JOC The Journal of Organic Chemistry

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Synthesis of Pyrido[1,2-*a*]indole Malonates and Amines through Aryne Annulation

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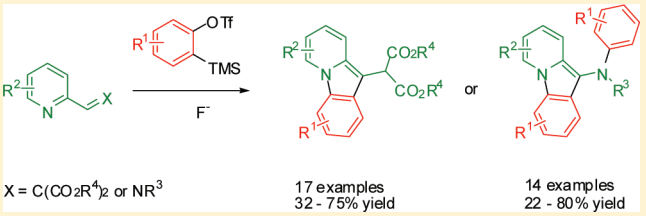
Supporting Information

ABSTRACT: Pyrido[1,2-*a*]indoles are known as medicinally and pharmaceutically important compounds, but there is a lack of efficient methods for their synthesis. We report a convenient and efficient route to these privileged structures starting from easily accessible 2-substituted pyridines and aryne precursors. A small library of compounds has been synthesized utilizing the developed method, affording variously substituted pyrido[1,2-*a*]-indoles in moderate to good yields.



INTRODUCTION

Selected examples of pyridoindoles have been shown to possess important biological activities (Figure 1). (−)-Goniomitine

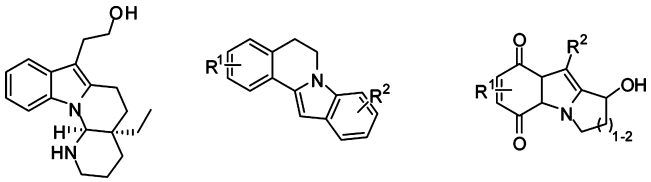


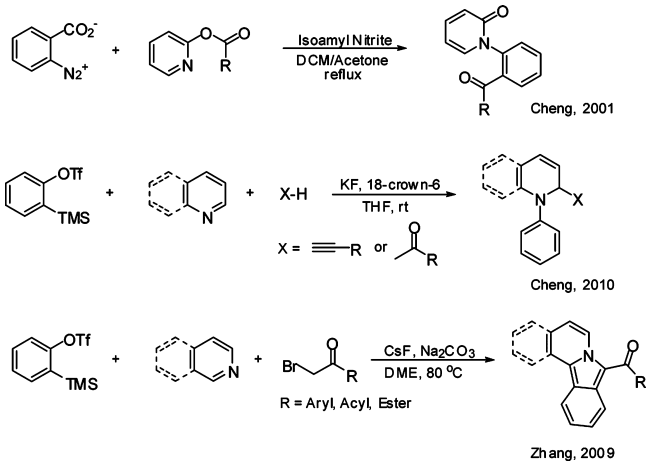
Figure 1. Biologically active compounds containing a pyridoindole core.

isolated from the root bark of *Gonioma malagasy* has shown significant antitumor activity against several types of cancer cells.[1] A series of indolo[2,1-*a*]isoquinoline compounds have been shown to possess a wide range of biological activities, including cytostatic,[2,3] antiviral,[4] immunosuppressive,[5] and tubulin polymerization inhibiting activities.[6] Another series of compounds known as metosenes have shown significant antitumor activity.[7] However, the fully aromatic pyridoindole core has been mentioned in the literature only briefly, mainly due to the challenges in the preparation of this system.[8] Recent efforts, as shown herein, have focused on utilizing the nucleophilic nature of carefully designed pyridines for the synthesis of pyrido[1,2-*a*]indoles.

The highly electrophilic nature of arynes, combined with the ability to fine-tune their generation by employing various combinations of solvents, temperatures, and fluoride sources, has given rise to an impressive number of useful synthetic reactions between arynes and a wide variety of nucleophiles.[9] As a result, aryne intermediates have provided chemists with the ability to rapidly access a plethora of interesting heterocycles and carbocycles, including indoles,[10] xanthones,[11] acridines,[12] indazoles,[13] and benzotriazoles,[14] among others, using mild and functional group tolerant reaction conditions. The ability to expediously synthesize biologically important compounds continues to motivate our laboratories to explore the full potential of aryne-based methodologies.[15]

To the best of our knowledge, there have been no reports that incorporate pyridines into larger ring systems through an initial attack onto arynes by the pyridyl nitrogen. On the other hand, a few reports have demonstrated related pyridine-aryne couplings. In 2001, Cheng and co-workers reported the reaction of 2-pyridyl carboxylates and benzynes (Scheme 1).[16]

Scheme 1. Aryne-Mediated Processes Involving Pyridines



In 2010, the same group reported that the multicomponent reaction of pyridines, arynes, and terminal acetylenes or methyl ketones leads to a series of 1,2-disubstituted pyridines, also proceeding through initial attack by a pyridyl nitrogen on an aryne.[17]

