Synthesis V. Z. Shirinian et al. Paper

Practical and Efficient Synthesis of Polyaryl(hetaryl)-Substituted Cyclohexenones and Salicylates

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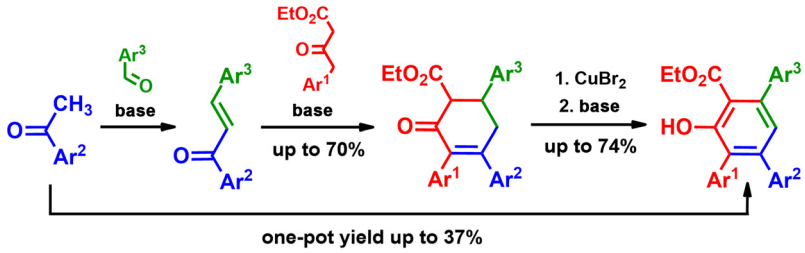

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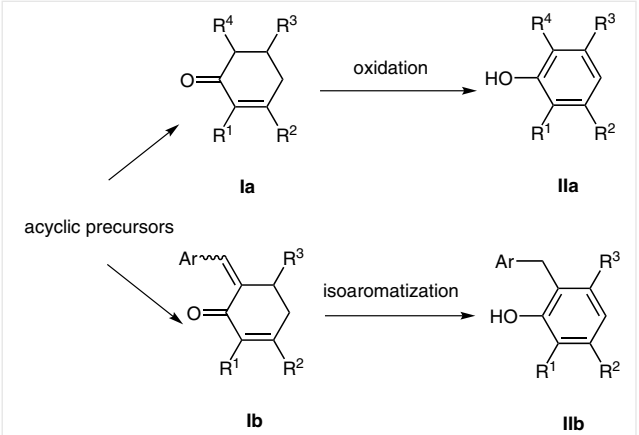
Abstract A new efficient method was developed for the synthesis of triaryl-substituted cyclohexenones and salicylates. The method is based on the Robinson annulation of readily available keto esters and chalcones, followed by the aromatization of the cyclohexenone moiety. The aromatization can be accomplished either by reaction with bromine in boiling chloroform or bromination with copper(II) bromide in ethanol followed by treatment with pyridine or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). The new synthetic method was also implemented in a one-pot protocol, which in some cases resulted in higher yields of the final product compared to those obtained in the stepwise synthesis.

Key words cyclohexenones, salicylates, polyaryl-substituted phenols, Robinson annulation, chalcones, bromination

There is an ever-growing need for new chemical products to sustain and improve our lives, e.g. medicines, polymers, dyes, food additives, etc. One approach to tackling this problem is to develop facile and efficient methods for the synthesis of these compounds from simple and readily available precursor molecules. A perfect example of this synthesis is the preparation of phenol and salicylic acid derivatives from commercially available synthons.[1] Phenol derivatives are widely used in various applications, such as medicine, agriculture, organic synthesis (fine chemicals), polymers, etc.[2] In particular, a very good example of the practical application of substituted phenols is the use of salicylates (aspirin and its analogues) as efficient analgesic and anti-inflammatory drugs.[3]

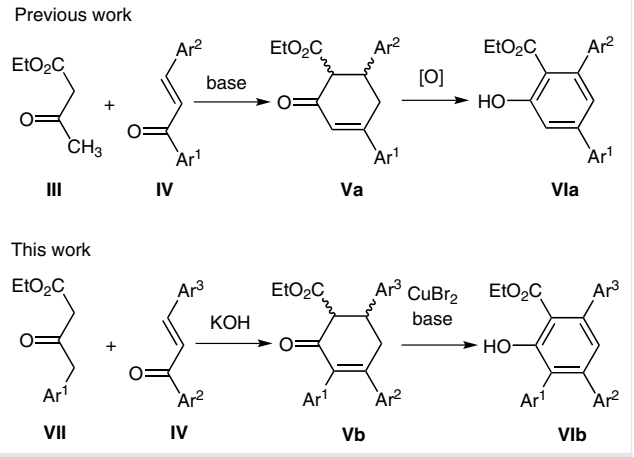
Numerous known synthetic protocols for the preparation of phenol derivatives include an approach based on the Robinson annulation followed by the aromatization of the cyclohexenone moiety. The Robinson annulation is commonly used for the assembly of the cyclohexenone ring by utilizing acetoacetic ester derivatives and various Michael acceptors as building blocks.[4] Six-membered carbocycles can also be constructed by the Claisen reaction,[5] intramolecular condensation of 1,5-dicarbonyl compounds,[6] lactone transformations,[7] and metathesis reactions.[8] The subsequent transformation of cyclohexenones **I** to phenols **II** can be performed by means of oxidation (the reaction with bromine followed by the elimination of hydrogen bromide,[4a,d] oxidation with various reagents[7,9]) or isoaromatization of benzylidene derivatives (Scheme 1).[8,10]



Scheme 1 Synthesis of phenols **II** from polysubstituted cyclohexenones **I**

The conventional method for the synthesis of cyclohexenones **Va** involves the Robinson annulation of readily available acetoacetic ester **III**[4a–d] (or its derivatives[11]) and chalcones **IV** followed by the oxidation of the resulting cyclohexenones **Va** to give 4,6-diaryl-substituted salicylates **VIa** (Scheme 2). The use of γ-aryl-substituted derivatives (ethyl 4-aryl-3-oxobutanoates) **VII** instead of acetoacetic

ester could provide a route to 3,4,6-triaryl-substituted salicylates **VIb**; however, almost no data concerning this approach are available in the scientific literature.



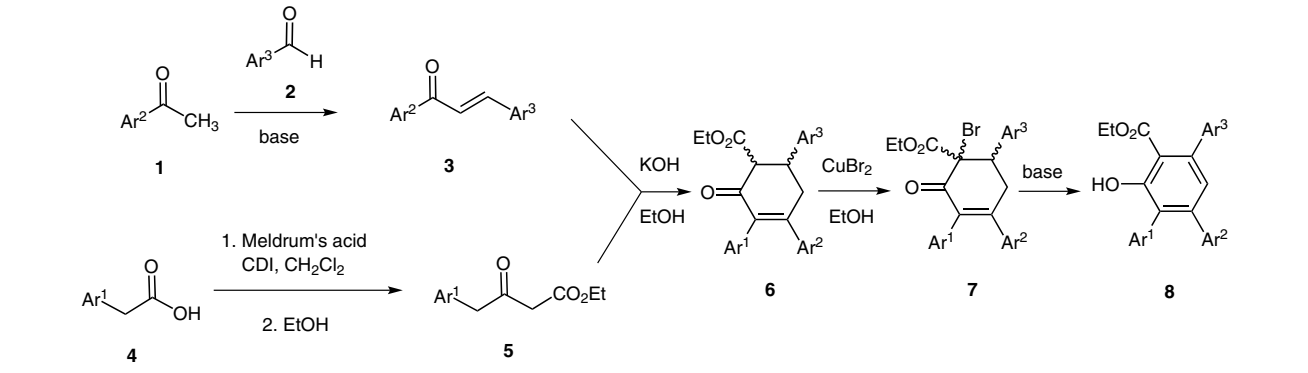
Scheme 2 Synthesis of cyclohexenones and phenols from keto esters and chalcones

