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Silver-catalyzed regioselective synthesis of acridines, quinolines, and naphthalenes from 3-(2-alkynyl)aryl-β-ketoesters

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ABSTRACT

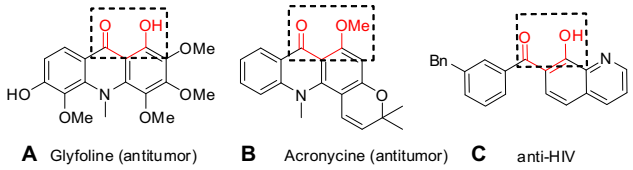
A facile, efficient, and general synthetic method for a wide range of medicinally useful 2-carboxylate derivatives of acridinols, quinolinols, and naphthalenols has been developed via silver-catalyzed electrophilic cyclization of 3-(2-alkynyl)aryl-β-ketoesters. The designed reaction involved selective C–C bond formation on more electrophilic alkynyl carbon, which resulted in the regioselective 6-*endo-dig* cyclized product, as confirmed by X-ray crystallographic studies. The deuterium labeling experiments were performed to support the proposed mechanism. The synthetic methodology accommodates wide functional group variations on alkyne, which proves to be highly advantageous for structural and biological activity assessments.

1. Introduction

Transition-metal-catalyzed electrophilic cyclization of alkynes and carbon–carbon bond formation using enolates have made a large contribution in organic chemistry for the synthesis of a variety of natural products, heterocycles, and carbocycles.[1] Among the various transition metals employed, silver-catalyzed reactions have gathered remarkable importance because of their ability to activate various π-systems at low-catalyst loading.[2]

The biochemical properties and therapeutic applications of polycyclic compounds largely depend on substituents in the basic structure. Acridines, quinolines and naphthalenes, have demonstrated significant biological activity against cancer,[3] viruses,[4] bacteria,[5] parasites,[6] fungus,[7] Alzheimer's disease,[8] and HIV/AIDS.[9] Substrates with diketoacid (DKAs) functionality have been disclosed as promising HIV-1 integrase (IN) inhibitor.[10] Acridine based alkaloids, such as Glyfoline, Acronycine (Fig. 1, **A** and **B**), and quinoline based compound **C** with analogous DKAs functionality, have found their application as potential antitumor and anti-HIV agents.[11] Thus, the development of novel and efficient routes for rapid access to such functionalized heterocycles under mild conditions are of high demand.

Although several reports are available for synthesis of these heterocycles, yet the efficient and general routes to synthesize such heterocyclic compounds with requisite DKAs functionality under mild reaction condition still have to be explored. The most common approaches for the synthesis of acridines proceed via corresponding acridones,[12] aminobenzannulation[13] cycloisomerisation,[14] and [4+2] annulations of benzynes.[15] Most of the methods for the synthesis of acridines require rather harsh conditions.[16]



A Glyfoline (antitumor) **B** Acronycine (antitumor) **C** anti-HIV

Fig. 1. Selected biologically active acridines and quinolines.

Prompted by importance of these heterocycles and in continuation of our ongoing efforts in the synthesis of heterocycles[17] by the electrophilic cyclization of alkynes, we herein, report a straight forward approach for the synthesis of acridinol, quinolinol, naphthalenol and benzothiophenol via silver-catalyzed electrophilic cyclization of 3-(2-alkynyl)aryl-β-ketoesters (**3a**–**t**) with requisite DKAs functionality in excellent regioselectivity at room temperature. *ortho*-Alkynyl-β-keto esters **3** required for the reaction were readily prepared from easily accessible *ortho*-alkynyl aldehydes **1**, by reacting it with ethyl 2-diazoacetate **2** using $NbCl_5$ in CH_2Cl_2 at

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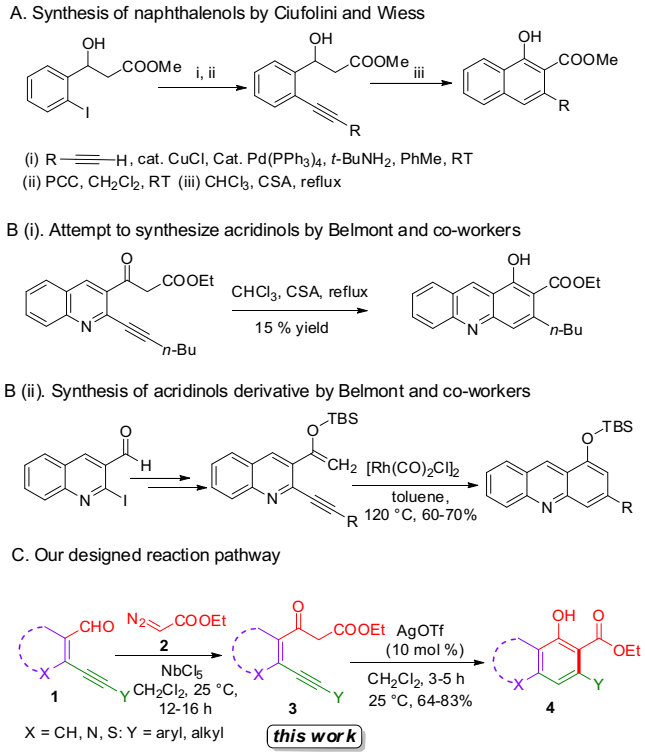
25 °C.[18] Alkynes **3** were then subjected to electrophilic cyclization using AgOTf as a catalyst in CH_2Cl_2 to afford the desired product **4** (Scheme 1, C).



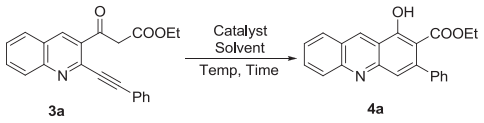
Scheme 1. Previous approaches and our designed reaction pathway.

Previously, Ciufolini and Weiss[19] have reported electrophilic cyclization on the parent benzaldehyde moiety using camphor sulphonic acid (CSA) in $CHCl_3$ under reflux condition for 8–12 h (Scheme 1, A). However, the methodology failed on quinolinecarbaldehyde moiety when Belmont and co-workers[20] used same reaction condition and ended up only with the 15% yield of the desired product {Scheme 1, B(i)}. This forced them to design a new strategy for the synthesis of acridinol derivatives[14,20] {Scheme 1, B(ii)}. Our designed strategy accomodates various substrates like quinolinecarbaldehyde, nicotinaldehyde, benzaldehyde and benzothiophenecarbaldehyde, which afforded various 2-carboxylate derivative of acridinols, quinolinols, naphthalenols and benzothiophenols, respectively, under mild reaction condition in good yields. Reaction afforded the *6-endo-dig* cyclized products by selective C–C bond formation on the more electrophilic alkynyl carbon (Scheme 1, C).

2. Results and discussion

In order to find the optimal reaction condition, we first analyzed various factors affecting reaction by using ethyl 3-oxo-3-(2-(phenylethynyl)quinolin-3-yl)propanoate **3a** (0.5 mmol) as a starting substrate. First of all, the reaction was performed with 5.0 mol % $AgNO_3$ in 2.0 mL of $CHCl_3$ at 25 °C, the cyclized product **4a** was obtained in only 22% yield after 3 h (Table 1, entry 1). However, when the reaction was further allowed to stir for 5 h, the product **4a** was obtained in 30% yield (Table 1, entry 2). Increasing the amount of $AgNO_3$ from 5 mol % to 10 mol %, led to the formation of **4a** in 44% yield (entry 3). Further efforts were made to come up with better conditions, which could afford the product in good yield. Among the various factors, we first varied silver salt. Employing AgOTf instead of $AgNO_3$, afforded the desired product **4a** in 58% yield (entry 4). Various solvents like CH_3CN, CH_2Cl_2, H_2O, DMSO, DMF, and methanol were screened at low and elevated temperatures to find an appropriate system for the proposed reaction. From entries 5–10 in Table 1, it is apparent that CH_2Cl_2 was found to be quite successful for the transformation, as compound **4a** was obtained in a 75% yield. The use of AgOAc afforded the desired product **4a** only in 45% yield; whereas, other triflates like CuOTf and HOTf were found to be ineffective (entries 11–13). The combination of AgOTf (10.0 mol %) in CH_2Cl_2 (2.0 mL) at 25 °C was found to be most suitable for the reaction.

Table 1
Optimization of reaction condition[a]



Entry	Solvent	Catalyst (mol %)	T °C	Time (h)	Yield[b] (%)
1	$CHCl_3$	$AgNO_3$ (5)	25	3 h	22
2	$CHCl_3$	$AgNO_3$ (5)	25	5 h	30
3	$CHCl_3$	$AgNO_3$ (10)	25	5 h	44
4	$CHCl_3$	AgOTf (10)	25	5 h	58
5	CH_3CN	AgOTf (10)	25	5 h	48
6	CH_2Cl_2	AgOTf (10)	25	5 h	75
7	H_2O	AgOTf (10)	80	5 h	68
8	DMSO	AgOTf (10)	120	5 h	28
9	DMF	AgOTf (10)	120	5 h	32
10	MeOH	AgOTf (10)	70	5 h	Trace
11	CH_2Cl_2	AgOAc (10)	25	5 h	45
12	CH_2Cl_2	CuOTf (10)	25	5 h	Trace
13	CH_2Cl_2	HOTf (10)	25	5 h	Trace

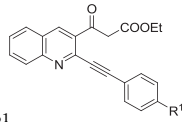
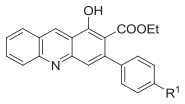
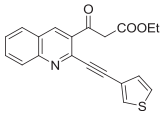
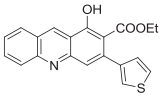
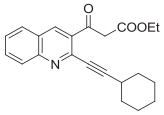
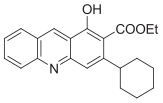
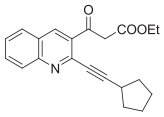
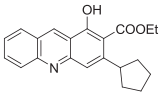
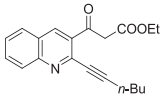
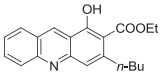
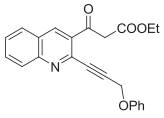
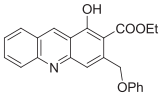
[a] All reactions were performed using 0.5 mmol of the alkyne **3a**, in 2.0 mL of solvent.
[b] Isolated yields.

The scope and limitation of this silver-catalyzed electrophilic cyclization process were next examined by employing various alkynes bearing different substituents. The alkyne **3a** bearing phenyl substituent, afforded the desired cyclized product **4a** in 75% yield (Table 2, entry 1). Substrates **3b–d** bearing electron-releasing methyl, ethyl, and methoxy groups on the phenyl, *para* to the triple bond resulted 6-*endo-dig* cyclized product **4b–d** in 78–83% yields (entries 2–4). Alkyne bearing biphenyl substituent **3e** provided the cyclized product **4e** in 76% yield (entry 5). Alkyne **3f** bearing an electron-withdrawing CF_3 group on phenyl, *para* to the triple bond, afforded the product **4f** in 64% yield (entry 6). Having studied the effect of phenyl ring, we further employed the protocol for alkyne bearing an electron-rich heterocycle, i.e., thiophene, afforded the desired product **4g** in 82% yield (entry 7). Alkynes **3h–j** having alicyclic and alkyl substituents were found successful for the reaction, and the desired cyclized products **4h–j** were obtained in 70–72% yields (entries 8–10). The propargylphenoxy substituted alkyne **3k** was also subjected to this cyclization and we were pleased to obtain cyclized product **4k** in 69% yield (entry 11).

After obtaining the successful results with *ortho*-alkynylquinolines **3a–k**, we further extended the scope of this reaction on other substrates bearing electron-deficient (**3l–n**), neutral (**3o–s**) and electron-rich (**3t**) heterocyclic nucleus. Alkynes ethyl 3-oxo-3-(2-(arylethynyl)pyridin-3-yl)propanoate bearing *p*-tolyl and 1,3-dimethoxybenzene **3l,m** afforded the desired cyclized product **4l,m** in 72–79% yields (Table 3, entries 1–2). Furthermore, ethyl 3-oxo-3-(3-(*p*-tolylethynyl)pyridin-4-yl)propanoate **3n** provided the product **4n** in 73% yield (entry 3).

