71.3, 119.3, 125.9, 127.5, 128.0, 128.3, 128.4, 128.5, 128.8, 134.0, 134.1, 134.9, 135.2, 136.2, 141.7, 143.0, 147.7, 156.9, 185.8, 190.7 (1C were not observed). Anal. Calcd for $C_{27}H_{24}O_4S_2$: C, 68.04; H, 5.08. Found: C, 68.40; H, 4.95.

(5-(Phenoxy)-4-hydroxy-1,3-phenylene)bis(phenylmethanone) (6i).

Yield 46% (55 mg), yellow powder, mp 163–165 °C. IR (ATR): 3062, 2960, 1631, 1573, 1287, 1120, 1021, 879, 694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.05 (d, J = 8.0 Hz, 2H, H-2, H-6 Ph), 7.12 (t, J = 7.4 Hz, 1H, H-4 Ph), 7.36 (t, J = 8.0 Hz, 2H, H-3, H-5 Ph), 7.44 (t, J = 7.7 Hz, 2H, H-3, H-5 Ph), 7.51 (t, J = 7.7 Hz, 2H, H-3, H-5 Ph), 7.55 (tt, J = 7.5 Hz, J = 1.1 Hz, 1H, H-4 Ph), 7.61 (tt, J = 7.5 Hz, J = 1.0 Hz, 1H, H-4 Ph), 7.70–7.75 (m, 4H, 2Ph), 7.75 (d, J = 1.9 Hz, 1H, H-6 Ph), 7.99 (d, J = 1.9 Hz, 1H, H-2 Ph), 12.65 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 117.6, 119.7, 123.6, 127.3, 128.0, 128.4, 128.6, 129.4, 129.7, 129.9, 131.7, 132.5, 132.8, 137.1, 146.3, 157.0, 159.0, 193.9, 201.2 (1C was not observed); HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{26}H_{19}O_4$ 395.1283; Found 395.1268.

(5-(Phenoxy)-4-hydroxy-1,3-phenylene)bis(thiophen-2-ylmethanone) (6j).

Yield 52% (64 mg), yellow powder, mp 120–122 °C. IR (ATR): 3081, 2675, 1615, 1582, 1488, 1410, 1281, 1106, 864 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 7.06 (d, J = 8.0 Hz, 2H, H-2, H-6 Ph), 7.13 (t, J = 7.2 Hz, 1H, H-4 Ph), 7.15 (t, J = 4.3 Hz, 1H, H-4 Th), 7.23 (t, J = 4.5 Hz, 1H, H-4 Th), 7.36 (t, J = 7.9 Hz, 2H, H-3, H-5 Ph), 7.64 (d, J = 3.5 Hz, 1H, H-3 Th), 7.71 (d, J = 4.8 Hz, 1H, H-5 Th), 7.80 (d, J = 1.6 Hz, 1H, H-4 Ph), 7.81 (d, J = 4.9 Hz, 1H, H-5 Th), 7.86 (d, J = 3.5 Hz, 1H, H-3 Th), 8.42 (d, J = 1.6 Hz, 1H, H-2 Ph), 12.19 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 117.7, 120.4, 123.6, 126.3, 128.1, 128.5, 128.6, 128.9, 129.9, 134.2, 134.3, 135.3, 141.5, 142.8, 146.4, 156.9, 158.0, 185.3, 190.5. Anal. Calcd for $C_{22}H_{14}O_4S_2$: C, 65.01; H, 3.47. Found: C, 65.04; H, 3.50.

(5-(Methoxy)-4-hydroxy-1,3-phenylene)bis(phenylmethanone) (6k).

Yield 29% (29 mg), grey powder, mp 140–142 °C. IR (ATR): 3068, 2980, 2933, 1654, 1622, 1597, 1448, 1305, 1273, 1128, 978, 724 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 4.02 (s, 3H, Me), 7.42–7.50 (m, 4H, Ph), 7.53–7.61 (m, 2H, Ph), 7.67–7.72 (m, 4H, Ph), 7.72–7.77 (m, 2H, Ph), 12.74 (s, 1H, OH). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 55.5, 115.8, 117.0, 126.6, 127.3, 127.4, 127.8, 128.3, 128.6, 131.3, 131.6, 136.1, 136.5, 148.3, 156.4, 193.6, 200.3; HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{21}H_{17}O_4$ 333.1127; Found 333.1129.

General method for the preparation of diacyl-substituted phenoles 9.

