JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

$SnCl_2$-Catalyzed Selective Atom Economic Imino Diels–Alder Reaction: Synthesis of 2-(1*H*-Pyrrolo[2,3-*b*]pyridin-3-yl)quinolines

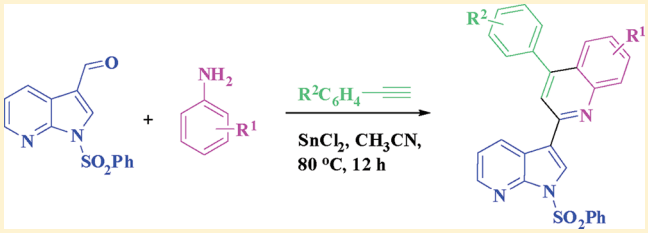
Rajendran Suresh,[†,‡] Shanmugam Muthusubramanian,*[,†] Rajendran Senthilkumaran,[‡] and Govindaswamy Manickam[‡]

[†]Department of Organic Chemistry, School of Chemistry, Madurai Kamaraj University, Madurai, 625 021, India

[‡]Syngene International Limited, Biocon, Bangalore, 560 099, India

Supporting Information

ABSTRACT: The synthesis of 2-(1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)quinolines by a $SnCl_2$-catalyzed multicomponent reaction has been described. The reaction proceeds chemo- and regioselectively in an atom-economic way, generating a library of 24 quinoline derivatives.



INTRODUCTION

Heterocyclic compounds embedded with nitrogen are prevalent in nature and present in numerous natural products and pharmaceutical leads. Among the nitrogen heterocycles, quinoline derivatives are important motifs, widely found in many natural products, many of them displaying biological activities such as antimalarial, antimicrobial, antifungal, antineoplastic, anti-HIV, antituberclosis, anticancer, and antibacterial properties.[1−3] Owing to their biological importance, these derivatives attract the attention of synthetic chemists, and hence, many synthetic strategies are dedicated to access these frameworks. Skraup reaction,[4a,b] Combes synthesis,[4c] Friedländer synthesis[4d] and Doebner–Miller reaction[4e] are a few well-recognized synthetic protocols employed for the preparation of quinoline derivatives.[5] Recently, the imino Diels–Alder reaction, known as Povarov reaction, has become one of the most important protocols for the synthesis of tetrahydroquinoline derivatives.[6] Interestingly, Povarov reaction can be promoted either by Lewis acid[7a−e] or protic acid[7f−h] or by even iodine[7i] through cycloaddition of *N*-aryl aldimine, generated in situ from aniline and aldehyde, with alkene yielding the tetrahydroquinoline derivatives.[8] To get quinoline from tetrahydro/dihydroquinoline, the latter should be subjected to oxidation under harsh conditions[9] or dehydrogenation by hydrogen transfer process[10] or acid-catalyzed elimination reactions.[11] On the other hand, one can utilize acetylene derivative as dienophile to form dihydroquinoline, which in situ undergoes aerobic oxidation[12] to the corresponding quinoline.[13]

Azaindole is yet another nucleus known to be part of many biologically active compounds, occupying a unique position in medicinal and pharmaceutical chemistry and serving as a building block in synthetic chemistry.[14]

RESULTS AND DISCUSSION

We have planned to link two biologically important nuclei, quinolines and azaindoles, to generate a new set of compounds, (1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)quinoline analogues, using Povarov reaction by the cycloaddition of aldimine containing 7-azaindole unit and alkyne. It must be mentioned that usage of alkyne as a component for Povarov reaction is not as popular as with alkene.[13] The general synthetic strategy of the present investigation is shown in Scheme 1. Following the literature procedure, 7-azaindole-3-carboxaldehyde **1** was obtained from 7-azaindole in two steps.[15] Treatment of **1** with substituted aniline **2** under acidic condition would have formed the intermediate *N*-aryl aldimine **3**, which subsequently undergoes [4 + 2]-cycloaddition with substituted alkyne **4** followed by aerobic dehydrogenation to afford directly quinoline derivatives **5**.

In order to select the suitable acid to promote this one-pot Povarov reaction, the reaction has been screened with azaindole **1**, 4-methoxyaniline (**2b**), and phenylacetylene (**4a**), taken with different Lewis acids in stoichiometric ratio. The choice between toluene, ethanol, and acetonitrile as a solvent has also been optimized. The details are presented in Table 1. It can be seen that the reaction leads to a mixture of products having quinoline **5b** and the deprotected (1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)-quinoline derivative **6b**. Though boron triflouride diethyl etherate has been widely used for Povarov reactions, it is noticed that stannous chloride is competent enough as the acid source. When only 20 mol % of stannous chloride in acetonitrile was used, very good yield of **5b**, with negligible amount of **6b**, has been achieved. It is noteworthy that (i) titanium(IV) chloride in acetonitrile gives exclusively **6b** with no trace of **5b**, (ii) when titanium(IV) isopropoxide is employed, the reaction does not go at all, (iii) camphorsulfonic acid is not effective in this conversion,

Received: November 17, 2011
Published: January 9, 2012

Scheme 1. Synthesis of 4-Substituted-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)quinoline

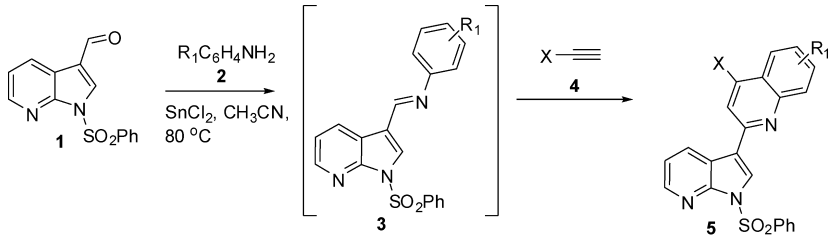
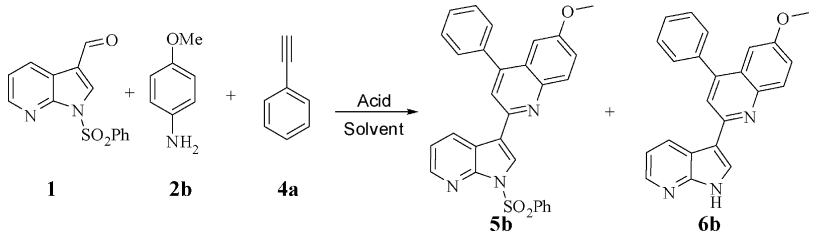


Table 1. Screening Impact of Solvents and Lewis Acids



entry	Lewis acid (100 mol %)	Solvent at reflux temp[a]	yield of **5b** (%)[b]	yield of **6b** (%)[b]
1	$BF_3{\cdot}OEt_2$	EtOH	4	62
2	$BF_3{\cdot}OEt_2$	toluene	18	36
3	$BF_3{\cdot}OEt_2$	CH_3CN	42	34
4	CSA	CH_3CN	4	
5	$InCl_3$	CH_3CN	31	29
6	*p*-TsOH	toluene	9	33
7	$Sc(OTf)_3$	CH_3CN	40	39
9	$FeCl_3$	CH_3CN	19	54
10	$La(OTf)_3$	CH_3CN	13	67
11	$ZnCl_2$	CH_3CN	8	42
12	$InBr_3$	CH_3CN	29	46
13	$TiCl_4$	CH_3CN		76
14	$Ti(OPr)_4$	CH_3CN		
15	AgOTf	CH_3CN	28	45
16	$SnCl_2$	CH_3CN	47	42
17	$SnCl_2$[c]	CH_3CN	86	5

[a]Reaction time:12 h. [b]Isolated yield. [c]20 mol % catalyst used.

and (iv) acetonitrile is found to be superior as solvent over ethanol or toluene. The reaction has been carried out under the optimized conditions (20 mol % of $SnCl_2$, acetonitrile, 80 °C) for various combinations of aryl amines and acetylene derivatives to get different **5**. Under this condition, **6** was obtained only in traces.

The amines employed were *ortho*-, *para*-, or *meta*-substituted anilines, naphthylamines, and some heterocyclic amines, while a variety of aryl/heteroaryl and cyclohexenyl acetylenes have been used as the dienophiles, yielding a range of products with good yield (Table 2). 2-Aminopyridine, 4-aminopyridine, and 2-aminopyrazine have not undergone this reaction, no matter which acetylenic component was employed. The reduced nucleophilicity of the amino group could be the reason for this, as the imine formation itself would have been difficult in these cases.

Products have been adequately characterized by ^1H, ^{13}C, and mass spectral data. The reaction proceeds regioselectively, and the regiochemistry of the product formed has been unambiguously assigned by the single crystal X-ray analysis of **5b** (see the Supporting Information for more details). The substituent of the alkyne occupies the fourth position of the quinoline and not the third position. It is the double bond of the *N*-aryl ring, not that of the 7-azaindole, that plays part of the diene in this imino Diels–Alder reaction, exhibiting another selectivity. Another selectivity has been noticed during the formation of **5d**, **5m**, and **5o**, where it is the triple bond, not the double bond, of 1-ethynyl cyclohexene that has participated in the cycloaddition. In addition, the reaction works well, whether electron-donating or -withdrawing groups are present in the *o*- or *p*-position of the aniline ring.

