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Iodine-Mediated Solvent-Controlled Selective Electrophilic Cyclization and Oxidative Esterification of *o*-Alkynyl Aldehydes: An Easy Access to Pyranoquinolines, Pyranoquinolinones, and Isocumarins

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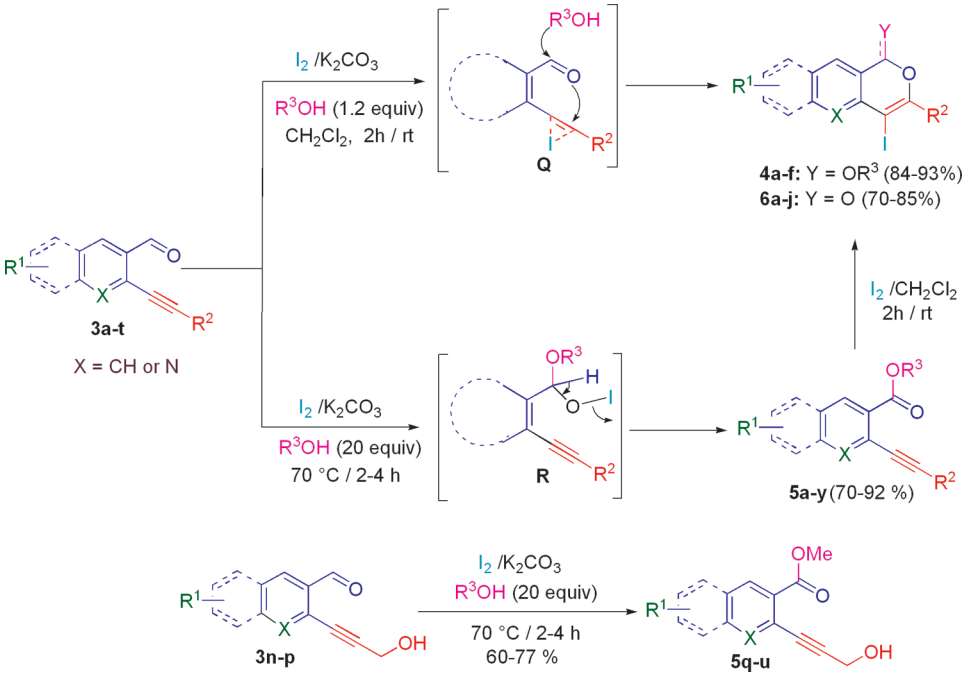
Received August 11, 2010



Chemoselective behavior of iodine in different solvents in the electrophilic iodocyclization of *o*-alkynyl aldehydes is described. *o*-Alkynyl aldehydes **3a**−**t** on reaction with I_2 in CH_2Cl_2 with appropriate nucleophiles provides pyrano[4,3-*b*]quinolines **4a**−**f**, via formation of cyclic iodonium intermediate **Q**; however, using alcohols as a solvent as well as nucleophile, *o*-alkynyl esters **5a**−**y** were obtained selectively in good to excellent yields via formation of hypoiodide intermediate **R**. Subsequently, *o*-alkynyl esters were converted in to pyranoquinolinones **6a**−**i** and isocoumarin **6j** by electrophilic iodocyclization. This developed oxidative esterification provides a novel access for the chemoselective synthesis of esters **5q**−**u** from aldehydes **3n**−**p** without oxidizing primary alcohol present in the substrate.

Introduction

Substituted heterocycles are structural components of a vast number of biologically active natural and non-natural compounds. Synthesis of various heterocycles has been a research objective for over a century, and a variety of well-established methods are available in the literature. Development of new approaches for their syntheses, employing efficient and economical routes, is currently a popular research area.[1] Among

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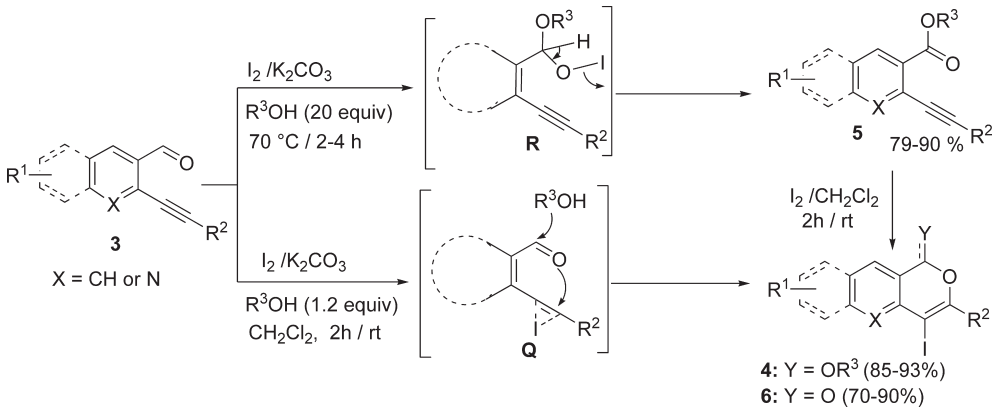
DOI: 10.1021/jo101526b Published on Web 10/29/2010

SCHEME 1



the electrophilic cyclizations leading to nitrogen-containing heterocycles, electrophilic iodocyclization is a widely used process and has emerged as an effective protocol in the preparation of a variety of heterocyclic and carbocyclic compounds.[2−5] Pyranoquinoline, pyranoquinolinone, and isocumarin moieties are known to be present in many alkaloids and possess a wide range of pharmacological activities and biological activities such as anticoagulant, coronary constricting, optical brightening, antifungal, antihistamine, and antiallergic activities.[6]

o-Alkynyl esters are important synthetic intermediates for the synthesis of pharmaceutically and medicinally important isocumarins, α-pyranones, and pyranoquinolinone and are structural subunits in numerous natural products.[7] Halogen-containing quinoline and their derivatives are of significant interest as the halogen atom plays a pivotal role in the compound's bioactivity, and such compounds provide a further avenue for structure elaboration.[8]

Reported methods for the synthesis of pyranoquinolines, quinolinones, and isocoumarins[9] are limited and multistep and suffer from availability of starting material.[10] Iodocyclization on 2-arylalkynyl aldehydes has been much studied; however, electrophilic iodocyclization on quinoline substrate has not been much explored.[11] Recently, tandem cyclization on a quinoline substrate has been reported using expensive gold and silver complexes to synthesize pyranoquinolines.[12] It is noteworthy that in the long history of electrophilic iodocyclization, the effect of solvents on the reactions has not been much explored, and also to the best our knowledge none of the reported procedures describe the direct and chemoselective oxidative esterification of aldehydes bearing an alcoholic group.

In continuation of our interest in the synthesis of nitrogen heterocycles,[13] and our recent report on the synthesis of 4-iodo-pyrano[4,3-*b*]quinolines **4** and 4-iodopyrano[4,3-*b*]-quinolinones **6** by the iodine-catalyzed and solvent-controlled selective electrophilic cyclization and oxidative esterification of *o*-alkynyl aldehydes[14] (Scheme 1), we herein report full details of our work on the selective synthesis of 4-iodo-pyrano[4,3-*b*]quinolines **4a**−**f**, 4-iodo-pyrano[4,3-*b*]-quinolinones **6a**−**i**, and isocumarins **6j** and extension of developed methodology to afford for the first time chemoselective oxidative esterification of aldehydes without oxidizing an unprotected primary alcoholic group present in the substrate. This chemistry employs the use of iodine,

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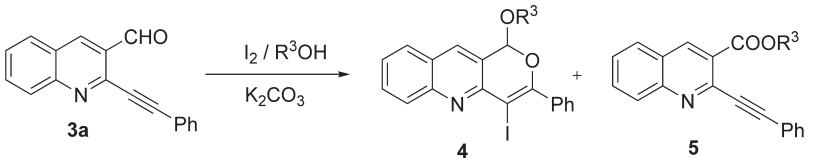
TABLE 1. Optimization of Reaction Conditions[a]



entry	R_3OH	solvent	base	T (°C)	t (h)	yield (%)[g]	ratio **4**:**5**:**3**
1	MeOH	CH_2Cl_2	K_2CO_3	25	6.0	50[b]	50:00:50
2	MeOH	CH_2Cl_2	K_2CO_3	25	2.0	70[c]	70:00:30
3	MeOH	CH_2Cl_2	K_2CO_3	25	2.0	93	100:00:00
4	MeOH	CH_2Cl_2		25	4.0	00[d]	00:00:100
5	MeOH	$CHCl_3$	K_2CO_3	25	2.0	88	90:00:10
6	MeOH	CH_2Cl_2	$KHCO_3$	25	4.0	70	75:00:25
7	MeOH	CH_2Cl_2	NEt_3	25	24	0	00:00:100
8	*n*-PrOH	CH_2Cl_2	K_2CO_3	25	4.0	78	90:00:10
9	MeOH	MeOH	K_2CO_3	40	3.0	55	00:70:30
10	MeOH	MeOH	K_2CO_3	70	2.5	92	00:100:00
11	MeOH	MeOH	K_2CO_3	70	5.0	92	00:100:00
12	MeOH	MeOH	K_2CO_3	50	4.0	55[b]	05:45:50
13	EtOH	EtOH	K_2CO_3	50	2.0	44	10:45:45
14	EtOH	EtOH	K_2CO_3	70	4.0	82	05:85:05
15	EtOH	EtOH	K_2CO_3	70	8.0	80	05:85:05
16	*n*-BuOH	*n*-BuOH	K_2CO_3	70	5.0	75	15:70:15
17	*t*-BuOH	CH_2Cl_2	K_2CO_3	25	2.0	90	100:00:00
18	*t*-BuOH	*t*-BuOH	K_2CO_3	80	2.0	85	90:00:10
19	MeOH	CH_2Cl_2	K_2CO_3	25	2.5	84[e]	100:00:00
20	MeOH	MeOH	K_2CO_3	25	6.0	00[e]	00:00:100