In the present study, we describe an efficient method for the synthesis of triaryl(hetaryl)-substituted cyclohexenone and salicylic acid derivatives involving the Robinson annulation as a key step. This method includes preparative steps based on commercially available starting compounds, primarily acetyl and formyl derivatives of aromatic and heteroaromatic compounds. Aryl (or hetaryl) substituents in the cyclohexenone and phenol moieties were chosen because of the interest in studying photochemical transformations of these compounds[12] and their biological activity. The development of this synthetic protocol was made possible because the starting keto esters (4-aryl-3-oxobutanoates) became available and can be prepared from appropriate arylacetic acids by the proposed method.[13]

The synthetic protocol for the preparation of the cyclohexenone and salicylic acid derivatives is based on the Robinson annulation of 4-aryl-3-oxobutanoates **5** and chalcones **3** followed by the bromination and aromatization of the resulting six-membered ring (Scheme 3). Readily available aryl- or hetarylethanones **1**, aryl- or hetarylcarbaldehydes **2**, as well as acetic acids of various carbo- and heteroaromatic derivatives **4**, were used as the starting compounds. In the cases where the aryl- or hetarylacetic acids were commercially unavailable, they were synthesized from appropriate aryl- or hetarylethanones by the Willgerodt–Kindler reaction.[14] To develop an efficient practical method for the synthesis of polyaryl(hetaryl)-substituted cyclohexenones **6** and salicylates **8**, we performed a step-by-step optimization of this synthetic protocol. The optimized conditions were used for the synthesis of a wide range of salicylates based on benzene, naphthalene, thiophene, oxazole, and thiazole derivatives (Table 1).

Our studies demonstrated that potassium hydroxide (1.0 equiv) in aqueous ethanol (water–ethanol, 1:1) is the reagent of choice for the step giving the chalcones **3**. The use of alternative conditions (sodium ethoxide in anhydrous ethanol, potassium carbonate in anhydrous DMF, sodium hydroxide in ethanol, piperidine in ethanol, etc.) proved to be less efficient and, in some cases, resulted in the formation of byproducts and a decrease in the yields of the final chalcones (the examination of these conditions was important for the development also of the one-pot protocol). The reaction time depends on the nature of the aryl substituents and the solubility of the starting compounds in an aqueous ethanol solution and varies from 15 minutes to 2 hours.

The second step of this synthetic procedure is based on the Robinson annulation of keto esters **5** with chalcones **3** in ethanol in the presence of an alkali (Scheme 3). This step is the most intricate and unpredictable. Due to the presence of acidic protons in the resulting cyclohexenone system, these compounds are very sensitive to various transformations under basic conditions and, depending on the structure of the resulting cyclohexenone, the reaction can afford the enol form as potassium enolate, which adds complexity to the workup of the reaction mixture.

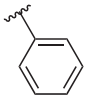
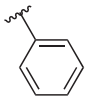
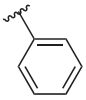
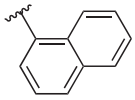
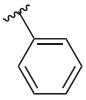
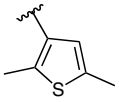
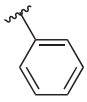
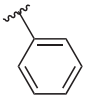
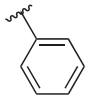
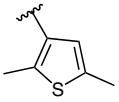
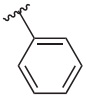
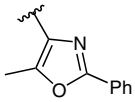
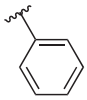
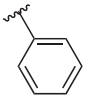
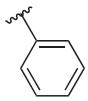
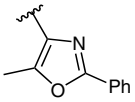
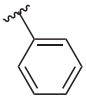
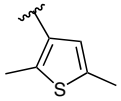
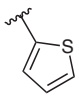
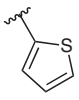
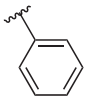
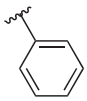
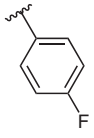
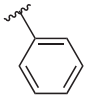
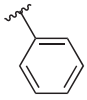
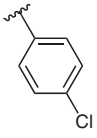
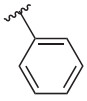
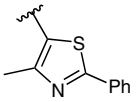
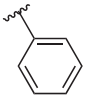


Scheme 3 Synthetic method to triaryl(hetaryl)-substituted cyclohexenones and phenols

The Robinson annulation is also catalyzed by bases, but, as opposed to the synthesis of chalcones, the best results were obtained when using 0.2–0.5 equivalents potassium hydroxide in an aqueous ethanol solution. An increase in the amount of potassium hydroxide (more than 0.5 equiv) led to a decrease in the yields of the target cyclohexenones.

The conditions of choice for the Robinson annulation include running the reaction at room temperature, at which the reaction is complete in approximately 25–30 hours. In reactions using azole derivatives as Ar^1 or Ar^2 (entries 5, 6, and 10; in Table 1), a temperature rise results in an increase in the yields of the target products. Therefore, the reaction

Table 1 Synthesis of Triarylcyclohexenones **6** and Phenols **8**

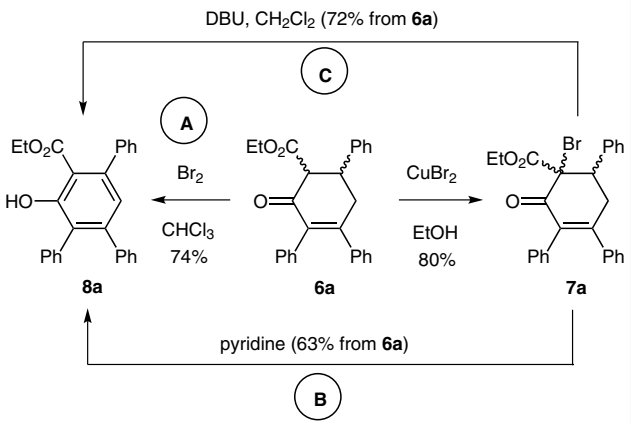
Entry	**6**/**8**	Ar^1	Ar^2	Ar^3	Yield of **6** (%)[a]	Yield of **8** (%)[b,c]	One-pot yield of **8** (%)[d]
1	**a**				70	74 (A)	25
2	**b**				34	55 (A)	30
3	**c**				39	60 (B)	29
4	**d**				34	49 (B)	30
5	**e**				40	49 (C)	37
6	**f**				63	64 (B)	30
7	**g**				45	61 (C)	22
8	**h**				60	50 (C)	28
9	**i**				63	35 (C)	23
10	**j**				68	71 (C)	30

[a] Yield of cyclohexenone **6** from chalcone **3**.
[b] Yield of phenol **8** from cyclohexenone **6**.
[c] Method given in parentheses: A: Br_2, $CHCl_3$; B: 1. $CuBr_2$, EtOH; 2. pyridine; C: 1. $CuBr_2$, EtOH; 2. DBU, CH_2Cl_2.
[d] Overall yield from ketone **1**.

for these compounds was performed under reflux. The reaction with sodium ethoxide as a base in anhydrous ethanol is also efficient for the azole derivatives; however, this method can be implemented only in a stepwise protocol.