A mixture of the corresponding enaminodione **8** (1.214 mmol), $Si(OEt)_4$ (126.5 mg, 0.607 mmol), and LiH (11.6 mg, 1.458 mmol) was refluxed in 1,2-dimethoxyethane (2 mL) for 5 h or dioxane (2 mL) (for enaminodiones **8e,f,h,j,k**) for 8 h using a reflux condenser equipped with a calcium chloride drying tube. After that (in the case of enaminodiones **8b,d,e,h,i,l**), the reaction mixture was quenched with HCl (1 : 2) to pH = 2 at 0 ºC and stirred for 30 min. The precipitate was filtered and recrystallized from EtOH or aq. EtOH (for **9l**). If the participate did not form (in the case of enaminodiones **8a,c,f,g,j,k**) after the acidification, the reaction mixture was diluted with H_2O (6 mL) and the product was extracted with EtOAc (3 × 10 mL). The combined extracts were washed with water (10 mL) and brine (10 mL). The organic phase was dried with anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was diluted with EtOH (2 mL) and

maintained at –20 ºC for 24 h. The precipitate that formed was filtered off.

(4-Hydroxy-1,3-phenylene)bis(phenylmethanone) (9a).

Yield 62% (114 mg), grey solid, mp 91–92 °C (lit.[19] mp 101 °C). IR (ATR): 3055, 2966, 1621, 1477, 1339, 1250, 987, 795, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.16 (d, J = 8.7 Hz, 1H, H-5 Ph), 7.44–7.53 (m, 4H, Ph), 7.54–7.63 (m, 2H, Ph), 7.69–7.77 (m, 4H, Ph), 8.02 (dd, J = 8.7 Hz, J = 2.2 Hz, 1H, H-6 Ph), 8.20 (d, J = 2.2 Hz, 1H, H-2 Ph), 12.49 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, ppm) δ 118.5, 128.3, 128.4, 128.5, 129.3, 129.6, 132.3, 132.6, 136.6, 137.0, 137.4, 137.8, 166.6, 194.4, 201.3 (1C was not observed); HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{15}O_3$ 303.1021; Found 303.1019.

(4-Hydroxy-1,3-phenylene)bis((4-methoxyphenyl)methanone) (9b).

Yield 91% (200 mg), yellow powder, mp 108–110 °C. IR (ATR): 3000, 2838, 1646, 1598, 1506, 1246, 1026, 765 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 3.89 (s, 6H, Me), 6.96 (d, J = 8.8 Hz, 2H, H-3, H-5 Ar), 6.99 (d, J = 8.8 Hz, 2H, H-3, H-5 Ar), 7.13 (d, J = 8.7 Hz, 1H, H-5 Ar), 7.75 (d, J = 8.8 Hz, 2H, H-2, H-6 Ar), 7.78 (d, J = 8.8 Hz, 2H, H-2, H-6 Ar), 7.95 (dd, J = 8.7 Hz, J = 2.1 Hz, 1H, H-6 Ar), 8.18 (d, J = 2.1 Hz, 1H, H-2 Ar), 12.38 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 55.5, 55.6, 113.7, 113.9, 118.2, 118.8, 128.9, 129.7, 130.1, 132.0, 132.2, 135.8, 137.2, 163.2, 163.4, 166.0, 193.5, 199.6. Anal. Calcd for $C_{22}H_{18}O_5$: C, 72.92; H, 5.01. Found: C, 72.64; H, 5.07.

(4-Hydroxy-1,3-phenylene)bis((3-methoxyphenyl)methanone) (9c).

Yield 94% (207 mg), yellow liquid. IR (ATR): 3068, 2936, 2834, 1716, 1623, 1576, 1425, 1256, 1039, 882 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 3.85 (s, 3H, MeO), 3.86 (s, 3H, MeO), 7.08–7.14 (m, 2H, Ar), 7.15 (d, J = 8.7 Hz, 1H, H-5 Ar), 7.23–7.31 (m, 4H, Ar), 7.33–7.43 (m, 2H, Ar), 8.03 (dd, J = 8.7 Hz, J = 2.2 Hz, 1H, H-6 Ar), 8.22 (d, J = 2.2 Hz, 1H, H-2 Ar), 12.45 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 55.4, 55.5, 114.1, 114.2, 118.4, 118.5, 118.6, 118.7, 121.8, 122.2, 128.4, 129.3, 129.5, 136.7, 137.8, 138.3, 138.8, 159.6, 159.7, 166.7, 194.2, 201.1; HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{19}O_5$ 363.1232; Found 363.1231.