[a]Reaction was performed using 0.50 mmol of **3a** and R^3OH (1.2 equiv), I_2 (2.5 equiv), and K_2CO_3 (2.5 equiv) in CH_2Cl_2 at 25 °C unless otherwise noted. [b]1.2 equiv of I_2 and K_2CO_3 was used. [c]2.0 equiv of I_2 and 2.0 equiv of K_2CO_3 was used. [d]Reaction was carried out in the absence of K_2CO_3. [e]2.5 equiv of ICl was used. [g]Isolated yield.

which is more economical, eco-friendly, and convenient to use than (IPy_2BF_4).[15]

Mori et al.[16] reported the esterification on simple aliphatic alcohols using molecular iodine. Recently, Karade et al.[17] reported oxidative esterification of simple aromatic aldehydes using diacetoxyiodobenzene (DIB) combined with a catalytic quantity of molecular iodine that required longer reaction time (10−14 h). However, they failed to bring about esterification alone with molecular iodine; also none of the reported procedure explained the selectivity.

The developed chemistry provides an efficient and green protocol for the direct and selective synthesis of *o*-alkynyl esters **5a**−**y** from *o*-alkynyl aldehydes in very mild conditions without affecting the triple bond and primary alcoholic group present in the molecule. The developed process is also successful with hindered aldehydes (Table 3, entry 31) and tolerates various functional groups such as aryl carboxylic acid and alcoholic groups, which are sensitive toward Lewis acids.

Results and Discussion

A two-step approach to pyranoquinolines **4a**−**f** and *o*-alkynyl esters **5a**−**y** has been examined involving (i) preparation of 2-(arylalkynyl)quinoline-3-carbaldehydes **3a**−**t** by Sonogashira coupling reaction and (ii) solvent-controlled electrophilic iodocyclization.

Interesting observations emerge from the data in Table 1. When 2-(2-phenylethynyl)quinoline-3-carbaldehyde (**3a**) (0.5 mmol) was reacted with 1.2 equiv of I_2, 1.2 equiv of methanol, and 1.2 equiv of K_2CO_3 in 2.0 mL of CH_2Cl_2 at 25 °C for 6 h, 4-iodo-1-methoxy-3-phenyl-1*H*-pyrano-[4,3-*b*]quinoline (**4a**) was obtained in only 50% yield, along with starting material **3a** in 50% yield (Table 1, entry 1). However, increasing the amount of I_2 and K_2CO_3 from 1.2 equiv to 2.0 and 2.5 equiv afforded the compound **4a** in 70% and 93% yields, respectively, in 2 h (entries 2 and 3). Chloroform was also found effective for the reaction and afforded the iodocyclized product **4a** in an 88% yield (entry 5). No reaction was observed (monitored by TLC) in the absence of base (entry 4). $KHCO_3$ and NEt_3 were also investigated as bases. Although $KHCO_3$ provided a slightly lower yield of the desired product **4a** compared with K_2CO_3 (entries 3 and 6), NEt_3 proved to be ineffective, and none of the desired product was detected (entry 7). *n*-Propanol provided the desired product **4** in lower yield in comparison to methanol (entry 3 and 8). Interesting results were obtained in the course of this study, where simple modification of the reaction conditions employed in the synthesis of pyranoquinoline **4**, i.e., increasing the amount of alcohol from 1.2 equiv to using alcohol as solvent as well as nucleophile at 70 °C, afforded 2-arylalkynyl ester **5a**, an oxidative esterification product, selectively in 92% yield (entry 10).

Reaction temperature and solvents were found to have dramatic effects on the reaction, and higher yield of product **5a** was obtained when the reaction was performed at higher

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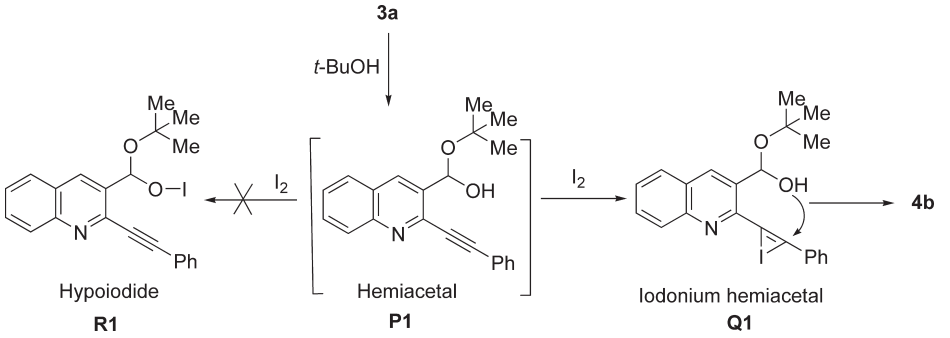
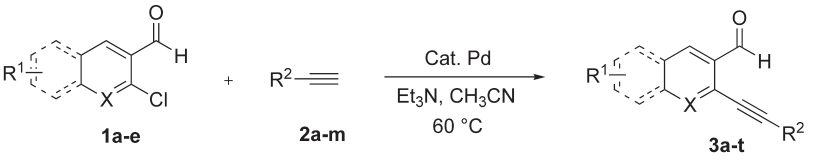
(17) Karade, N. N.; Budhewar, V. H.; Katkar, A. N.; Tiwari, G. B. *Arkivoc* **2006**, *xi*, 162.

SCHEME 2



SCHEME 3. Sonogashira Reaction of Heteroaryl Chloride with Different Alkynes



temperature using alcohols as the solvent (entry 10). No change in yield was observed when the reaction mixture was allowed to stir for a longer time (entry 11). At lower temperature (40 °C), a mixture of compound **5a** and **3a** were obtained (entry 9). Higher alcohols provided the desired products in lower yields (entries 13−16). Screening of solvents suggested that methanol is most suitable for the reaction (entries 3 and 10).

In the case of a hindered alcohol like *t*-BuOH, iodocyclized product **4b** was obtained in a 90% yield at room temperature in CH_2Cl_2 (entry 17), and the same product **4b** was obtained even if *t*-BuOH was used as a solvent as well as nucleophile at 80 °C (entry 18), probably due to steric hindrance of the *tert*-butyl group that favors the attack of iodine on triple bond and forms iodonium intermediate **Q1** rather than attacking on hemiacetal carbon bearing the bulky *tert*-butyl group to form hypoiodide intermediate **R1** (Scheme 2). ICl was also found effective for the iodocyclization and afforded the product **4a** in 84% yield; however, no oxidative esterification product **5a** was obtained using ICl as electrophile (entries 19 and 20).

The 2-(arylalkynyl)aryl-3-carbaldehydes **3a**−**t** required for our approach were readily prepared by Sonogashira coupling[18] of the 2-haloaryl-3-carbaldehydes **1a**−**e** with terminal alkynes **2a**−**m**. The yields of this process range from 70% to 89%, and this procedure should readily accommodate a large variety of functional groups (Scheme 3).

Having established the optimal conditions, we then further explored the scope of *o*-alkynyl aldehydes **3a**−**t** that could participate in iodocyclization. Various nucleophiles have been tested in this process using 2-(phenylethynyl)-quinoline-3-carbaldehyde (**3a**) and I_2. Alcohols, such as MeOH and *t*-BuOH, all reacted well and afforded the iodocyclized product **4a** and **4b** in 88% and 85% yields, respectively (Table 2, entries 1 and 2). Using ICl as electrophile, the desired product **4a** was obtained in an 84% yield (entry 1). Electron-rich arylacetylenes **3c** and **3m** provided the 4-iodo-pyrano[4,3-*b*]quinolines **4c** and **4d** in 93% and 91% yield, respectively (entries 3 and 4). Alkynes bearing an alkyl substituent also reacted well and provided the desired iodocyclized product **4e** in 85% yield (entry 5). In all cases, 6-*endo*-*dig* cyclized products were obtained regioselectively (entries 1−5).