Received: December 15, 2011
Published: February 22, 2012

dx.doi.org/10.1021/jo2025543 | *J. Org. Chem.* 2012, 77, 2743–2755

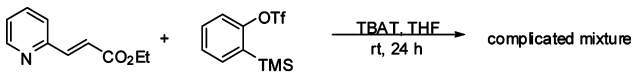
Before that, similar work was reported using acetonitrile as the proton source and secondary nucleophile in place of the terminal acetylene.[18] Additionally, Zhang has reported the reaction of arynes with in situ generated pyridyl analogues from pyridines (and quinoline) and alpha-bromo carbonyl compounds (Scheme 1).[19]

A challenge when designing pyridine-based aryne coupling reactions is neutralization of the newly formed quaternary nitrogen cation. Through careful reaction design, one can surmount this difficulty, as was previously demonstrated by the authors whose methodologies are shown in Scheme 1. Wanting to incorporate the pyridine ring system into a larger ring system, a series of electrophilic groups were envisioned to be compatible mechanistically with arynes, namely Michael acceptors and imines. In both scenarios, neutralization steps led to the stabilized pyrido[1,2-*a*]indole aromatic ring system.

RESULTS AND DISCUSSION

To test our hypothesis that pyridine-containing Michael acceptors should react with arynes to form pyridoindoles, the reaction of ethyl *E*-3-(pyridin-2-yl)acrylate (**1**) and Kobayashi's benzyne precursor[20] has been examined. However, to our disappointment, we observed a complicated mixture and very low yields of the desired product, ethyl 2-(pyrido[1,2-*a*]indol-10-yl)acetate (Scheme 2).

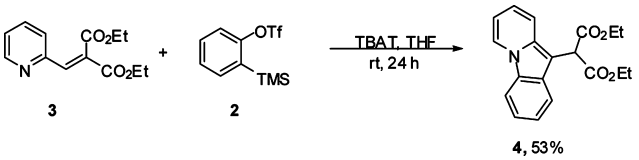
Scheme 2. Reaction of *E*-3-(Pyridine-2-yl)acrylate and Benzyne



1 2

In an attempt to increase the electrophilicity of the Michael acceptor, diethyl 2-(pyridin-2-ylmethylene)malonate (**3**) was synthesized by condensing diethyl malonate with 2-pyridinecarboxaldehyde. This substrate reacted cleanly with benzyne to form diethyl 2-(pyrido[1,2-*a*]indol-10-yl)malonate (**4**) in a 53% yield (Scheme 3). However, a significant portion of the starting material remained. Thus, further optimization was needed.

Scheme 3. Reaction of 2-(Pyridin-2-ylmethylene)malonate and Benzyne



3 2 4, 53%

In an effort to optimize this reaction, various fluoride sources, solvents, temperatures, and stoichiometries in the reaction shown in Scheme 3 were examined (Table 1). In the case of substrate **3** (Scheme 3), 2.0 or 3.0 equiv of the benzyne precursor afforded yields similar to reactions employing 1.75 equiv of the benzyne precursor, while 1.5 equiv of the benzyne precursor yielded significantly less product (Table 1, entries 1−4). TBAT proved to be the most effective fluoride source, and it was found that 1.25 equiv per 1.0 equiv of the benzyne precursor were sufficient (Table 1, entry 5). Other fluoride sources, such as CsF, TBAF, or TMAF, usually resulted in

Table 1. Optimization of Aryne Annulations with 2-(Pyridin-2-ylmethylene)malonates

entry	**2** (equiv)	fluoride source (equiv)	solvent (ratio)	temp (°C)	% yield[a]
1	1.5	TBAT	THF	rt	59
2	1.75	TBAT	THF	rt	68
3	2.0	TBAT	THF	rt	71
4	3.0	TBAT	THF	rt	73
5	1.75	TBAT	THF	50	57
6	1.75	CsF	THF	65	19
7	1.75	CsF	MeCN	rt	23
8	1.75	TMAF	THF	rt	46
9	1.75	TBAF	THF	rt	24
10	1.75	TBAT	THF/MeCN (1:1)	rt	59
11	1.75	TBAT	THF/toluene (1:1)	rt	47
12[b]	1.75	TBAT	THF	rt	56

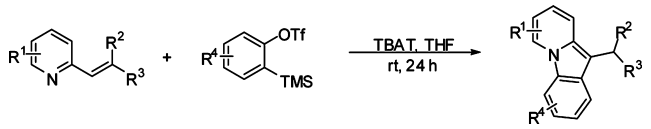
[a]Isolated yields. [b]Slow addition over 6 h.