We have also revealed some trends in the effects of substituents on aryl moieties on the reactions of chalcones with keto esters. It was found that the nature of the aryl moiety (Ar^3) of the aldehyde component **2** substantially influences the formation of the cyclohexenone ring (Robinson cyclization). In the case of compounds containing a 4-halogen-substituted phenyl moiety (F, Cl), the cyclization occurs in low yields, apparently due to the electron-withdrawing inductive effect of the halogen atom that has an effect on the reactivity of chalcone **3** in the conjugate addition, although the starting chalcones **3** containing these substituents are produced in high yields. It was also found that chalcones **3** containing a heterocyclic moiety at the first position (Ar^2) react more readily with keto esters compared to compounds containing phenyl substituents. This can be attributed to the difference in solubility.

The third step in this synthesis involves the oxidation of the cyclohexenone ring giving phenol derivatives. The conventional method for this transformation is based on bromination with molecular bromine in chloroform under reflux.[15] The reaction results in the dehydrobromination of the primary halogen derivative and gives the phenol derivative in good yield. We tested this method for model compound **6a**, the bromination of which afforded phenol **8a** in 74% yield (Scheme 4). However, the drawback of this method is the sensitivity of aromatic substituents on the cyclohexenone ring to molecular bromine. In particular, we found that the aromatization of thiophene-containing compounds is accompanied by the bromination of the aromatic ring, which results in a decrease in the yield and interferes with purification of the target products. For this reason, we examined different aromatization methods for the cyclohexenone system.



Scheme 4 Different approaches for the aromatization of **6a**

Scheme 4 displays the results of the investigation of the aromatization of the model compound, cyclohexenone **6a** containing three phenyl substituents. We studied various brominating and oxidizing systems, in particular, iodine in ethanol, DDQ, copper acetate, etc. The best results were obtained with the use of copper(II) bromide[16] for the bromination, followed by treatment with pyridine or DBU. The bromination was found to be the most efficient with the use of 2.2 equivalents of $CuBr_2$ in ethanol at 60–80 °C. In this case, product **7a** was isolated in 80% yield.

After the usual workup of the reaction mixture, one of two procedures for the aromatization of **7a** can be applied (Scheme 4). In the one method, the solvent is removed by distillation and the residue is heated in pyridine at 80 °C until the starting bromine derivative is completely consumed. An alternative method involves the use of DBU as the dehydrobrominating agent and dichloromethane as the solvent. A twofold excess of DBU is added to a dichloromethane solution of **7a** obtained in the previous step, the reaction mixture is stirred for 30 minutes and then successively washed with hydrochloric acid and water, then the solvent is removed by distillation, and the residue is purified by flash chromatography. It is an alternative method that is less laborious and more efficient than the approach using pyridine (pyridine as solvent, reflux, 20–24 h), but it requires a more expensive reactant (DBU) as the dehydrobrominating agent. The bromination in ethanol and subsequent dehydrobromination and aromatization using DBU (method C) is an operationally simple and efficient workup method that leads to high yields of the target phenols, and excludes the possibility of bromination of a heteroaromatic system.

We applied these procedures to synthesize a number of previously unknown triaryl-substituted salicylates **8** (Table 1). The structures of the resulting compounds were established by ^1H and ^{13}C NMR spectroscopy and high-resolution mass spectrometry. The structure of compound **8e** was also confirmed by X-ray crystal structure analysis[17] (Figure 1).

This synthetic route to salicylates **8** was also accomplished in a one-pot protocol starting from 1-aryl- or 1-hetarylethanones **1**. The first two steps are performed in an aqueous ethanol solution in the presence of potassium hydroxide. We found that 0.8–1.0 equivalents of KOH is the optimum quantity of the base for the first two steps. An increase in the amount of the hydroxide has a very positive impact on the yields in the first step, but negatively affects the cyclization. In contrast, a decrease in the amount of the base results in lower yields of chalcones **3**, but has a positive effect on the formation of the cyclohexenone derivatives **6** (for this stage, catalytic amounts of base are required). Then, in order to neutralize the base, an equimolar amount of NH_4Cl (with respect to the amount of potassium hydroxide used) and $CuBr_2$ (2.1 equiv) as the brominating agent are added. The bromination proceeds under reflux in ethanol for 4–6 hours. After extraction and drying of the

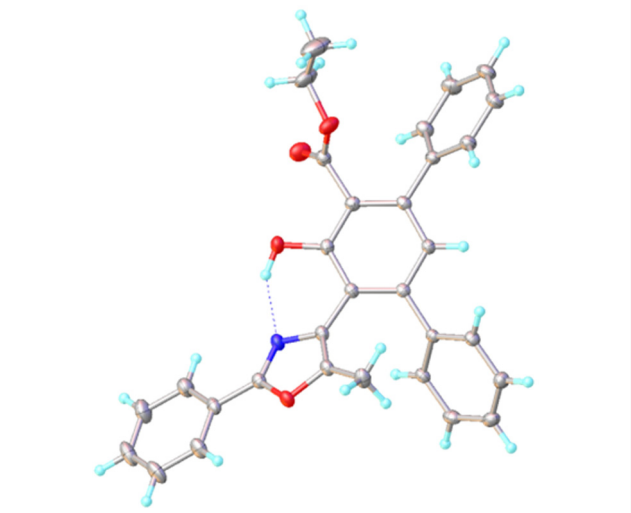
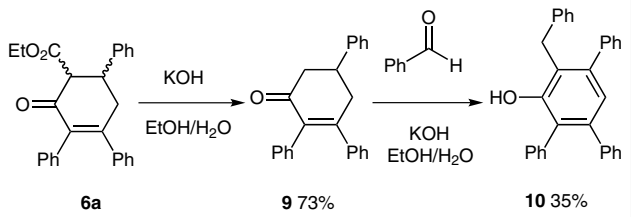


Figure 1 Structure of compound **8e** as determined by X-ray crystallographic analysis

bromine derivative **7**, an excess of DBU in dichloromethane is added to a dichloromethane solution of **7** as in the stepwise procedure.

A comparative analysis of the yields obtained in the stepwise method and in the one-pot protocol shows that in some cases (entries 2–5 in the Table 1) the one-pot method is more efficient, which can probably be attributed to losses during the workup of the reaction mixture and purification of the final products in these steps. Molecular bromine can also be used as the brominating agent. However, it should be taken into account that this method is not suitable for the synthesis of compounds sensitive to this reactant. The bromination with $CuBr_2$ is a versatile and efficient method and can be applied to any substrate. It was also shown that DBU is an operationally convenient and efficient reagent in the steps of elimination of HBr and aromatization.