The formation of iodocyclized products **4** was confirmed by ^1H and ^{13}C NMR and finally by X-ray crystallographic analysis[19] of compounds **4a** (Figure 1) (see Supporting Information).

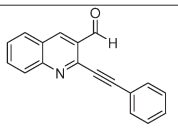
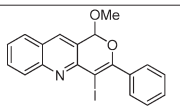
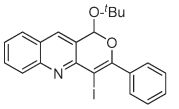
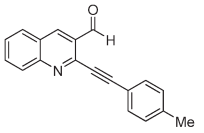
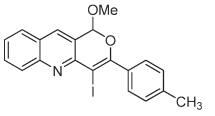
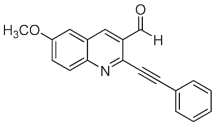
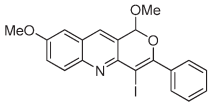
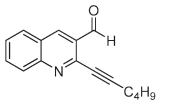
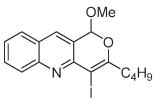
2-Arylalkynyl esters **5a**−**y** were obtained selectively in good to excellent yields by the oxidative esterification of corresponding 2-alkynyl aldehydes **3a**−**t** (Table 3, entries 1−25). Various alcohols such as MeOH, EtOH, *n*-PrOH, and *n*-BuOH were successfully employed as solvents as well as nucleophiles in our standard oxidative esterification conditions. Using methanol as a nucleophile as well as solvent provided the desired product **5a** in an 92% yields (entry 1). Reactions using EtOH as a nucleophile as well as a solvent provided the alkynyl esters **5b** and **5d** in 80% and 75% yields (entries 2 and 4), and those using *n*-PrOH, *n*-BuOH afforded the alkynyl esters **5c** and **5f** in comparatively lower yields (entries 3 and 6). This is probably because oxidative esterification of aldehydes with alcohols is sensitive to steric hindrance and electronic effect, since the formation of hemiacetal is the key step.[14]

To further examine the generality of this chemistry, acetylenic aldehydes bearing different substituents on the carbon−carbon triple bond were then allowed to react under our standard oxidative esterification conditions to afford the

(18) Chandra, A.; Singh, B.; Upadhaya, S.; Singh, R. M. *Tetrahedron* **2008**, *64*, 11680.

(19) CCDC 784808(4a) and 784809(6c) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/request/cif.

TABLE 2. Iodine-Catalyzed Selective Synthesis of Iodo-pyrano[4,3-*b*]quinolines[a]

Entry	Substrate		Nucleophile	Product		Yield (%)[c]
1		**3a**	MeOH		**4a**	88, 84[b]
2		**3a**	*t*-BuOH		**4b**	85
3		**3c**	MeOH		**4c**	93
4		**3m**	MeOH		**4d**	91
5		**3d**	MeOH		**4e**	85

[a]The reactions were performed using *o*-alkynylaldehyde **3** (0.50 mmol), 1.2 equiv of the nucleophile, 2.5 equiv of K_2CO_3, and 2.5 equiv of I_2 in 2.0 mL of CH_2Cl_2 at room temperature for 2 h, unless otherwise noted. [b]2.5 equiv of ICl. [c]Yield of isolated product.

corresponding 2-arylalkynyl esters. 2-Arylalkynyl aldehydes **3c** and **3e**−**h** bearing an electron-donating aryl substituents on the triple bond afforded the desired oxidative esterification products **5d**−**i** in good to excellent yields in lesser reaction (table 3, entries 4−9). In case of 2-((4-methoxyphenyl)ethynyl)quinoline-3-carbaldehyde **3b**, oxidative esterification product **5k** was obtained with in 10 min, in 92% yield using 2.0 equiv of iodine (entry 11), whereas 2-((3,5-dimethoxyphenyl)ethynyl)quinoline-3-carbaldehyde (**3i**), bearing two methoxy groups at the 3 and 5 position afforded the desired product **5j** in appreciable yield in longer reaction time (entry 10). Modification of the quinoline ring made no appreciable difference in the reactivity toward oxidative esterification; alkynyl aldehyde **3m** afforded the oxidative esterification product **5l** in 85% yield (entry 12).

2-Alkynyl aldehydes **3d** and **3j**−**k** bearing an alkyl substituent such as butyl, cyclohexyl, and *t*ert-butyl reacted well and provided the desired oxidative esterification products **5m**−**o** in good to appreciable yields (entries 13−15). Substrate bearing a hydroxyl functional group (**3l**) did not interfere in the oxidative esterification, affording selectively the desired product methyl 2-((1-hydroxycyclohexyl)-ethynyl)quinoline-3-carboxylate (**5p**) in comparable yield (entry 16).

During the course of this study we have found that this new, mild, and selective procedure allows chemoselective oxidation of aldehyde **3** in the presence of alcohol without competition from a primary alcoholic group present in the substrate. For this we have screened aldehydes **3n**−**p** bearing a primary alcoholic group. Reaction proceeded well in the presence of methanol and afforded the oxidative esterification products **5q**, **5s**, and **5t** in 75%, 77%, and 72% yields, respectively, without oxidation of the primary alcoholic group (entries 17, 19, and 20), whereas comparatively lower yield was obtained in case of ethanol (entries 18 and 21). None of the reported methods allow this type of selectivity for the direct conversion of aldehydes into esters chemoselectively.

Pyridinecarboxaldehyde derivatives **3q**−**s** have also been allowed to react under our standard cyclization conditions using MeOH as a nucleophile as well as solvent. The electron-deficient aromatic ring of these aldehydes did not affect the reaction and afforded the desired products **5v**−**x** in 70−85% yields, respectively (entries 22−24). 2-Alkynyl aldehyde **3t** also afforded the desired product **5y** in 89% yield (entry 25).

The potential scope of this oxidative esterification was then extended to a range of various aromatic aldehydes (entries 26−30). Aromatic aldehydes having electron-withdrawing and electron-donating substituents underwent oxidative methyl esterification in appreciable yields. Hindered aldehyde 2-(4-methoxyphenyl)nicotinaldehyde (**1h**), prepared by Suzuki reaction, having a bulky aromatic group adjacent to the aldehyde, underwent facile oxidative esterification (entry 31).

When phenol **8** was used as solvent as well as nucleophile at 80 °C, iodocyclized product 4-(4-iodo-3-phenyl-1*H*-pyrano[4,3-*b*]quinolin-1-yl)phenol (**4f**) was obtained instead of phenyl 2-(phenylethynyl)quinoline-3-carboxylate (**5ff**) (Scheme 4).

To further explore the scope of analogous esters, we carried out electrophilic cyclization on 2-arylalkynyl esters using iodine in dichloromethane at room temperature[20]

(20) Larock, R. C.; Yao, T. *J. Org. Chem.* **2003**, *68*, 5936.

TABLE 3. Solvent-Controlled Synthesis of *o*-Alkynyl Esters and Substituted Arylaldehydes[a]

Entry	Substrate	Nu	Product	Yield (%)[d]
1		**3a** MeOH	**5a**	92
2		**3a** EtOH	**5b**	80
3		**3a** *n*-BuOH	**5c**	70
4		**3c** EtOH	**5d**	75
5		**3e** MeOH	**5e**	91
6		**3e** *n*-PrOH	**5f**	71
7		**3f** MeOH	**5g**	87
8		**3g** MeOH	**5h**	87
9		**3h** MeOH	**5i**	79
10		**3i** MeOH	**5j**	80