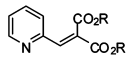
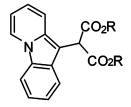
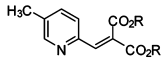
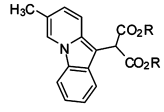
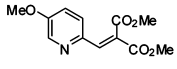
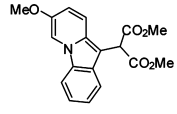
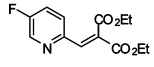
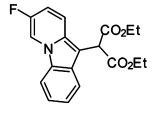
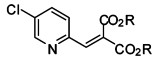
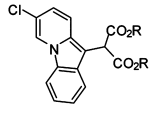
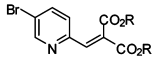
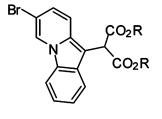
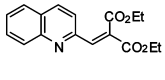
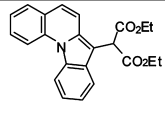
complicated mixtures (Table 1, entries 6−9). Ambient temperatures provided a cleaner reaction and a higher yield compared to using TBAT at higher temperatures, which mainly resulted in more spots upon TLC analysis and lower yields (Table 1, entries 5 and 6). However, according to TLC analysis, a significant amount of starting material still remained for reactions at ambient temperatures. Therefore, further efforts to promote the conversion of substrate **3** were undertaken by varying the rate at which benzyne is formed in situ. Thus, combination solvent systems, such as MeCN/THF or toluene/THF, should speed up or slow down the rate, respectively, of benzyne generation because of their increased or decreased polarities (Table 1, entries 10 and 11). However, lower yields were obtained in both cases. Additionally, other pure solvents in conjunction with TBAT, such as MeCN, DME, and toluene, failed to improve the yield using either ambient or elevated temperatures. Lastly, in an attempt to decrease the amount of available benzyne at a given time, slow addition (Table 1, entry 12) and portion-wise addition (results not shown) of the precursor were examined, but lower yields were obtained in both cases.

After finding optimal annulation conditions for the synthesis of 2-(pyrido[1,2-*a*]indol-10-yl)malonates (Table 1, entry 2), the scope and limitations of this process were studied (Table 2). The methodology seems to tolerate a variety of different esters, in addition to the parent substrate **3**, including a dimethyl ester, a di-*t*-butyl ester, and a dibenzyl ester (Table 2, entries 1−4). Except for the sterically hindered di-*t*-butyl ester (Table 2, entry 3), good yields of the corresponding pyrido[1,2-*a*]-indoles were obtained. Mixed results were observed when various substituents were placed on the pyridine ring. For example, a methyl substituent placed at the 5-position of the pyridine ring (**11** and **13**) drastically reduced the yield of the desired product when compared to the corresponding unsubstituted pyridines **3** and **5** (Table 2, entries 5 and 6). Similar results were realized when a halogen-containing pyridine was subjected to the optimized conditions. As seen in entries 8−12 (Table 2), the yields suffered drastically in comparison. One interesting trend noted is the fact that the yields seemed to increase as the halogen decreased in electronegativity, providing yields closer to that of the unsubstituted pyridines. As seen previously, the dimethyl ester pyridines seemed to yield marginally higher quantities of the desired

dx.doi.org/10.1021/jo2025543 | J. Org. Chem. 2012, 77, 2743−2755

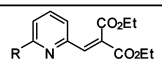
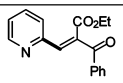
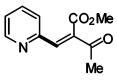
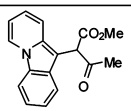
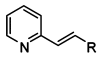
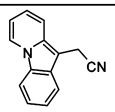
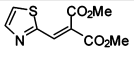
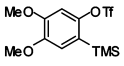
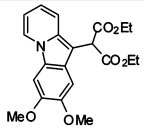
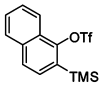
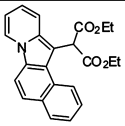
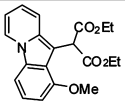
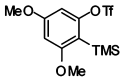
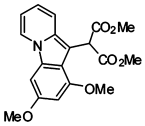
Table 2. Synthesis of Pyridoindoles from 2-(Pyridin-2-yl-methylene)malonates and Arynes[a]



entry	starting material	aryne	product	yield (%)[b]
		**2**		
1	R = Et, **3**		R = Et, **4**	68
2	R = Me, **5**		R = Me, **6**	74
3	R = t-Bu, **7**		R = t-Bu, **8**	40
4	R = Bn, **9**		R = Bn, **10**	72
		**2**		
5	R = Et, **11**		R = Et, **12**	59
6	R = Me, **13**		R = Me, **14**	63
		**2**		
7	**15**		**16**	41
		**2**		
8	**17**		**18**	39
		**2**		
9	R = Et, **19**		R = Et, **20**	43
10	R = Me, **21**		R = Me, **22**	45
		**2**		
11	R = Et, **23**		R = Et, **24**	47
12	R = Me, **25**		R = Me, **26**	51
		**2**		
13	**27**		**28**	32

dx.doi.org/10.1021/jo2025543 | J. Org. Chem. 2012, 77, 2743−2755

Table 2. continued

entry	starting material	aryne	product	yield (%)[b]
14	 R = 4-FC$_6$H$_4$, **29**	**2**	-	-[c]
15	R = 4-MeOC$_6$H$_4$, **30**		-	-[c]
16	 **31**	**2**	-	-[c,e]
17	 **32**	**2**	 **33**	61
18	 R = CN, **34**	**2**	 **35**	9
19	R = NO_2, **36**		-	-[b,d]
20	 **37**	**2**	-	-[b,d]
21	**3**	 **38**	 **39**	64
22	**3**	 **40**	 **41**	66
23	**3**	 **42**	 **43**	75
24	**5**	 **44**	 **45**	73