We have also applied an alternative method to synthesize a phenol derivative from decarboxylated cyclohexenone **9** (Scheme 5). The condensation of **9** with benzaldehyde in an aqueous ethanol solution of an alkali afforded phenol **10** in 35% yield via a 1,3-sigmatropic shift, resulting in the aromatization of the cyclohexenone system.[8,10,18]



Scheme 5 Alternative aromatization route

To summarize, we have developed a new efficient method for the synthesis of polyaryl(hetaryl)substituted cyclohexenones and salicylates from readily available starting compounds. It was shown that polyaromatic derivatives of phenol and salicylic acid can be synthesized in good yields from simple and readily available acyclic starting compounds – aromatic (heteroaromatic) aldehydes, ketones, and acetic acid derivatives. This synthetic protocol involves the Robinson annulation of keto esters with chalcones as a key step. Various benzene, naphthalene, thiophene, oxazole, and thiazole derivatives were used as aryl moieties. The aromatization can be accomplished either by reaction with bromine in refluxing chloroform or bromination with copper(II) bromide in ethanol followed by treatment with pyridine or DBU. The new method was also implemented in a one-pot protocol, which in some cases resulted in the formation of the final products in higher yields compared to those obtained in the stepwise procedure. This method can be applied to synthesize desired polyaryl(hetaryl)-substituted salicylates containing different predetermined aromatic substituents.

^{1}H and ^{13}C NMR spectra of samples in deuterated solvents were recorded at 293 K (300 MHz for ^{1}H, 75 MHz for ^{13}C). Melting points were recorded by using an apparatus and are not corrected. Mass spectra were obtained on a mass spectrometer (70 eV) with direct sample injection into the ion source. High resolution mass spectra were obtained on a TOF mass spectrometer with an ESI source. All chemicals and anhydrous solvents were purchased from commercial sources and used without further purification. Column chromatography was performed by using silica gel 60 (70–230 mesh); TLC analysis was conducted on silica gel 60 F254 plates. Keto esters **5** were described previously.[13,19]

Cyclohexenones 6; General Procedure

KOH (0.6 mmol) was added to a solution of the keto ester **5** (1.23 mmol) and the chalcone **3** (1.23 mmol) in EtOH (4 mL). The resulting suspension was stirred for 24 h at r.t. After the completion of the reaction (TLC control) the precipitated product formed was collected by filtration, washed with H_2O (50 mL) and cold EtOH (5 mL), and dried under vacuum. Additional quantities of the product were obtained as following: filtrate was poured into H_2O (50 mL), extracted with EtOAc (3 × 30 mL), washed with brine (70 mL), dried ($MgSO_4$), and evaporated under vacuum. The residue was purified by column chromatography (silica gel, PE–EtOAc, 6:1).

Ethyl 3′-Oxo-5′-phenyl-3′,4′,5′,6′-tetrahydro-[1,1′:2′,1″-terphenyl]-4′-carboxylate (6a)

Colorless crystals; yield: 341 mg (70%); mp 160–161 °C.

IR (KBr): 3024, 2993, 1741, 1664, 1256, 1032, 697 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (t, *J* = 7.1 Hz, 3 H, CH_3), 3.05–3.19 (m, 2 H, CH_2), 3.92–4.16 (m, 4 H, CH+CH+CH_2), 6.91–7.43 (m, 15 H, H^{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 40.4, 43.4, 60.1, 61.0, 127.1, 127.2 (2 C), 127.4, 127.6 (2 C), 128.0 (2 C), 128.2 (3 C), 128.8 (2 C), 131.0 (2 C), 134.7, 136.8, 139.9, 141.1, 156.6, 169.3, 193.2.

MS (EI, 70 eV): *m*/*z* (%) = 396 (60) [M]$^+$, 323 (100) [M – CO_2Et]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{24}O_3$: 397.1798; found: 397.1782.

Ethyl 6′-(1-Naphthyl)-5′-oxo-2′,3′,4′,5′-tetrahydro-[1,1′:3′,1″-terphenyl]-4′-carboxylate (6b)

Pale-red powder; yield: 187 mg (34%); mp 225–226 °C.

IR (KBr): 3056, 1734, 1667, 1315, 1142, 779, 701 cm^{-1}.

(Double set of some signals in the ^{1}H and ^{13}C NMR spectra indicates dynamic NMR effect.)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 and 1.13 (t, *J* = 7.1 Hz, 3 H, CH_3), 3.10–3.38 (m, 2 H, CH_2), 4.00–4.20 (m, 4 H, CH+CH+CH_2), 6.92–7.89 (m, 17 H, H^{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 40.0, 40.4, 43.7, 43.8, 61.1, 61.2, 125.2, 125.4, 125.5, 125.7, 125.9, 126.1, 126.2, 126.7, 126.8, 127.1, 127.3, 127.4, 127.6, 127.9, 128.0, 128.1, 128.4, 128.5, 128.6, 128.8, 128.9, 129.0, 132.6, 132.9, 133.3, 133.4, 136.0, 136.1, 139.7, 139.8, 141.1, 141.2, 158.2, 158.3, 169.2, 169.4, 193.0, 193.2.

MS (EI, 70 eV): *m*/*z* (%) = 446 (80) [M]$^+$, 373 (100) [M – CO_2Et]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{26}O_3$: 447.1955; found: 447.1952.

Ethyl 6′-(2,5-Dimethyl-3-thienyl)-5′-oxo-2′,3′,4′,5′-tetrahydro-[1,1′:3′,1″-terphenyl]-4′-carboxylate (6c)

Yellow crystals; yield: 206 mg (39%); mp 117–118 °C.

IR (KBr): 2917, 1732, 1662, 1147, 754, 702 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.11 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.81 (s, 3 H, CH_3), 2.34 (s, 3 H, CH_3), 3.03–3.20 (m, 2 H, CH_2), 3.89–4.16 (m, 4 H, CH+CH+CH_2), 6.38 (s, 1 H, $H^{thiophene}$), 7.05–7.41 (m, 10 H, H^{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8, 14.0, 15.2, 39.8, 43.4, 60.1, 60.9, 127.2 (2 C), 127.4, 127.7 (2 C), 127.8, 128.0 (2 C), 128.5, 128.8 (2 C), 130.6, 131.7, 134.3, 135.1, 139.9, 141.1, 157.1, 169.2, 193.3.

MS (EI, 70 eV): *m*/*z* (%) = 430 (20) [M]$^+$, 357 (35) [M – CO_2Et]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{26}O_3S$: 431.1675; found: 431.1663.

Ethyl 5′-(2,5-Dimethyl-3-thienyl)-3′-oxo-1′,2′,3′,6′-tetrahydro-[1,1′:4′,1″-terphenyl]-2′-carboxylate (6d)

Yellow amorphous powder; yield: 180 mg (34%).