Further exploring the developed protocol to ethyl 3-oxo-3-(2-(arylethynyl)phenyl)propanoate **3o–s**, the desired products **4o–s** were obtained in moderate to good yields (Table 3, entries 4–8). The

Table 2
Synthesis of 3-aryl/alkylacridinol-2-carboxylates[a]

Entry	Substrate **3**		Product **4**		Yield[b] (%)
					
	R^1		R^1		
1	H	**3a**	H	**4a**	75
2	Me	**3b**	Me	**4b**	79
3	Et	**3c**	Et	**4c**	78
4	OMe	**3d**	OMe	**4d**	83
5	Ph	**3e**	Ph	**4e**	76
6	CF_3	**3f**	CF_3	**4f**	64
7		**3g**		**4g**	82
8		**3h**		**4h**	70
9		**3i**		**4i**	72
10		**3j**		**4j**	70
11		**3k**		**4k**	69

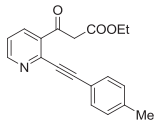
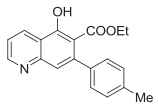
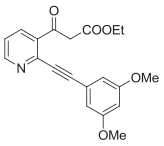
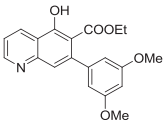
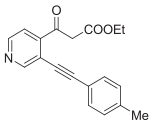
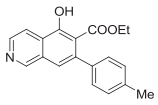
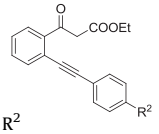
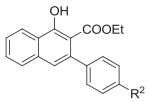
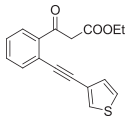
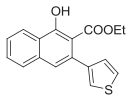
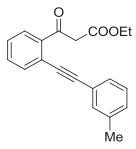
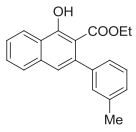
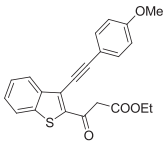
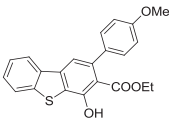
[a] All reactions were performed with 0.5 mmol of the alkynes **3a**–**k**, AgOTf (10.0 mol %) in CH_2Cl_2 (2.0 mL) at 25 °C for 3–5 h.
[b] Isolated yields.

methyl and methoxy group present at *para* of alkynes **3p**–**q**, resulted the cyclized products **4p**–**q**, in 74% and 79% yields, respectively (entries 5–6). The electron-rich thiophene substituted alkyne **3r**, proved favorable for the reaction and afforded desired product **4r** in 80% yield (entry 7). The substitution at *meta* position of the phenyl ring afforded the cyclized product **4s** in comparatively lower, i.e., 69% yield (entry 8). Electron-rich alkyne ethyl-3-(3-((4-methoxy phenyl) ethynyl)benzo-[*b*]thiophen-2-yl)-3-oxopropano ate **3t** afforded the desired cyclized product **4t** in 75% yield (entry 9).

All the synthesized products were fully characterized by the ^1H and ^{13}C NMR method and mass spectroscopic data. The regioselective *6-endo-dig* cyclization was unambiguously confirmed by X-ray crystallographic studies of compounds **4f** and **4p** (Figs. 2 and 3).

To support the proposed mechanism, reaction of alkyne **3d** was performed in $CHCl_3$ and quenched with D_2O, product **5** was observed (Scheme 2). Similar result was obtained, when we performed the reaction in $CDCl_3$ and quenched it with D_2O/CD_3OD. The product **4d** was obtained when the same reaction was carried out in $CDCl_3$ and quenched with H_2O.[21] However, when the reaction was carried out in $CDCl_3$ with 10.0 equiv of CD_3OD, both the compounds **5** and **6** were obtained in 2:3 ratios. Whereas, the formation of compound **6** occurred because of the presence of D^+ ion in the reaction medium, sourced by CD_3OD. These experiments indicate that H^+ ion, which replaces Ag^+ ion, is being accomplished before workup.

Table 3
Synthesis of naphthalenes, quinolines, and dibenzothiophenes with DKAs functionality[a]

Entry	Substrate **3**		Product **4**		Yield (%)[b]
1		**3l**		**4l**	79
2		**3m**		**4m**	72
3		**3n**		**4n**	73
					
	R^2		R^2		
4	H	**3o**	H	**4o**	70
5	Me	**3p**	Me	**4p**	74
6	OMe	**3q**	OMe	**4q**	79
7		**3r**		**4r**	80
8		**3s**		**4s**	69
9		**3t**		**4t**	75

[a] All reactions were performed with 0.50 mmol of the alkynes **3l**–**t**, AgOTf (10.0 mol %) in CH_2Cl_2 (2.0 mL) at 25 °C for 3–5 h.
[b] Isolated yields.

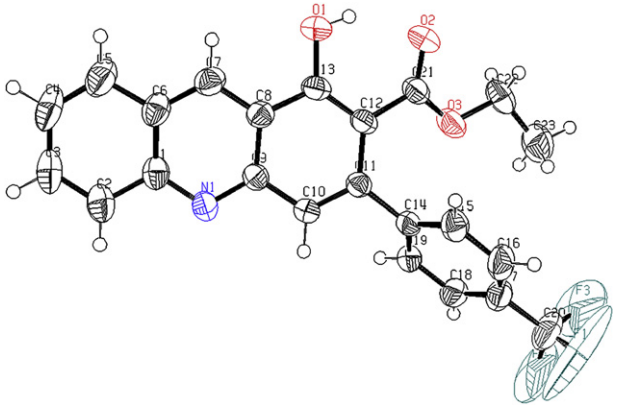


Fig. 2. X-ray crystallographic ORTEP drawing of compound **4f**.

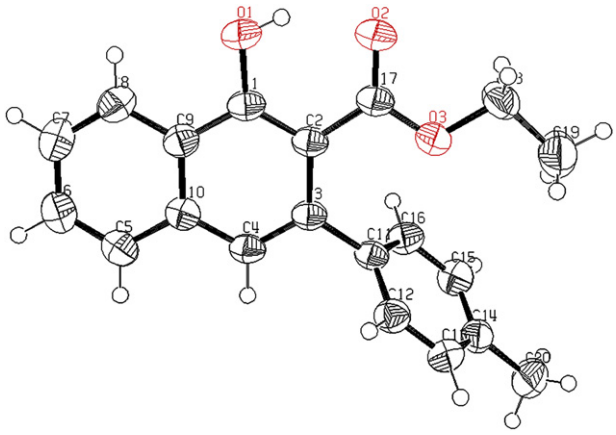
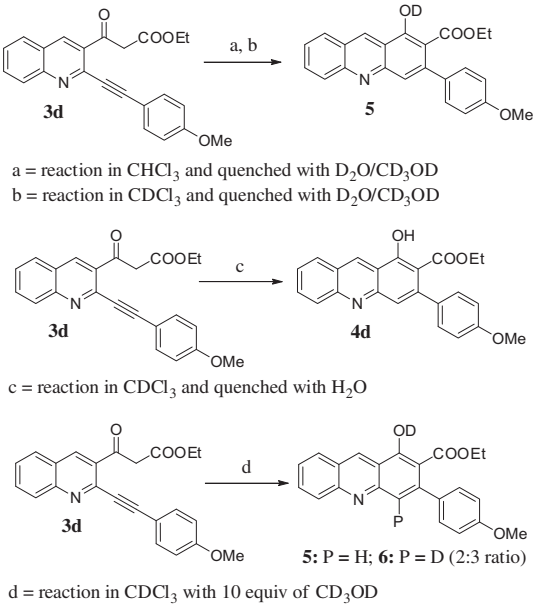
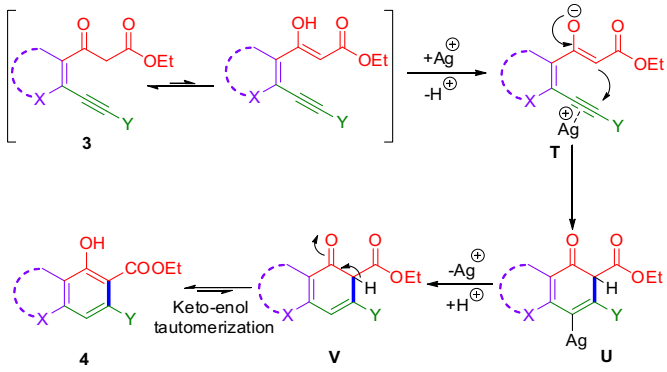


Fig. 3. X-ray crystallographic ORTEP drawing of compound **4p**.



Scheme 2. Deuterium-labeling experiments.

On the basis of above observations, along with deuterium labeling experiments, an assumed pathway for the formation of cyclized product **4** is illustrated in Scheme 3. Firstly, the AgOTf coordinates to the triple bond of **3** to form a π-complex **T**,[14] which undergoes intramolecular nucleophilic attack by the C2 position of β-keto ester onto alkynyl carbon to form the species **U**.



Scheme 3. Proposed mechanism.

Subsequently, replacement of silver ion by H^+ ion and keto-enol tautomerization of **V** led to desired cyclized product **4**.

3. Conclusions

In summary, a mild and efficient approach for the direct synthesis of medicinally important acridinol, naphthalenol, quinolinol and benzothiophenol bearing 2-carboxylate group have been demonstrated. This milder and feasible silver-catalyzed electrophilic cyclization have been advantageously employed to tolerate high functional group variation, thereby achieving diversity and regioselectivity in good yields, which makes it ideal for the generation of libraries of functionally-substituted scaffolds. The regioselective 6-*endo-dig* formation was confirmed by X-ray crystallographic studies. The deuterium labeling experiments proved to be an additional support for the proposed mechanism.

4. Experimental section

4.1. General method

^{1}H NMR (300 MHz or 400 MHz) and ^{13}C NMR (75 MHz or 100 MHz) spectra were recorded in $CDCl_3$ or in DMSO as specified and were obtained using Jeol JNM ECX400P (400 MHz) spectrometer and Bruker AV300 (300 MHz) spectrometer. Chemical shifts for protons are reported in parts per million from tetramethylsilane with the residual $CHCl_3$ resonance as internal reference. Chemical shifts for carbons are reported in ppm from tetramethylsilane and are referenced to the carbon resonance of the solvent. Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, dd=doublet of doublet), coupling constants in hertz, and integration. High-resolution mass spectra were recorded on Applied Biosystems QSTAR® Elite Hybrid (QqTOF) from Department of Biomedical & Pharmaceutical Sciences, College of Pharmacy, University of Rhode Island, Kingston-02881, Rhode Island, USA. Crystal structure analysis was accomplished on Oxford diffraction (Xcaliber S) single crystal X-ray diffractometer. TLC analysis was performed on commercially prepared 60 F_{254} silica gel plates and visualized by either UV irradiation or by staining with I_2. Anhydrous forms of all reagents, such as diethyl ether, hexanes, ethyl acetate, CH_2Cl_2, 2-chloroquinoline-3-carbaldehyde, 2-bromonicotinaldehyde, 3-bromoisonicotin aldehyde, 2-bromobenzaldehyde, 3-bromobenzo [*b*] thiophene-2-carbaldehyde, ethyl diazoacetate, terminal alkynes, Et_3N, and the silver salts were used directly as obtained commercially unless otherwise noted.

4.2. General procedure for the niobium-catalyzed formation of the *ortho*-alkynyl-β-keto esters (3a–t)

To a solution of CH_2Cl_2 (10.0 mL), $NbCl_5$ (10.0 mol %) and *ortho*-alkynyl aldehydes (1 mmol), ethyl 2-diazoacetate (1.2 mmol) was added and the reaction mixture was allowed to stir at 25 °C for 12–16 h. The reaction mixture was filtered and diluted with ethyl acetate and washed with brine solution. The combined organic fractions were dried over anhydrous Na_2SO_4 and concentrated under vacuum to yield the crude product. The crude product was purified by column chromatography on silica gel using ethyl acetate/hexane as the eluent.