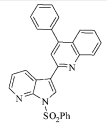
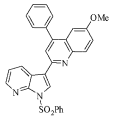
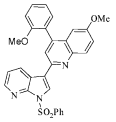
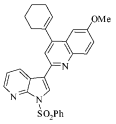
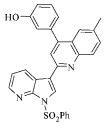
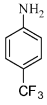
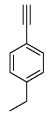
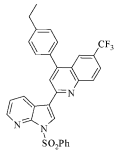
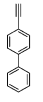
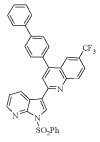
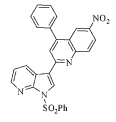
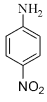
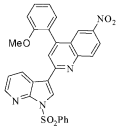
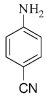
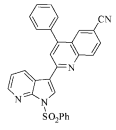
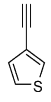
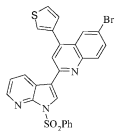
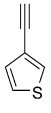
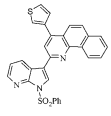
When *m*-substituted anilines were used as the amine component, both 5- and 7-substituted regioisomers were obtained in almost equal amounts and have been successfully separated. It is easy to distinguish between these two isomers from their NMR data. These two regioisomers could not be isolated in the case of **5w** and **5w′**, though the crude NMR spectrum suggests a nearly 1:1 ratio of these isomers.

The suitability of this protocol to this class of compounds has been tested with another reaction. 7-Azaindole-2-caroxaldehyde **7**, which was prepared from 7-azaindole by a literature method,[16] underwent smooth Povarov reaction with **2b** and **4a** (Scheme 2).

dx.doi.org/10.1021/jo202256z | *J. Org. Chem.* 2012, 77, 1468–1476

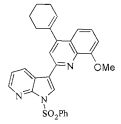
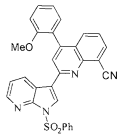
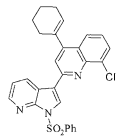
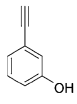
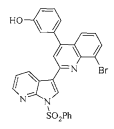
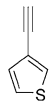
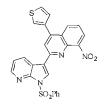
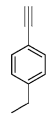
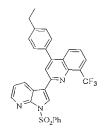
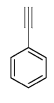
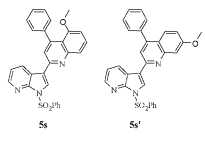
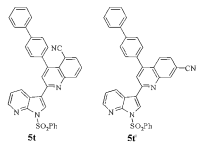
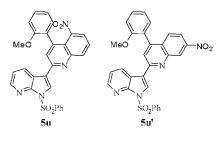
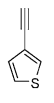
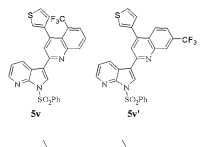
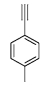
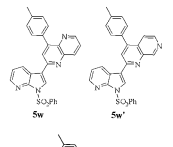
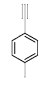
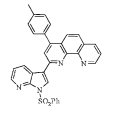
However, only the deprotected quinoline derivatives **8** were obtained, in this case in 76% yield. It is not understood why the cycloadduct originating from azaindole 2-aldehyde **7** undergoes total deprotection giving **8**, while that is not the case with **5**. The possible hydrogen bonding of N−H with the quinoline nitrogen may be a stabilizing factor in **8**.

Table 2. Synthesis of 4-Substituted-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)quinoline 5

Compd	Amine, 2	Alkyne, 4	Product, 5	Yield (%)	mp (°C)
5a				83	236-239
5b				86	222-224
5c				88	211-213
5d				83	231-233
5e				79	214-216
5f				82	212-214
5g				81	195-197
5h				86	228-230
5i				79	237-239
5j				86	236-238
5k				79	239-241
5l				84	218-220

dx.doi.org/10.1021/jo202256z | *J. Org. Chem.* 2012, 77, 1468−1476

Table 2. continued

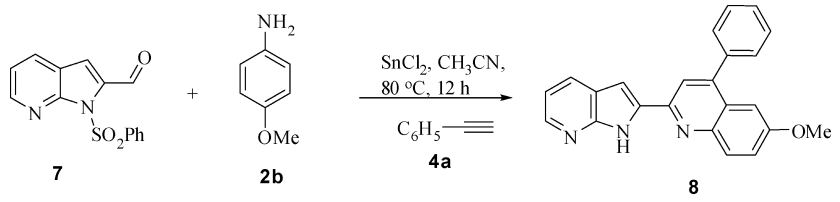
Compd	Amine, 2	Alkyne, 4	Product, 5	Yield (%)	mp (°C)
5m				81	230-232
5n				78	218-220
5o				79	226-228
5p				72	239-241
5q				80	246-248
5r				74	205-207
5s				**5s** = 39 **5s'** = 37	220-223 214-216
5t				**5t** = 38 **5t'** = 37	228-230 210-211
5u				**5u** = 36 **5u'** = 35	198-200 194-197
5v				**5v** = 42 **5v '**= 44	240-242 225-227
5w				71[a]	-
5x				85	267-269

[a]The mixture of regioisomers could not be separated.

It must be mentioned that the reaction proceeded even with the unprotected 7-azaindole **9a**, but the yield was relatively poor. When unprotected 7-azaindole-3-carboxaldehyde **9a** reacted with differently substituted acetylenes and anilines, a few derivatives of **6** (**6b**, **6c**, **6d**, **6j**, and **6n**) have been prepared and characterized (Table 3). In order to check the role of the

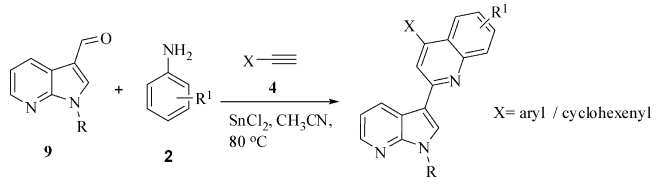
dx.doi.org/10.1021/jo202256z | J. Org. Chem. 2012, 77, 1468–1476

Scheme 2. Synthesis of 6-Methoxy-4-phenyl-2-(1*H*-pyrrolo[2,3-*b*]pyridin-2-yl)quinoline



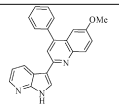
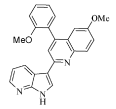
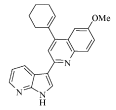
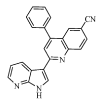
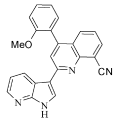
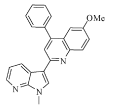
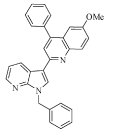
7 2b 4a 8

Table 3. Synthesis of 4-Substituted-2-(1-(substituted)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)quinoline 5



9a R=H
9b R=Me
9c R=Benzyl

6 R=H
10 R=Me
11 R=Benzyl

Compd	Amine, 2	Alkyne, 4	Product, 6/10/11	Yield (%)	mp (°C)
6b				52	248-250
6c				59	232-235
6d				56	224-226
6j				58	253-255
6n				61	262-264
10				78	195-197
11				82	205-207

protecting group in this aza Diels–Alder reaction, the reaction has been carried out with *N*-methyl-[17] and *N*-benzyl-derived[18] azaindoles (**9b** and **9c**). The reaction went on smoothly in these cases too, with appreciable yields of **10** and **11**, respectively (Table 3).

CONCLUSION

In summary, a facile and efficient method is described for the one-pot synthesis of a range of quinoline derivatives linked to azaindole by a Povarov reaction in good yields. $SnCl_2$, a cheap Lewis acid, has been used to promote the reaction for the first time. The reaction has been found to be chemo- and regioselective with good atom efficiency.

EXPERIMENTAL SECTION

General Remarks. Nuclear magnetic resonance (^{1}H and ^{13}C NMR) spectra were recorded on a 400 MHz spectrometer in $CDCl_3$ using TMS as internal standard. Chemical shifts are reported in parts per million (δ), coupling constants (*J*-values) are reported in hertz (Hz), and spin multiplicities are indicated by the following symbols: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), bs (broad singlet). ^{13}C NMR spectra were routinely run with broadband decoupling.

dx.doi.org/10.1021/jo202256z | *J. Org. Chem.* 2012, 77, 1468–1476

General Procedure for the Synthesis of 4-Substituted-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl)quinoline. The mixture of 7-azaindole-3-carboxaldehyde **1** (1.0 mmol), amine **2** (1.05 mmol) in acetonitrile, and stannous chloride (0.2 mmol) was stirred at room temperature for 10 min, and then alkyne **4** (1.5 mmol) was added to the above mixture. The stirring was then continued at 80 °C for 12 h. The reaction mixture was then quenched with ammonium chloride solution and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over sodium sulfate, and concentrated in vacuum. Crude product was purified by column chromatography using ethyl acetate−hexane as the solvent to get quinoline derivative **5**.