[a]For the details of the experimental procedure, see the Experimental Section. [b]Isolated yield after column chromatography. [c]The product was not observed or isolated. [d]No reaction. [e]A complicated mixture was observed on TLC analysis.

product compared to the diethyl esters. The yields seemed to diminish even further when a substituent was placed at the 6-position of the pyridine ring (Table 2, entries 13−15). Poor yields of the desired product **28** were obtained when quinoline substrate **27** was allowed to react, whereas substrates **29** and **30** did not seem to react at all. Only the starting material was observed on TLC analysis.

dx.doi.org/10.1021/jo2025543 | J. Org. Chem. 2012, 77, 2743−2755

β-Keto esters have also been condensed with 2-pyridinecarboxaldehyde in order to obtain the corresponding pyridine-containing Michael acceptor. Phenyl ketone **31** reacted with benzyne to yield an inseparable mixture of products (Table 2, entry 16). However, it is believed that the desired product was indeed formed, because of the appearance of a distinct yellow spot observed on TLC analysis, as seen in all other successful reactions. On the other hand, the methyl ketone **32**, as a mixture of *E* and *Z* isomers, reacted favorably to give product **33** in a 61% yield (Table 2, entry 17). Cyano-alkene **34** produced the desired product **35** (Table 2, entry 18), albeit in a very low 9% yield, using CsF as the fluoride source and MeCN as the solvent. Unfortunately, the nitro-alkene **36** did not react favorably and produced a complicated mixture upon TLC analysis (Table 2, entry 19). Next, a thiazole malonate derivative **37** was synthesized, but, despite multiple efforts to optimize the subsequent reaction with benzyne, the desired product could not be isolated (Table 2, entry 20).

It was pleasing to see that our conditions tolerated a variety of different benzyne precursors (Table 2, entries 21−24). Symmetrical benzyne precursor **38** produced a respectable 64% yield of pyrido[1,2-*a*]indole **39** (Table 2, entry 21). A series of unsymmetrical benzyne precursors **40**, **42**, and **44** have been examined, and all produced single regioisomers in good yields (Table 2, entries 22−24). These results are in good agreement with previously reported studies on the regioselectivity of reactions involving unsymmetrical arynes[21] and provide additional evidence that the aryne is initially attacked by the nitrogen of the pyridine ring.

A series of quick and convenient 1D-NOESY and/or 1D-COSY experiments confirmed the structures shown (Figure 2).

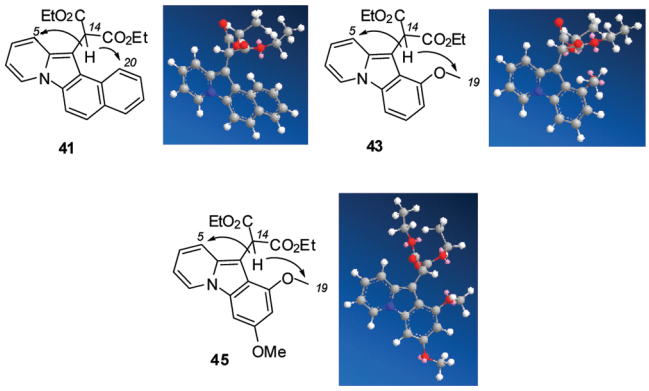
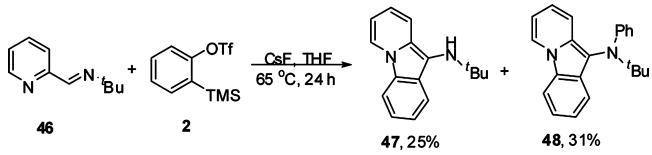


Figure 2. Characteristic NOEs observed in the ^{1}H−^{1}H NOESY analysis (NOESY, 400 MHz, $CDCl_3$) and 3D structures (generated in Chem3D, C: gray; H: white; N: blue; O: red) for compounds **41**, **43**, and **45**.

For example, an NOE interaction was observed between the malonate hydrogen at C14 of **41** and two doublet protons (C5 and C20). Furthermore, using a 1D-COSY experiment, these two doublets were observed to couple to two triplet protons. If the other regioisomer had been formed, the two doublets found to interact with the malonate hydrogen at through 1D-NOESY experiment would have coupled to both a triplet proton and a doublet proton in a 1D-COSY experiment. For compounds **43** and **45**, NOE interactions between the malonate hydrogen (C14) and the methoxy protons (C19) were observed along with coupling to the doublet hydrogen at C5.