IR (KBr): 2914, 1737, 1663, 1258, 766, 698 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.81 (s, 3 H, CH_3), 2.33 (s, 3 H, CH_3), 2.91–3.00 (m, 2 H, CH_2), 3.86–4.13 (m, 4 H, CH+CH+CH_2), 6.46 (s, 1 H, $H^{thiophene}$), 7.00–7.09 (m, 2 H, H^{arom}), 7.14–7.40 (m, 8 H, H^{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 14.2, 15.0, 40.5, 43.2, 60.4, 61.0, 125.3, 127.0, 127.2 (2 C), 127.4 (3 C), 128.8 (2 C), 130.6 (2 C), 133.6, 134.7, 136.3, 136.8, 137.2, 141.1, 153.1, 169.3, 192.9.

MS (EI, 70 eV): *m*/*z* (%) = 430 (100) [M]$^+$, 357 (95) [M – CO_2Et]$^+$.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{26}O_3S$: 431.1675; found: 431.1669.

Ethyl 6′-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)-5′-oxo-2′,3′,4′,5′-tetrahydro-[1,1′:3′,1″-terphenyl]-4′-carboxylate (6e)

Yellow crystals; yield: 235 mg (40%); mp 129–130 °C.

IR (KBr): 2981, 1734, 1681, 1266, 1256, 698 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.89 (s, 3 H, CH_3), 3.03–3.21 (m, 2 H, CH_2), 3.94–4.17 (m, 4 H, CH+CH+CH_2), 7.16–7.46 (m, 13 H, H^{arom}), 7.85–8.01 (m, 2 H, H^{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.7, 14.1, 40.4, 43.4, 60.1, 61.0, 126.1 (2 C), 127.3, 127.6 (2 C), 127.7, 127.8, 128.0, 128.3, 128.5 (2 C), 128.6 (2 C), 128.9 (4 C), 129.8, 130.5, 139.5, 141.0, 146.8, 159.6, 160.3, 169.1, 192.7.

MS (EI, 70 eV): *m*/*z* (%) = 477 (60) [M]$^+$, 404 (100) [M – CO_2Et]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{27}NO_4$: 478.2013; found: 478.2025.

Ethyl 5′-(5-Methyl-2-phenyl-1,3-oxazol-4-yl)-3′-oxo-1′,2′,3′,6′-tetrahydro-[1,1′:4′,1″-terphenyl]-2′-carboxylate (6f)

Yellow powder; yield: 370 mg (63%); mp 131–134 °C.

IR (KBr): 2978, 1731, 1668, 1261, 1136, 696 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.57 (s, 3 H, CH_3), 2.99 (dd, *J* = 19.1, 9.1 Hz, 1 H, 0.5CH_2), 3.53 (dd, *J* = 19.1, 3.8 Hz, 1 H, 0.5CH_2), 3.91–4.11 (m, 4 H, CH+CH+CH_2), 7.13–7.47 (m, 13 H, H^{arom}), 7.90–8.00 (m, 2 H, H^{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.2, 14.0, 38.3, 42.9, 60.5, 60.9, 126.0 (2 C), 127.0, 127.3 (3 C), 127.9, 128.0 (2 C), 128.1 (2 C), 128.7 (2 C), 130.3 (2 C), 130.8, 134.6, 134.9, 136.6, 141.1, 146.7, 148.2, 160.1, 169.2, 193.0.

MS (EI, 70 eV): *m*/*z* (%) = 477 (80) [M]$^+$, 404 (100) [M – CO_2Et]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{27}NO_4$: 478.2013; found: 478.2005.

Ethyl 3-(2,5-Dimethyl-3-thienyl)-2-oxo-4,6-di-2-thienylcyclohex-3-ene-1-carboxylate (6g)

Gray powder; yield: 245 mg (45%); mp 111–113 °C.

IR (KBr): 3096, 2915, 1734, 1656, 1371, 1277, 1150, 707 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.99 and 2.08 (s, 3 H, CH_3), 2.43 (s, 3 H, CH_3), 3.11–3.34 (m, 1 H), 3.43–3.61 (m, 1 H), 3.76–3.93 (m, 1 H), 4.03–4.30 (m, 3 H, CH+CH_2), 6.31 (s, 1 H, $H^{thiophene}$), 6.90–7.09 (m, 3 H, $H^{thiophene}$), 7.17–7.50 (m, 3 H, $H^{thiophene}$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.4, 14.1, 15.4, 38.0, 38.1, 60.9, 61.2, 124.1, 124.8, 126.3, 126.7, 126.9, 128.9, 130.3, 130.7, 132.3, 136.2, 137.3, 140.8, 144.7, 147.1, 169.0, 192.1.

MS (EI, 70 eV): *m*/*z* (%) = 442 (100) [M]$^+$, 369 (75) [M – CO_2Et]$^+$.

HRMS (ESI-TOF) *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{23}O_3S_3$: 443.0804; found: 443.0792.

Ethyl 5′-(4-Fluorophenyl)-3′-oxo-3′,4′,5′,6′-tetrahydro-[1,1′:2′,1″-terphenyl]-4′-carboxylate (6h)

White powder; yield: 306 mg (60%); mp 153–155 °C.

IR (KBr): 2978, 1735, 1665, 1510, 1141, 843, 700 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 (t, *J* = 7.1 Hz, 3 H, CH_3), 3.05–3.17 (m, 2 H, CH_2), 3.86–4.24 (m, 4 H, CH+CH+CH_2), 6.97–7.25 (m, 12 H, H^{arom}), 7.30–7.47 (m, 2 H, H^{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 40.4, 42.7, 60.3, 61.1, 115.7 (d, $^2J_{CF}$ = 21.4 Hz, 2 C), 127.1, 127.7 (2 C), 128.1 (4 C), 128.3, 128.5, 128.8 (d, $^3J_{CF}$ = 8.1 Hz, 2 C), 131.0 (2 C), 134.5, 136.8, 156.5, 162.0 (d, $^1J_{CF}$ = 245.8 Hz), 169.1, 193.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{23}FO_3$: 415.1704; found: 415.1691.

Ethyl 5′-(4-Chlorophenyl)-3′-oxo-3′,4′,5′,6′-tetrahydro-[1,1′:2′,1″-terphenyl]-4′-carboxylate (6i)

White powder, yield: 333 mg (63%); mp 105–107 °C (dec.).

IR (KBr): 2923, 1660, 1734, 1315, 1139, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.00–1.20 (m, 3 H, CH_3), 3.00–3.17 (m, 2 H, CH_2), 3.85–4.30 (m, 4 H, CH+CH+CH_2), 6.90–7.25 (m, 12 H, H^{arom}), 7.26–7.52 (m, 2 H, H^{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 40.2, 42.8, 60.0, 61.2, 127.2, 127.7 (2 C), 128.1, 128.2 (2 C), 128.4 (2 C), 128.5 (2 C), 128.7 (2 C), 129.0, 131.0 (2 C), 133.2, 134.5, 136.8, 139.6, 156.4, 169.1, 192.9.