4-Phenyl-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)quinoline (5a). Isolated as orange solid: mp 236−239 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (dd, J = 8.0, 4.8 Hz, 1H, Ar−H), 7.48 (t, J = 8.0 Hz, 2H, Ar−H), 7.48 (s, 1H, Ar−H), 7.53−7.61 (m, 6H, Ar−H), 7.77 (t, J = 7.6 Hz, 1H, Ar−H), 7.77 (s, 1H, Ar−H), 7.92 (d, J = 7.6 Hz, 1H, Ar−H), 8.21 (d, J = 7.2 Hz, 1H, Ar−H), 8.26 (d, J = 7.6 Hz, 2H, Ar−H), 8.37 (bs, 1H, Ar−H), 8.53 (dd, J = 4.8, 1.6 Hz, 1H, Ar−H), 9.15 (d, J = 7.2, Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.9, 119.8, 121.6, 121.9, 125.5, 125.6, 125.8, 126.4, 127.2, 128.1, 128.6, 128.7, 128.9, 129.0, 129.3, 129.5, 129.7, 132.4, 134.2, 137.9, 138.0, 145.6, 147.9, 152.1; UPLC (M + 1) 462.3. Anal. Calcd for $C_{28}H_{19}N_3O_2S$: C, 72.87; H, 4.15; N, 9.10. Found: C, 72.80; H, 4.19; N, 9.18.

6-Methoxy-4-phenyl-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]-pyridin-3-yl)quinoline (5b). Isolated as pale yellow solid: mp 222−224 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.81 (s, 3H, −OMe), 7.20 (d, J = 2.8 Hz, 1H, Ar−H), 7.35 (dd, J = 8.0, 4.8 Hz, 1H, Ar−H), 7.40 (dd, J = 9.2, 2.8 Hz, 1H, Ar−H), 7.48 (t, J = 8.0 Hz, 2H, Ar−H), 7.50−7.60 (m, 6H, Ar−H), 7.69 (s, 1H, Ar−H), 8.11 (d, J = 8.8 Hz, 1H, Ar−H), 8.24 (d, J = 8.0 Hz, 2H, Ar−H), 8.30 (s, 1H, Ar−H), 8.52 (d, J = 4.4 Hz, 1H, Ar−H), 9.10 (d, J = 8.0 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2, 103.7, 118.69, 119.7, 120.1, 120.9, 121.5, 125.7, 126.9, 127.6, 128.6, 128.7, 129.5, 129.6, 131.1, 132.6, 134.9, 137.4, 137.5, 143.8, 145.3, 146.8, 147.2, 149.9, 157.4; UPLC (M + 1) 492.4. Anal. Calcd for $C_{29}H_{21}N_3O_3S$: C, 70.86; H, 4.31; N, 8.55. Found: C, 70.73; H, 4.26; N, 8.62.

6-Methoxy-4-(2-methoxyphenyl)-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)quinoline (5c). Isolated as orange solid: mp 211−213 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (s, 3H, −OMe), 3.78 (s, 3H, −OMe), 6.88 (d, J = 2.8 Hz, 1H, Ar−H), 7.12 (d, J = 8.4 Hz, 1H, Ar−H), 7.16 (t, J = 7.6 Hz, 1H, Ar−H), 7.32−7.38 (m, 3H, Ar−H), 7.46−7.57 (m, 4H, Ar−H), 7.70 (s, 1H, Ar−H), 8.08 (d, J = 9.2 Hz, 1H, Ar−H), 8.22 (dd, J = 7.2, 1.6 Hz, 2H, Ar−H), 8.27 (s, 1H, Ar−H), 8.51 (dd, J = 4.8, 1.6 Hz, 1H, Ar−H), 9.08 (dd, J = 8.0, 1.6.Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 55.5, 104.4, 111.2, 119.6, 120.0, 120.2, 120.9, 121.6, 121.7, 124.7, 126.8, 127.2, 128.0, 129.0, 130.1, 131.0, 131.2, 132.3, 134.1, 138.2, 144.4, 145.1, 145.5, 147.9, 149.7, 156.7, 157.6; UPLC (M + 1) 522.4. Anal. Calcd for $C_{30}H_{23}N_3O_4S$: C, 69.08; H, 4.44; N, 8.06. Found: C, 69.01; H, 4.48; N, 8.02.

4-Cyclohexenyl-6-methoxy-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)quinoline (5d). Isolated as orange solid: mp 231−233; °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.83−1.87 (m, 2H), 1.89−1.94 (m, 2H), 2.34−2.35 (m, 2H), 2.45−2.46 (m, 2H), 3.94 (s, 3H, −OMe), 5.93 (bs, 1H, −CH), 7.27−7.39 (m, 3H, Ar−H), 7.49 (t, J = 8.0 Hz, 2H, Ar−H),7.56−7.60 (m, 2H, Ar−H), 8.05 (bs, 1H, Ar−H), 8.25−8.31 (m, 3H, Ar−H), 8.51 (dd, J = 4.8, 1.6 Hz, 1H, Ar−H), 9.05 (bs, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.1, 23.0, 25.5, 30.1, 55.5, 104.0, 117.5, 119.7, 119.9, 121.4, 121.7, 124.7, 126.5, 128.0, 128.8, 129.0, 131.1, 132.3, 134.2, 135.8, 138.2, 144.5, 145.5, 147.9, 149.9, 150.7, 157.5; UPLC (M + 1) 496.4. Anal. Calcd for $C_{29}H_{25}N_3O_3S$: C, 70.28; H, 5.08; N, 8.48. Found: C, 70.24; H, 5.05; N, 8.52.

3-(6-Methyl-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)quinolin-4-yl)phenol (5e). Isolated as orange solid: mp 214−216 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.44 (s, 3H, $-CH_3$), 6.95 (dd, J = 8.0, 2.0 Hz, 1H, Ar−H), 6.99 (s, 1H, Ar−H), 7.03 (d, J = 7.6 Hz, 1H, Ar−H), 7.40 (t, J = 8.0 Hz, 1H, Ar−H), 7.47 (dd, J = 8.0, 4.8 Hz, 1H, Ar−H), 7.61−7.64 (m, 4H, Ar−H), 7.72 (t, J = 7.6 Hz, 1H, Ar−H), 8.08 (d, J = 8.8 Hz, 1H, Ar−H), 8.18 (d, J = 8.0 Hz, 2H, Ar−H), 8.20 (s, 1H, Ar−H), 8.46 (d, J = 4.8 Hz, 1H, Ar−H), 9.03 (s, 1H, Ar−H), 9.25 (dd, J = 8.0, 0.8 Hz, 1H, Ar−H), 9.73 (s, 1H, −OH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.4, 115.4, 116.4, 118.6, 119.1, 120.1, 120.3, 120.9, 124.1, 124.8, 127.3, 127.6, 129.3, 129.6, 129.7, 131.7, 132.6, 134.8, 136.0, 137.4, 138.7, 145.3, 146.4, 147.2, 147.7, 151.4, 157.5; UPLC (M + 1) 492.3. Anal. Calcd for $C_{29}H_{21}N_3O_3S$: C, 70.86; H, 4.31; N, 8.55. Found: C, 70.75; H, 4.27; N, 8.62.

4-(4-Ethylphenyl)-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]-pyridin-3-yl)-6-(trifluoromethyl)quinoline (5f). Isolated as orange solid: mp 212−214; °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (t, J = 7.6 Hz, 3H, $-CH_3$), 2.83 (q, J = 7.6 Hz, 2H, $-CH_2$), 7.38 (dd, J = 8.0, 4.8 Hz, 1H, Ar−H), 7.44−7.53 (m, 6H, Ar−H), 7.60 (t, J = 7.6 Hz, 1H, Ar−H), 7.83 (s, 1H, Ar−H), 7.91 (d, J = 8.8 Hz, 1H, Ar−H), 8.26−8.32 (m, 4H, Ar−H), 8.43 (s, 1H, Ar−H), 8.54 (d, J = 8.4 Hz, 1H, Ar−H), 9.13 (d, J = 8.0 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.5, 28.7, 119.9, 120.9, 121.3, 123.8, 123.9, 124.8, 125.4, 125.5, 126.2, 127.8, 128.1, 128.2, 128.5, 129.1, 129.4, 130.7, 132.4, 134.2, 134.3, 137.9, 145.5, 145.8, 147.8, 149.9, 154.2; UPLC (M + 1) 558.3. Anal. Calcd for $C_{31}H_{22}F_3N_3O_2S$: C, 66.78; H, 3.98; N, 7.54. Found: C, 66.81; H, 4.02; N, 7.59.