We postulated that imines might serve equally well as the electrophilic trap after initial coupling to the aryne. Thus, imine **46** was synthesized from 2-pyridinecarboxaldehyde, and this imine was allowed to react favorably with benzyne to form a mixture of pyridoindoles **47** and **48** in a combined yield of 56% (Scheme 4). Unlike substrate **3** (Scheme 3), substrate **46**

Scheme 4. Reaction of 2-Imino-pyridine 46 with Benzyne



provided a mixture of the desired annulation product **47** and the subsequent arylation product **48**.

Attempts were made to inhibit the subsequent arylation process (Table 3). However, in all cases, roughly equimolar

Table 3. Optimization of Aryne Annulations with Pyridin-2-ylmethanimines

entry	**2** (equiv)	fluoride source (equiv)	temp (°C)	% yield[a]
1	1.0	TBAT	rt	62 (34:28)[b]
2	1.2	CsF (3)	65	56 (25:31)[b]
3	2.0	CsF (3)	65	67 (36:31)[b]
4	3.0	CsF (6)	65	70 (55:15)[b]
5	1.2	TBAF (1.4)	−78 to 100	18[c]
6	3.0	CsF (6)	100	72[d]

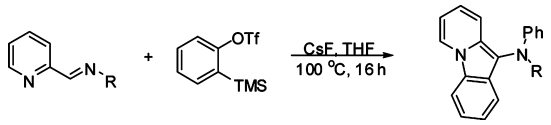
[a]Isolated yields. [b]Combined yield (**47**:**48**). [c]Yield of **47**. [d]Yield of **48**.

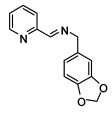
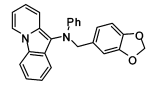
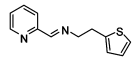
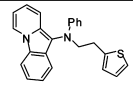
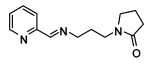
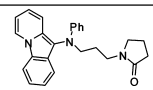
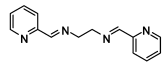
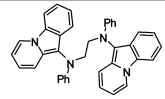
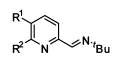
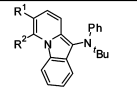
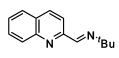
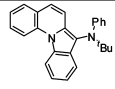
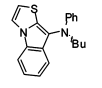
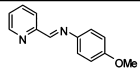
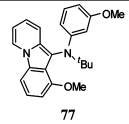
mixtures of **47** and **48** were obtained in modest yields (Table 3, entries 1−4). After evaluating the reaction conditions that should favor formation of the free amino product (Table 3, entry 5), we were able to suppress the formation of product **48** and obtain product **47** exclusively, albeit in just an 18% yield. Alternatively, the subsequent arylation product **48** could be promoted by using an excess of the benzyne precursor (3 equiv) and an elevated reaction temperature (Table 3, entry 6).

With optimal conditions in hand for the synthesis of *N*-aryl-2-pyrido[1,2-*a*]indoles, a series of electronically and sterically diverse imines were allowed to react with benzyne precursor **2** (Table 4). To our delight, our optimized conditions provided good yields of the corresponding pyridoindoles starting from a variety of alkyl imines, even the sterically bulky adamantyl imine **53** and allyl imine **55** (Table 4, entries 1−5). Conversely, propargyl imine **57** did not provide any of the desired product for reasons unknown (Table 4, entry 6). Additionally, a couple of heterocycle-containing primary amines were condensed with 2-pyridinecarboxaldehyde to form another series of imines capable of reacting with benzyne (Table 4, entry 7), including substrates containing the medicinally relevant methylenedioxy unit (Table 4, entry 8) and amide functionality (Table 4, entry 9). A major drawback was the fact that all substrates that contained a CH_2 unit directly attached to the imine nitrogen afforded pyridoindoles that were not stable on silica gel and polymerized rapidly. This caused some problems with purification of these compounds, but we found that the addition of 5% triethylamine to both the silica gel and the eluent helped stabilize the compounds and afforded clean products in slightly higher yields. However, despite the instability of the product, even the

dx.doi.org/10.1021/jo2025543 | J. Org. Chem. 2012, 77, 2743−2755

Table 4. Synthesis of Pyridoindoles from *N*-Pyridin-2-yl-methanimines and Arynes[a]



entry	starting material	aryne	product	yield (%)[b]
		2		
1	R = ^{t}Bu, **46**		R = ^{t}Bu, **48**	72
2	R = ^{i}Pr, **49**		R = ^{i}Pr, **50**	66
3	R = Cy, **51**		R = Cy, **52**	75
4	R = Ada, **53**		R = Ada, **54**	62
5	R = Allyl, **55**		R = Allyl, **56**	54
6	R = Propargyl, **57**		R = Propargyl, -	0[c]
		2		
7	**58**		**59**	78
		2		
8	**60**		**61**	70
		2		
9	**62**		**63**	60
		2		
10	**64**		**65**	51
		2		
11	R^1 = Br, R^2 = H, **66**		R^1 = Br, R^2 = H, **67**	34[d]
12	R^1 = F, R^2 = H, **68**		R^1 = F, R^2 = H, **69**	22[d]
13	R^1 = H, R^2 = Br, **70**		-	0[e]
14	R^1 = H, R^2 = 4-OMeC$_6$H$_4$, **71**		-	0[e]
		2		
15	**72**		**73**	75
		2		
16	**74**		**75**	27
		2		
17	**76**		-	trace[f]
		42		
18	**47**		**77**	80