*4.2.1. Ethyl 3-oxo-3-(2-(phenylethynyl)quinolin-3-yl)propanoate (**3a**).* The product was obtained as a brown oil (247.2 mg, 72%); R_f (15% ethyl acetate/hexane) 0.33; the compound was obtained as a mixture of keto and enol forms in the ratio of 2:1, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.58 (s, 0.4H, O*H*) (enol), 8.51 (d, *J*=2.9 Hz, 1H, $CH_{aromatic}$) (keto), 8.17–8.10 (m, 1.4H, $CH_{aromatic}$) (keto+enol), 7.83–7.70 (m, 2.8H,

$CH_{aromatic}$) (keto+enol), 7.67–7.63 (m, 2.8H, $CH_{aromatic}$) (keto+enol), 7.54–7.47 (m, 2.0H, $CH_{aromatic}$) (keto+enol), 7.35–7.30 (m, 4.4H, $CH_{aromatic}$) (keto+enol), 6.33 (s, 0.4H, C=CH) (enol), 4.30–4.24 (m, 2.8H, C=OCH_2C=O+CH_2CH_3) (keto+enol), 4.12 (q, J=7.3 Hz, 2H, CH_2CH_3) (keto), 1.30 (t, J=7.3 Hz, 1.6H, CH_2CH_3) (enol), 1.13 (t, J=7.3 Hz, 3H, CH_2CH_3) (keto); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 193.5, 172.7, 171.2, 168.3, 166.9, 163.6, 148.7, 147.9, 147.0, 139.9, 139.7, 138.1, 136.5, 136.3, 132.8, 132.2, 132.1, 131.3, 129.6, 129.63, 129.55, 129.35, 128.8, 128.76, 128.67, 128.3, 128.25, 128.17, 128.0, 127.1, 127.29, 127.22, 126.1, 121.84, 121.79, 124.4, 106.0, 94.3, 93.7, 93.1, 88.47, 88.41, 88.0, 61.4, 61.0, 60.4, 48.3, 14.1, 13.8; HRMS calcd for $C_{22}H_{18}NO_3$ ([M+H]$^+$) 344.1287; found 344.1296.

*4.2.2. Ethyl 3-oxo-3-(2-(p-tolylethynyl)quinolin-3-yl)propanoate (**3b**).* The product was obtained as a brown oil (268.0 mg, 75%); R_f (15% ethyl acetate/hexane) 0.31; the compound was obtained as a mixture of keto and enol forms in the ratio of 2:1, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.62 (s, 0.5H, OH) (enol), 8.60–8.55 (m, 1.5H, $CH_{aromatic}$) (keto+enol), 8.19–8.00 (m, 3H, $CH_{aromatic}$) (keto+enol), 7.92–7.78 (m, 4.2H, $CH_{aromatic}$) (keto+enol), 7.63–7.52 (m, 6H, $CH_{aromatic}$) (keto+enol), 7.40–7.21 (m, 6.2H, $CH_{aromatic}$) (keto+enol), 6.41 (s, 0.5H, C=CH) (enol), 4.38–4.31 (m, 3H, C=OCH_2C=O+CH_2CH_3) (keto+enol), 4.18 (q, J=7.3 Hz, 2H, CH_2CH_3) (keto), 2.68 (s, 4.5H, PhCH_3) (keto+enol), 1.38 (t, J=7.3 Hz, 1.7H, CH_2CH_3) (enol), 1.21 (t, J=7.3 Hz, 3H, CH_2CH_3) (keto); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.8, 173.1, 171.6, 162.4, 161.4, 150.9, 149.7, 143.5, 143.0, 134.9, 134.2, 131.8, 130.8, 130.0, 129.2, 127.9, 127.1, 126.5, 126.0, 125.8, 124.8, 122.3, 121.8, 118.6, 95.5, 94.6, 91.8, 86.3, 86.1, 61.2, 60.2, 60.7, 21.4, 16.3, 15.9; HRMS calcd for $C_{23}H_{20}NO_3$ (M^+) 357.1365; found 357.1366.

*4.2.3. Ethyl 3-(2-((4-ethylphenyl)ethynyl)quinolin-3-yl)-3-oxopropanoate (**3c**).* The product was obtained as a brown oil (278.4 mg, 75%); R_f (15% ethyl acetate/hexane) 0.31; the compound was obtained as a mixture of keto and enol forms in the ratio of 1.3:1, ^{1}H NMR (300 MHz, $CDCl_3$) δ: 12.53 (s, 0.7H, OH) (enol), 7.85–7.79 (m, 1.7H, $CH_{aromatic}$) (keto+enol), 7.66–7.59 (m, 1.7H, $CH_{aromatic}$) (keto+enol), 7.55–7.49 (m, 4.4H, $CH_{aromatic}$) (keto-+enol), 7.48–7.41 (m, 2.7H, $CH_{aromatic}$) (keto+enol), 7.40–7.20 (m, 4.1H, $CH_{aromatic}$) (keto+enol), 6.26 (s, 0.7H, C=CH) (enol), 4.36–4.29 (m, 3.4H, C=OCH_2C=O+CH_2CH_3) (keto+enol), 4.19 (q, J=7.2 Hz, 2H, CH_2CH_3) (keto), 2.69 (q, J=7.2 Hz, 3.7H, CH_2CH_3) (keto+enol), 1.38 (t, J=7.3 Hz, 2.2H, CH_2CH_3) (enol), 1.30–1.20 (m, 8.6H, CH_2CH_3) (keto); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 194.9, 173.2, 170.4, 167.6, 145.6, 145.1, 139.2, 135.2, 133.9, 133.6, 131.8, 131.6, 131.5, 129.9, 129.2, 128.28, 128.13, 128.07, 127.95, 122.1, 121.4, 120.2, 119.7, 96.2, 95.2, 92.2, 87.7, 87.3, 61.3, 60.3, 48.6, 28.9, 15.3, 14.3, 14.0; HRMS calcd for $C_{24}H_{22}NO_3$ ([M+H]$^+$) 372.1600; found 372.1576.

*4.2.4. Ethyl 3-(2-((4-methoxyphenyl)ethynyl) quinolin-3-yl)-3-oxopropanoate (**3d**).* The product was obtained as a brown oil (280.0 mg, 75%); R_f (15% ethyl acetate/hexane) 0.25; the compound was obtained as a mixture of keto and enol forms in the ratio of 2.5:1, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.54 (s, 0.4H, OH) (enol), 8.52 (d, J=5.8 Hz, 1H, $CH_{aromatic}$) (keto), 8.08–8.06 (m, 1.4H, $CH_{aromatic}$) (keto+enol), 7.84–7.70 (m, 2.8H, $CH_{aromatic}$) (keto+enol), 7.59–7.58 (m, 2.7H, $CH_{aromatic}$) (keto+enol), 7.53–7.48 (m, 1.4H, $CH_{aromatic}$) (keto+enol), 7.19 (s, 0.4H, $CH_{aromatic}$) (enol), 6.86–6.82 (m, 2.8H, $CH_{aromatic}$) (keto+enol), 6.34 (s, 0.4H, C=CH) (enol), 4.30–4.25 (m, 2.8H, C=OCH_2C=O+CH_2CH_3) (keto+enol), 4.11 (q, J=7.3 Hz, 2H, CH_2CH_3) (keto), 3.77 (s, 4.4H, PhOCH_3) (keto+enol), 1.38 (t, J=6.6 Hz, 1.4H, CH_2CH_3) (enol), 1.13 (t, J=7.3 Hz, 3H, CH_2CH_3) (keto); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 193.9, 172.9, 168.5, 167.2, 160.8, 160.6, 148.9, 147.9, 138.2, 133.95, 133.92, 133.3, 128.92, 128.83, 128.3, 127.9, 127.7, 126.2, 125.9, 114.2, 114.0, 113.5, 93.2, 87.3, 61.5, 60.5, 55.3, 48.5, 14.3, 14.0; HRMS calcd for $C_{23}H_{19}NO_4$ (M^+) 373.1314; found 373.1314.

*4.2.5. Ethyl 3-(2-(biphenyl-4-ylethynyl)quinolin-3-yl)-3-oxopropanoate (**3e**).* The product was obtained as a brown oil (293.6 mg, 70%); R_f (15% ethyl acetate/hexane) 0.28; the compound was obtained as a mixture of keto and enol forms in the ratio of 2:1, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.55 (s, 0.5H, OH) (enol), 8.54–8.48 (m, 1.5H, $CH_{aromatic}$) (keto+enol), 8.10–8.00 (m, 3.1H, $CH_{aromatic}$) (keto+enol), 7.86–7.64 (m, 4.8H, $CH_{aromatic}$) (keto+enol), 7.62–7.49 (m, 8.3H, $CH_{aromatic}$) (keto+enol), 7.35–7.28 (m, 8.0H, $CH_{aromatic}$) (keto+enol), 6.31 (s, 0.5H, C=CH) (enol), 4.29–4.24 (m, 2.8H, C=OCH_2C=O+CH_2CH_3) (keto+enol), 4.10 (q, J=7.3 Hz, 2H, CH_2CH_3) (keto), 1.30 (t, J=7.3 Hz, 1.6H, CH_2CH_3) (enol), 1.12 (t, J=7.3 Hz, 3H, CH_2CH_3) (keto); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 193.9, 173.4, 171.5, 167.7, 149.8, 148.5, 144.3, 140.8, 139.6, 136.7, 135.2, 132.5, 130.1, 129.8, 129.20, 129.08, 128.7, 128.29, 128.26, 128.06, 128.01, 126.31, 126.12, 125.88, 125.72, 125.4, 125.0, 124.2, 123.9, 123.4, 121.2, 118.6, 96.2, 95.0, 92.1, 86.1, 85.8, 61.4, 61.2, 47.5, 13.2, 13.0; HRMS calcd for $C_{28}H_{22}NO_3$ ([M+H]$^+$) 420.1600; found 420.1598.

*4.2.6. Ethyl 3-oxo-3-(2-((4-(trifluoromethyl)phenyl) ethynyl)quinolin-3-yl)propanoate (**3f**).* The product was obtained as a brown oil (284.1, 69%); R_f (15% ethyl acetate/hexane) 0.28; the compound was obtained as a mixture of keto and enol forms in the ratio of 2.5:1, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.63 (s, 0.4H, OH) (enol), 8.61 (d, J=6.6 Hz, 1H, $CH_{aromatic}$) (Keto), 8.53–8.37 (m, 0.4H, $CH_{aromatic}$) (enol), 8.23–8.10 (m, 1.9H, $CH_{aromatic}$) (keto+enol), 7.95–7.87 (m, 2.9H, $CH_{aromatic}$) (keto+enol), 7.86–7.78 (m, 2.8H, $CH_{aromatic}$) (keto+enol), 7.69–7.58 (m, 4.6H, $CH_{aromatic}$) (keto+enol), 6.29 (s, 0.4H, C=CH) (enol), 4.37–4.30 (m, 2.9H, C=OCH_2C=O+CH_2CH_3) (keto+enol), 4.17 (q, J=7.3 Hz, 2H, CH_2CH_3) (keto), 1.38 (t, J=7.3 Hz, 2.0H, CH_2CH_3) (enol), 1.20 (t, J=7.3 Hz, 3H, CH_2CH_3) (keto); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.2, 173.4, 171.1, 163.1, 162.4, 150.9, 149.3, 146.6, 144.8, 141.7, 140.2, 135.8, 134.7, 134.3, 132.1, 131.0, 129.13, 129.09, 128.5, 127.7, 126.16, 126.14, 125.6, 124.51, 124.47, 124.43, 122.9, 122.5, 120.3, 119.3, 118.8, 96.2, 94.9, 91.6, 87.8, 87.3, 61.4, 61.2, 48.4, 13.7, 12.7; HRMS calcd for $C_{23}H_{17}F_3NO_3$ ([M+H]$^+$) 412.1161; found 412.1156.