TABLE 3. Continued

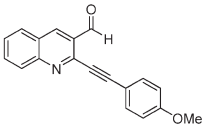
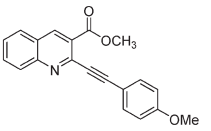
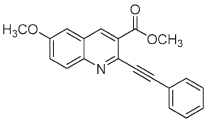
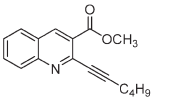
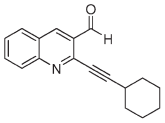
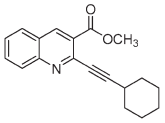
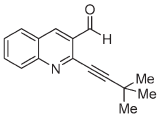
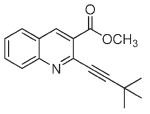
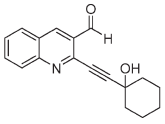
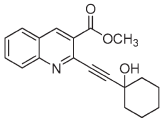
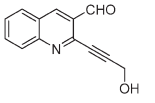
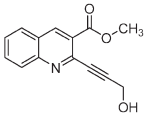
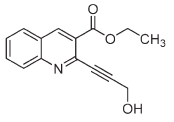
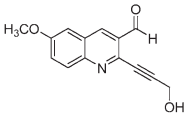
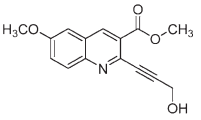
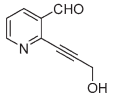
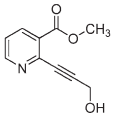
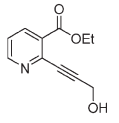
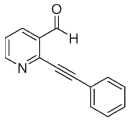
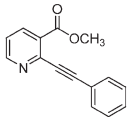
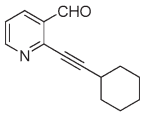
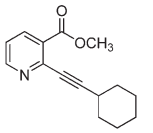
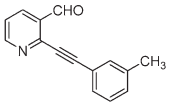
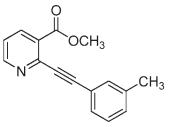
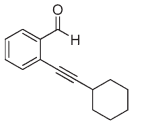
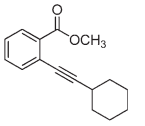
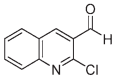
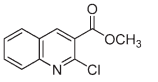
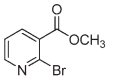
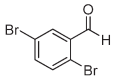
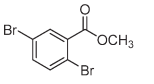
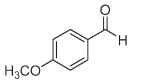
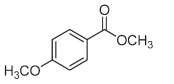
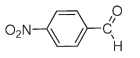
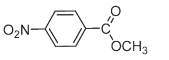
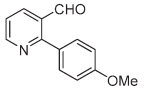
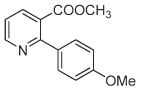
Entry	Substrate		Nu	Product		Yield (%)[d]
11		**3b**	MeOH		**5k**	92[b]
12		**3m**	MeOH		**5l**	85
13		**3d**	MeOH		**5m**	85
14		**3j**	MeOH		**5n**	79
15		**3k**	MeOH		**5o**	80
16		**3l**	MeOH		**5p**	78
17		**3n**	MeOH		**5q**	75
18		**3n**	EtOH		**5r**	60
19		**3o**	MeOH		**5s**	77
20		**3p**	MeOH		**5t**	72
21		**3p**	EtOH		**5u**	61
22		**3q**	MeOH		**5v**	85

TABLE 3. Continued

Entry	Substrate		Nu	Product		Yield (%)[d]
23		**3r**	MeOH		**5w**	70
24		**3s**	MeOH		**5x**	75
25		**3t**	MeOH		**5y**	89
26		**1a**	MeOH		**5z**	93
27		**1c**	MeOH		**5aa**	92
28		**1e**	MeOH		**5bb**	89
29		**1f**	MeOH		**5cc**	90
30		**1g**	MeOH		**5dd**	85
31		**1h**	MeOH		**5ee**	68[c]

[a]The reactions were performed using *o*-alkynylaldehyde **3**/arylaldehydes **1** (0.50 mmol), 20 equiv of nucleophile, 2.5 equiv of K_2CO_3, and 2.5 equiv of I_2 at 70 °C for 2−4 h. [b]Using 2.0 equiv of I_2 for 10 min. [c]3.0 equiv of I_2. [d]Yield of isolated product.

(Table 4). Electrophilic iodocyclization on 2-arylalkynyl esters afforded the corresponding 4-iodo-pyran[4,3-*b*]-quinolinones **6a**−**i** and isocoumarin **6j** in 70−85% and 82% yields, respectively (Table 4, entries 1−12). Alkynyl esters **5m**, **5n**, **5o**, **5w**, and **5hh**, bearing alkyl and alicyclic substituents such as *n*-butyl, cyclohexyl, and *tert*-butyl, reacted well and provided desired iodocyclized products **6e**−**h** in good yields (entries 6−10).

The formation of 4-iodo-pyrano[4,3-*b*]quinolinone **6** was confirmed by ^1H, ^{13}C NMR and finally by X-ray crystallographic analysis[19] of compound **6c** (Figure 2) (see Supporting Information).

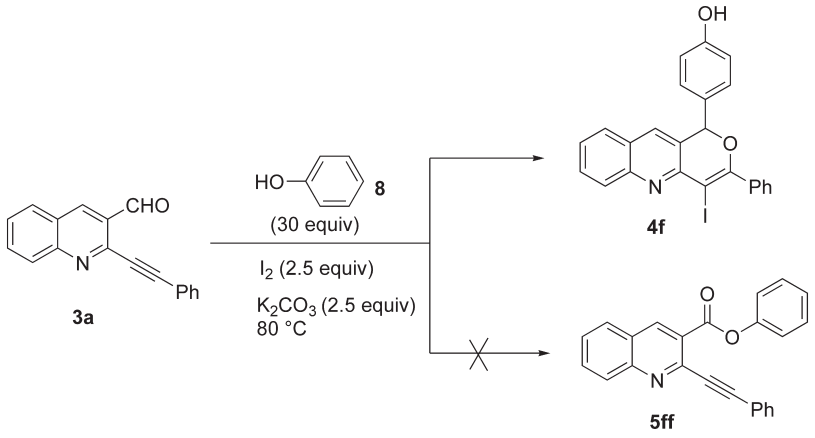
We rationalized these results with the assumption that the quinoline nitrogen being close to the phenylethynyl group might first coordinate to the electrophile to form an ammonium cation (Scheme 5). Because of this coordination, electrophilic attack of the triple bond might then occur in an intramolecular fashion.[21]

The cyclization process selectively proceeds via the more stable benzyl cationic intermediate **C** in which the positive charge is better stabilized by the aromatic ring, bearing an electron-donating group rather than proceeding through the formation of less stable intermediate **B** in which the positive charge is adjacent to electron-deficient ortho position of the quinoline ring. Subsequently 6-*endo*-*dig* cyclization is favored over 5-*exo*-*dig* cyclization. This leads to the formation of regioselective six-membered cyclized product.

We believe that this approach to 4-iodopyranoquinolines is quite useful for the synthesis of additional more highly substituted pyranoquinolines, particularly when one considers

(21) Huang, Q.; Hunter, J. A.; Larock, R. C. *Org. Lett.* **2001**, *3*, 2973.

SCHEME 4



that there are many ways to transform the resulting iodide functional group into other substituents. For example **4a** and **4d** produced by this strategy can be further functionalized by applying palladium-catalyzed coupling reactions such as Suzuki[22] and Heck[23] reactions to afford the corresponding products **10**, **11**, and **12** in 85%, 81%, and 70% yields, respectively (Scheme 6).

Conclusion

In conclusion, we have realized for the first time iodine-catalyzed and solvent-controlled selective synthesis of iodo-pyrano[4,3-*b*]quinolines and *o*-alkynyl esters from *o*-alkynyl aldehydes in mild reaction conditions. The developed novel oxidative esterification process provides a powerful tool for the preparation of a wide range of functionalized pyrano-quinolinones as well as isocoumarin. This direct selective oxidative transformation of aldehydes to esters is an extremely useful and selective functional group interconversion in organic synthesis. This chemoselective esterification affords esters from aldehydes having alkyne and unprotected alcohols without any side reaction on the primary alcoholic group present in the substrate. The developed methodology accommodates a variety of functional groups, affording iodo-pyrano[4,3-*b*]quinolines that are then readily elaborated to more complex products using organopalladium chemistry.

This methodology is tolerant toward a variety of functional groups including primary alcohol, carboxyl, and methoxy groups. This provides a handle for further organic transformations. Further investigations to expand the reaction scope are ongoing and will be reported in due course.

Experimental Section

General Procedure for the Synthesis of 4-Iodo-1*H*-pyrano[4,3-*b*]-quinolines (4b−f). Into a solution of the 2-(alkynyl)quinoline-3-carbaldehyde (0.50 mmol), K_2CO_3 (2.5 equiv) and the nucleophile (1.2 equiv) in CH_2Cl_2 (2.0 mL) was added I_2 (2.5 equiv), and the solution was stirred at room temperature until the total disappearance of the starting material as determined by TLC analysis. The reaction mixture was then quenched with satd aq $Na_2S_2O_3$ (5.0 mL) and water (5.0 mL). The resulting solution was extracted using ethyl acetate. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash column chromatography (hexane/EtOAc) to afford pure compounds.

1-*tert*-Butoxy-4-iodo-3-phenyl-1*H*-pyrano[4,3-*b*]quinoline (4b). The product was obtained as a yellow solid, mp 108−110 °C: ^{1}H NMR (300 MHz, [D]CHCl$_3$) δ 8.18 (d, J = 8.4 Hz, 1H), 7.87 (s, 1H), 7.82 (d, J = 8.1 Hz, 1H), 7.72−7.67 (m, 3H), 7.50−7.43 (m, 4H), 6.56 (s, 1H), 1.44 (s, 9H); ^{13}C NMR (CDCl$_3$) δ 158.7, 148.8, 148.5, 137.1, 131.8, 130.3, 130.0, 129.4, 128.2, 127.9, 127.8, 127.6, 126.2, 123.7, 94.9, 77.5, 29.7, 29.0; HRMS (ESI) calcd for $C_{22}H_{20}INO_2$ (M+H$^+$) 457.0539, found 457.0541.