(4-Hydroxy-1,3-phenylene)bis((2-methoxyphenyl)methanone) (9d).

Yield 82% (180 mg), brown powder, mp 81–83 °C. IR (ATR): 3063, 3011, 2965, 1656, 1624, 1596, 1429, 1014, 907, 769 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 3.63 (s, 3H, MeO), 3.69 (s, 3H, MeO), 6.89 (d, J = 8.4 Hz, 1H, Ar), 6.94 (d, J = 8.4 Hz, 1H, Ar), 6.99 (td, J = 7.5 Hz, J = 0.6 Hz, 1H, Ar), 7.02–7.07 (m, 2H, Ar), 7.25–7.32 (m, 2H, Ar), 7.41 (ddd, J = 8.3 Hz, J = 7.5 Hz, J = 1.7 Hz, 1H, Ar), 7.47 (ddd, J = 8.3 Hz, J = 7.5 Hz, J = 1.7 Hz, 1H, Ar), 7.91 (dd, J = 8.7 Hz, J = 2.2 Hz, 1H, H-6 Ar), 7.94 (d, J = 2.1 Hz, 1H, H-2 Ar), 12.67 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 55.4, 55.5, 111.3, 111.6, 180.0, 119.4, 120.6, 120.7, 127.0, 128.5, 128.9, 129.1, 129.3, 131.8, 132.5, 137.2, 137.7, 156.6, 156.9, 166.6, 194.0, 202.0; HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{19}O_5$ 363.1232; Found 363.1229.

(4-Hydroxy-1,3-phenylene)bis(*p*-tolylmethanone) (9e).

Yield 80% (160 mg), yellow powder, mp 80–82 °C. IR (ATR): 3325, 2924, 1648, 1627, 1600, 1560, 1155, 914, 790 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.43 (s, 3H, Me), 2.44 (s, 3H, Me), 7.13 (d, J = 8.7 Hz, 1H, H-5 Ar), 7.24–7.33 (m, 4H, Ar); 7.63 (d, J = 8.2 Hz, 2H, H-2, H-6 Ar), 7.67 (d, J = 8.2 Hz, 2H, H-2, H-6 Ar), 7.97 (dd, J = 8.7 Hz, J = 2.2 Hz, 1H, H-6 Ar), 8.20 (d, J = 2.2 Hz, 1H, H-2 Ar), 12.46 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 21.64, 21.66, 118.3, 118.7, 128.7, 129.0, 129.3, 129.6, 129.9, 134.5, 134.8, 136.3, 137.6, 143.2, 143.5, 166.4, 194.3, 201.0. Anal. Calcd for $C_{22}H_{18}O_3$: C, 79.98; H, 5.49. Found: C, 79.62; H, 5.49.

(4-Hydroxy-1,3-phenylene)bis((4-chlorophenyl)methanone) (9f).

Yield 51% (114 mg), brown powder, mp 92–94 °C. IR (ATR): 3300, 1647, 1627, 1584, 1276, 1090, 777 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.16 (d, J = 8.7 Hz, 1H, H-5 Ph), 7.46 (d, J = 8.5 Hz, 2H, H-3, H-5 Ar), 7.50 (d, J = 8.5 Hz, 2H, H-3, H-5 Ar), 7.66 (d, J = 8.5 Hz, 2H, H-2, H-6 Ar), 7.69 (d, J = 8.5 Hz, 2H, H-2, H-6 Ar), 7.96 (dd, J = 8.7 Hz, J = 2.1 Hz, 1H, H-6 Ar), 8.13 (d, J = 2.1 Hz, 1H, H-2 Ar), 12.32 (s, 1H, OH). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 118.5, 118.7, 128.2, 128.8, 129.0, 130.7, 131.1, 135.3, 135.6, 135.9, 137.8, 139.0, 139.3, 166.6, 193.1, 199.9. Anal. Calcd for $C_{20}H_{12}Cl_2O_3$: C, 64.71; H, 3.26. Found: C, 64.82; H, 3.41.

(4-Hydroxy-1,3-phenylene)bis((4-nitrophenyl)methanone) (9g).