*4.2.7. Ethyl 3-oxo-3-(2-(thiophen-3-ylethynyl) quinolin-3-yl)propanoate (**3g**).* The product was obtained as a brown oil (255.0 mg, 73%); R_f (15% ethyl acetate/hexane) 0.33; the compound was obtained as a mixture of keto and enol forms in the ratio of 2.5:1 ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.50 (s, 0.4H, OH) (enol), 7.81–7.76 (m, 1.4H, $CH_{aromatic}$) (keto+enol), 7.62–7.55 (m, 2.8H, $CH_{aromatic}$) (keto+enol), 7.51–7.47 (m, 1.4H, $CH_{aromatic}$) (keto+enol), 7.43–7.37 (m, 2.8H, $CH_{aromatic}$) (keto+enol), 7.33–7.30 (m, 1.5H, $CH_{aromatic}$) (keto+enol), 7.24–7.21 (m, 1.8H, $CH_{aromatic}$) (keto+enol), 6.18 (s, 0.4H, C=CH) (enol), 4.27 (q, J=7.3 Hz, 0.8H, CH_2CH_3) (enol), 4.25 (s, 2H, C=OCH_2C=O) (keto), 4.17 (q, J=7.3 Hz, 2H, CH_2CH_3) (keto), 1.34 (t, J=7.3 Hz, 1.2H, CH_2CH_3) (enol), 1.20 (t, J=7.3 Hz, 3H, CH_2CH_3) (keto); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.1, 171.5, 169.6, 163.7, 162.6, 150.8, 149.6, 146.4, 143.1, 141.8, 140.8, 139.8, 137.1, 135.4, 134.2, 131.9, 130.7, 129.16, 129.07, 128.1, 127.6, 127.3, 127.0, 126.3, 126.0, 125.9, 122.3, 118.7, 95.1, 94.6, 92.8, 85.4, 84.9, 61.0, 60.8, 48.1, 14.1, 13.9; HRMS calcd for $C_{20}H_{15}NO_3S$ (M^+) 349.0773; found 349.0773.

*4.2.8. Ethyl 3-(2-(cyclohexylethynyl)quinolin-3-yl)-3-oxopropanoate (**3h**).* The product was obtained as a brown oil (258.6 mg, 74%); R_f (15% ethyl acetate/hexane) 0.31; the compound was obtained as a mixture of keto and enol forms in the ratio of 1.8:1, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.50 (s, 0.5H, OH) (enol), 8.76–8.64 (m, 1.6H, $CH_{aromatic}$) (keto+enol), 8.13–8.09 (m, 1.6H, $CH_{aromatic}$) (keto+enol), 7.54–7.52 (m, 1.8H, $CH_{aromatic}$) (keto+enol), 7.38–7.17 (m, 4.2H, $CH_{aromatic}$) (keto+enol), 6.35 (s, 0.5H, C=CH) (enol), 4.34–4.29 (m, 3H, C=OCH_2C=O+CH_2CH_3) (keto+enol), 4.17 (q, J=7.3 Hz, 2H,

CH_2CH_3) (keto), 3.55–3.50 (m, 1.3H, C*H*) (keto+enol), 2.05–2.02 (m, 2.2H, CH_2) (keto+enol), 1.93–1.90 (m, 2H, CH_2) (keto+enol), 1.82–1.79 (m, 1.3H, CH_2) (keto+enol), 1.65–1.56 (m, 2.2H, CH_2) (keto+enol), 1.42–1.25 (m, 7.8H, CH_2+CH_2CH_3) (keto+enol), 1.24–1.18 (m, 4.1H, CH_2+CH_2CH_3) (keto+enol); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.4, 172.6, 172.3, 166.9, 166.6, 149.8, 133.8, 128.3, 126.3, 126.0, 125.6, 125.2, 124.7, 121.8, 121.5, 119.1, 118.8, 108.8, 100.6, 99.4, 99.2, 92.1, 61.2, 61.0, 32.2, 29.7, 25.8, 24.7, 13.9, 13.7; HRMS calcd for $C_{22}H_{23}NO_3$ (M^+) 349.1678; found 349.1678.

*4.2.9. Ethyl 3-(2-(cyclopentylethynyl)quinolin-3-yl)-3-oxopropanoate (**3i**).* The product was obtained as a brown oil (238.1 mg, 71%); R_f (15% ethyl acetate/hexane) 0.31; the compound was obtained as a mixture of keto and enol forms in the ratio of 2.5:1, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.58 (s, 0.4H, O*H*) (enol), 8. 51 (d, J=4.2 Hz, 0.4H, C$H_{aromatic}$), 8.07–8.03 (m, 1.4H, C$H_{aromatic}$) (keto+enol), 7.91 (s, 1H, C$H_{aromatic}$) (Keto), 7.84–7.64 (m, 3.5H, C$H_{aromatic}$) (keto+enol), 7.54–7.46 (m, 1.8H, C$H_{aromatic}$) (keto+enol), 7.28–7.25 (m, 1.4H, C$H_{aromatic}$) (keto+enol), 6.81 (s, 0.4H, C=C*H*) (enol), 4.32–4.25 (m, 2.8H, C=OCH_2C=O+CH_2CH_3) (keto+enol), 4.17 (q, J=7.3 Hz, 2H, CH_2CH_3) (enol), 3.87–3.79 (m, 1.3H, C*H*) (keto+enol), 2.05–1.95 (m, 3H, CH_2) (keto+enol), 1.80–1.77 (m, 6H, CH_2) (keto+enol), 1.67–1.62 (m, 3H, CH_2+CH_2CH_3) (keto+enol), 1.23–1.18 (m, 6.5H) (keto+enol, CH_2+CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 193.5, 172.3, 171.8, 160.5, 159.2, 141.9, 133.7, 132.9, 128.3, 127.6, 126.8, 124.7, 121.5, 118.8, 108.8, 102.9, 100.7, 99.4, 98.4, 70.7, 61.9, 61.8, 33.4, 30.8, 24.9, 14.1, 13.9; HRMS calcd for $C_{21}H_{21}NO_3$ (M^+) 335.1521; found 335.1521.

*4.2.10. Ethyl 3-(2-(hex-1-ynyl)quinolin-3-yl)-3-oxo propanoate (**3j**).* The product was obtained as a brown oil (239.3 mg, 74%); R_f (15% ethyl acetate/hexane) 0.31; the compound was obtained as a mixture of keto and enol forms in the ratio of 2.5:1, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.60 (s, 0.4H, O*H*) (enol), 8.58–8.27 (m, 1.3H, C$H_{aromatic}$) (keto+enol), 8.25–8.09 (m, 2.9H, C$H_{aromatic}$) (keto+enol), 8.04–7.90 (m, 3.7H, C$H_{aromatic}$) (keto+enol), 7.76–7.68 (m, 2.2H, C$H_{aromatic}$) (keto+enol), 7.51–7.42 (m, 0.5H, C$H_{aromatic}$) (keto+enol), 6.29 (s, 0.4H, C=C*H*) (enol), 4.31–4.18 (m, 3H, C=OCH_2C=O+CH_2CH_3) (keto+enol), 3.98–3.93 (m, 2H, CH_2CH_3) (keto), 2.58–2.44 (m, 3.4H, CH_2) (keto+enol), 1.76–1.60 (m, 6.6H, CH_2) (keto+enol), 1.76–160 (m, 6.6H, CH_2) (keto+enol), 1.58–1.42 (m, 2.4H, CH_2) (keto+enol), 1.35–1.10 (m, 5H, CH_2+CH_2CH_3) (keto+enol), 1.00–0.92 (m, 4.9H, CH_2+CH_2CH_3) (keto+enol); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.8, 173.2, 171.6, 168.0, 159.6, 141.8, 133.8, 129.5, 128.3, 127.1, 126.0, 124.8, 121.5, 119.3, 118.8, 108.9, 103.1, 102.8, 102.20, 102.12, 92.1, 71.0, 61.9, 61.0, 30.4, 21.9, 144.1, 13.9, 13.6; HRMS calcd for $C_{20}H_{22}NO_3$ ([M+H]$^+$) 324.1600; found 324.1599.

*4.2.11. Ethyl 3-oxo-3-(2-(3-phenoxyprop-1-ynyl) quinolin-3-yl) propanoate (**3k**).* The product was obtained as a brown oil (257.6 mg, 69%); R_f (15% ethyl acetate/hexane) 0.25; the compound was obtained as a mixture of keto and enol forms in the ratio of 1.6:1, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 13.26 (s, 0.7H, O*H*) (enol), 8.18–8.08 (m, 1.4H, C$H_{aromatic}$) (keto+enol), 8.02–7.77 (m, 4.6H) (keto+enol, C$H_{aromatic}$), 7.71–7.38 (m, 4.7H, C$H_{aromatic}$) (keto+enol), 7.24–7.20 (m, 1.6H, C$H_{aromatic}$) (keto+enol), 6.99–6.89 (m, 4.1H, C$H_{aromatic}$) (keto+enol), 6.19 (s, 0.7H, C=C*H*) (enol), 5.41 (s, 3.2H, PhOCH_2) (keto+enol), 4.39 (q, J=7.3 Hz, 2H, CH_2CH_3) (keto), 4.20–4.06 (m, 5.2H, C=OCH_2C=O+CH_2CH_3) (keto+enol), 1.29 (t, J=7.3 Hz, 2.6H, CH_2CH_3) (enol), 1.23–1.11 (m, 3H, CH_2CH_3) (keto); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.6, 171.8, 169.6, 167.3, 160.7, 159.7, 143.5, 140.7, 139.1, 133.2, 132.2, 132.9, 128.2, 126.6, 125.4, 125.3, 125.2, 124.78, 124.57, 123.3, 122.7, 122.4, 120.9, 119.8, 119.4, 113.8, 95.7, 82.1, 82.0, 72.4, 72.3, 61.6, 61.0, 47.6, 14.2, 13.9; HRMS calcd for $C_{23}H_{20}NO_4$ ([M+H]$^+$) 374.1393; found 374.1389.

*4.2.12. Ethyl 3-oxo-3-(2-(p-tolylethynyl)pyridin-3-yl)propanoate (**3l**).* The product was obtained as light brown oil (224.3 mg, 73%); R_f (15% ethyl acetate/hexane) 0.21; the compound was obtained as a mixture of keto and enol forms in the ratio of 1.6:1, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.51 (s, 0.6H, O*H*) (enol), 8.76–8.65 (m, 1.6H, C$H_{aromatic}$) (keto+enol), 8.12–8.10 (m, 1.6H, C$H_{aromatic}$) (keto-+enol), 7.55–7.42 (m, 3.3H, C$H_{aromatic}$) (keto+enol), 7.39–7.31 (m, 1.6H, C$H_{aromatic}$) (keto+enol), 7.26–7.17 (m, 3.6H, C$H_{aromatic}$) (keto+enol), 6.36 (s, 0.6H, C=C*H*) (enol), 4.34–4.29 (m, 3.2H, C=OCH_2C=O+CH_2CH_3) (keto+enol), 4.17 (q, J=7.3 Hz, 2H, CH_2CH_3) (keto), 2.39 (s, 4.9H, PhCH_3) (keto+enol), 1.37 (t, J=7.3 Hz, 1.9H, CH_2CH_3) (enol), 1.20 (t, J=7.3 Hz, 3H, CH_2CH_3) (keto); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.0, 172.9, 168.1, 167.1, 152.6, 150.9, 141.1, 140.2, 139.8, 137.0, 135.8, 135.5, 132.0, 131.7, 129.3, 129.2, 122.6, 122.3, 122.0, 118.9, 118.3, 96.0, 94.9, 93.1, 87.4, 87.0, 61.5, 60.6, 48.4, 21.6, 14.3, 13.9; HRMS calcd for $C_{19}H_{17}NO_3$ (M^+) 307.1208; found 307.1208.

*4.2.13. Ethyl 3-(2-((3,5-dimethoxyphenyl)ethynyl) pyridin-3-yl)-3-oxopropanoate (**3m**).* The product was obtained as light brown oil (257.9 mg, 73%); R_f (15% ethyl acetate/hexane) 0.18; the compound was obtained as a mixture of keto and enol forms in the ratio of 2.5:1, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.50 (s, 0.4H, O*H*) (enol), 7.81–7.76 (m, 1.4H, C$H_{aromatic}$) (keto+enol), 7.62–7.55 (m, 2.8H, C$H_{aromatic}$) (keto+enol), 7.51–7.47 (m, 1.4H, C$H_{aromatic}$) (keto+enol), 7.43–7.37 (m, 2.8H, C$H_{aromatic}$) (keto+enol), 7.33–7.30 (m, 1.5H, C$H_{aromatic}$) (keto+enol), 7.24–7.21 (m, 1.8H, C$H_{aromatic}$) (keto+enol), 6.18 (s, 0.6H, C=C*H*) (enol), 4.27 (q, J=7.3 Hz, 0.8H, CH_2CH_3) (enol), 4.25 (s, 2H, C=OCH_2C=O) (keto), 4.17 (q, J=7.3 Hz, 2H, CH_2CH_3) (keto), 3.85 (s, 8.6H, PhOCH_3) (keto+enol), 1.34 (t, J=7.3 Hz, 1.2H, CH_2CH_3) (enol), 1.20 (t, J=7.3 Hz, 3H, CH_2CH_3) (keto); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.4, 174.3, 171.6, 168.7, 159.7, 158.8, 150.8, 149.6, 143.0, 135.3, 134.2, 129.3, 129.13, 129.01, 125.8, 119.3, 118.6, 113.8, 113.0, 96.2, 94.9, 91.6, 85.2, 84.8, 61.2, 60.7, 55.3, 48.7, 13.8, 13.2; HRMS calcd for $C_{20}H_{19}NO_5$ ([M]$^+$) 353.1263; found 353.1264.