4-Iodo-1-methoxy-3-*p*-tolyl-1*H*-pyrano[4,3-*b*]quinoline (4c). The product was obtained as a yellow solid, mp 110−112 °C: ^{1}H NMR (300 MHz, [D]CHCl$_3$) δ 8.20 (d, J = 8.4 Hz, 1H), 7.97 (s, 1H), 7.83 (d, J = 8.1 Hz, 1H), 7.76−7.62 (m, 3H), 7.51 (t, J = 7.5 Hz, 1H), 7.29−7.25 (m, 2H), 6.23 (s, 1H), 3.72 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (CDCl$_3$) δ 157.8, 148.9, 148.0, 140.1, 134.1, 133.1, 130.3, 129.9, 129.5, 128.7, 127.5, 126.3, 121.9, 100.4, 56.5, 21.6; HRMS (ESI) calcd for $C_{20}H_{16}INO_2$ (M + H$^+$) 429.0226, found 429.0230.

4-Iodo-1,8-dimethoxy-3-phenyl-1*H*-pyrano[4,3-*b*]quinoline (4d). The product was obtained as a yellow solid, mp 150−152 °C: ^{1}H NMR (300 MHz, [D]CHCl$_3$) δ 8.09 (d, J = 9.0 Hz, 1H), 7.85 (s, 1H), 7.71 (d, J = 5.1 Hz, 2H), 7.4−7.37 (m, 4H), 7.09 (s, 1H), 6.20 (s, 1H), 3.92 (s, 3H), 3.70 (s, 3H); ^{13}C NMR (CDCl$_3$) δ 157.8, 156.6, 145.7, 145.0, 137.1, 131.8, 131.00, 130.00, 129.7, 128.6, 128.0, 122.9, 122.1, 105.2, 100.5, 78.1, 56.4, 55.6; HRMS (ESI) calcd for $C_{20}H_{16}INO_3$ (M + H$^+$) 445.0175, found 445.0180.

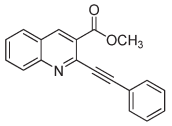
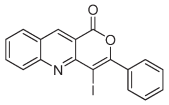
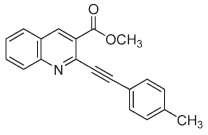
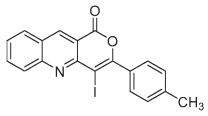
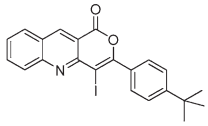
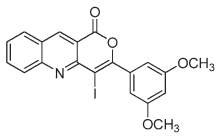
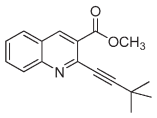
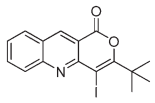
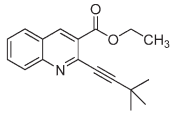
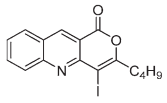
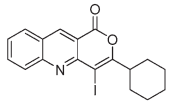
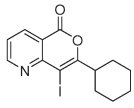
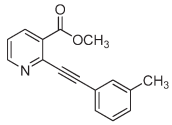
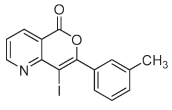
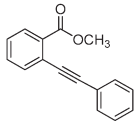
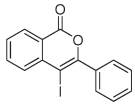
3-Butyl-4-iodo-1-methoxy-1*H*-pyrano[4,3-*b*]quinoline (4e). The product was obtained as a yellow sticky solid: ^{1}H NMR (300 MHz, [D]CHCl$_3$) δ 8.1 (t, J = 8.4 Hz, 1H), 7.89−7.76(m, 2H), 7.72−7.67 (m, 2H), 6.09 (s, 1H), 3.62 (s, 3H), 2.96−2.80 (m, 2H), 1.83−1.65 (m, 2H), 1.53−1.41 (m, 2H), 1.03-.098 (m, 3H); ^{13}C NMR (CDCl$_3$) δ 161.7, 148.8, 147.4, 133.0, 130.4, 129.4, 127.4, 126.0, 121.5, 120.4, 94.2, 78.5, 56.0, 37.9, 29.3, 22.3, 14.0; HRMS (ESI) calcd for $C_{17}H_{18}INO_2$ (M+H$^+$) 395.0382, found 395.0387.

4-(4-Iodo-3-phenyl-1*H*-pyrano[4,3-*b*]quinolin-1-yl)phenol (4f). The product was obtained as a brown solid, mp 120−124 °C: ^{1}H NMR (300 MHz, [D]CHCl$_3$) δ 8.92 (s, 1H), 8.55 (s,1H), 8.03 (d, J = 8.4 Hz, 1H), 7.8 (d, J = 8.1 Hz, 1H), 7.71−7.62 (m, 2H), 7.57−7.55 (m, 1H), 7.37−7.34 (m, 1H), 7.23−7.21 (m, 1H), 6.94 (d, J = 8.4 Hz, 1H), 6.80−6.75 (m, 2H), 6.30 (d, J = 3.9 Hz, 1H), 5.45 (s, 1H); ^{13}C NMR (CDCl$_3$) δ 161.6, 160.7, 151.8, 149.2, 146.9, 144.8, 144.6, 138.9, 138.06, 137.8, 135.3, 135.1, 134.5,

(22) (a) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147. (b) Miyura, N. *Chem. Rev.* **1995**, *95*, 2457.

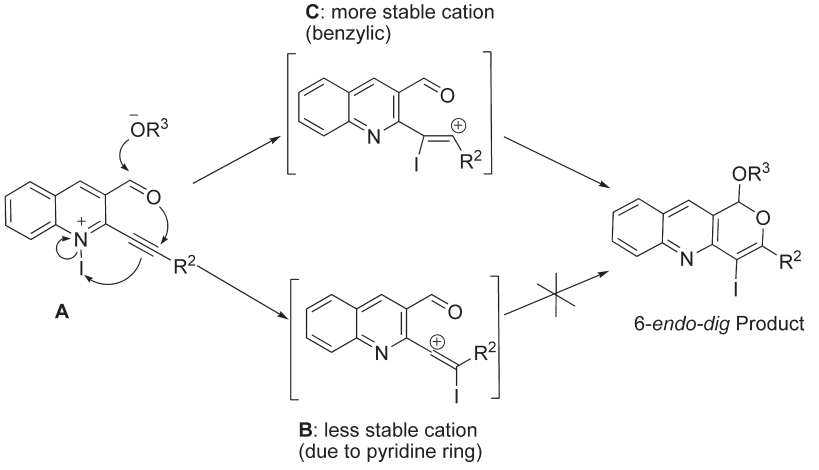
(23) Yao, Q.; Kinney, E. P.; Yang, Z. *J. Org. Chem.* **2003**, *68*, 7528.

TABLE 4. Synthesis of 4-Iodo-pyrano[4,3-*b*]quinolinones 6a−i and 4-Iodo-isocoumarin and 6j from *o*-Alkynyl Esters[a]

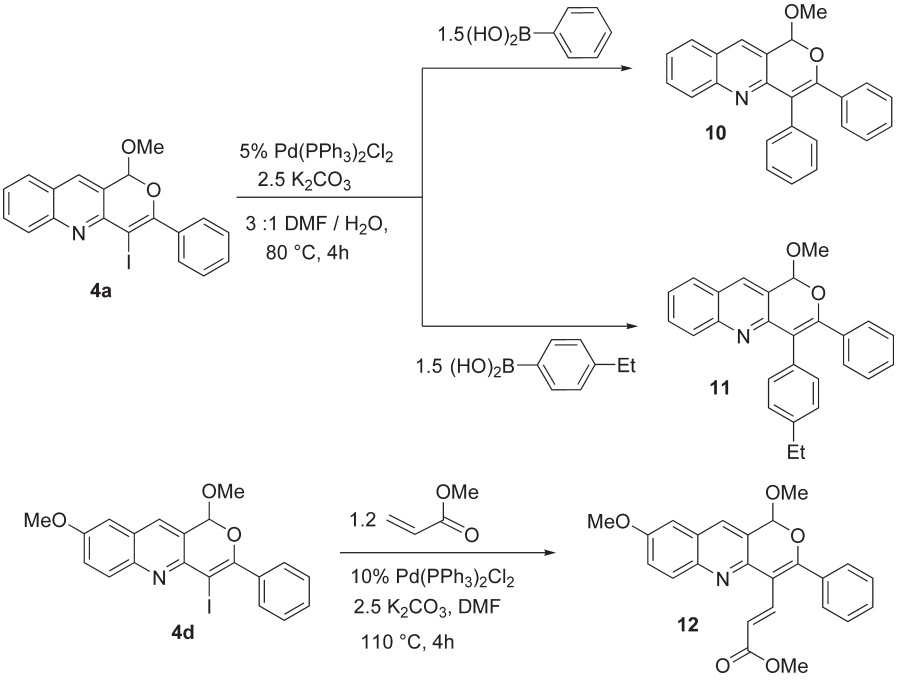
Entry	Substrate		Product		Yield(%)[b]
1		**5a**		**6a**	85
2		**5b**		**6a**	78
3		**5gg**		**6b**	76
4		**5h**		**6c**	77
5		**5j**		**6d**	70
6		**5o**		**6e**	75
7		**5hh**		**6e**	70
8		**5m**		**6f**	77
9		**5n**		**6g**	80
10		**5w**		**6h**	70
11		**5x**		**6i**	78
12		**5ii**		**6j**	82

[a]0.50 mmol of *o*-alkynylesters **5** and 2.0 equiv of I_2 in 2.0 mL of CH_2Cl_2 at room temperature. [b]Yield of isolated product.