HRMS (ESI-TOF) *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{23}ClO_3$: 431.1408; found:431.1393.

Ethyl 5′-(4-Methyl-2-phenyl-1,3-thiazol-5-yl)-3′-oxo-1′,2′,3′,6′-tetrahydro-[1,1′:4′,1″-terphenyl]-2′-carboxylate (6j)

Pale-yellow powder; yield: 412 mg (68%); mp 162–164 °C.

IR (KBr): 2978, 1733, 1670, 1258, 1023, 700 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.11 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.99 (s, 3 H, CH_3), 3.03–3.23 (m, 2 H, CH_2), 3.94–4.22 (m, 4 H, CH+CH+CH_2), 7.05–7.60 (m, 13 H, H^{arom}), 7.77–7.92 (m, 2 H, H^{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 16.8, 41.7, 43.1, 60.2, 61.1, 126.4 (2 C), 127.2 (2 C), 127.6, 127.8, 127.9 (2 C), 128.8, 128.9 (4 C), 130.3, 130.4, 130.5 (2 C), 133.0, 134.1, 140.6, 147.2, 150.7, 167.4, 168.9, 192.3.

HRMS (ESI-TOF) *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{27}NO_3S$: 494.1784; found: 494.1775.

Phenols 8

Method A: Cyclohexenone **6** (0.3 mmol) was dissolved in $CHCl_3$ (2 mL), then Br_2 (16 µL, 0.3 mmol) was added, and the resulting mixture was refluxed for 3 h. Then the reaction mixture was poured into H_2O (50 mL) and extracted with EtOAc (3 × 30 mL) and the combined organic phases were washed with H_2O (50 mL), dried ($MgSO_4$), and evaporated under vacuum. The residue was purified by flash chromatography (silica gel, PE–EtOAc 20:1).

Method B: Cyclohexenone **6** (0.3 mmol) was dissolved in EtOH (2 mL) and $CuBr_2$ (168 mg, 0.75 mmol) was added. The reaction mixture was refluxed for 6 h. The resulting mixture was poured into H_2O (75 mL) and extracted with EtOAc (3 × 40 mL); then the combined organic phases were washed with brine (4 × 70 mL), dried ($MgSO_4$), and evaporated under vacuum (compound **7a** was isolated by recrystallization from EtOH). The residue was dissolved in pyridine (2 mL) and stirred at 90 °C for 3 h; the mixture was subsequently evaporated under vacuum and purified by flash chromatography (silica gel, PE–EtOAc 20:1).

Method C: Cyclohexenone **6** (0.3 mmol) was suspended in EtOH (2 mL) and $CuBr_2$ (168 mg, 0.75 mmol) was added. The reaction mixture was refluxed for 6 h. The resulting mixture was poured into H_2O (75 mL) and extracted with EtOAc (3 × 40 mL), and the combined organic phases were washed with brine (4 × 70 mL), dried ($MgSO_4$), and evaporated under vacuum. The residue was dissolved in CH_2Cl_2 (20 mL) and then DBU (90 µL, 0.6 mmol) was added to the solution; the resulting solution was then washed with 5% aq HCl, evaporated, and purified by flash chromatography (silica gel, PE–EtOAc, 20:1 or 30:1).

One-pot method: KOH (1.1 mmol) was added to a solution of ketone **1** (1.23 mmol) and aldehyde **2** (1.23 mmol) in EtOH (4 mL). The mixture was stirred at r.t. for 2 h. Then keto ester **5** (1.23 mmol) was added to the obtained suspension and the mixture was left overnight. The next day, NH_4Cl (107 mg, 2 mmol) and $CuBr_2$ (685 mg, 3.06 mmol) were added and the mixture was refluxed for 6 h. Then the reaction mixture was cooled, poured into H_2O (100 mL), and extracted with CH_2Cl_2 (3 × 50 mL); the combined organic phases were washed with brine (2 × 50 mL), dried ($MgSO_4$), and evaporated. The residue was dissolved in CH_2Cl_2 (30 mL) and then DBU (0.37 mL, 2.45 mmol) was added; the resulting solution was then washed with 5% aq HCl, evaporated, and purified by flash chromatography (silica gel, PE–EtOAc, from 20:1 to 30:1). (Overall yields of phenols **8** obtained by one-pot protocol are given in Table 1).

Ethyl 4′-Bromo-3′-oxo-5′-phenyl-3′,4′,5′,6′-tetrahydro-[1,1′:2′,1″-terphenyl]-4′-carboxylate (7a)

Pale grey powder; yield: 114 mg (80%); mp 222–225 °C.

IR (KBr): 3057, 3029, 2981, 1756, 1730, 1670, 1263, 1221, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.0 Hz, 3 H, CH_3), 3.06 (dd, *J* = 4.3, 19.2 Hz, 1 H, 0.5CH_2), 3.43 (dd, *J* = 10.7, 19.2 Hz, 1 H, 0.5CH_2), 4.17–4.28 (m, 3 H, CH+CH_2), 7.00–7.54 (m, 15 H, H^{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0, 37.5, 47.1, 63.2, 72.5, 127.3, 127.5, 127.7 (2 C), 128.1 (2 C), 128.2 (2 C), 128.4 (3 C), 128.9 (2 C), 130.8 (2 C), 134.0, 134.5, 137.2, 139.5, 157.3, 165.9, 188.4.

MS (EI, 70 eV): *m*/*z* (%) = 396 (90) [M + H – Br]$^+$, 349 (85), 323 (100).

HRMS (ESI-TOF) *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{23}BrO_3$: 475.0903 (^{79}Br), 477.0884 (^{81}Br); found: 475.0892 (^{79}Br), 477.0873 (^{81}Br).

Ethyl 5′-Hydroxy-6′-phenyl-1,1′:3′,1″-terphenyl-4′-carboxylate (8a)

White powder; method A: yield: 87 mg (74%), method B: yield: 75 mg (63%), method C: yield: 85 mg (72%); mp 173–176 °C.

IR (KBr): 3058, 2989, 1651, 1379, 1303, 1224, 755, 696 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, *J* = 7.1 Hz, 3 H, CH_3), 4.04 (q, *J* = 7.1 Hz, 2 H, CH_2), 6.96 (s, 1 H, H^{arom}), 7.07–7.44 (m, 15 H, H^{arom}), 11.12 (s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.1, 61.2, 111.2, 124.3, 126.9, 127.1, 127.5, 127.7 (2 C), 127.8 (4 C), 128.3 (2 C), 128.8, 129.6 (2 C), 131.2 (2 C), 135.9, 140.4, 142.9, 143.8, 146.3, 159.1, 171.2.

MS (EI, 70 eV): *m*/*z* (%) = 394 (70) [M]$^+$, 348(100) [M – EtOH]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{22}O_3$: 395.1642; found: 395.1636.