4-(Biphenyl-4-yl)-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]-pyridin-3-yl)-6-(trifluoromethyl)quinoline (5g). Isolated as pale yellow solid: mp 195−197 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.56 (m, 6H, Ar−H), 7.61 (t, J = 7.6 Hz, 1H, Ar−H), 7.68 (d, J = 8.0 Hz, 2H, Ar−H), 7.75 (d, J = 9.2 Hz, 2H, Ar−H), 7.87 (dd, J = 6.4, 1.6 Hz, 2H, Ar−H),7.89 (s, 1H, Ar−H), 7.93 (dd, J = 8.8, 2.0 Hz, 1H, Ar−H), 8.27−8.30 (m, 2H, Ar−H), 8.33 (d, J = 8.8 Hz, 1H, Ar−H), 8.46 (s, 1H, Ar−H), 8.55 (dd, J = 4.8, 1.6 Hz, 2H, Ar−H), 9.16 (dd, J = 8.0, 1.6 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.9, 119.8, 119.9, 121.4, 122.6, 123.7, 123.8, 124.7, 125.4, 126.2, 127.2, 127.7, 127.9, 128.2, 129.0, 129.1, 129.9, 130.8, 132.4, 134.3, 135.8, 137.9, 140.2, 142.1, 145.8, 147.8, 149.6, 149.8, 154.2; UPLC (M + 1) 606.3. Anal. Calcd for $C_{35}H_{22}F_3N_3O_2S$: C, 69.41; H, 3.66; N, 6.94. Found: C, 69.37; H, 3.69; N, 6.87.

6-Nitro-4-phenyl-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]-pyridin-3-yl)quinoline (5h). Isolated as orange solid: mp 228−230 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (dd, J = 8.0, 4,8 Hz, 1H, Ar−H), 7.52 (t, J = 8.0 Hz, 2H, Ar−H), 7.58−7.67 (m, 6H, Ar−H), 7.89 (s, 1H, Ar−H), 8.27−8.31 (m, 3H, Ar−H), 8.48 (s, 1H, Ar−H), 8.49 (dd, J = 7.6, 2.4 Hz, 1H, Ar−H), 8.55 (dd, J = 8.4, 0.8 Hz, 1H, Ar−H), 8.84 (d, J = 2.4 Hz, 1H, Ar−H), 9.15 (dd, J = 8.4, 0.8 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.6, 120.0, 120.3, 121.2, 122.9, 123.3, 124.6, 126.9, 128.3, 129.2, 129.3, 129.4, 129.6, 131.2, 132.4, 134.5, 136.5, 137.8, 145.4, 146.0, 147.8, 150.9, 151.0, 155.5; UPLC (M + 1) 507.4. Anal. Calcd for $C_{28}H_{18}N_4O_4S$: C, 66.39; H, 3.58; N, 11.06. Found: C, 66.29; H, 3.52; N, 11.10.

4-(2-Methoxyphenyl)-6-nitro-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)quinoline (5i). Isolated as orange solid: mp 237−239 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.72 (s, 3H, $-OCH_3$), 7.25 (t, J = 7.6 Hz, 1H, Ar−H), 7.34 (d, J = 8.4 Hz, 1H, Ar−H), 7.49−7.52 (m, 2H, Ar−H), 7.65 (t, J = 7.6 Hz, 3H, Ar−H), 7.75 (t, J = 7.6 Hz, 1H, Ar−H), 8.21 (d, J = 7.2 Hz, 2H, Ar−H), 8.31 (s, 1H, Ar−H), 8.35 (d, J = 9.2 Hz, 1H, Ar−H), 8.45−8.50 (m, 3H, Ar−H), 9.20 (s, 1H, Ar−H), 9.27 (d, J = 7.6 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 56.1, 112.3, 118.4, 120.8, 121.1, 121.5, 122.2, 123.1, 123.4, 125.0, 125.2, 128.2, 129.8, 130.2, 131.5, 131.6, 131.8, 133.2, 135.5, 137.7, 145.0, 146.1, 147.7, 148.4, 150.2, 156.5, 156.7; UPLC (M + 1) 537.4. Anal. Calcd for $C_{29}H_{20}N_4O_5S$: C, 64.92; H, 3.76; N, 10.44. Found: C, 64.87; H, 3.72; N, 10.38.

4-Phenyl-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)quinoline-6-carbonitrile (5j). Isolated as off white solid: mp 236−238 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (dd, J = 8.0, 4.8 Hz, 1H, Ar−H), 7.49−7.56 (m, 4H, Ar−H), 7.59−7.65 (m, 4H, Ar−H), 7.86−7.89 (m, 2H, Ar−H), 8.27−8.29 (m, 4H, Ar−H), 8.46 (s, 1H, Ar−H), 8.55 (dd, J = 4.4, 1.2 Hz, 1H, Ar−H), 9.13 (dd, J = 8.0, 1.2 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 109.7, 118.6, 118.9, 120.0, 120.2, 121.2, 125.2, 126.7, 128.3, 129.2, 129.3, 129.4, 129.5,

dx.doi.org/10.1021/jo202256z | J. Org. Chem. 2012, 77, 1468−1476

130.5, 130.9, 132.3, 132.4, 134.4, 136.5, 137.8, 145.9, 147.8, 149.6, 149.7, 154.9; UPLC (M + 1) 487.4. Anal. Calcd for $C_{29}H_{18}N_4O_2S$: C, 71.59; H, 3.73; N, 11.52. Found: C, 71.50; H, 3.68; N, 11.47.

6-Bromo-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)-4-(thiophen-3-yl)quinoline (5k). Isolated as off white solid: mp 239−241 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48−7.50 (m, 2H, Ar−H), 7.50 (t, J = 7.6 Hz, 2H, Ar−H), 7.57−7.61 (m, 3H, Ar−H), 7.79 (s, 1H, Ar−H), 7.80 (dd, J = 7.6, 2.4 Hz, 1H, Ar−H), 8.05(d, J = 8.8 Hz, 1H, Ar−H), 8.18 (d, J = 2.0 Hz, 1H, Ar−H), 8.27 (d, J = 8.4 Hz, 2H, Ar−H), 8.38 (s, 1H, Ar−H), 8.52 (dd, J = 4.8, 1.6 Hz, 1H, Ar−H), 9.09 (dd, J = 8.0, 1.6 Hz, 1H, Ar−H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 119.1, 119.3, 119.8, 120.5, 121.4, 125.4, 125.7, 126.8, 126.9, 127.8, 128.2, 128.6, 129.0, 131.3, 132.4, 133.2, 134.3, 137.7, 138.0, 143.0, 145.7, 147.3, 147.9, 152.6; UPLC (M + 1) 548.3. Anal. Calcd for $C_{26}H_{16}BrN_3O_2S_2$: C, 57.15; H, 2.95; N, 7.69. Found: C, 57.08; H, 2.99; N, 7.62.

2-(1-(Phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)-4-(thiophen-3-yl)benzo[h]quinoline (5l). Isolated as off white solid: mp 218−220 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.63 (m, 7H, Ar−H), 7.73−7.77 (m, 3H, Ar−H), 7.81−7.98 (m, 3H, Ar−H), 8.29 (dd, J = 1.4 Hz, 2H, Ar−H), 8.42 (s, 1H, Ar−H), 8.58 (dd, J = 4.8, 1.6 Hz, 1H, Ar−H), 9.21 (dd, J = 8.0, 1.6 Hz, 1H, Ar−H), 9.41 (d, J = 8.2 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 119.0, 119.4, 119.6, 121.2, 122.4, 122.9, 124.4, 124.6, 124.7, 126.0, 126.7, 127.0, 127.4, 127.7, 127.9, 128.6, 128.7, 131.2, 131.6, 133.3, 133.8, 137.7, 138.4, 143.5, 145.2, 146.5, 147.5, 150.3; UPLC (M + 1) 518.4. Anal. Calcd for $C_{30}H_{19}N_3O_2S_2$: C, 69.61; H, 3.70; N, 8.12. Found: C, 69.55; H, 3.75; N, 8.07.

4-Cyclohexenyl-8-methoxy-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)quinoline (5m). Isolated as orange solid: mp 230−232 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.81−1.84 (m, 2H), 1.87−1.91 (m, 2H), 2.32−2.33 (m, 2H), 2.44−2.45 (m, 2H), 4.10 (s, 3H, −OMe), 5.90 (t, 1H, J = 1.6 Hz, −CH), 7.05 (d, J = 8.0 Hz, 1H, Ar−H), 7.34−7.48 (m, 5H, Ar−H), 7.55 (t, J = 1.2 Hz, 1H, Ar−H), 7.60 (s, 1H, Ar−H), 8.21 (d, 2H, J = 8.0 Hz, Ar−H), 8.31 (s, 1H, Ar−H), 8.50 (dd, J = 4.8, 1.6 Hz, 1H, Ar−H), 9.05 (dd, J = 8.0, 1.6 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 22.5, 25.0, 29.9, 55.7, 107.4, 116.9, 117.3, 119.6, 120.1, 121.6, 124.5, 125.5, 126.3, 127.6, 128.5, 128.6, 132.0, 133.7, 135.4, 137.7, 140.0, 145.1, 147.6, 150.4, 151.5, 155.3; UPLC (M + 1) 496.4. Anal. Calcd for $C_{29}H_{25}N_3O_3S$: C, 70.28; H, 5.08; N, 8.48. Found: C, 70.21; H, 5.02; N, 8.54.