*4.2.14. Ethyl 3-oxo-3-(3-(p-tolylethynyl)pyridin-4-yl)propanoate (**3n**).* The product was obtained as light brown oil (215.1 mg, 70%); R_f (15% ethyl acetate/hexane) 0.22; the compound was obtained as a mixture of keto and enol forms in the ratio of 1.7:1, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.50 (s, 0.6H, O*H*) (enol), 8.13–7.90 (m, 1.7H, C$H_{aromatic}$) (keto+enol), 7.80–7.73 (m, 1.5H, C$H_{aromatic}$) (keto-+enol), 7.57–7.51 (m, 3.6H, C$H_{aromatic}$) (keto+enol), 7.37–7.30 (m, 1.6H, C$H_{aromatic}$) (keto+enol), 7.22–7.17 (m, 3.3H, C$H_{aromatic}$) (keto+enol), 6.36 (s, 0.6H, C=C*H*) (enol), 4.35–4.29 (m, 3.2H, C=OCH_2C=O+CH_2CH_3) (keto+enol), 4.17 (q, J=7.3 Hz, 2H, CH_2CH_3) (keto), 2.39 (s, 5.2H, PhCH_3) (keto+enol), 1.37 (t, J=7.3 Hz, 1.7H, CH_2CH_3) (enol), 1.20 (t, J=7.3 Hz, 3H, CH_2CH_3) (keto); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.2, 173.0, 167.9, 166.9, 152.6, 151.2, 141.2, 140.1, 139.8, 137.0, 136.0, 135.5, 132.0, 131.9, 131.7, 129.3, 129.2, 122.6, 122.4, 121.8, 118.9, 118.3, 95.9, 94.6, 92.9, 87.6, 87.2, 61.5, 60.5, 48.4, 21.6, 14.3, 13.9; HRMS calcd for $C_{19}H_{18}NO_3$ ([M+H]$^+$) 308.1287; found 308.1291.

*4.2.15. Ethyl 3-oxo-3-(2-(phenylethynyl)phenyl) propanoate (**3o**).* The product was obtained as a brown oil (207.5 mg, 71%); R_f (10% ethyl acetate/hexane) 0.35; the compound was obtained as a mixture of keto and enol forms in the ratio of 2.5:1, ^{1}H NMR (300 MHz, $CDCl_3$) δ: 12.53 (s, 0.5H, O*H*) (enol), 7.75–7.69 (m, 1.4H, C$H_{aromatic}$) (keto+enol), 7.57–7.53 (m, 1.2H, C$H_{aromatic}$) (keto+enol), 7.50–7.41 (m, 4.3H, C$H_{aromatic}$) (keto+enol), 7.37–7.26 (m, 6.2H, C$H_{aromatic}$) (keto+enol), 6.12 (s, 0.4H, C=C*H*) (enol), 4.25–4.18 (m, 2.8H, C=OCH_2C=O+CH_2CH_3) (keto+enol), 4.08 (q, J=7.2 Hz, 2H, CH_2CH_3) (keto), 1.27 (t, J=7.2 Hz, 1.4H, CH_2CH_3) (enol), 1.12 (t, J=7.2 Hz, 3H, CH_2CH_3) (keto); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 194.8, 173.1, 170.4, 167.5, 139.3, 135.4, 134.0, 131.8, 131.61, 131.53, 129.9, 129.1, 128.9, 128.60, 128.46, 128.35, 128.1, 123.0, 122.5, 121.8, 121.1, 97.7, 94.8, 92.3, 88.3, 87.8, 61.3,

60.3, 48.5, 14.3, 14.0; HRMS calcd for $C_{19}H_{16}O_3$ (M^+) 292.1099; found 292.1088.

*4.2.16. Ethyl 3-oxo-3-(2-(p-tolylethynyl)phenyl) propanoate (**3p**).* The product was obtained as a brown oil (223.6 mg, 73%); R_f (10% ethyl acetate/hexane) 0.33; the compound was obtained as a mixture of keto and enol forms in the ratio of 3.3:1, ^{1}H NMR (300 MHz, $CDCl_3$) δ: 12.50 (s, 0.3H, O*H*) (enol), 7.82–7.76 (m, 1.3H, C*H*$_{aromatic}$) (keto+enol), 7.63–7.59 (m, 1.3H, C*H*$_{aromatic}$) (keto+enol), 7.52–7.37 (m, 5.1H, C*H*$_{aromatic}$) (keto+enol), 7.19–7.15 (m, 2.5H, C*H*$_{aromatic}$) (keto+enol), 6.22 (s, 0.3H, C=C*H*) (enol), 4.30–4.26 (m, 2.8H, C=OCH_2C=O+CH_2CH$_3$) (keto+enol), 4.17 (q, J=7.2 Hz, 2H, CH_2CH$_3$) (keto), 2.38 (s, 3.8H, PhCH_3) (keto+enol), 1.35 (t, J=7.2 Hz, 1.4H, CH$_2$CH_3) (enol), 1.20 (t, J=7.2 Hz, 3H, CH$_2$CH_3) (keto); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 194.9, 173.1, 170.4, 167.6, 139.3, 136.8, 133.9, 133.6, 131.9, 131.52, 131.43, 129.9, 129.25, 129.17, 128.27, 128.13, 122.1, 121.3, 120.0, 119.6, 96.1, 95.1, 92.2, 87.7, 87.7, 87.3, 61.3, 60.3, 48.6, 21.6, 14.4, 14.0; HRMS calcd for $C_{20}H_{18}O_3$ (M^+) 306.1256; found 306.1255.

*4.2.17. Ethyl 3-(2-((4-methoxyphenyl)ethynyl) phenyl)-3-oxopropanoate (**3q**).* The product was obtained as a brown oil (238.5 mg, 74%); R_f (10% ethyl acetate/hexane) 0.25; the compound was obtained as a mixture of keto and enol forms in the ratio of 2.5:1, ^{1}H NMR (300 MHz, $CDCl_3$) δ: 12.50 (s, 0.4H, O*H*) (enol), 7.82–7.79 (m, 1.3H, C*H*$_{aromatic}$) (keto+enol), 7.62–7.58 (m, 1.4H, C*H*$_{aromatic}$) (keto+enol), 7.50–7.47 (m, 4.3H, C*H*$_{aromatic}$) (keto+enol), 7.42–7.36 (m, 2H, C*H*$_{aromatic}$) (keto+enol), 6.91–6.86 (m, 3.2H, C*H*$_{aromatic}$) (keto+enol), 6.22 (s, 0.4H, C=C*H*) (enol), 4.31–4.26 (m, 2.8H, C=OCH_2C=O+CH_2CH$_3$) (keto+enol), 4.17 (q, J=7.2 Hz, 2H, CH_2CH$_3$) (keto), 3.84 (s, 4.5H, PhOCH_3) (keto+enol), 1.35 (t, J=7.2 Hz, 1.1H, CH$_2$CH_3) (enol), 1.18 (t, J=7.2 Hz, 3H, CH$_2$CH_3) (keto); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 194.9, 173.2, 170.5, 167.6, 160.2, 159.2, 139.1, 133.8, 133.4, 133.15, 133.01, 131.8, 129.9, 129.1, 128.1, 127.9, 122.3, 114.6, 114.12, 114.01, 96.1, 95.1, 92.1, 87.2, 86.8, 61.2, 60.3, 55.3, 48.6, 14.3, 14.0; HRMS calcd for $C_{20}H_{18}O_4$ (M^+) 322.1205; found 322.1207.

*4.2.18. Ethyl 3-oxo-3-(2-(thiophen-3-ylethynyl) phenyl)propanoate (**3r**).* The product was obtained as a brown oil (226.7 mg, 76%); R_f (10% ethyl acetate/hexane) 0.33; the compound was obtained as a mixture of keto and enol forms in the ratio of 2.5:1, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.50 (s, 0.4H, O*H*) (enol), 8.59 (d, J=7.2 Hz, 1H, C*H*$_{aromatic}$) (keto), 8.14 (t, J=7.2 Hz, 1H, C*H*$_{aromatic}$) (keto), 7.92–7.72 (m, 3.2H, C*H*$_{aromatic}$) (keto+enol), 7.66–7.61 (m, 5H, C*H*$_{aromatic}$) (keto+enol), 7.26 (s, 1.6H, C*H*$_{aromatic}$) (keto+enol), 6.94–6.90 (m, 3.9H, C*H*$_{aromatic}$) (keto+enol), 6.41 (s, 0.4H, C=C*H*) (enol), 4.37–4.33 (m, 3.0H, C=OCH_2C=O+CH_2CH$_3$) (keto+enol), 4.18 (q, J=7.3 Hz, 2H, CH_2CH$_3$) (keto), 1.38 (t, J=7.3 Hz, 1.5H, CH$_2$CH_3) (enol), 1.20 (t, J=7.3 Hz, 3H, CH$_2$CH_3) (keto); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.7, 173.1, 170.4, 167.5, 139.1, 135.2, 133.9, 133.4, 131.8, 129.9, 125.6, 129.16, 128.96, 128.34, 128.21, 128.13, 125.6, 125.4, 122.1, 121.9, 121.6, 121.1, 92.1, 91.1, 90.2, 87.8, 87.4, 61.3, 60.3, 48.5, 14.3, 13.9; HRMS calcd for $C_{17}H_{14}O_3S$ (M^+) 298.0664; found 298.0668.

*4.2.19. Ethyl 3-oxo-3-(2-(m-tolylethynyl)phenyl) propanoate (**3s**).* The product was obtained as a brown oil (220.5 mg, 72%); R_f (10% ethyl acetate/hexane) 0.31; the compound was obtained as a mixture of keto and enol forms in the ratio of 1.8:1, ^{1}H NMR (300 MHz, $CDCl_3$) δ: 12.53 (s, 0.5H, O*H*) (enol), 7.82–7.77 (m, 1.4H, C*H*$_{aromatic}$) (keto+enol), 7.64–7.59 (m, 1.5H, C*H*$_{aromatic}$) (keto+enol), 7.50–7.48 (m, 1H, C*H*$_{aromatic}$) (keto), 7.44–7.36 (m, 4.8H, C*H*$_{aromatic}$) (keto+enol), 7.29–7.22 (m, 1.8H, C*H*$_{aromatic}$) (keto+enol), 7.20–7.15 (m, 1.5H, C*H*$_{aromatic}$) (keto+enol), 6.22 (s, 0.5H, C=C*H*) (enol), 4.33–4.26 (m, 2.9H, C=OCH_2C=O+CH_2CH$_3$) (keto+enol), 4.16 (q, J=7.2 Hz, 2H, CH_2CH$_3$) (keto), 2.36 (s, 4.5H, PhCH_3) (keto+enol), 1.35 (t, J=7.2 Hz, 1.8H, CH$_2$CH_3) (enol), 1.20 (t, J=7.2 Hz, 3H, CH$_2$CH_3) (keto); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 194.9, 173.2, 170.4, 167.5, 139.3, 138.2, 135.3, 134.0, 133.7, 132.13, 132.09, 131.9, 129.95, 129.89, 129.5, 129.2, 128.9, 128.73, 128.63, 128.38, 128.26, 128.16, 122.9, 122.4, 122.0, 121.2, 96.1, 95.1, 92.2, 87.9, 61.3, 60.3, 48.6, 21.2, 14.3, 14.0; HRMS calcd for $C_{20}H_{18}O_3$ (M^+) 306.1256; found 306.1259.