SCHEME 5. Regioselectivity



SCHEME 6. Pd-Catalyzed Diversification of Iodopyranoquinoline



134.3, 133.6, 132.6, 132.2, 131.9, 130.6, 125.9; HRMS (ESI) calcd for $C_{22}H_{14}INO_2S$ ($M + H^+$) 482.9790, found 482.9780.

General Procedure for the Synthesis of Alkyl 2-(Alkynyl)-quinoline-3-carboxylates. Into a solution of I_2 (2.5 equiv) in 20 equiv of nucleophile were added 2-(alkynyl)quinoline-3-carbaldehydes **3** (0.50 mmol) and K_2CO_3 (2.5 equiv). The resulting reaction mixture was heated under an Ar atmosphere at 70 °C until the total disappearance of the starting material as determined by TLC analysis. The reaction mixture was then quenched with satd aq $Na_2S_2O_3$ (5.0 mL) and water (5.0 mL). The resulting solution was extracted using ethyl acetate. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash column chromatography (100−200 mesh silica gel, hexane/EtOAc) to afford pure compounds.

Butyl 2-(*m*-Tolylethynyl)quinoline-3-carboxylate (5c). The product was obtained as an orange oil with 30% mixture of starting material (**3a**): ^{1}H NMR (300 MHz, [D]CHCl$_3$) δ 8.77 (s, 1H), 8.19−8.15(m, 1H), 7.98−7.82 (m, 2H), 7.80−7.71 (m, 2H), 7.70−7.66 (m, 1H), 7.44−7.39(m, 3H), 4.44 (t, J = 6.0 Hz, 2H), 1.86−1.77 (m, 2H), 1.53−1.45 (m, 2H), 0.94 (t, J = 7.5 Hz, 3H); ^{13}C NMR (CDCl$_3$) δ 165.3, 149.0, 141.6, 139.5, 137.1, 132.3, 132.1, 129.6, 129.4, 128.9, 127.7 126.5, 125.9, 122.5, 93.3, 88.5, 65.7, 30.8, 19.3, 13.70.

Propyl 2-(*m*-Tolylethynyl)quinoline-3-carboxylate (5f). The product was obtained as an orange oil: ^{1}H NMR (300 MHz, [D]CHCl$_3$) δ 8.78(s, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.89 (d, J = 8.1 Hz, 1H), 7.82 (t, J = 9.0 Hz, 1H), 7.63−7.58 (m, 1H), 7.53−7.50 (m, 2H), 7.31−7.19 (m, 2H), 4.41 (t, J = 6.9 Hz, 2H), 2.37 (s, 3H), 1.91−1.79 (m, 2H), 1.05 (t, J = 7.5 Hz, 3H); ^{13}C NMR (CDCl$_3$) δ 165.3, 149.0, 141.7, 139.5, 138.0, 132.9, 130.1, 129.4, 129.2, 128.5, 128.2, 127.8, 125.9, 125.8, 122.2, 93.6, 88.2, 67.3, 29.7, 22.1, 21.3, 10.6; HRMS (ESI) calcd for $C_{22}H_{19}NO_2$ ($M + H^+$) 329.1416, found 329.1419.

Methyl 2-((4-*tert*-Butylphenyl)ethynyl)quinoline-3-carboxylate (5h). The product was obtained as an orange solid, mp 94−96 °C: ^{1}H NMR (300 MHz, [D]CHCl$_3$) δ 8.79 (s, 1H), 8.16 (d, J = 8.7 Hz, 1H), 7.90−7.79 (m, 2H), 7.67−7.57 (m, 3H), 7.41

(dd, J = 6.6 and 1.8 Hz, 2H), 4.04 (s, 3H), 1.34 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 165.8, 152.7, 149.0, 141.8, 139.7, 132.7, 132.2, 129.1, 128.5, 127.8, 125.7, 125.6, 125.5, 119.3, 93.9, 88.0, 55.6, 34.9, 31.1; HRMS (ESI) calcd for $C_{23}H_{21}NO_2$ (M + H^+) 343.1572, found 343.1569.

Methyl 2-((6-Methoxynaphthalen-2-yl)ethynyl)quinoline-3-carboxylate (5i). The product was obtained as an orange solid, mp 126−128 °C: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.81 (s, 1H), 8.17(d, J = 7.2 Hz, 2H), 7.90−7.80(m, 3H), 7.77−7.73(m, 2H), 7.60(t, J = 6.9 Hz, 1H), 7.16 (td, J = 9.0 and 2.4 Hz, 2H), 4.07 (s, 3H), 3.93 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.7, 158.7, 149.1, 141.8, 139.8, 134.8, 132.7, 132.2, 129.7, 129.3, 129.1, 128.6, 128.4, 127.8, 126.9, 125.8, 125.4, 119.5, 117.2, 105.9, 94.4, 88.4, 55.4, 52.7; HRMS (ESI) calcd for $C_{24}H_{17}NO_3$ (M + H^+) 367.1208, found 367.1210.

Methyl 2-((3,5-Dimethoxyphenyl)ethynyl)quinoline-3-carboxylate (5j). The product was obtained as an orange solid, mp 118−120 °C: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.81 (s, 1H), 8.16 (d, J = 9.0 Hz, 1H), 7.91−7.81(m, 2H), 7.61(t, J = 6.9 Hz, 1H), 6.88 (s, 2H), 6.52 (s, 1H), 4.05 (s, 3H), 3.82 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 165.6, 160.5, 149.0, 141.4, 139.8, 132.2, 129.1, 128.5, 127.9, 125.8, 125.5, 123.6, 110.0, 102.9, 93.3, 87.9, 55.5, 52.6; HRMS (ESI) calcd for $C_{21}H_{17}NO_4$ (M + H^+) 347.1158, found 347.1160.

Methyl 2-((4-Methoxyphenyl)ethynyl)quinoline-3-carboxylate (5k). The product was obtained as an orange solid, mp 82−84 °C: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.80 (s, 1H), 8.15 (d, J = 6.5 Hz, 1H), 7.90−7.81 (m, 2H), 7.68−7.60 (m, 3H), 6.92 (d, J = 6.8 Hz, 2H), 4.05 (s, 3H), 3.85 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.7, 160.5, 149.0, 141.9, 139.7, 134.0, 132.1, 129.1, 128.5, 127.7, 125.6, 125.4, 114.4, 114.1, 94.0, 87.6, 55.3, 52.6; HRMS (ESI) calcd for $C_{20}H_{15}NO_3$ (M + H^+) 317.1052, found 317.1050.

Methyl 2-((1-Hydroxycyclohexyl)ethynyl)quinoline-3-carboxylate (5p). The product was obtained as a yellow solid, mp 122−124 °C: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.74 (s, 1H), 8.13 (d, J = 8.4 Hz, 1H), 7.87−7.77 (m, 2H), 7.61−7.56 (m, 1H), 3.98 (s, 3H), 2.98 (s, 1H), 2.14 (d, J = 6.3 Hz, 3H), 1.80−1.60 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 165.7, 148.8, 141.2, 139.6, 132.1, 129.1, 128.5, 127.9, 125.8, 125.6, 97.7, 83.1, 69.0, 52.6, 39.6, 25.2, 23.1; HRMS (ESI) calcd for $C_{19}H_{19}NO_3$ (M + H^+) 309.1365, found 309.1370.

Methyl 2-(3-Hydroxyprop-1-ynyl)quinoline-3-carboxylate (5q). The product was obtained as a yellow solid, mp 100−102 °C: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.75 (s, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.92−7.78 (m, 2H), 7.60 (t, J = 8.1 Hz, 1H), 4.67 (s, 2H), 3.99 (s, 3H), 3.51 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 165.3, 148.7, 141.0, 139.8, 132.4, 128.8, 128.5, 128.0, 125.8, 124.9, 94.5, 92.5, 52.6, 51.4; HRMS (ESI) calcd for $C_{14}H_{11}NO_3$ (M + H^+) 241.0739, found 241.0740.