Ethyl 5′-Hydroxy-6′-(1-naphthyl)-1,1′:3′,1″-terphenyl-4′-carboxylate (8b)

Colorless crystals; method A: yield: 73 mg (55%); mp 195–196 °C.

IR (KBr): 3055, 3036, 2958, 2927, 1657, 1602, 1377, 1223, 1129, 778, 700 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, *J* = 7.1 Hz, 3 H, CH_3), 4.07 (q, *J* = 7.1 Hz, 2 H, CH_2), 7.00–7.11 (m, 5 H, H^{arom}), 7.19 (d, *J* = 7.0 Hz, 1 H, H^{arom}), 7.33–7.51 (m, 9 H, H^{arom}), 7.19 (d, *J* = 7.8 Hz, 2 H, H^{arom}),7.83–7.92 (m, 1 H, H^{arom}), 11.01 (s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.1, 61.2, 111.1, 124.3, 125.3, 125.6, 126.0, 126.1, 126.5, 126.9, 127.1, 127.6 (2 C), 127.7 (2 C), 127.8, 128.3 (2 C), 128.4, 128.6, 128.7 (2 C), 132.8, 133.3, 134.2, 140.2, 142.9, 144.2, 147.4, 159.6, 171.1.

MS (EI, 70 eV): *m*/*z* (%) = 444 (90) [M]$^+$, 398 (100) [M – EtOH]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{24}O_3$: 445.1798; found: 445.1798.

Ethyl 6′-(2,5-Dimethyl-3-thienyl)-5′-hydroxy-1,1′:3′,1″-terphenyl-4′-carboxylate (8c)

Yellow amorphous powder; method B: yield: 77 mg (60%).

IR (KBr): 2957, 2919, 1731, 1657, 1599, 1375, 1261, 1142, 699 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.93 (s, 3 H, CH_3), 2.40 (s, 3 H, CH_3), 4.04 (q, *J* = 7.1 Hz, 2 H, CH_2), 6.51 (s, 1 H, $H^{thiophene}$), 6.95 (s, 1 H, H^{arom}), 7.12–7.41 (m, 10 H, H^{arom}), 11.06 (s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.0, 13.8, 15.3, 61.1, 111.1, 123.0, 123.9, 126.8, 127.2, 127.7 (2 C), 127.8 (2 C), 128.0, 128.2 (2 C), 128.9 (2 C), 129.3, 131.5, 134.3, 135.3, 140.4, 142.9, 146.8, 159.6, 171.1.

MS (EI, 70 eV): *m*/*z* (%) = 428 (75) $[M]^+$, 382 (100) $[M - EtOH]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{27}H_{24}O_3S$: 429.1519; found: 429.1520.

Ethyl 5′-(2,5-Dimethyl-3-thienyl)-3′-hydroxy-1,1′:4′,1″-terphenyl-2′-carboxylate (8d)

Yellow amorphous powder; method B: yield: 63 mg (49%).

IR (KBr): 2958, 2924, 1741, 1658, 1601, 1378, 1251, 1177, 699 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, *J* = 7.1 Hz, 3 H, CH_3), 2.02 (s, 3 H, CH_3), 2.28 (s, 3 H, CH_3), 4.04 (q, *J* = 7.1 Hz, 2 H, CH_2), 6.28 (s, 1 H, $H^{thiophene}$), 6.85 (s, 1 H, H^{arom}), 7.18–7.42 (m, 10 H, H^{arom}), 11.13 (s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.0, 13.9, 15.0, 61.2, 111.1, 124.6, 126.7, 126.8, 127.5 (2 C), 127.6 (2 C), 128.2 (2 C), 128.3, 128.9, 130.7 (2 C), 135.1, 135.9, 136.7, 141.9, 142.9, 143.3, 158.9, 171.2.

MS (EI, 70 eV): *m*/*z* (%) = 428 (90) $[M]^+$, 382 (100) $[M - EtOH]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{27}H_{24}O_3S$: 429.1519; found: 429.1511.

Ethyl 5′-Hydroxy-6′-(5-methyl-2-phenyl-1,3-oxazol-4-yl)-1,1′:3′,1″-terphenyl-4′-carboxylate (8e)

Yellow crystals; method C: yield: 70 mg (49%); mp 189–191 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.89 (m, 3 H, CH_3), 1.80 (s, 3 H, CH_3), 4.09 (m, 2 H, CH_2), 7.00 (s, 1 H, H^{arom}), 7.25–7.45 (m, 13 H, H^{arom}), 8.02–8.12 (m, 2 H, H^{arom}), 11.00 (s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.6, 13.2, 61.2, 114.1, 117.2, 126.2, 127.8 (2 C), 128.2 (4 C), 128.3, 128.5 (2 C), 128.7 (2 C), 129.0 (2 C), 129.5, 130.1, 131.2, 140.4, 142.1, 144.2, 146.4 (2 C), 158.9, 159.8, 170.2.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{31}H_{25}NO_4$: 476.1856; found: 476.1765.

Ethyl 3′-Hydroxy-5′-(5-methyl-2-phenyl-1,3-oxazol-4-yl)-1,1′:4′,1″-terphenyl-2′-carboxylate (8f)

Yellow crystals; method B: yield: 91 mg (64%), mp 111–113 °C.

IR (KBr): 3059, 2978, 2927, 1656, 1598, 1374, 1244, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.74 (s, 3 H, CH_3), 4.03 (q, *J* = 7.1 Hz, 2 H, CH_2), 7.16 (s, 1 H, H^{arom}), 7.22–7.45 (m, 13 H, H^{arom}), 7.91–8.00 (m, 2 H, H^{arom}), 11.20 (s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.7, 13.0, 61.2, 111.8, 124.5, 126.0 (2 C), 126.8, 127.0, 127.5, 127.6 (2 C), 127.9 (2 C), 128.3 (2 C), 128.7 (2 C), 129.9, 131.0 (2 C), 132.6, 134.1, 135.7, 136.8, 139.4, 143.8, 145.7, 159.0, 159.6, 171.2.

MS (EI, 70 eV): *m*/*z* (%) = 475 (100) $[M]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{31}H_{25}NO_4$: 476.1856; found: 476.1846.

Ethyl 3-(2,5-Dimethyl-3-thienyl)-2-hydroxy-4,6-di-2-thienylbenzoate (8g)

Brownish amorphous powder; method C: yield: 81 mg (61%).

IR (KBr): 2957, 2917, 1655, 1599, 1396, 1257, 689 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.98 (t, *J* = 7.1 Hz, 3 H, CH_3), 2.07 (s, 3 H, CH_3), 2.46 (s, 3 H, CH_3), 4.13 (q, *J* = 7.1 Hz, 2 H, CH_2), 6.49 (s, 1 H, $H^{thiophene}$), 6.90–6.95 (m, 1 H, $H^{thiophene}$), 6.97–7.09 (m, 3 H, H^{arom}+$H^{thiophene}$), 7.25–7.30 (m, 2 H, $H^{thiophene}$), 7.33–7.37 (m, 1 H, $H^{thiophene}$), 10.76 (s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.3, 13.6, 61.5, 112.3, 123.0, 123.7, 125.2, 126.1, 126.2, 126.7, 126.9, 127.4, 127.5, 127.8, 128.0, 131.3, 135.8, 136.6, 138.9, 141.5, 143.4, 159.7, 170.6.