[a]For the details of the experimental procedure, see the Experimental Section. [b]Isolated yield after column chromatography. [c]The product was not observed or isolated. [d]The yield was determined by ^{1}H NMR spectral analysis. [e]Recovered unreacted starting material. [f]The reaction afforded a complicated mixture that contained trace amounts of the desired product on the basis of ^{1}H NMR spectral analysis.

dx.doi.org/10.1021/jo2025543 | J. Org. Chem. 2012, 77, 2743−2755

diimine **64**, derived from 1,2-diaminoethane, afforded the corresponding double-annulation product **65** in a 51% yield (Table 4, entry 10). The halogenated substrates **66** and **68** reacted poorly compared to the corresponding parent substrate **46**, affording the corresponding pyridoindoles **67** and **69** in 34 and 22% yields (Table 4, entries 11 and 12). Furthermore, the 6-substituted pyridinylmethanimines **70** and **71** did not react at all with benzyne according to TLC analysis (Table 4, entries 13 and 14), as was seen previously with substrates **29** and **30** in Table 2. Unlike substrate **27** of Table 2, the quinoline-based imine **72** reacted smoothly to form the desired product in a 75% yield (Table 4, entry 15). Finally, the thiazole derivative **74** was allowed to react using our optimized reaction conditions to form the desired product **75**, albeit in only a 27% yield (Table 4, entry 16). Unfortunately, the 4-methoxyaniline-derived imine **76** under our optimized reaction conditions afforded a complicated mixture with only trace amounts of the desired pyridoindole on the basis of ^{1}H NMR data (Table 4, entry 17).

Additionally, an unsymmetrical aryne precursor **42** has been employed in the reaction with imine **47**, which provided compound **77** in an 80% yield. The exact structure of the compound **77** has been determined by COSY and NOE experiments (Figure 3).

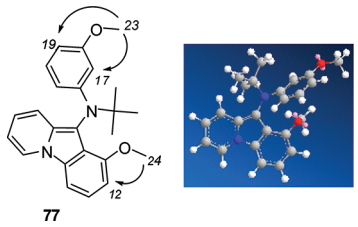
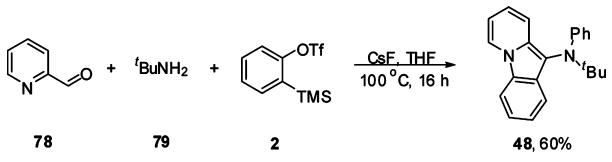


Figure 3. Characteristic NOEs observed in the ^{1}H−^{1}H NOESY analysis (NOESY, 400 MHz, $CDCl_3$) and 3D structure (generated in Chem3D, C: gray; H: white; N: blue; O: red) for compound 77.

An NOE experiment showed the methoxy protons (C24) coupling to the doublet (C12) and the methoxy protons (C23) coupling to a singlet (C17) and a doublet (C19). If a different isomer had been formed, then the methoxy group (C23) should have ended up ortho to the nitrogen; thus, only one coupling of hydrogens at C23 should have been observed.

In addition, we studied the possibility of converting the reaction presented in Scheme 4 into a one-pot protocol without isolation of the imine **46**. We were pleased to find that reaction between the aldehyde **78**, amine **79** (1 equiv), and aryne precursor **2** under the optimized reaction conditions afforded the desired pyridoindole product **48** in a 60% yield (Scheme 5).

Scheme 5. One-Pot Approach for the Synthesis of Pyridoindoles



A similar mechanism is assumed for the reactions of both the pyridine malonates and the imines (Scheme 6). Presumably, the pyridyl nitrogen initially attacks the aryne as a nucleophile, pushing electrons onto an adjacent aromatic carbon. Then, the newly formed aryl carbanion presumably attacks the neighboring electrophile to form intermediate **A**, which subsequently abstracts a hydrogen to afford the neutralized aromatic structure **B**. In the case of *N*-pyridin-2-yl-methanimines (X = NR), a subsequent aryne reaction takes place to form the arylated amine **C**.