Ethyl 2-(3-Hydroxyprop-1-ynyl)quinoline-3-carboxylate (5r). The product was obtained as brown solid, mp 80−82 °C: ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 8.89 (s, 1H), 8.18 (dd, J = 7.8, 1.4 Hz, 1H), 8.05−7.97 (m, 1H), 7.94−7.87 (m, 1H), 7.74−7.67 (m, 1H), 4.45−4.34 (m, 4H), 1.36 (t, J = 6.9 Hz, 3H); HRMS (ESI) calcd for $C_{15}H_{13}NO_3$ (M + H^+) 255.0895, found 255.0898.

Methyl 2-(3-Hydroxyprop-1-ynyl)-6-methoxyquinoline-3-carboxylate (5s). The product was obtained as a yellow solid, mp 116−118 °C: ^{1}H NMR (400 MHz, [D]$CHCl_3$) δ 8.65 (s, 1H), 8.02 (d, J = 9.1 Hz, 1H), 7.42 (dd, J = 9.1, 2.7 Hz, 1H), 7.65 (d, J = 2.7 Hz, 1H), 4.55 (s, 2H), 3.94 (s, 3H), 3.88 (s, 3H), 2.47 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 165.4, 159.10, 144.7, 138.6, 138.2, 130.2, 127.3, 125.8, 125.3, 105.5, 92.3, 84.2, 55.8, 52.7, 51.7; HRMS (ESI) calcd for $C_{15}H_{13}NO_4$ (M + H^+) 271.0845, found 271.0849.

Methyl 2-(3-Hydroxyprop-1-ynyl)nicotinate (5t). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, [D]$CHCl_3$) δ 8.63 (dd, J = 1.2, 3.2 Hz, 1H), 8.18 (dd, J = 1.8, 5.9 Hz, 1H), 7.61−7.56 (m, 1H), 4.50 (s, 2H), 3.87 (s, 3H), 2.88 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 165.2, 152.4, 138.2, 132.0, 128.4, 122.5, 93.3, 83.7, 52.6, 51.3; HRMS (ESI) calcd for $C_{10}H_9NO_3$ (M + H^+) 191.0582, found 191.0588.

Ethyl 2-(3-Hydroxyprop-1-ynyl)nicotinate (5u). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, [D]$CHCl_3$ + $(CD_3)_2SO$) δ 8.48 (t, J = 4.8 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.36−7.34 (m, 1H), 4.30 (s, 2H), 4.16−4.13 (m, 2H), 1.24−1.21 (m, 3H); ^{13}C NMR ($CDCl_3$ + $(CD_3)_2SO$): 165.0, 151.5, 138.1, 131.8, 128.4, 122.3, 93.8, 82.9, 61.6, 50.7, 14.1; HRMS (ESI) calcd for $C_{11}H_{11}NO_3$ (M + H^+) 205.0739, found 205.0742.

Methyl 2-(Phenylethynyl)nicotinate (5v). The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.75 (t, J = 4.8 Hz, 1H), 8.27 (d, J = 7.8 Hz, 1H), 7.68−7.65 (m, 2H), 7.39−7.37 (m, 3H), 7.35−7.26 4.67 (m, 1H), 4.0 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.6, 152.6, 142.8, 142.6, 138.2, 132.3, 129.3, 128.4, 122.3, 122.2, 94.2, 87.9, 52.6; HRMS (ESI) calcd for $C_{15}H_{11}NO_2$ (M + H^+) 237.0790, found 237.0792.

Methyl 2-(Cyclohexylethynyl)nicotinate (5w). The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.67 (dd, J = 1.8, 4.8 Hz, 1H), 8.18 (dd, J = 1.8, 8.1 Hz, 1H), 7.28−7.24 (m, 1H), 3.94 (s, 3H), 2.78−2.69 (m, 1H), 1.95−1.91 (m, 2H), 1.83−1.77 (m, 2H), 1.64−1.56 (m, 3H), 1.40−1.34 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 166.0, 152.3, 143.1, 138.0, 128.4, 121.6, 100.3, 79.4, 52.4, 32.1, 29.9, 25.8, 24.8; HRMS (ESI) calcd for $C_{15}H_{17}NO_2$ (M + H^+) 243.1259, found 243.1256.

Methyl 2-(*m*-Tolylethynyl)nicotinate (5x). The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.747 (d, J = 4.5 Hz, 1H), 8.26 (d, J = 8.1 Hz, 1H), 7.47 (d, J = 8.4 Hz, 2H), 7.34−7.29 (m, 1H), 7.24−7.18 (m, 2H), 4.00 (s, 3H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.5, 152.5, 142.8, 138.1, 138.1, 132.8, 130.2, 129.3, 128.3, 128.3, 122.1, 122.0, 94.4, 87.5, 52.5, 21.2; HRMS (ESI) calcd for $C_{16}H_{13}NO_2$ (M + H^+) 251.0946, found 251.0950.

Methyl 2-(Cyclohexylethynyl)benzoate (5y). The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 7.47 (d, J = 7.5, 1H), 7.33 (d, J = 6.9, 1H), 7.24−7.17 (m, 2H), 3.33 (s, 3H), 2.60−2.57 (m, 1H), 1.62−1.89 (m, 4H), 1.60−1.19 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 138.3, 131.2, 127.2, 126.5, 124.8, 122.0, 101.9, 98.1, 76.9, 53.5, 31.7, 28.8, 24.9, 23.8; HRMS (ESI) calcd for $C_{16}H_{18}O_2$ (M + H^+) 242.1307, found 242.1310.

Methyl 2-Chloroquinoline-3-carboxylate (5z). The product was obtained as white solid: mp 70−72 °C: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.69(s, 1H), 8.04 (d, J = 8.4 Hz, 1H), 7.90−7.80 (m, 2H), 7.62 (t, J = 7.2 Hz, 1H), 4.01 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.0, 148.3, 147.6, 141.7, 132.7, 128.5, 128.2, 127.9, 125.8, 124.1, 52.9; HRMS (ESI) calcd for $C_{11}H_8ClNO_2$ (M + H^+) 221.0244, found 221.0248.

Methyl 2-Bromonicotinate (5aa). The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.49 (dd, J = 1.8, 4.8 Hz, 1H), 8.08 (dd, J = 1.8, 4.8 Hz, 1H), 7.38−7.34 (m, 1H), 3.96 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.4, 152.1, 140.7, 139.6, 129.6, 122.3, 53.0; HRMS (ESI) calcd for $C_7H_6BrNO_2$ (M + H^+) 214.9582, found 214.9588.

Methyl 2,5-Dibromobenzoate (5bb). The product was obtained as an orange solid, mp 46−48 °C: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.00 (d, J = 1.8 Hz, 1H), 7.54−7.4 (m, 2H), 3.94 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.2, 135.8, 135.5, 134.2, 134.1, 121.0, 120.5, 52.8; HRMS (ESI) calcd for $C_8H_6Br_2O_2$ (M + H^+) 291.8735, found 291.8732.

Methyl 4-Methoxybenzoate (5cc). The product was obtained as white solid: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 7.99 (d, J = 7.2 Hz, 2H), 6.91 (d, J = 9.0 Hz, 2H), 3.88 (s, 3H), 3.85 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 166.9, 163.4, 131.2, 122.6, 113.6, 55.5, 51.9; HRMS (ESI) calcd for $C_9H_{10}O_3$ (M + H^+) 166.0630, found 166.0634.

Methyl 4-Nitrobenzoate (5dd). The product was obtained as a yellow solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35−8.20 (m, 4H), 3.98 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.2, 150.5, 135.5, 130.8,

123.6, 52.9; HRMS (ESI) calcd for $C_8H_7NO_4$ (M + H^+) 181.0375, found 181.0378.

Methyl 2-(4-Methoxyphenyl)nicotinate (5ee). The product was obtained as an orange oil: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.75−8.73 (m, 1H), 8.06−8.03 (m, 1H), 7.57−7.50 (m, 2H), 7.30−7.27 (m, 1H), 7.05−6.95, (m, 2H), 3.85(s, 3H), 3.73 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 168.9, 160.2, 158.1, 151.2, 137.8, 132.3, 131.9, 129.9, 126.6, 121.0, 114.1, 113.6, 55.3, 52.3; HRMS (ESI) calcd for $C_{14}H_{13}NO_3$ (M + H^+) 243.0895, found 243.0891.

Methyl 2-(*p*-Tolylethynyl)quinoline-3-carboxylate (5gg). The product was obtained as a yellow solid, mp 110−112 °C: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.78 (s, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.80−7.79 (m, 2H), 7.62−7.56 (m, 3H), 7.19 (d, J = 8.1 Hz, 2H), 4.04 (s, 3H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.7, 149.0, 141.7, 139.7, 139.6, 132.3, 132.1, 129.1, 129.1, 128.5, 127.8, 125.7, 125.5, 119.3, 93.7, 88.0, 52.6, 21.6; HRMS (ESI) calcd for $C_{20}H_{15}NO_2$ (M + H^+) 301.1103, found 301.1100.