MS (EI, 70 eV): *m*/*z* (%) = 440 (100) $[M]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{20}O_3S_3$: 441.0647; found: 441.0636.

Ethyl 5′-(4-Fluorophenyl)-3′-hydroxy-[1,1′:2′,1″-terphenyl]-4′-carboxylate (8h)

White powder; method C: yield: 62 mg (50%); mp 139–141 °C.

IR (KBr): 2978, 1668, 1603, 1513, 1380, 1214, 1155, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.2 Hz, 3 H, CH_3), 4.08 (q, *J* = 7.2 Hz, 2 H, CH_2), 6.93 (s, 1 H, H^{arom}), 7.08–7.34 (m, 14 H, H^{arom}), 11.21 (s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.2, 61.3, 114.5 (d, $^2J_{CF}$ = 21.6 Hz, 2 C), 124.3, 126.9, 127.1, 127.8 (4 C), 128.4, 129.6 (2 C), 129.8 (d, $^3J_{CF}$ = 7.8 Hz, 2 C), 131.1 (2 C), 135.7, 138.9, 140.3, 142.6, 144.3, 146.4, 159.3, 171.0.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{27}H_{21}FO_3$: 413.1547; found: 413.1538.

Ethyl 5′-(4-Chlorophenyl)-3′-hydroxy-[1,1′:2′,1″-terphenyl]-4′-carboxylate (8i)

White powder; method C: yield: 45 mg (35%); mp 178–181 °C.

IR (KBr): 2985, 1649, 1492, 1374, 1219, 1089, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.2 Hz, 3 H, CH_3), 4.09 (q, *J* = 7.2 Hz, 2 H, CH_2), 6.90 (s, 1 H, H^{arom}), 7.08–7.34 (m, 12 H, H^{arom}), 7.36–7.43 (m, 2 H, H^{arom}), 11.26 (s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.2, 61.4, 110.9, 124.1, 127.0, 127.1, 127.8 (6 C), 128.6, 129.5 (2 C), 129.6 (2 C), 131.1 (2 C), 132.9, 135.7, 140.2, 141.4, 142.4, 146.5, 159.4, 171.0.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{27}H_{21}ClO_3$: 451.1071; found: 451.1064.

Ethyl 3′-Hydroxy-5′-(4-methyl-2-phenyl-1,3-thiazol-5-yl)-1,1′:4′,1″-terphenyl-2′-carboxylate (8j)

Pale-yellow powder; method C: yield: 105 mg (71%); mp 143–145 °C.

IR (KBr): 2963, 1683, 1656, 1312, 1261, 1108, 1014, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, *J* = 7.2 Hz, 3 H, CH_3), 2.23 (s, 3 H, CH_3), 4.07 (q, *J* = 7.2 Hz, 2 H, CH_2), 7.02 (s, 1 H, H^{arom}), 7.25–7.52 (m, 13 H, H^{arom}), 7.80–8.94 (m, 2 H, H^{arom}), 11.16 (s, 1 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.0, 16.1, 61.4, 112.4, 125.2, 126.3 (2 C), 127.1, 127.6, 127.8 (2 C), 128.0 (2 C), 128.2 (2 C), 128.8 (2 C), 129.9, 130.1, 130.2, 130.6 (2 C), 133.4, 135.2, 136.3, 142.4, 143.7, 150.4, 159.1, 166.7, 170.9.

HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{31}H_{25}NO_3S$: 492.1628; found: 492.1618.

5′-Phenyl-5′,6′-dihydro-[1,1′:2′,1″-terphenyl]-3′(4′*H*)-one (9)

A solution of KOH (112 mg, 2.0 mmol) in H_2O (2 mL) was added to a solution of cyclohexenone **6a** (0.4 mmol) in EtOH (2 mL). The resulting mixture was refluxed until completion of the reaction (TLC control), poured into H_2O (75 mL), and extracted with EtOAc (3 × 40 mL); the combined organic phases were washed with brine, dried with $MgSO_4$, and evaporated under vacuum. The obtained residue was purified by column chromatography (silica gel, PE–EtOAc, 6:1); this gave target compound **9**.

Colorless crystals; yield: 95 mg (73%); mp 184–186 °C.

IR (KBr): 3057, 3028, 1669, 1492, 751, 697 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.89–3.14 (m, 4 H, CH_2+CH_2), 3.57–3.71 (m, 1 H, CH), 6.94–7.46 (m, 15 H, H^{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 40.4, 40.9, 44.8, 126.8 (2 C), 126.9, 127.1, 127.7 (2 C), 128.0 (2 C), 128.2 (2 C), 128.5, 128.8 (2 C), 131.0 (2 C), 135.3, 137.6, 140.5, 143.1, 157.0, 198.1.

MS (EI, 70 eV): *m*/*z* (%) = 324 (40) $[M]^+$, 220 (100).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{21}O$: 325.1587; found: 325.1590.

2′-Benzyl-1,1′:4′,1″-terphenyl-3′-ol (10)

Cyclohexenone **9** (178 mg, 0.55 mmol) was suspended in EtOH (2 mL), and benzaldehyde (56 µL, 0.55 mmol) was added; then a solution of KOH (176 mg, 4.4 mmol) in H_2O (1.5 mL) was added. The resulting mixture was refluxed for 2 h. After completion of the reaction (TLC control) the reaction mixture was cooled, poured into H_2O (75 mL), and extracted with EtOAc (3 × 40 mL); the combined organic phases were washed with brine, dried ($MgSO_4$), and evaporated under vacuum. The obtained residue was purified by flash chromatography (silica gel, PE–EtOAc, 15:1); this gave target compound **10**.

White powder; yield: 79 mg (35%); mp 210–212 °C.

IR (KBr): 3530, 3056, 3025, 2923, 1599, 1493, 1392, 1262, 756, 700 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.13 (s, 2 H, CH_2), 5.34 (s, 1 H, OH), 7.05 (s, 1 H, H^{arom}), 7.11–7.42 (m, 20 H, H^{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.3, 123.7, 123.9, 125.6, 126.4, 127.1, 127.5, 127.6 (2 C), 127.8, 128.0 (2 C), 128.1 (2 C), 128.3 (2 C), 129.1 (2 C), 129.3 (2 C), 129.7 (2 C), 131.1 (2 C), 131.4, 135.3, 139.8, 140.9, 141.4, 143.4, 151.4.

MS (EI, 70 eV): *m*/*z* (%) = 412 (100) $[M]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{31}H_{25}O$: 413.1900; found: 413.1885.

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Supporting Information

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