4-(2-Methoxyphenyl)-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)quinoline-8-carbonitrile (5n). Isolated as orange solid: mp 218−220 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (s, 3H, OMe), 7.11−7.20 (m, 3H, Ar−H), 7.33−7.60 (m, 6H, Ar−H), 7.82 (d, J = 8.4 Hz, 1H, Ar−H), 7.87 (s, 1H, Ar−H), 8.10 (d, J = 7.2 Hz, 1H, Ar−H), 8.26 (d, J = 8.0 Hz, 2H, Ar−H), 8.42 (s, 1H, Ar−H), 8.54 (d, J = 8.6 Hz, 1H, Ar−H), 9.55 (d, J = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.5, 111.2, 112.7, 118.1, 118.9, 120.6, 120.7, 121.0, 121.4, 124.9, 125.6, 126.2, 126.3, 128.2, 129.1, 130.7, 131.0, 131.4, 133.6, 134.4, 135.2, 137.9, 145.8, 145.9, 147.1, 147.8, 154.2, 156.6; UPLC (M + 1) 517.2. Calcd for $C_{30}H_{20}N_4O_3S$: C, 69.75; H, 3.90; N, 10.85. Found: C, 69.81; H, 3.84; N, 10.91.

8-Chloro-4-cyclohexenyl-2-(1-(phenylsulfonyl)-1*H*-pyrrolo-[2,3-b]pyridin-3-yl)quinoline (5o). Isolated as orange solid: mp 226−228 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.80−1.85 (m, 2H), 1.88−1.94 (m, 2H), 2.32−2.34 (m, 2H), 2.42−2.44 (m, 2H), 5.91 (bs, 1H, −CH), 7.37−7.41 (m, 2H, Ar−H), 7.49 (t, J = 8.0 Hz, 2H, Ar−H), 7.58 (t, J = 7.6 Hz, 1H, Ar−H), 7.66 (s, 1H, Ar−H), 7.82 (d, 1H, J = 8.4 Hz, Ar−H), 7.92 (d, 1H, J = 8.4 Hz, Ar−H), 8.25 (d, J = 8.4 Hz, 2H, Ar−H), 8.38 (s, 1H, Ar−H), 8.52 (dd, J = 4.8, 1.6 Hz, 1H, Ar−H), 9.05 (dd, J = 8.0, 1.6 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 22.9, 25.4, 30.4, 117.4, 119.7, 120.2, 121.6, 124.6, 125.5, 125.6, 127.0, 128.1, 129.0, 129.5, 129.6, 133.3, 133.9, 134.3, 135.3, 138.1, 144.7, 145.7, 147.9, 152.4, 152.6; UPLC (M + 1) 500.4. Anal. Calcd for $C_{28}H_{22}ClN_3O_2S$: C, 67.26; H, 4.43; N, 8.40. Found: C, 67.20; H, 4.39; N, 8.33.

3-(8-Bromo-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)quinolin-4-yl)phenol (5p). Isolated as off white solid: mp 239−241 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01−7.13 (m, 3H, Ar−H), 7.33−7.59 (m, 6H, Ar−H), 7.81 (s, 1H, Ar−H), 7.90 (d, J = 7.4 Hz, 2H, Ar−H), 8.08 (d, J = 8.4 Hz, 1H, Ar−H), 8.26 (d, J = 7.6 Hz, 2H, Ar−H), 8.40 (s, 1H, Ar−H), 8.55 (d, J = 4.8 Hz, 1H, Ar−H), 9.58 (d, 1H, J = 8.0 Hz); Sample is not sufficiently soluble to record ^{13}C NMR spectrum; UPLC (M + 1) 558.3. Calcd for $C_{28}H_{18}BrN_3O_3S$: C, 60.44; H, 3.26; N, 7.55. Found: C, 60.49; H, 3.21; N, 7.50.

8-Nitro-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)-4-(thiophen-3-yl)quinoline (5q). Isolated as orange solid: mp 246−248 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.42 (m, 2H, Ar−H), 7.48−7.63 (m, 6H, Ar−H), 7.92 (s, 1H, Ar−H), 8.05 (d, J = 7.6 Hz, 1H, Ar−H), 8.25 (t, J = 8.4 Hz, 3H, Ar−H), 8.42 (s, 1H, Ar−H), 8.52 (d, J = 4.8 Hz, 1H, Ar−H), 9.09 (d, J = 7.6 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.8, 119.7, 120.5, 121.3, 123.9, 124.7, 125.8, 126.3, 127.2, 128.2, 128.5, 129.1, 129.8, 133.0, 134.4, 137.3, 137.9, 144.1, 146.0, 148.3, 154.4, 160.0, 164.2, 166.6; UPLC (M + 1) 513.2. Calcd for $C_{26}H_{16}N_4O_4S_2$: C, 60.93; H, 3.15; N, 10.93. Found: C, 60.82; H, 3.11; N, 10.85.

4-(4-Ethylphenyl)-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]-pyridin-3-yl)-8-(trifluoromethyl)quinoline (5r). Isolated as off white solid: mp 205−207 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (t, J = 7.6 Hz, 3H), 2.82 (q, J = 7.6 Hz, 2H), 7.39−7.52 (m, 8H, Ar−H), 7.59 (t, J = 6.8 Hz, 1H, Ar−H), 7.86 (s, 1H, Ar−H), 8.09 (d, 1H, J = 7.6 Hz), 8.14 (d, 1H, J = 6.8 Hz), 8.26 (d, J = 7.6 Hz, 2H, Ar−H), 8.41 (s, 1H, Ar−H), 8.53 (dd, J = 4.8, 1.6 Hz, 1H, Ar−H), 9.33 (dd, J = 8.0, 1.6 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 28.3, 118.8, 118.9, 119.8, 121.1, 124.2, 125.6, 125.8, 126.2, 127.6, 127.7, 127.8, 127.9, 128.7, 129.1, 130.1, 132.5, 133.9, 134.3, 137.6, 144.7, 144.8, 145.4, 147.5, 148.9, 152.3; LCMS (M + 1) 558.2. Calcd for $C_{31}H_{22}F_3N_3O_2S$: C, 66.78; H, 3.98; N, 7.54. Found: C, 66.71; H, 3.93; N, 7.60.

5-Methoxy-4-phenyl-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)quinoline (5s). Isolated as orange solid: mp 220−223 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.02 (s, 3H, −OMe), 7.11 (dd, J = 8.4, 2.0 Hz, 1H, Ar−H), 7.37 (dd, J = 7.6, 4.8 Hz, 1H, Ar−H), 7.48−7.62 (m, 10H, Ar−H), 7.80 (d, J = 8.8 Hz, 1H, Ar−H), 8.25 (d, J = 8.0 Hz, 2H, Ar−H), 8.34(s, 1H, Ar−H), 8.53(d, J = 4.4 Hz, 1H, Ar−H), 9.09 (d, J = 8.0 Hz, 1H, Ar−H); Sample is not sufficiently soluble to record ^{13}C NMR spectrum; UPLC (M + 1) 492.4. Anal. Calcd for $C_{29}H_{21}N_3O_3S$: C, 70.86; H, 4.31; N, 8.55. Found: C, 70.92; H, 4.28; N, 8.49.

7-Methoxy-4-phenyl-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)quinoline (5s′). Isolated as orange solid: mp 214−216 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.55 (s, 3H, −OMe), 7.14 (dd, J = 9.2, 2.8 Hz, 1H, Ar−H), 7.37 (dd, J = 7.6, 6.4 Hz, 1H, Ar−H), 7.48−7.62 (m, 10H, Ar−H), 7.83 (d, J = 8.4 Hz, 1H, Ar−H), 8.24 (d, J = 8.0 Hz, 2H, Ar−H), 8.32 (s, 1H, Ar−H), 8.52 (dd, J = 4.8, 1.6 Hz, 1H, Ar−H), 9.12 (d, J = 8.0 Hz, 1H, Ar−H); Sample is not sufficiently soluble to record ^{13}C NMR spectrum; UPLC (M + 1) 492.4. Anal. Calcd for $C_{29}H_{21}N_3O_3S$: C, 70.86; H, 4.31; N, 8.55. Found: C, 70.78; H, 4.35; N, 8.51.

4-(Biphenyl-4-yl)-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]-pyridin-3-yl)quinoline-5-carbonitrile (5t). Isolated as off white solid: mp 228−230 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27−7.61 (m, 9H, Ar−H), 7.73−7.81 (m, 5H, Ar−H), 7.86 (s, 1H, Ar−H), 7.97 (d, J = 7.2 Hz, 1H, Ar−H), 8.28 (d, J = 8.0 Hz, 2H, Ar−H), 8.45 (s, 1H, Ar−H), 8.50 (d, J = 8.4 Hz, 1H, Ar−H),8.55 (dd, J = 4.8, 1.6 Hz, 1H, Ar−H), 9.12 (d, J = 8.0 Hz, 1H, Ar−H); Sample was not sufficiently soluble to record ^{13}C NMR spectrum; UPLC (M + 1) 563.5. Anal. Calcd for $C_{35}H_{22}N_4O_2S$: C, 74.71; H, 3.94; N, 9.96. Found: C, 74.65; H, 3.89; N, 9.99.