*4.2.20. Ethyl 3-(3-((4-methoxyphenyl)ethynyl) benzo[b]thiophen-2-yl)-3-oxopropanoate (**3t**).* The product was obtained as a yellow semi solid (295.2 mg, 78%); R_f (10% ethyl acetate/hexane) 0.18; the compound was obtained as a mixture of keto and enol forms in the ratio of 2.5:1, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 13.52 (s, 0.4H, O*H*) (enol), 8.12–8.07 (m, 0.9H, C*H*$_{aromatic}$) (keto+enol), 7.86–7.76 (m, 1.2H, C*H*$_{aromatic}$) (keto+enol), 7.62–7.59 (m, 2.3H, C*H*$_{aromatic}$) (keto+enol), 7.54–7.45 (m, 3.3H, C*H*$_{aromatic}$) (keto+enol), 6.96–6.88 (m, 2.8H, C*H*$_{aromatic}$) (keto+enol), 4.26–4.17 (m, 5.4H, C=OCH_2C=O+CH_2CH$_3$) (keto+enol), 3.86 (s, 3H, PhOCH_3) (keto), 3.83 (s, 0.8H, PhOCH_3) (enol), 1.29 (t, J=7.2 Hz, 3H, CH$_2$CH_3) (keto), 1.20 (t, J=7.2 Hz, 1H, CH$_2$CH_3) (enol); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 187.1, 169.7, 167.4, 160.9, 143.5, 140.5, 140.4, 133.5, 133.1, 128.3, 125.41, 125.33, 125.20, 124.6, 123.3, 122.8, 122.1, 114.3, 114.0, 113.8, 101.5, 81.8, 68.2, 61.5, 61.0, 55.4, 47.6, 39.4, 14.14, 13.99; HRMS calcd for $C_{22}H_{18}O_4S$ (M^+) 378.0926; found 378.0924.

4.3. General procedure for the silver-catalyzed formation of the 2-carboxylate-acridinols, quinolinols, naphthlenols, and benzothiophenol (4a–t)

To a solution of CH_2Cl_2 (2 mL), and AgOTf (10 mol %), *ortho*-alkynyl-β-keto esters (**3a**–**t**) (0.5 mmol) were added and the reaction mixture was allowed to stir at 25 °C for 3–5 h. The completion of reaction was monitored by TLC. The reaction mixture was filtered and diluted with ethyl acetate and washed with brine solution. The combined organic fractions were dried over anhydrous Na_2SO_4 and concentrated under vacuum to yield the crude product. The crude product was purified by column chromatography on silica gel using ethyl acetate/hexane as the eluent.

*4.3.1. Ethyl 1-hydroxy-3-phenylacridine-2-carboxylate (**4a**).* The product was obtained as brown crystals in hexane/CH_2Cl_2 (128.7 mg, 75%); mp 140–144 °C; R_f (10% ethyl acetate/hexane) 0.46; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.67 (s, 1H, O*H*), 9.30 (s, 1H, C*H*$_{aromatic}$), 8.12 (d, J=8.8 Hz, 1H, C*H*$_{aromatic}$), 8.02 (d, J=8.8 Hz, 1H, C*H*$_{aromatic}$), 7.77 (t, J=7.3 Hz, 1H, C*H*$_{aromatic}$), 7.52–7.48 (m, 2H, C*H*$_{aromatic}$), 7.33–7.28 (m, 5H, C*H*$_{aromatic}$), 3.99 (q, J=6.6 Hz, 2H, CH_2CH$_3$), 0.73 (t, J=6.6 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.5, 162.6, 150.9, 149.6, 143.4, 142.9, 134.2, 131.9, 129.1, 128.2, 127.6, 126.8, 126.0, 125.9, 122.4, 118.7, 104.5, 61.2, 12.9; HRMS calcd for $C_{22}H_{18}NO_3$ ([M+H]$^+$) 344.1287; found 344.1285. IR ν (cm^{-1}) (liquid film): 2920, 2850, 1654, 1514, 1463, 1401, 1375, 1324, 1260, 1161, 1097, 1019, 800.

*4.3.2. Ethyl 1-hydroxy-3-p-tolylacridine-2-carboxylate (**4b**).* The product was obtained as light yellow crystalline solid from hexane/CH_2Cl_2 (141.2 mg, 79%); mp 155–157 °C; R_f (10% ethyl acetate/hexane) 0.41; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.19 (s, 1H, O*H*), 9.32 (S, 1H, C*H*$_{aromatic}$), 8.20 (d, J=6.88 Hz, 1H, C*H*$_{aromatic}$), 8.00 (d, J=8.2 Hz, 1H, C*H*$_{aromatic}$), 7.81–7.77 (M, 1H, C*H*$_{aromatic}$), 7.56 (M, 1H, C*H*$_{aromatic}$), 7.53–7.49 (M, 1H, C*H*$_{aromatic}$), 7.19 (d, J=8.7 Hz, 2H, C*H*$_{aromatic}$), 7.13 (d, J=6.9 Hz, 2H, C*H*$_{aromatic}$), 4.02 (q, J=6.4 Hz, 2H, CH_2CH$_3$), 2.35 (s, 3H, PhCH_3), 0.75 (t, J=7.2 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.5, 162.4, 149.8, 148.4, 144.5, 139.6, 136.7, 135.2, 132.5, 129.2, 128.3, 128.1, 126.1, 125.8, 121.5, 118.6, 104.9, 61.4, 21.8, 13.0;

HRMS calcd $C_{23}H_{20}NO_3$ (M^+) 357.1365; found 357.1366. IR ν (cm^{-1}) (liquid film): 3075, 2981, 2927, 2855, 1633, 1619, 1561, 1513, 1495, 1444, 1374, 1263, 1068, 960, 822, 703, 677, 624.

*4.3.3. Ethyl 3-(4-ethylphenyl)-1-hydroxyacridine-2-carboxylate (**4c**).* The product was obtained as brown crystals in hexane/CH_2Cl_2 (144.7 mg, 78%); mp 138–141 °C; R_f (10% ethyl acetate/hexane) 0.43; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.60 (s, 1H, O*H*), 9.29 (s, 1H, C*H*$_{aromatic}$), 8.12 (d, *J*=8.8 Hz, 1H, C*H*$_{aromatic}$), 8.00 (d, *J*=8.1 Hz, 1H, C*H*$_{aromatic}$), 7.78–7.74 (m, 1H, C*H*$_{aromatic}$), 7.52–7.49 (m, 2H, C*H*$_{aromatic}$), 7.22 (d, *J*=8.1 Hz, 2H, C*H*$_{aromatic}$), 7.15 (d, *J*=8.1 Hz, 2H, C*H*$_{aromatic}$), 4.09 (q, *J*=7.3 Hz, 2H, C*H*$_2$CH$_3$), 2.64 (q, *J*=7.0 Hz, 2H, C*H*$_2$CH$_3$), 1.22 (t, *J*=7.3 Hz, 3H, CH$_2$C*H*$_3$), 0.73 (t, *J*=7.3 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.6, 162.5, 150.9, 149.7, 143.5, 143.0, 140.0, 134.2, 131.8, 129.2, 128.2, 127.1, 126.0, 125.8, 122.3, 118.7, 104.7, 61.2, 28.6, 15.9, 12.9; HRMS calcd for $C_{24}H_{22}NO_3$ ($[M+H]^+$) 372.1600; found 372.1589. IR ν (cm^{-1}) (liquid film): 2925, 2853, 1617, 1515, 1440, 1396, 1338, 1263, 1180, 1100, 963, 807, 747.

*4.3.4. Ethyl 1-hydroxy-3-(4-methoxyphenyl)acridine-2-carboxylate (**4d**).* The product was obtained as brown crystals in hexane/CH_2Cl_2 (154.9 mg, 83%); mp 170–172 °C; R_f (10% ethyl acetate/hexane) 0.23; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.61 (s, 1H, O*H*), 9.28 (s, 1H, C*H*$_{aromatic}$), 8.11 (d, *J*=8.8 Hz, 1H, C*H*$_{aromatic}$), 7.99 (d, *J*=8.0 Hz, 1H, C*H*$_{aromatic}$), 7.76 (t, *J*=8.1 Hz, 1H, C*H*$_{aromatic}$) 7.50–7.46 (m, 2H, C*H*$_{aromatic}$), 7.23 (d, *J*=8.8 Hz, 2H, C*H*$_{aromatic}$), 6.87 (d, *J*=8.8 Hz, 2H, C*H*$_{aromatic}$), 4.02 (q, *J*=7.3 Hz, 2H, C*H*$_2$CH$_3$), 3.80 (s, 3H, PhOC*H*$_3$), 0.81 (t, *J*=7.3 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.6, 162.5, 158.8, 150.8, 149.6, 143.1, 135.3, 134.2, 131.9, 129.31, 129.13, 129.01, 125.96, 125.81, 122.2, 118.6, 113.0, 104.7, 61.3, 55.3, 13.2; HRMS calcd $C_{23}H_{20}NO_4$ ($[M+H]^+$) 374.1393; found 374.1395. IR ν (cm^{-1}) (liquid film): 2924, 2853, 1617, 1512, 1441, 1374, 1339, 1232, 1264, 1181, 1101, 1019, 961, 810, 748, 698.

*4.3.4.1. Procedure for the silver-catalyzed formation of compound (**5**+**6**).* To a solution of $CDCl_3$ (2 mL), and AgOTf (10 mol %), ethyl 3-(2-((4-methoxyphenyl)ethynyl)quinolin-3-yl)-3-oxopropanoate (**3d**) (0.5 mmol) was added followed by 10 equiv of CD_3OD and reaction mixture was allowed to stir at 25 °C for 5 h and the resulting solution was filtered and washed with D_2O and extracted with ethyl acetate (3×10 mL). The combined organic fractions was dried over anhydrous Na_2SO_4 and concentrated under vacuum to yield the crude product. The crude product was purified by column chromatography on silica gel using ethyl acetate/hexane as the eluent. The product was obtained as brown crystals in hexane/CH_2Cl_2; mp 175–176 °C; R_f (10% ethyl acetate/hexane) 0.24; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.36 (s, 1H, C*H*$_{aromatic}$), 8.22 (d, *J*=8.4 Hz, 1H, C*H*$_{aromatic}$), 8.05 (d, *J*=8.1 Hz, 1H, C*H*$_{aromatic}$), 7.83 (t, *J*=7.3 Hz, 1H, C*H*$_{aromatic}$), 7.60 (s, 0.4H, C*H*$_{aromatic}$), 7.55 (t, *J*=7.3 Hz, 1H, C*H*$_{aromatic}$), 7.28 (d, *J*=8.0 Hz, 2H, C*H*$_{aromatic}$), 6.82 (d, *J*=8.8 Hz, 2H, C*H*$_{aromatic}$), 4.08 (q, *J*=6.6 Hz, 2H, C*H*$_2$CH$_3$), 3.85 (s, 3H, PhOC*H*$_3$), 0.86 (t, *J*=7.3 Hz, 3H, CH$_2$C*H*$_3$).

*4.3.5. Ethyl 3-(biphenyl-4-yl)-1-hydroxyacridine-2-carboxylate (**4e**).* The product was obtained as brown crystals in hexane/CH_2Cl_2 (159.4 mg, 76%); mp 173–175 °C; R_f (10% ethyl acetate/hexane) 0.30; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.69 (s, 1H, O*H*), 9.31 (s, 1H, C*H*$_{aromatic}$), 8.13 (d, *J*=8.8 Hz, 1H, C*H*$_{aromatic}$), 8.00 (d, *J*=8.8 Hz, 1H, C*H*$_{aromatic}$), 7.79–7.75 (m, 1H, C*H*$_{aromatic}$), 7.60–7.56 (m, 5H, C*H*$_{aromatic}$), 7.49 (t, *J*=7.3 Hz, 1H, C*H*$_{aromatic}$), 7.42–7.37 (m, 4H, C*H*$_{aromatic}$), 7.30 (t, *J*=7.3 Hz, 1H, C*H*$_{aromatic}$), 4.01 (q, *J*=7.3 Hz, 2H, C*H*$_2$CH$_3$), 0.74 (t, *J*=7.3 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.5, 162.7, 149.6, 143.0, 141.9, 140.8, 139.8, 134.3, 131.9, 129.16, 129.07, 128.8, 128.6, 127.3, 127.0, 126.3, 126.0, 125.9, 122.3, 118.7, 104.5, 61.0, 14.1; HRMS calcd for $C_{28}H_{21}NO_3$ (M^+) 419.1521; found 419.1521. IR ν (cm^{-1}) (liquid film): 2923, 2852, 1615, 1373, 1269, 1102, 1019, 845, 754, 694.