Ethyl 2-(3,3-Dimethylbut-1-ynyl)quinoline-3-carboxylate (5hh). The product was obtained as a yellow oil: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.65 (s, 1H), 8.12 (d, J = 8.3 Hz, 1H), 7.84 (d, J = 8.1 Hz, 1H), 7.79 (t, J = 6.3 Hz, 1H), 7.56 (t, J = 7.8 Hz, 1H), 4.47 (q, J = 7.2 Hz, 2H), 1.46 (t, J = 7.2 Hz, 3H), 1.42 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 165.7, 148.7, 141.7, 138.9, 131.7, 129.0, 128.3, 127.4, 126.5, 125.6, 103.1, 78.6, 61.5, 30.5, 28.2, 14.4; HRMS (ESI) calcd for $C_{18}H_{19}NO_2$ (M + H^+) 281.1416, found 281.1412.

General Procedure for the Synthesis of 4-Iodo-3-aryl-1*H*-pyrano[4,3-*b*]quinolin-1-one (6a−j). Into a solution of I_2 (2.5 equiv) in CH_2Cl_2 (2.0 mL) was added a 2-(alkynyl) quinoline-3-carboxylate (0.50 mmol). The resulting reaction mixture was stirred under an Ar atmosphere at room temperature until the total disappearance of the starting material as determined by TLC analysis. The reaction mixture was then quenched with satd aq $Na_2S_2O_3$ (5.0 mL) and water (5.0 mL). The resulting solution was extracted using ethyl acetate. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified by recrystallization.

3-(4-*tert*-Butylphenyl)-4-iodo-1*H*-pyrano[4,3-*b*]quinolin-1-one (6c). The product was obtained as an orange solid, mp 192−194 °C: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 9.13 (s, 1H), 8.30 (d, J = 8.4 Hz, 1H), 8.17 (d, J = 6.6 Hz, 1H), 8.05 (d, J = 8.1 Hz, 1H), 7.94 (t, J = 8.4 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.52 (d, J = 6.9 Hz, 2H), 7.31−7.26 (m, 1H), 1.39 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 161.7, 154.0, 151.7, 150.7, 140.7, 133.6, 131.7, 131.3, 29.8, 129.0, 128.1, 127.7, 125.2, 125.0, 114.2, 81.1, 34.9, 31.2; HRMS (ESI) calcd for $C_{22}H_{18}INO_2$ (M + H^+) 455.0382, found 455.03879.

3-(3,5-Dimethoxyphenyl)-4-iodo-1*H*-pyrano[4,3-*b*]quinolin-1-one (6d). The product was obtained as an orange solid, mp 202−204 °C: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 9.1 (s, 1H), 8.31(d, J = 8.4 Hz, 1H), 8.06 (d, J = 8.1 Hz, 1H), 7.95 (t, J = 8.1 Hz, 1H), 7.68 (t, J = 7.5 Hz, 1H), 6.95 (s, 2H), 6.6 (s, 1H), 3.9 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 161.6, 160.3, 157.5, 151.7, 150.5, 140.7, 136.3, 133.7, 129.7, 129.1, 127.8, 127.4, 114.3, 108.1, 102.6, 81.7, 55.6; HRMS (ESI) calcd for $C_{20}H_{14}INO_4$ (M + H^+) 458.9968, found 458.9967.

3-*tert*-Butyl-4-iodo-1*H*-pyrano[4,3-*b*]quinolin-1-one (6e). The product was obtained as an orange solid, mp 140−142 °C: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 9.07 (s, 1H), 8.27 (d, J = 8.7 Hz, 1H), 8.02 (d, J = 8.4 Hz, 1H), 7.94−7.84 (m, 1H), 7.63 (t, J = 7.8 Hz, 1H), 1.68 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 165.5, 161.7, 151.5, 150.7, 140.3, 133.4, 129.6, 128.9, 127.48, 127.4, 113.8, 80.1, 39.4, 29.0; HRMS (ESI) calcd for $C_{16}H_{14}INO_2$ (M + H^+) 379.0069, found 379.0071.

7-Cyclohexyl-8-iodo-5*H*-pyrano[4,3-*b*]pyridin-5-one (6h). The product was obtained as an orange solid, mp 116−118 °C: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.99 (dd, J = 1.8, 4.8 Hz, 1H), 8.47(dd, J = 1.5, 7.8 Hz, 1H), 7.46−7.42 (m, 1H), 3.37−3.28 (m, 1H), 1.91−1.87 (m, 4H), 1.46−1.22 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 164.8, 161.8, 156.4, 137.8, 123.4, 116.3, 79.1, 77.4, 46.4, 29.4, 25.9, 25.5; HRMS (ESI) calcd for $C_{14}H_{14}INO_2$ (M + H^+) 355.0069, found 355.0071.

8-Iodo-7-*m*-tolyl-5*H*-pyrano[4,3-*b*]pyridin-5-one (6i). The product was obtained as an orange solid, mp 124−126 °C: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 9.07 (s, 1H), 8.55(d, J = 7.5 Hz, 1H), 7.61−7.58 (m, 2H), 7.54−7.50 (m, 1H), 7.41−7.30 (m, 2H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 161.5, 158.4, 156.5, 153.4, 138.0, 137.9, 134.3, 131.4, 130.3, 128.0, 127.2, 123.9, 116.4, 80.1, 21.4; HRMS (ESI) calcd for $C_{15}H_{10}INO_2$ (M + H^+) 362.9756, found 362.9759.

1-Methoxy-3,4-diphenyl-1*H*-pyrano[4,3-*b*]quinoline (10). The product was obtained as white solid, mp 138−140 °C: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.09 (s, 1H), 7.97 (d, J = 6.9 Hz, 1H), 7.81 (d, J = 7.2 Hz, 1H), 7.61 (t, J = 7.2 Hz, 1H), 7.46−7.16 (m, 11H), 6.32 (s, 1H), 3.75 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 153.4, 149.8, 148.8, 135.4, 135.3, 132.8, 132.4, 129.9, 129.6, 129.5, 128.6, 127.8, 127.7, 127.5, 126.9, 126.8, 125.8, 122.5, 117.6, 100.1, 56.21; HRMS (ESI) calcd for $C_{25}H_{19}NO_2$ (M + H^+) 365.1416, found 365.1410.

4-(4-Ethylphenyl)-1-methoxy-3-phenyl-1*H*-pyrano[4,3-*b*]quinoline (11). The product was obtained as an orange solid, mp 92−94 °C: ^{1}H NMR (300 MHz, [D]$CHCl_3$) δ 8.05 (s, 1H), 7.97 (d, J = 8.4 Hz, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.60 (td, J = 6.9, 1.2 Hz, 1H), 7.42 (t, J = 8.1 Hz, 1H), 7.35−7.31 (m, 4H), 7.23−7.13 (m, 5H), 6.29 (s, 1H), 3.74 (s, 3H), 2.67 (q, J = 7.5 Hz, 2H), 1.26 (t, J = 7.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 153.2, 150.0, 148.8, 143.7, 135.5, 132.7, 132.3, 132.2, 129.9, 129.5, 128.7, 128.4, 128.0, 127.6, 127.3, 126.8, 126.4, 125.7, 122.6, 117.5, 100.0, 56.1, 28.6, 15.4; HRMS (ESI) calcd for $C_{27}H_{23}NO_2$ (M + H^+) 393.1729, found 393.1730.

(*E*)-Methyl 3-(1,8-Dimethoxy-3-phenyl-1*H*-pyrano[4,3-*b*]-quinolin-4-yl)acrylate (12). The product was obtained as a yellow oil: ^{1}H NMR (400 MHz, [D]$CHCl_3$) δ 8.19 (d, J = 9.1 Hz, 1H), 8.02 (s, 1H), 7.83−7.79 (m, 1H), 7.632−7.622 (m, 3H), 7.49−7.48 (m,3H), 7.40 (dd, J = 2.7, 9.2 Hz, 1H), 7.09 (d, J = 2.0 Hz, 1H), 6.21 (s, 1H), 3.93 (s, 3H), 3.77 (s, 3H), 3.74 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 168.8, 166.7, 161.5, 157.8, 146.2, 139.9, 139.1, 133.6, 132.1, 130.6, 130.1, 128.4, 127.7, 123.1, 122.9, 119.8, 111.0, 105.2, 100.6, 56.7, 55.5, 51.4; HRMS (ESI) calcd for $C_{24}H_{21}NO_5$ (M + H^+) 403.1420, found 403.1430.

Acknowledgment. We gratefully acknowledge the University of Delhi for financial support and USIC for providing instrumentation facilties. Our sincere thanks to Dr. Rajeev Gupta for his kind help in solving X-ray crystallographic data. V.R. and T.A. thank CSIR and DST for a fellowship.

Supporting Information Available: X-ray crystallographic data of compound **4a** and **6c** in CIF format and copies of ^{1}H and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.