CONCLUSION

In conclusion, readily obtainable pyridine-containing Michael acceptors and imines, when allowed to react with arynes, give a variety of biologically relevant pyrido[1,2-*a*]indoles generally in good overall yields under mild reaction conditions. Although mixed results were observed for the 2-(pyrido[1,2-*a*]indol-10-yl)-malonates, a new route to an otherwise elusive heterocyclic ring system has been developed. The optimized methodology tolerates a variety of ester types, while substrates bearing substitution around the pyridine ring have reacted with only modest success. 2-(Pyrido[1,2-*a*]indol-10-yl)malonates containing a substituent at the 6-position seemed not to react at all. On the other hand, the unsubstituted 2-(pyrido[1,2-*a*]indol-10-yl)malonates **3** and **5** reacted with various benzyne precursors, both symmetrical and unsymmetrical, to yield the desired pyrido[1,2-*a*]indoles in good yields. Additionally, *N*-aryl-2-(pyrido[1,2-*a*]indol-10-yl)amines have been synthesized in good yields. In this case, a large variety of imines are apparently well tolerated, including imines with various alkyl substituents and heterocycles.

EXPERIMENTAL SECTION

General Methods. The ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz or 400 and 100 MHz, respectively. Thin layer chromatography was performed using commercially prepared 60-mesh silica gel plates, and visualization was effected with short wavelength UV light (254 nm). All melting points are uncorrected. All reagents were used directly as obtained commercially.

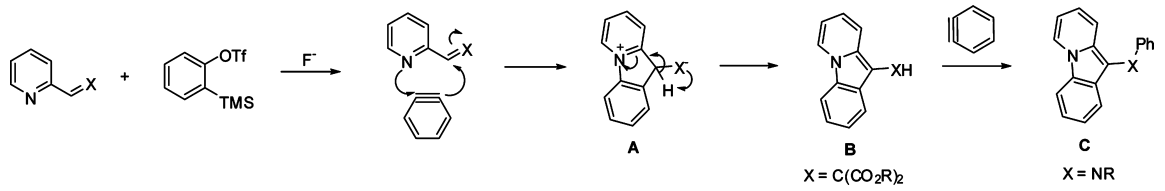
General Procedure for Preparation of the 2-(Pyridin-2-ylmethylene)malonates. To a 100 mL round-bottom flask equipped with a magnetic stir bar and ethanol (in the case of ethyl esters) or methanol (in the case of methyl esters and all other substrates) were added the commercially available corresponding aldehyde (4.24 mmol) and malonate (1.02 equiv), followed by redistilled piperidine (0.2 mL). The resulting solution was allowed to stir at 40 °C overnight (substrates **16a** and **17a** were allowed to stir at rt for 6 h). The reaction mixture was then poured into a separatory funnel containing water (50 mL) and chloroform (50 mL). The organic layer was removed, and the aqueous layer was extracted twice more with chloroform (25 mL each). The organic layer was then dried over anhydrous Na_2SO_4, and the solvent was removed to afford the crude product, which was purified by column chromatography using gradient solvent combinations of hexanes and ethyl acetate.

*Diethyl 2-(Pyridin-2-ylmethylene)malonate (**3**).*[22] The product was isolated as a tan solid: mp 46−48 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (d, J = 3.9 Hz, 1 H), 7.72 (td, J = 7.8, 1.8 Hz, 1 H), 7.64 (s, 1 H), 7.40 (d, J = 7.8 Hz, 1 H), 7.26 (m, 1 H), 4.42 (q, J = 7.2 Hz, 2 H), 4.32 (q, J = 7.2 Hz, 2 H), 1.35 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 163.5, 150.7, 149.3, 138.7, 136.5, 128.7, 125.9, 124.2, 61.3, 60.9, 13.7, 13.6; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{13}H_{15}NO_4$) 250.1074, found 250.1078.

*Dimethyl 2-(Pyridin-2-ylmethylene)malonate (**5**).*[23] The product was isolated as a white solid: mp 86−88 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 3.0 Hz, 1 H), 7.71 (t, J = 8.0 Hz, 1 H), 7.66 (s, 1 H), 7.39 (d, J = 8.0 Hz, 1 H), 7.26 (t, J = 8.0 Hz, 1 H), 3.90 (s, 3 H), 3.84 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 164.2, 150.8, 149.9, 139.8, 136.8, 128.2, 126.3, 124.6, 52.7, 52.3; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{11}H_{11}NO_4$) 222.0761, found 222.0763.

dx.doi.org/10.1021/jo2025543 | J. Org. Chem. 2012, 77, 2743−2755

Scheme 6. Proposed Mechanism for Formation of the Pyrido[1,2-*a*]indoles



*Di-tert-butyl 2-(Pyridin-2-ylmethylene)malonate (**7**).* The product was isolated as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, J = 3.9 Hz, 1 H), 7.68 (td, J = 7.7, 1.5 Hz, 1 H), 7.47 (s, 1 H), 7.37 (d, J = 7.8 Hz, 1 H), 7.24 (dd, J = 7.0, 4.9 Hz, 1 H), 1.59 (s, 6 H), 1.54 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 163.5, 152.0, 149.6, 137.43, 137.40, 136.6, 132.0, 125.7, 124.1, 82.4, 82.0, 28.3; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{17}H_{23}NO_4$) 306.1700, found 306.1707.