*4.3.6. Ethyl 1-hydroxy-3-(4-(trifluoromethyl) phenyl)acridine-2-carboxylate (**4f**).* The product was obtained as yellow crystals in hexane/CH_2Cl_2 (131.7 mg, 64%); mp 173–175 °C; R_f (10% ethyl acetate/hexane) 0.37; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.89 (s, 1H, O*H*), 9.33 (s, 1H, C*H*$_{aromatic}$), 8.17 (d, *J*=8.8 Hz, 1H, C*H*$_{aromatic}$), 8.03 (d, *J*=8.1 Hz, 1H, C*H*$_{aromatic}$), 7.85–7.81 (m, 1H, C*H*$_{aromatic}$), 7.66 (d, *J*=8.0 Hz, 2H, C*H*$_{aromatic}$), 7.58–7.54 (m, 1H, C*H*$_{aromatic}$), 7.52 (s, 1H, C*H*$_{aromatic}$), 7.48 (d, *J*=8.0 Hz, 2H, C*H*$_{aromatic}$), 4.05 (q, *J*=7.3 Hz, 2H, C*H*$_2$CH$_3$), 0.77 (t, *J*=7.3 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.1, 163.1, 150.9, 149.3, 146.6, 141.7, 134.3, 132.1, 129.13, 129.09, 128.5, 126.2, 126.1, 124.51, 124.47, 124.43, 122.5, 118.8, 103.7, 61.4, 12.8; HRMS calcd for $C_{23}H_{16}F_3NO_3$ (M^+) 411.1082; found 411.1082. IR ν (cm^{-1}) (KBr): 2924, 1653, 1615, 1513, 1371, 1337, 1311, 1240, 1101, 962, 877, 748, 588, 536. Crystallographic data for **4f** have been deposited with the Cambridge Crystallographic Data Centre. CCDC 864805, contain all crystallographic details of this publication and is available free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or can be ordered from the following address: Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB21EZ; fax: (+44)1223-336-033; or email: deposit@ccdc.cam.ac.uk.

*4.3.7. Ethyl 1-hydroxy-3-(thiophen-3-yl)acridine-2-carboxylate (**4g**).* The product was obtained as brown crystals in hexane/CH_2Cl_2 (143.2 mg, 82%); mp 147–150 °C; R_f (10% ethyl acetate/hexane) 0.46; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.69 (s, 1H, O*H*), 9.28 (s, 1H, C*H*$_{aromatic}$), 8.11 (d, *J*=8.8 Hz, 1H, C*H*$_{aromatic}$), 7.99 (d, *J*=8.1 Hz, 1H, C*H*$_{aromatic}$), 7.76 (t, *J*=7.3 Hz, 1H, C*H*$_{aromatic}$), 7.56 (s, 1H, C*H*$_{aromatic}$), 7.49 (t, *J*=7.3 Hz, 1H, C*H*$_{aromatic}$), 7.24–7.21 (m, 2H, C*H*$_{aromatic}$), 7.02 (d, *J*=5.9 Hz, 1H, C*H*$_{aromatic}$) 4.07 (q, *J*=7.3 Hz, 2H, C*H*$_2$CH$_3$), 0.91 (t, *J*=7.3 Hz, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.5, 162.6, 150.9, 149.6, 142.9, 138.0, 134.2, 131.9, 129.17, 129.12, 128.98, 126.07, 125.96, 124.1, 122.5, 121.5, 118.8, 104.5, 61.4, 13.2; HRMS calcd for $C_{20}H_{15}NO_3S$ (M^+) 349.0773; found 349.0779. IR ν (cm^{-1}) (liquid film): 3060, 2920, 2850, 2658, 1723, 1614, 1574, 1514, 1372, 1251, 1131, 1016, 857, 757, 691, 660.

*4.3.8. Ethyl 3-cyclohexyl-1-hydroxyacridine-2-carboxylate (**4h**).* The product was obtained as green needle crystals in hexane/CH_2Cl_2 (122.3 mg, 70%); mp 80–85 °C; R_f (10% ethyl acetate/hexane) 0.44; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 13.06 (s, 1H, O*H*), 9.31 (s, 1H, C*H*$_{aromatic}$), 8.15 (d, *J*=8.8 Hz, 1H, C*H*$_{aromatic}$), 8.04 (d, *J*=8.1 Hz, 1H, C*H*$_{aromatic}$), 7.84–7.80 (m, 1H, C*H*$_{aromatic}$), 7.62 (s, 1H, C*H*$_{aromatic}$), 7.55–7.51 (m, 1H, C*H*$_{aromatic}$), 4.53 (q, *J*=6.6 Hz, 2H, C*H*$_2$CH$_3$), 3.57–3.49 (m, 1H, C*H*), 2.50–2.02 (m, 2H, C*H*$_2$), 1.93–1.90 (m, 2H, C*H*$_2$), 1.82–1.79 (m, 1H, C*H*$_2$), 1.56–1.40 (m, 5H, C*H*$_2$), 1.36–1.24 (m, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.3, 164.4, 142.4, 139.1, 136.1, 132.8, 130.9, 129.5, 128.8, 128.0, 127.1, 125.5, 118.4, 106.1, 62.0, 48.0, 34.3, 29.7, 25.0, 14.4. HRMS calcd for $C_{22}H_{23}NO_3$ (M^+) 349.1678; found 349.1675. IR ν (cm^{-1}) (liquid film): 2957, 2922, 2852, 1731, 1634, 1608, 1515, 1402, 1379, 1326, 1179, 1112, 1016, 956, 853, 832, 772, 617.

*4.3.9. Ethyl 3-cyclopentyl-1-hydroxyacridine-2-carboxylate (**4i**).* The product was obtained as green needle crystals in hexane/CH_2Cl_2 (120.7 mg, 72%); mp 87–88 °C; R_f (10% ethyl acetate/hexane) 0.44; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.86 (s, 1H, O*H*), 9.23 (s, 1H, C*H*$_{aromatic}$), 8.11 (d, *J*=8.7 Hz, 1H, C*H*$_{aromatic}$), 7.94 (d, *J*=8.1 Hz, 1H, C*H*$_{aromatic}$), 7.74 (t, *J*=7.7 Hz, 1H, C*H*$_{aromatic}$), 7.55 (s, 1H, C*H*$_{aromatic}$), 7.44 (t, *J*=7.3 Hz, 1H, C*H*$_{aromatic}$), 4.44 (q, *J*=7.3 Hz, 2H, C*H*$_2$CH$_3$), 3.46–3.41 (m, 1H, C*H*), 1.95–1.92 (m, 2H, C*H*$_2$), 1.84–1.81 (m, 2H, C*H*$_2$), 1.73–1.70 (m, 1H, C*H*$_2$), 1.48–1.22 (m, 6H, C*H*$_2$+CH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.3, 162.9, 150.1,

147.8, 139.5, 134.3, 131.8, 129.7, 129.2, 128.8, 125.5, 117.3, 105.5, 103.4, 61.2, 43.8, 34.2, 25.0, 13.9; HRMS calcd for $C_{21}H_{22}NO_3$ ($[M+H]^+$) 336.1600; found 336.1589. IR ν (cm^{-1}) (liquid film): 2961, 2924, 2855, 1716, 1633, 1615, 1558, 1511, 1463, 1337, 1374, 1262, 1099, 1019, 861, 844, 796, 750, 628.

*4.3.10. Ethyl 3-butyl-1-hydroxyacridine-2-carboxylate (**4j**).* The product was obtained as greenish yellow needle crystals in hexane/CH_2Cl_2 (113.2 mg, 70%); mp 100–103 °C; R_f (10% ethyl acetate/hexane) 0.38; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 13.33 (s, 1H, O*H*), 9.31 (s, 1H, C$H_{aromatic}$), 8.16 (d, J=8.8 Hz, 1H, C$H_{aromatic}$), 8.03 (d, J=8.1 Hz, 1H, C$H_{aromatic}$), 7.84–7.80 (m, 1H, C$H_{aromatic}$), 7.53 (t, J=7.3 Hz, 1H, C$H_{aromatic}$), 7.49 (s, 1H, C$H_{aromatic}$), 4.52 (q, J=7.3 Hz, 2H, CH_2CH$_3$), 3.12 (t, J=7.3 Hz, 2H, CH_2), 1.70–1.62 (m, 2H, CH_2), 1.50–1.41 (m, 5H, CH_2+CH$_2$CH_3), 0.96 (t, J=7.3 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.4, 164.0, 150.8, 150.0, 144.3, 134.4, 131.8, 129.2, 128.9, 125.8, 125.5, 121.1, 118.5, 104.3, 61.9, 37.1, 33.7, 22.8, 14.10, 14.06; HRMS calcd for $C_{20}H_{22}NO_3$ ($[M+H]^+$) 324.1600; found 324.1598. IR ν (cm^{-1}) (liquid film): 2952, 2924, 2858, 1630, 1615, 1458, 1371, 1338, 1264, 1107, 818, 744.

*4.3.11. Ethyl 1-hydroxy-3-(phenoxymethyl)acridine-2-carboxylate (**4k**).* The product was obtained as green semi solid (128.8 mg, 69%); R_f (10% ethyl acetate/hexane) 0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 13.32 (s, 1H, O*H*), 9.37 (s, 1H, C$H_{aromatic}$), 8.21 (d, J=8.8 Hz, 1H, C$H_{aromatic}$), 8.07 (d, J=8.8 Hz, 1H, C$H_{aromatic}$), 7.96 (s, 1H, C$H_{aromatic}$), 7.85 (t, J=7.3 Hz, 1H, C$H_{aromatic}$), 7.57 (t, J=7.7 Hz, 1H, C$H_{aromatic}$), 7.33–7.29 (m, 2H, C$H_{aromatic}$), 7.03–6.96 (m, 3H, C$H_{aromatic}$), 5.48 (s, 2H, CH_2OPh), 4.04 (q, J=7.3 Hz, 2H, CH_2CH$_3$), 1.36 (t, J=7.3 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.8, 169.7, 164.2, 158.7, 143.2, 140.0, 137.8, 135.4, 134.6, 132.2, 129.5, 129.1, 126.1, 120.9, 119.5, 119.0, 114.7, 102.8, 68.2, 61.0, 14.1; HRMS calcd for $C_{23}H_{19}NO_4$ (M^+) 373.1314; found 373.1314. IR ν (cm^{-1}) (KBr): 2984, 2931, 1655, 1631, 1617, 1229, 1509, 1371, 1327, 1280, 1161, 1116, 849, 754, 637.

*4.3.12. Ethyl 5-hydroxy-7-p-tolylquinoline-6-carboxylate (**4l**).* The product was obtained as brown needle crystals in hexane/CH_2Cl_2 (121.4 mg, 79%); mp 107–110 °C; R_f (10% ethyl acetate/hexane) 0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.19 (s, 1H, O*H*), 8.98 (dd, J=1.5, 4.4 Hz, 1H, C$H_{aromatic}$), 8.72–8.70 (m, 1H, C$H_{aromatic}$), 7.48 (s, 1H, C$H_{aromatic}$), 7.44–7.40 (m, 1H, C$H_{aromatic}$), 7.23–7.18 (m, 4H, C$H_{aromatic}$), 4.03 (q, J=7.3 Hz, 2H, CH_2CH$_3$), 2.36 (s. 3H, PhCH_3), 0.81 (t, J=7.3 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.4, 160.8, 153.5, 149.9, 143.3, 139.8, 136.5, 132.4, 128.26, 128.16, 122.5, 120.6, 119.2, 106.8, 61.3, 21.2, 13.0; HRMS calcd for $C_{19}H_{17}NO_3$ (M^+) 307.1208; found 307.1208. IR ν (cm^{-1}) (liquid film): 2926, 1645, 1515, 1374, 1321, 1258, 1155, 1094, 1020, 799, 614.