4-(Biphenyl-4-yl)-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]-pyridin-3-yl)quinoline-7-carbonitrile (5t′). Isolated as off white solid: mp 210−211 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27−7.36 (m, 1H, Ar−H), 7.47 (d, J = 7.6 Hz, 1H, Ar−H), 7.51 (d, J = 6.8 Hz, 2H, Ar−H), 7.55 (d, J = 6.8 Hz, 2H, Ar−H), 7.60−7.68 (m, 3H, Ar−H), 7.74 (d, J = 8.4 Hz, 2H, Ar−H), 7.90 (d, J = 8.0 Hz, 2H, Ar−H), 7.93 (s, 1H, Ar−H), 8.11 (d, J = 8.8 Hz, 2H, Ar−H), 8.30 (d, J = 7.6 Hz, 2H, Ar−H), 8.50 (s, 1H, Ar−H), 8.56 (dd, J = 4.8, 1.6 Hz, 1H, Ar−H), 8.65 (d, J = 0.8 Hz, 1H, Ar−H), 9.11(dd, J = 8.0, 1.6 Hz,

dx.doi.org/10.1021/jo202256z | J. Org. Chem. 2012, 77, 1468−1476

1H, Ar−H); Sample is not sufficiently soluble to record ^{13}C NMR spectrum; UPLC (M + 1) 563.5. Anal. Calcd for $C_{35}H_{22}N_4O_2S$: C, 74.71; H, 3.94; N, 9.96. Found: C, 74.66; H, 3.97; N, 9.99.

4-(2-Methoxyphenyl)-5-nitro-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)quinoline (5u). Isolated as pale yellow solid: mp 198−200 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.71 (s, 3H, −OMe), 6.99 (d, J = 8.4 Hz, 1H, Ar−H), 7.14 (t, J = 7.4 Hz, 1H, Ar−H), 7.34−7.39 (m, 2H, Ar−H), 7.47−7.62 (m, 4H, Ar−H), 7.74 (t, J = 7.6 Hz, 1H, Ar−H), 7.75 (d, J = 7.6 Hz, 1H, Ar−H), 7.79 (s, 1H, Ar−H), 8.27 (d, J = 7.6 Hz, 2H, Ar−H), 8.40 (d, J = 7.4 Hz, 1H, Ar−H), 8.41 (s, 1H, Ar−H), 8.54 (d, J = 4.2 Hz, 1H, Ar−H), 9.12 (d, J = 7.8 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 54.8, 110.2, 117.9, 118.2, 119.5, 120.5, 120.8, 122.1, 123.4, 125.9, 126.3, 127.2, 127.8, 128.7, 129.3, 130.2, 131.9, 133.9, 134.0, 137.4, 143.1, 145.4, 147.4, 148.4, 148.5, 153.0, 155.3; UPLC (M + 1) 537.4. Calcd for $C_{29}H_{20}N_4O_5S$: C, 64.92; H, 3.76; N, 10.44. Found: C, 64.88; H, 3.70; N, 10.41.

4-(2-Methoxyphenyl)-7-nitro-2-(1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)quinoline (5u′). Isolated as yellow solid: mp 194−197 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76 (s, 3H, −OMe), 7.14 (d, J = 8.4 Hz, 1H, Ar−H), 7.20 (t, J = 7.6 Hz, 1H, Ar−H), 7.36 (dd, J = 7.4, 1.6 Hz, 1H, Ar−H), 7.42 (dd, J = 8.0, 4.8 Hz, 1H, Ar−H), 7.50−7.64 (m, 4H, Ar−H), 7.74 (d, J = 9.2 Hz, 1H, Ar−H), 7.89 (s, 1H, Ar−H), 8.18 (dd, J = 9.2, 2.4 Hz, 1H, Ar−H), 8.28 (d, J = 7.4 Hz, 2H, Ar−H), 8.42 (s, 1H, Ar−H), 8.56 (dd, J = 4.8, 1.6 Hz, 1H, Ar−H), 9.08 (d, J = 2.4 Hz, 1H, Ar−H), 9.20 (dd, J = 8.0, 1.6 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.5, 111.3, 117.8, 119.4, 120.0, 121.1, 121.2, 122.4, 124.8, 125.2, 127.0, 128.2, 128.3, 129.1, 129.6, 131.0, 131.1, 132.2, 134.4, 137.8, 146.0, 146.6, 147.5, 147.7, 148.3, 154.2, 156.5; UPLC (M + 1) 537.4. Calcd for $C_{29}H_{20}N_4O_5S$: C, 64.92; H, 3.76; N, 10.44%. Found: C, 64.81; H, 3.71; N, 10.50.%.

2-(1-(Phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)-4-(thiophen-3-yl)-5-(trifluoromethyl)quinoline (5v). Isolated as orange solid: mp 240−242 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, J = 4.8 Hz, 1H, Ar−H), 7.33−7.44 (m, 3H, Ar−H), 7.51 (dd, J = 9.6, 1.6, Hz, 2H, Ar−H), 7.59 (t, J = 1.4 Hz, 1H, Ar−H), 7.74 (s, 1H, Ar−H), 7.78 (t, J = 7.8 Hz, 1H, Ar−H), 7.98 (d, J = 7.4 Hz, 1H, Ar−H), 8.27 (dd, J = 7.6, 1.4 Hz, 2H, Ar−H), 8.37 (s, 1H, Ar−H), 8.40 (d, J = 7.4 Hz, 1H, Ar−H), 8.54 (dd, J = 4.6, 1.6 Hz, 1H, Ar−H), 9.12 (dd, J = 8.0, 1.6 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.3, 119.8, 121.3, 123.2, 123.3, 124.6, 126.0, 127.5, 127.6, 127.7, 127.9, 128.2, 129.1, 129.2, 132.3, 134.3, 135.0, 137.9, 140.4, 140.5, 143.6, 145.8, 147.8, 149.7, 151.9; UPLC (M + 1) 536.3. Calcd for $C_{27}H_{16}F_3N_3O_2S_2$: C, 60.55; H, 3.01; N, 7.85. Found: C, 60.48; H, 3.06; N, 7.80.

2-(1-(Phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)-4-(thiophen-3-yl)-7-(trifluoromethyl)quinoline (5v′). Isolated as orange solid: mp 225−227 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.42 (m, 2H, Ar−H), 7.52 (t, J = 7.8 Hz, 2H, Ar−H), 7.59−7.69 (m, 4H, Ar−H), 7.90 (s, 1H, Ar−H), 8.18 (d, J = 8.8 Hz, 1H, Ar−H), 8.29 (d, J = 8.0 Hz, 2H, Ar−H), 8.42 (s, 1H, Ar−H), 8.49 (s, 1H, Ar−H), 8.55 (d, J = 4.6 Hz, 1H, Ar−H), 9.18 (d, J = 8.0 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.5, 119.5, 119.7, 120.9, 121.5, 125.0, 125.5, 126.5, 126.6, 126.8, 127.0, 127.1, 127.8, 128.2, 128.7, 130.9, 131.2, 132.1, 133.9, 137.2, 143.4, 145.5, 147.4, 147.5, 153.3; UPLC (M + 1) 536.3. Calcd for $C_{27}H_{16}F_3N_3O_2S_2$: C, 60.55; H, 3.01; N, 7.85. Found: C, 60.51; H, 2.97; N, 7.90.

2-(1-(Phenylsulfonyl)-1*H*-pyrrolo[2,3-b]pyridin-3-yl)-4-p-tolyl-1,10-phenanthroline (5x). Isolated as orange solid: mp 267−269 °C; (^{1}H NMR 400 MHz, $CDCl_3$) 2.53 (s, 3H, $-CH_3$), 7.42−7.59 (m, 8H, Ar−H), 7.66 (dd, J = 8.0, 4.4 Hz, 1H, Ar−H), 7.73 (d, J = 9.0 Hz, 1H, Ar−H), 7.95 (d, J = 7.8 Hz, 1H, Ar−H), 7.96 (s, 1H, Ar−H), 8.22−8.27 (m, 3H, Ar−H), 8.42 (s, 1H, Ar−H), 8.55 (dd, J = 4.8, 1.6 Hz, 1H, Ar−H), 9.25 (dd, J = 4.4, 1.6 Hz, 1H, Ar−H), 9.48 (dd, J = 8.0, 1.6 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 120.3, 120.5, 120.7, 122.2, 123.1, 124.2, 125.2, 125.6, 125.9, 128.0, 128.6, 129.0, 129.5, 129.6, 132.8, 134.2, 135.0, 135.8, 138.2, 138.6, 145.6, 146.4, 146.7, 148.0, 149.4, 150.5, 151.8; UPLC (M + 1) 527.4. Anal. Calcd for $C_{32}H_{22}N_4O_2S$: C, 72.98; H, 4.21; N, 10.64. Found: C, 72.89; H, 4.25; N, 10.59.