Yield 53% (252 mg), brown powder, mp 131–133 °C. IR (ATR): 3106, 1630, 1514, 1343, 1103, 850 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 7.22 (d, J = 8.6 Hz, 1H, H-5 Ar), 7.91 (s, 1H, H-2 Ar), 7.95–8.08 (m, 6H, Ar), 8.34–8.52 (m, 3H, Ar), 12.25 (s, 1H, OH); ^1H NMR (400 MHz, DMSO-d_6, ppm) δ 7.22 (d, J = 8.7 Hz, 1H, H-5 Ar), 7.63–8.54 (m, 10H, Ar), 11.48 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6, ppm) δ 117.1, 123.6, 123.7, 124.9, 127.2, 130.3, 130.4, 133.2, 135.4, 142.1, 143.0, 149.2, 149.8, 161.0, 192.5, 194.3. Anal. Calcd for $C_{20}H_{12}N_2O_7$: C, 61.23; H, 3.08; N, 7.14. Found: C, 61.05; H, 3.21; N, 6.82.

(4-Hydroxy-1,3-phenylene)bis(naphthalen-2-ylmethanone) (9h).

Yield 97% (237 mg), brown powder, mp 168–170 °C. IR (ATR): 3056, 2964, 1645, 1618, 1466, 1220, 906, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.22 (d, J = 8.7 Hz, 1H, H-5 Ar), 7.49–7.64 (m, 4H, Naph), 7.80 (dd, J = 8.5 Hz, J = 1.7 Hz, 1H, Naph), 7.83–7.95 (m, 7H, Naph), 8.10 (dd, J = 8.7 Hz, J = 2.2 Hz, 1H, H-6 Ar), 8.23 (s, 2H, H-1 2Naph), 8.32 (d, J = 2.2 Hz, 1H, H-2 Ar), 12.53 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 118.7, 118.8, 125.1, 125.6, 126.9,

127.1, 127.8, 127.9, 128.3, 128.4, 128.5, 128.6, 128.9, 129.28, 129.32, 130.8, 131.2, 132.2, 132.3, 134.4, 134.8, 135.1, 135.2, 136.6, 137.8, 166.7, 194.6, 201.2; HRMS (ESI/Q-TOF) m/z: $[M+H]^+$ Calcd for $C_{28}H_{19}O_3$ 403.1334; Found 403.1352.

(4-Hydroxy-1,3-phenylene)bis(thiophen-2-ylmethanone) (9i).

Yield 53% (102 mg), grey powder, mp 97–99 °C. IR (ATR): 1630, 1605, 1565, 1415, 1282, 1091, 862 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 7.17 (d, J = 8.6 Hz, 1H, H-5 Ar), 7.19 (dd, J = 5.0 Hz, J = 3.8 Hz, 1H, H-4 Th), 7.21 (dd, J = 5.0 Hz, J = 3.8 Hz, 1H, H-4 Th), 7.67 (dd, J = 3.8 Hz, J = 1.1 Hz, 1H, H-3 Th), 7.73 (dd, J = 5.0 Hz, J = 1.1 Hz, 1H, H-5 Th), 7.79 (dd, J = 5.0 Hz, J = 1.1 Hz, 1H, H-5 Th), 7.82 (dd, J = 3.8 Hz, J = 1.1 Hz, 1H, H-3 Th), 8.11 (dd, J = 8.6 Hz, J = 2.2 Hz, 1H, H-6 Ar), 8.61 (d, J = 2.2 Hz, 1H, H-2 Ar), 12.08 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 118.6, 119.1, 128.0, 128.4, 129.3, 133.9, 134.07, 134.11, 134.8, 135.1, 136.7, 141.5, 143.1, 165.9, 185.8, 190.7. Anal. Calcd for $C_{16}H_{10}O_3S_2$: C, 61.13; H, 3.21. Found: C, 61.04; H, 3.14.

(4-Hydroxy-5-methyl-1,3-phenylene)bis(phenylmethanone) (9j).

Yield 37% (72 mg), yellow powder, mp 86–88 °C. IR (ATR): 3061, 2918, 1650, 1669, 1598, 1444, 1278, 1183, 821 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.38 (s, 3H, CH_3), 7.43–7.51 (m, 4H, H-3, H-5, H-3′, H-5′ 2Ph), 7.53–7.61 (m, 2H, H-4, H-4′ 2Ph), 7.66–7.76 (m, 4H, H-2, H-6, H-2′, H-6′ 2Ph), 7.89–7.94 (m, 1H, H-6 Ar), 8.01 (d, J = 2.1 Hz, 1H, H-2 Ar), 12.80 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 15.7, 117.6, 127.6, 128.0, 128.3, 128.5, 129.3, 126.6, 132.2, 132.4, 134.6, 137.4, 137.7, 138.1, 165.3, 194.8, 201.6. Anal. Calcd for $C_{21}H_{16}O_3$: C, 79.73; H, 5.10. Found: C, 79.72; H, 4.88.