*4.3.13. Ethyl 7-(3,5-dimethoxyphenyl)-5-hydroxy quinoline-6-carboxylate (**4m**).* The product was obtained as light yellow crystals in hexane/CH_2Cl_2 (127.2 mg, 72%); mp 260–265 °C; R_f (10% ethyl acetate/hexane) 0.10; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.16 (s, 1H, O*H*), 8.92 (dd, J=1.4, 2.2 Hz, 1H, C$H_{aromatic}$), 8.65 (dd, J=1.4, 8.8 Hz, 1H, C$H_{aromatic}$), 7.44 (s, 1H, C$H_{aromatic}$), 7.39–7.35 (m, 1H, C$H_{aromatic}$), 6.43–6.37 (m, 3H, C$H_{aromatic}$), 4.04 (q, J=7.3 Hz, 2H, CH_2CH$_3$), 3.74 (s, 6H, PhOCH_3), 1.18 (t, J=7.3 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.2, 160.8, 160.1, 153.5, 149.8, 144.6, 143.1, 138.5, 132.5, 122.1, 120.8, 119.4, 106.7, 99.2, 61.3, 60.4, 55.4, 14.1; HRMS calcd for $C_{20}H_{19}NO_5$ (M^+) 353.1263; found 353.1268. IR ν (cm^{-1}) (liquid film): 2922, 2852, 1636, 1401, 1326, 1280, 1242, 1179, 1111, 1016, 832, 722.

*4.3.14. Ethyl 5-hydroxy-7-p-tolylisoquinoline-6-carboxylate (**4n**).* The product was obtained as yellow needle crystals in hexane/CH_2Cl_2 (112.2 mg, 73%); 110–112 mp °C; R_f (10% ethyl acetate/hexane) 0.28; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.22 (s, 1H, O*H*), 7.97 (d, J=2.9 Hz, 1H, C$H_{aromatic}$), 7.70 (d, J=8.0 Hz, 1H, C$H_{aromatic}$), 7.44–7.41 (m, 2H, C$H_{aromatic}$), 7.24–7.18 (m, 4H, C$H_{aromatic}$), 4.06 (q, J=7.3 Hz, 2H, CH_2CH$_3$), 2.42 (s, 3H, PhCH_3), 0.81 (t, J=7.3 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.5, 160.9, 153.7, 149.9, 143.6, 140.1, 136.7, 131.9, 128.2, 128.1, 122.5, 120.6, 119.2, 106.5, 61.7, 20.6, 11.9; HRMS calcd $C_{19}H_{17}NO_3$ (M^+) 307.1208; found 307.1205. IR ν (cm^{-1}) (liquid film): 2925, 2852, 1733, 1630, 1615, 1515, 1445, 1372, 1266, 1243, 1101, 1020, 963, 831, 749.

*4.3.15. Ethyl 1-hydroxy-3-phenyl-2-naphthoate (**4o**).* The product was obtained as light yellow semi solid (102.3 mg, 70%); R_f (5% ethyl acetate/hexane) 0.78; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.27 (s, 1H, O*H*), 8.17 (d, J=8.8 Hz, 1H, C$H_{aromatic}$), 8.00 (d, J=8.8 Hz, 1H, C$H_{aromatic}$), 7.78 (t, J=8.0 Hz, 1H, C$H_{aromatic}$), 7.50 (t, J=7.3 Hz, 1H, C$H_{aromatic}$), 7.36–7.29 (m, 5H, C$H_{aromatic}$), 7.19 (s, 1H, C$H_{aromatic}$), 3,98 (q, J=7.3 Hz, 2H, CH_2CH$_3$), 0.72 (t, J=6.6 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.8, 161.1, 140.6, 139.4, 136.1, 135.5, 129.7, 128.3, 128.1, 127.3, 125.6, 123.94, 123.89, 121.2, 106.1, 61.0, 13.0; HRMS calcd $C_{19}H_{16}O_3$ (M^+) 292.1099; found 292.1089. IR ν (cm^{-1}) (liquid film): 2923, 2852, 1630, 1457, 1258, 1018, 751.

*4.3.16. Ethyl 1-hydroxy-3-p-tolyl-2-naphthoate (**4p**).* The product was obtained as white crystals in hexane/CH_2Cl_2 (113.3 mg, 74%); mp 114–116 °C; R_f (5% ethyl acetate/hexane) 0.72; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 12.21 (s, 1H, O*H*), 8.41 (d, J=7.8 Hz, 1H, C$H_{aromatic}$), 7.72 (d, J=7.2 Hz, 1H, C$H_{aromatic}$), 7.60–7.58 (m, 1H, C$H_{aromatic}$), 7.54–7.49 (m, 2H, C$H_{aromatic}$), 7.36–7.19 (m, 4H, C$H_{aromatic}$), 4.04 (q, J=6.9 Hz, 2H, CH_2CH$_3$), 2.41 (s, 3H, PhCH_3), 0.79 (t, J=7.2 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 171.8, 161.1, 140.6, 139.4, 136.1, 135.5, 131.8, 129.6, 128.8, 128.1, 127.3, 125.6, 123.9, 121.1, 106.1, 61.0, 21.1, 13.0; HRMS calcd $C_{20}H_{18}O_3$ (M^+) 306.1256; found 306.1251. IR ν (cm^{-1}) (liquid film): 2924, 2854, 1731, 1660, 1651, 1608, 1514, 1373, 1305, 1261, 1108, 1020, 831, 805, 733. Crystallographic data for **4p** have been deposited with the Cambridge Crystallographic Data Centre. CCDC 847471, contain all crystallographic details of this publication and is available free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or can be ordered from the following address: Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB21EZ; fax: (+44)1223-336-033; or email: deposit@ccdc.cam.ac.uk.

*4.3.17. Ethyl 1-hydroxy-3-(4-methoxyphenyl)-2-naphthoate (**4q**).* The product was obtained as white crystals in hexane/CH_2Cl_2 (127.3 mg, 79%); mp 127–129 °C; R_f (5% ethyl acetate/hexane) 0.52; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 12.16 (s, 1H, O*H*), 8.33 (d, J=8.1 Hz, 1H, C$H_{aromatic}$), 7.64 (d, J=7.8 Hz, 1H, C$H_{aromatic}$), 7.53 (t, J=6.9 Hz, 2H, C$H_{aromatic}$), 7.46–7.41 (m, 1H, C$H_{aromatic}$), 7.18–7.14 (m, 2H, C$H_{aromatic}$), 6.84 (d, J=8.4 Hz, 2H, C$H_{aromatic}$), 3.98 (q, J=7.2 Hz, 2H, CH_2CH$_3$), 3.79 (s, 3H, PhOCH_3), 0.77 (t, J=7.2 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.8, 160.2, 157.5, 137.9, 135.1, 134.4, 128.6, 128.4, 126.2, 124.6, 122.8, 120.2, 111.9, 105.1, 60.0, 54.4, 12.2; HRMS calcd $C_{20}H_{18}O_4$ (M^+) 322.1205; found 322.1205. IR ν (cm^{-1}) (liquid film): 2924, 2851, 1629, 1401, 1326, 1280, 1242, 1179, 1111, 1016, 822, 772.

*4.3.18. Ethyl 1-hydroxy-3-(thiophen-3-yl)-2-naphthoate (**4r**).* The product was obtained as yellow crystals in hexane/CH_2Cl_2 (119.3 mg, 80%); mp 90–94 °C; R_f (5% ethyl acetate/hexane) 0.76; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.25 (s, 1H, O*H*), 8.34 (d, J=8.1 Hz, 1H, C$H_{aromatic}$), 7.64 (d, J=8.1 Hz, 1H, C$H_{aromatic}$), 7.55–7.51 (m, 1H, C$H_{aromatic}$), 7.46–7.42 (m, 1H, C$H_{aromatic}$), 7.21–7.19 (m, 1H, C$H_{aromatic}$), 7.17 (s, 1H, C$H_{aromatic}$), 7.11–7.09 (m, 1H, C$H_{aromatic}$), 6.96 (d, J=5.9 Hz, 1H, C$H_{aromatic}$), 4.04 (q, J=7.3 Hz, 2H, CH_2CH$_3$), 0.89 (t, J=7.3 Hz, 3H, CH$_2$CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.7, 161.3, 143.6, 135.5, 133.9, 129.7, 129.3, 127.2, 125.8, 124.2, 123.93, 123.81, 121.4, 120.9, 106.0, 61.1, 13.1; HRMS calcd $C_{17}H_{14}O_3S$ ($[M-H]^+$)

297.0650; found 297.0625. IR ν (cm^{-1}) (liquid film): 3109, 2923, 2853, 1636, 1441, 1402, 1369, 1274, 1168, 1102, 1013, 834, 807, 770, 670.

*4.3.19. Ethyl 1-hydroxy-3-m-tolyl-2-naphthoate (**4s**).* The product was obtained as white needle crystals in hexane/CH_2Cl_2 (105.7 mg, 69%); mp 109–111 °C; R_f (5% ethyl acetate/hexane) 0.74; ^1H NMR (400 MHz, $CDCl_3$) δ: 12.24 (s, 1H, O*H*), 8.42 (d, J=8.1 Hz, 1H, C$H_{aromatic}$), 7.72 (d, J=8.1 Hz, 1H, C$H_{aromatic}$), 7.60 (t, J=6.6 Hz, 1H, C$H_{aromatic}$), 7.51 (t, J=7.3 Hz, 1H, C$H_{aromatic}$), 7.27–7.23 (m, 2H, C$H_{aromatic}$), 7.15–7.09 (m, 3H, C$H_{aromatic}$), 4.03 (q, J=7.3 Hz, 2H, CH_2CH_3), 2.36 (s, 3H, PhCH_3), 0.79 (t, J=7.3 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.9, 161.2, 143.4, 139.5, 137.0, 135.4, 129.7, 129.2, 127.4, 127.3, 127.1, 125.7, 125.5, 123.9, 121.1, 106.0, 60.9, 21.4, 13.0; HRMS calcd for $C_{20}H_{18}O_3$ (M^+) 306.1256; found 306.1248. IR ν (cm^{-1}) (KBr): 2926, 1618, 1508, 1374, 1232, 1101, 1018, 958, 823, 785, 749, 613.

*4.3.20. Ethyl 4-hydroxy-2-(4-methoxyphenyl)dibenzo[b,d]thiophene-3-carboxylate (**4t**).* The product was obtained as yellow crystals in hexane/CH_2Cl_2 (141.9 mg, 75%); mp 122–125 °C; R_f (5% ethyl acetate/hexane) 0.41; ^1H NMR (400 MHz, $CDCl_3$) δ: 11.66 (s, 1H, O*H*), 8.02 (d, J=8.0 Hz, 1H, C$H_{aromatic}$), 7.84 (d, J=8.1 Hz, 1H, C$H_{aromatic}$), 7.48 (s, 1H, C$H_{aromatic}$), 7.44–7.41 (m, 1H, C$H_{aromatic}$), 7.40–7.36 (m, 1H, C$H_{aromatic}$), 7.19–7.16 (m, 2H, C$H_{aromatic}$), 6.86 (d, J=8.8 Hz, 2H, C$H_{aromatic}$), 3.99 (q, J=7.3 Hz, 2H, CH_2CH_3), 3.80 (s, 3H, PhOCH_3), 0.79 (t, J=7.3 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.3, 158.7, 157.4, 141.7, 140.9, 139.6, 135.9, 135.2, 129.6, 127.8, 126.2, 124.6, 123.2, 122.6, 115.8, 113.0, 108.7, 61.2, 55.4, 13.2; HRMS calcd $C_{22}H_{18}O_4S$ (M^+) 378.0926; found 378.0925. IR ν (cm^{-1}) (liquid film): 2953, 2853, 1731, 1651, 1608, 1463, 1394, 1372, 1304, 1260, 1175, 1018, 945, 831, 805, 783.

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Supplementary data

Supplementary data (^1H and ^{13}C NMR spectra, HRMS, IR) associated with this article can be found. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2012.08.068. These data include MOL files and InChIKeys of the most important compounds described in this article.

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