6-Methoxy-4-phenyl-2-(1*H*-pyrrolo[2,3-b]pyridin-3-yl)-quinoline (6b). Isolated as pale brown solid: mp 248−250 °C; (^{1}H NMR 400 MHz, DMSO-d_6) 3.75 (s, 3H, $-OCH_3$), 7.24−7.27 (m, 2H, Ar−H), 7.43 (d, J = 8.0 Hz, 1H, Ar−H), 7.54−7.67 (m, 5H, Ar−H), 7.98 (s, 1H, Ar−H), 8.08 (d, J = 9.2 Hz, 1H, Ar−H), 8.32 (d, J = 4.0 Hz, 1H, Ar−H), 8.52 (s, 1H, Ar−H), 9.17 (d, J = 7.2 Hz, 1H, Ar−H), 12.10 (br s, 1H, −NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 55.6, 104.4, 114.7, 117.1, 118.5, 119.5, 121.4, 125.5, 127.9, 128.9, 129.2, 129.8, 131.1, 131.2, 138.4, 143.8, 144.6, 146.8, 149.9, 152.9, 157.1; UPLC (M + 1) 352.3. Anal. Calcd for $C_{23}H_{17}N_3O$: C, 78.61; H, 4.88; N, 11.96. Found: C, 78.53; H, 4.83; N, 11.99.

6-Methoxy-4-(2-methoxyphenyl)-2-(1*H*-pyrrolo[2,3-b]-pyridin-3-yl)quinoline (6c). Isolated as brown solid: mp 232−235 °C; (^{1}H NMR 400 MHz, $CDCl_3$) 3.85 (s, 6H, $-OCH_3$), 6.87 (d, J = 2.8 Hz, 1H, Ar−H), 7.13−7.53 (m, 6H, Ar−H), 7.71 (s, 1H, Ar−H), 8.02 (s, 1H, Ar−H), 8.13 (d, J = 8.8 Hz, 1H, Ar−H), 8.42 (dd, J = 4.8, 1.4 Hz, 1H, Ar−H), 9.14 (dd, J = 8.0, 1.4 Hz, 1H, Ar−H), 11.56 (br s, 1H, −NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 55.6, 104.5, 111.2, 116.3, 118.7, 119.2, 120.2, 120.8, 121.2, 124.9, 126.6, 127.4, 129.8, 130.8, 131.3, 131.6, 143.2, 144.5, 144.6, 149.6, 151.9, 156.8, 156.9; UPLC (M + 1) 382.3. Anal. Calcd for $C_{24}H_{19}N_3O_2$: C, 75.57; H, 5.02; N, 11.02. Found: C, 75.63; H, 4.97; N, 10.97.

4-Cyclohexenyl-6-methoxy-2-(1*H*-pyrrolo[2,3-b]pyridin-3-yl)quinoline (6d). Isolated as orange solid: mp 224−226 °C; (^{1}H NMR 400 MHz, DMSO-d_6) 1.76−1.77 (m, 2H), 1.84−1.95 (m, 2H), 2.29−2.43 (m, 4H), 3.83 (s, 3H, −OMe), 5.90 (bs, 1H, −CH), 7.21−7.30 (m, 3H, Ar−H), 7.39 (d, J = 9.0 Hz, 1H, Ar−H), 7.81 (s, 1H, Ar−H), 7.99 (d, J = 8.0 Hz, 1H, Ar−H), 8.30 (d, J = 3.2 Hz, 1H, Ar−H), 8.48 (d, J = 2.4 Hz, 1H, Ar−H), 9.12 (d, J = 6.8 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 22.0, 22.9, 25.3, 29.9, 55.7, 104.5, 114.7, 117.2, 117.3, 118.5, 121.1, 125.4, 127.2, 128.6, 131.0, 131.3, 135.7, 143.8, 144.4, 149.4, 149.8, 152.7, 156.8; UPLC (M + 1) 356.3. Anal. Calcd for $C_{23}H_{21}N_3O$: C, 77.72; H, 5.96; N, 11.82. Found: C, 77.79; H, 6.01; N, 11.76.

4-Phenyl-2-(1*H*-pyrrolo[2,3-b]pyridin-3-yl)quinoline-6-carbonitrile (6j). Isolated as brown solid: mp 253−255 °C; (^{1}H NMR 400 MHz, DMSO-d_6) 7.30 (dd, J = 7.6, 4.8 Hz, 1H, Ar−H), 7.61−7.63 (m, 5H, Ar−H), 8.02−8.36 (m, 5H, Ar−H), 8.75 (s, 1H, Ar−H), 9.20 (d, J = 8.0 Hz, 1H, Ar−H), 12.36 (br s, 1H, −NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 107.9, 114.2, 117.7, 118.5, 119.5, 120.5, 124.4, 129.4,* 130.1, 130.6, 130.9,* 131.5, 131.9, 136.9, 144.3, 148.3, 150.0, 150.1, 157.9; UPLC (M + 1) 347.3. Anal. Calcd for $C_{23}H_{14}N_4$: C, 79.75; H, 4.07; N, 16.17. Found: C, 79.68; H, 4.12; N, 16.24 (* two carbons merged here).

4-(2-Methoxyphenyl)-2-(1*H*-pyrrolo[2,3-b]pyridin-3-yl)-quinoline-8-carbonitrile (6n). Isolated as yellow solid: mp 262−264 °C; (^{1}H NMR 400 MHz, DMSO-d_6) 3.69 (s, 3H, $-OCH_3$), 7.16−7.68 (m, 7H, Ar−H), 8.19 (s, 1H, Ar−H), 8.28−8.36 (m, 2H, Ar−H), 8.75 (s, 1H, Ar−H), 9.43 (d, J = 7.6 Hz, 1H, Ar−H), 12.35 (br s, 1H, −NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 55.9, 111.2, 112.0, 114.2, 117.8, 118.6, 118.8, 121.0, 121.3, 125.2, 125.5, 125.9,* 130.4, 131.0, 131.4, 131.6, 135.9, 144.4, 146.6, 148.3, 150.1, 156.9, 157.0; UPLC (M + 1) 377.3. Anal. Calcd for $C_{24}H_{16}N_4O$: C, 76.58; H, 4.28; N, 14.88. Found: C, 76.51; H, 4.32; N, 14.83 (* two carbons merged here).

6-Methoxy-4-phenyl-2-(1*H*-pyrrolo[2,3-b]pyridin-2-yl)-quinoline (8). Isolated as pale yellow solid: mp 212−214 °C; (^{1}H NMR 400 MHz, DMSO-d_6) 3.78 (s, 3H, $-OCH_3$), 7.11 (dd, J = 7.8, 4.6 Hz, 1H, Ar−H) 7.20 (d, J = 2.8 Hz, 1H, Ar−H), 7.39 (d, J = 2.0 Hz, 1H, Ar−H), 7.51 (dd, J = 9.2, 2.8 Hz, 1H, Ar−H), 7.58−7.72 (m, 5H, Ar−H), 8.02 (d, J = 6.8 Hz, 1H, Ar−H), 8.10 (d, J = 9.2 Hz, 1H, Ar−H), 8.14 (s, 1H, Ar−H), 8.30 (dd, J = 4.6, 1.4 Hz, 1H, Ar−H), 12.26 (br s, 1H, −NH); sample was not sufficiently soluble to record ^{13}C NMR spectrum; UPLC (M + 1) 352.3. Anal. Calcd for $C_{23}H_{17}N_3O$: C, 78.61; H, 4.88; N, 11.96. Found: C, 78.56; H, 4.81; N, 11.92.

6-Methoxy-2-(1-methyl-1*H*-pyrrolo[2,3-b]pyridin-3-yl)-4-phenylquinoline (10). Isolated as orange solid: mp 195−197 °C; (^{1}H NMR 400 MHz, DMSO-d_6) 3.75 (s, 3H, $-NCH_3$), 3.89

dx.doi.org/10.1021/jo202256z | J. Org. Chem. 2012, 77, 1468−1476

(s, 3H, $-OCH_3$), 7.13 (d, J = 2.4 Hz, 1H, Ar−H), 7.29 (dd, J = 7.6, 4.4 Hz, 1H, Ar−H), 7.43 (dd, J = 9.2, 2.4 Hz, 1H, Ar−H), 7.54−7.67 (m, 5H, Ar−H), 7.89 (s, 1H, Ar−H), 8.07 (d, J = 9.2 Hz, 1H, Ar−H), 8.37 (d, J = 4.4 Hz, 1H, Ar−H), 8.57 (s, 1H, Ar−H), 9.14 (d, J = 7.6 Hz, 1H, Ar−H); ^{13}C NMR spectrum could not be recorded due to poor solubility; UPLC (M + 1) 366.4. Anal. Calcd for $C_{24}H_{19}N_3O$: C, 78.88; H, 5.24; N, 11.50. Found: C, 78.83; H, 5.28; N, 11.57.