(4-Hydroxy-5-methyl-1,3-phenylene)bis(thiophen-2-ylmethanone) (9k).

Yield 36% (72 mg), grey powder, mp 104–105 °C. IR (ATR): 3072, 2916, 1618, 1557, 1512, 1408, 1231, 1112, 1055, 768 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.38 (s, 3H, Me), 7.16–7.22 (m, 2H, H-4, H-4′ 2Th), 7.67 (dd, J = 3.8 Hz, J = 1.0 Hz, 1H, H-3 Th), 7.72 (dd, J = 4.9 Hz, J = 1.0 Hz, 1H, H-5 Th), 7.77 (dd, J = 5.0 Hz, J = 1.0 Hz, 1H, H-5 Th), 7.79 (dd, J = 3.8 Hz, J = 1.0 Hz, 1H, H-3 Th), 7.95 (d, J = 1.9 Hz, 1H, H-6 Ar), 8.45 (d, J = 1.9 Hz, 1H, H-2 Ar), 12.38 (s, 1H, OH); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 15.8, 118.1, 128.0, 128.1, 128.3, 128.5, 131.7, 133.9, 134.0, 134.6, 135.0, 137.1, 141.7, 143.2, 164.5, 186.1, 191.1. Anal. Calcd for $C_{17}H_{12}S_2O_3$: C, 62.17; H, 3.68. Found: C, 61.94; H, 3.62.

Diethyl 4-hydroxyisophthalate (9l).

Yield 92% (134 mg), yellow powder, mp 49–51 °C. ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 1.40 (t, J = 7.1 Hz, 3H, Me), 1.45 (t, J = 7.1 Hz, 3H, Me), 4.37 (q, J = 7.1 Hz, 2H, CH_2), 4.45 (q, J = 7.1 Hz, 2H, CH_2), 7.01 (d, J = 8.7 Hz, 1H, H-5 Ar), 8.12 (dd, J = 8.7 Hz, J = 2.2 Hz, 1H, H-6 Ar), 8.56 (d, J = 2.2 Hz, 1H, H-2 Ar), 11.31 (s, 1H, OH). The analytical data are in accordance with those reported in the literature.[14]

(2*E*,4*Z*)-1-(3-Acetyl-4-hydroxyphenyl)-4-(1-hydroxyethylidene)hex-2-ene-1,5-dione (10).

A mixture of 3-((dimethylamino)methylene)pentane-2,4-dione (**8m**) (0.40 g, 2.58 mmol), $Si(OEt)_4$ (0.27 g, 1.29 mmol), and LiH (24.6 mg, 3.09 mmol) was refluxed in dioxane (2 mL) for 1 h using a reflux condenser equipped with a calcium chloride drying tube. After that, the reaction mixture was quenched with HCl (1 : 2) to pH = 2 at 0 ºC and stirred for 30 min. The reaction mixture was diluted with H_2O (6 mL), and the product was extracted with EtOAc (3 × 10 mL). The combined extracts were washed with water (10 mL) and brine (10 mL). The organic phase was dried with anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was diluted with EtOH (2 mL) and maintained at –20 ºC for 24 h. The precipitate that formed was filtered off. Yield 32% (79 mg), red powder, mp 125–128 ºC. IR (ATR): 2917, 1668, 1635, 1531, 1330, 1176, 983, 834 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.45 (s, 6H, 2Me), 7.06 (d, J = 8.7 Hz, 1H, H-5 Ar), 8.07 (dd, J = 8.7 Hz, J = 2.1 Hz, 1H, H-6 Ar), 7.09 (d, J = 15.4 Hz, 1H, CH), 7.95 (d, J = 15.4 Hz, 1H, CH), 8.48 (d, J = 2.1 Hz, 1H, H-2 Ar), 13.33 (s, 1H, OH), the OH proton was not observed due to broadening; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 25.3, 26.3, 110.4, 118.7, 119.4, 119.5, 128.5, 130.3, 136.1, 141.5, 167.2, 193.1, 195.2, 195.7. Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59. Found: C, 66.50; H, 5.59.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:
^1H and ^{13}C NMR spectra for compounds **3a–l**, **4a–l**, **6a–k**, **8c,d,j.k**, **9a–l**, **10** (PDF)

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Notes

The authors declare no competing financial interest.

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