2-(1-Benzyl-1*H*-pyrrolo[2,3-b]pyridin-3-yl)-6-methoxy-4-phenylquinoline (11). Isolated as orange solid: mp 205−207 °C; (^{1}H NMR 400 MHz, $CDCl_3$) 3.81 (s, 3H, $-OCH_3$), 5.60 (s, 2H, $-CH_2$), 7.16 (d, J = 2.4 Hz, 1H, Ar−H), 7.28−7.59 (m, 12H, Ar−H), 7.61 (s, 1H, Ar−H), 7.84 (s, 1H, Ar−H), 8.12 (d, J = 9.2 Hz, 1H, Ar−H), 8.45 (dd, J = 4.8, 1.6 Hz, 1H, Ar−H), 9.09 (d, J = 8.0, 1.6 Hz, 1H, Ar−H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 48.0, 55.4, 104.1, 115.4, 117.2, 119.0, 119.3, 121.3, 125.9, 127.5, 127.6, 127.8, 128.3, 128.6, 128.8, 129.3, 131.0, 131.1, 137.4, 138.7, 143.9, 144.9, 147.2, 148.6, 151.8, 157.2; UPLC (M + 1) 442.3. Anal. Calcd for $C_{30}H_{23}N_3O$: C, 81.61; H, 5.25; N, 9.52. Found: C, 81.70; H, 5.20; N, 9.45.

■ ASSOCIATED CONTENT

Supporting Information

General experimental procedures, ^{1}H, ^{13}C NMR and mass spectra for synthesized compounds **5a−x**, **6b**, **6c**, **6d**, **6j**, **6n**, **8**, **10**, and **11**, and crystallographic information file (CIF) of **5b**. This material is available free of cost via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: muthumanian2001@yahoo.com.

■ ACKNOWLEDGMENTS

R. Suresh is grateful to Syngene International Limited, Bangalore for providing necessary facilities to carry out this work.

■ REFERENCES

(1) (a) Jones, G. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, A. R., Eds.; Pergamon: New York, 1984; Vol. 2, p 395. (b) Balasubramanian, M.; Keay, J. G. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon Press: Oxford, 1996; Vol. 5, p 245.

(2) (a) Michael, J. P. *Nat. Prod. Rep.* **2007**, *24*, 223. (b) Jain, M.; Khan, S. I.; Tekwani, B. L.; Jacob, M. R.; Singh, S.; Singh, P. P.; Jain, R. *Bioorg. Med. Chem.* **2005**, *13*, 4458. (c) Lilienkampf, A.; Mao, J.; Wan, B.; Wang, Y.; Franzblau, S. G.; Kozikowski, A. P. *J. Med. Chem.* **2009**, *52*, 2109. (d) Chen, S.; Chen, R.; He, M.; Pang, R.; Tan, Z.; Yang, M. *Bioorg. Med. Chem.* **2009**, *17*, 1948.

(3) For reviews, see: (a) Michael, J. P. *Nat. Prod. Rep.* **1997**, *14*, 605. (b) Bray, P. G.; Ward, S. A.; O'Neil, P. M. *Curr. Top. Microbiol. Immunol.* **2005**, *295*, 3. (c) Michael, J. P. *Nat. Prod. Rep.* **2005**, *22*, 627.

(4) (a) Skraup, H. *Chem. Ber.* **1880**, *13*, 2086. (b) Mansake, R. H. F.; Kulka, M. *Org. React.* **1953**, *7*, 59. (c) Combes, A. *Compt. Rend.* **1888**, *106*, 142. (d) Friedländer, P. *Chem. Ber.* **1882**, *15*, 2772. (e) Doebner, O.; von Miller, W. *Chem. Ber.* **1881**, *14*, 2812.

(5) Yamashkin, S. A.; Oreshkina, E. A. *Chem. Heterocycl. Compd.* **2006**, *42*, 701.

(6) (a) Povarov, L. S.; Mikhailov, B. M. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1963**, 953. (b) Povarov, L. S.; Grigos, V. I.; Mikhailov, B. M. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1963**, 2039. (c) Povarov, L. S. *Russ. Chem. Rev.* **1967**, *36*, 656. (d) For recent review, see: Kouznetsov, V. V. *Tetrahedron* **2009**, *65*, 2721 and references cited therein. (e) Kouznetsov, V. V.; Bohórquez, A. R. R.; Stashenko, E. E. *Tetrahedron Lett.* **2007**, *48*, 8855. (f) Taranin, A. V.; Glushkov, V. A.; Mayorova, O. A.; Shcherbinina, I. A.; Tolstikov, A. G. *Mendeleev Commun.* **2008**, *18*, 188. (g) Guchhait, S. K.; Jadeja, K.; Madaan, C. *Tetrahedron Lett.* **2009**, *50*, 6861. (h) Rai, N. P.; Shashikanth, S.; Arunachalam, P. N. *Synth. Commun.* **2009**, *39*, 2125.

(7) (a) Palacios, F.; Alonso, C.; Arrieta, A.; Cossío, F. P.; Ezpeleta, J. M.; Fuertes, M.; Rubiales, G. *Eur. J. Org. Chem.* **2010**, 2091. (b) Manian, R. D. R. S.; Jayashankaran, J.; Raghunathan, R. *Tetrahedron Lett.* **2007**, *48*, 4139. (c) Lu, J.-M.; Shi, M. *Org. Lett.* **2007**, *9*, 1805. (d) Twin, H.; Batey, R. A. *Org. Lett.* **2004**, *6*, 4913. (e) Smith, C. D.; Gavrilyuk, J. I.; Lough, A. J.; Batey, R. A. *J. Org. Chem.* **2010**, *75*, 702. (f) Baudelle, R.; Melnyk, P.; Déprez, B.; Tartar, A. *Tetrahedron* **1998**, *54*, 4125. (g) Sundarajan, G.; Prabagaran, N.; Varghese, B. *Org. Lett.* **2001**, *3*, 1973. (h) Akiyama, T.; Morita, H.; Fuchibe, K. *J. Am. Chem. Soc.* **2006**, *128*, 13070. (i) Li, X.; Mao, Z.; Wang, Y.; Chen, W.; Lin, X. *Tetrahedron* **2011**, *67*, 3858.

(8) Katritzky, A. R.; Rachwal, S.; Rachwal, B. *Tetrahedron* **1996**, *52*, 15031.

(9) (a) Bortolotti, B.; Leardini, R.; Nanni, D.; Zanardi, G. *Tetrahedron* **1993**, *49*, 10157. (b) Hirashita, T.; Kawai, D.; Araki, S. *Tetrahedron Lett.* **2007**, *48*, 5421. (c) Shindoh, N.; Tokuyama, H.; Takasu, K. *Tetrahedron Lett.* **2007**, *48*, 4749.

(10) (a) Shindoh, N.; Tokuyama, H.; Takemoto, Y.; Takasu, K. *J. Org. Chem.* **2008**, *73*, 7451. (b) Zhoa, Y.-L.; Zhang, W.; Wang, S.; Liu, Q. *J. Org. Chem.* **2007**, *72*, 4985.

(11) (a) Savitha, G.; Perumal, P. T. *Tetrahedron Lett.* **2006**, *47*, 3589. (b) Demaude, T.; Knerr, L.; Pasau, P. *J. Comb. Chem.* **2004**, *6*, 768.

(12) Chen, Y.; Qian, L.; Zhang, W.; Han, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 9330.

(13) (a) Zhang, X.; Campo, M. A.; Larock, R. C. *Org. Lett.* **2005**, *7*, 763. (b) Gabriele, B.; Mancuso, R.; Salerno, G.; Ruffolo, G.; Plastina, P. *J. Org. Chem.* **2007**, *72*, 6873. (c) Amii, H.; Kishikawa, Y.; Uneyama, K. *Org. Lett.* **2001**, *3*, 1109. (d) Zhoa, Y.-L.; Zhang, W.; Wang, S.; Liu, Q. *J. Org. Chem.* **2007**, *72*, 4985.

(14) (a) Chavan, N. L.; Nayak, S. K.; Kusurkar, R. S. *Tetrahedron* **2010**, *66*, 1827. (b) Liger, F.; Popowycz, F.; Besson, T.; Picot, L.; Galmarini, C. M.; Joseph, B. *Bioorg. Med. Chem.* **2007**, *15*, 5615. (c) Dormoy, J. R.; Heymes, A. *Tetrahedron* **1993**, *49*, 2885. (d) Alvarez, M.; Fernandez, D.; Joule, J. A. *Synthesis* **1999**, 615. (e) Curtius, N. R.; Kulagowski, J. J.; Leeson, P. D.; Redgill, M. P.; Emms, F.; Freedman, S. B.; Patel, S. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 585. (f) Mazeas, D.; Guillaumet, G.; Viaud, M.-C. *Heterocycles* **1999**, *50*, 1065.

(15) (a) Mouaddib, A.; Joseph, B.; Hasnaoui, A.; Merour, J.-Y. *Tetrahedron Lett.* **1999**, *40*, 5853. (b) Chavan, N. L.; Sandip, K. N.; Radhika, S. K. *Tetrahedron* **2010**, *66*, 1827. (c) Verbiscar, A. J. *J. Med. Chem.* **1972**, *15*, 149.

(16) Desarbre, E.; Coudret, S.; Meheust, C.; Merour, J.-Y. *Tetrahedron* **1997**, *53*, 3637.

(17) Chavan, N. L.; Kusurkar, R. S.; Nayak, S. K *Tetrahedron* **2010**, *66*, 1827.

(18) Le Borgne, M.; Na, Y.; Pagniez, F.; Le Baut, G.; Le Pape, P.; Abdala, H. US patent, US2004/67998 A1, 2004.