*Dibenzyl 2-(Pyridin-2-ylmethylene)malonate (**9**).* The product was isolated as a white solid: mp 109−111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, J = 4.3 Hz, 1 H), 7.71 (s, 1 H), 7.66 (td, J = 7.7, 1.8 Hz, 1 H), 7.46−7.29 (m, 11 H), 7.22 (ddd, J = 7.7, 4.8, 0.9 Hz, 1 H), 5.40 (s, 2 H), 5.32 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 163.7, 150.9, 149.8, 140.1, 136.7, 135.6, 135.4, 128.7, 128.6, 128.4, 128.3, 128.2, 128.0, 126.2, 124.5, 67.3, 67.3; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{23}H_{19}NO_4$) 374.1387, found 374.1395.

*Diethyl 2-[(5-Methylpyridin-2-yl)methylene]malonate (**11**).* The product was isolated a white solid: mp 65−67 °C; ^{1}H NMR (400 MHz, acetone) δ 8.39 (s, 1 H), 7.57 (s, 1 H), 7.46 (d, J = 7.9 Hz, 1 H), 7.24 (d, J = 8.0 Hz, 1 H), 4.37 (q, J = 7.1 Hz, 2 H), 4.26 (q, J = 7.2 Hz, 2 H), 2.30 (s, 1 H), 1.30 (dt, J = 11.0, 7.1 Hz, 6 H); ^{13}C NMR (100 MHz, acetone) δ 166.7, 164.2, 150.5, 148.5, 139.3, 137.0, 134.7, 128.1, 125.8, 61.7, 61.4, 18.6, 14.2, 14.1; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{14}H_{17}NO_4$) 264.1230, found 264.1235.

*Dimethyl 2-[(5-Methylpyridin-2-yl)methylene]malonate (**13**).* The product was isolated as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.45 (d, J = 1.8 Hz, 1 H), 7.64 (s, 1 H), 7.51 (ddd, J = 7.9, 2.2, 0.7 Hz, 1 H), 7.29 (d, J = 7.9 Hz, 1 H), 3.90 (s, 3 H), 3.85 (s, 3 H), 2.35 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 164.7, 151.0, 148.5, 140.2, 137.2, 135.1, 127.5, 126.2, 52.9, 52.7, 18.8; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{12}H_{13}NO_4$) 236.0917, found 236.0921.

*Dimethyl 2-[(5-Methoxypyridin-2-yl)methylene]malonate (**15**).* The product was isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 2.4 Hz, 1 H), 7.49 (s, 1 H), 7.23 (d, J = 8.5 Hz, 1 H), 7.05 (dd, J = 8.6, 2.7 Hz, 1 H), 3.78 (s, 3 H), 3.74 (s, 3 H), 3.72 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 164.4, 156.2, 143.0, 139.3, 138.8, 127.5, 125.6, 119.3, 55.6, 52.5, 52.2; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{12}H_{13}NO_5$) 252.0872, found 252.0880.

*Diethyl 2-[(5-Fluoropyridin-2-yl)methylene]malonate (**17**).* The product was isolated as a white solid: mp 48−50 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1 H), 7.57 (d, J = 2.1 Hz, 1 H), 7.39 (m, 2 H), 4.31 (m, 4 H), 1.30 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 163.9, 161.2, 157.7, 147.6, 147.6, 138.8, 138.5, 137.6, 129.1, 129.1, 127.5, 127.4, 123.4, 123.2, 61.9, 61.5, 14.2, 14.1; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{13}H_{14}FNO_4$) 268.0980, found 268.0984.

*Diethyl 2-[(5-Chloropyridin-2-yl)methylene]malonate (**19**).* The product was isolated as a white solid: mp 65−67 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 2.4 Hz, 1 H), 7.70 (dd, J = 8.2, 2.5 Hz, 1 H), 7.59 (s, 1 H), 7.35 (d, J = 8.3 Hz, 1 H), 4.40 (q, J = 7.1 Hz, 2 H), 4.32 (q, J = 7.2 Hz, 2 H), 1.35 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 164.0, 149.5, 149.1, 137.8, 136.6, 133.1, 129.9, 126.8, 62.1, 61.7, 14.3, 14.2; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{13}H_{14}ClNO_4$) 284.0684, found 284.0691.

*Dimethyl 2-[(5-Chloropyridin-2-yl)methylene]malonate (**21**).* The product was isolated as a white solid: mp 103−105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 2.2 Hz, 1 H), 7.71 (dd, J = 8.3, 2.5 Hz, 1 H), 7.63 (s, 1 H), 7.36 (d, J = 8.2 Hz, 1 H), 3.90 (s, 3 H), 3.87 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 164.3, 149.3, 138.5, 136.6, 133.3, 129.0, 127.0, 53.1, 52.8; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{11}H_{10}ClNO_4$) 256.0371, found 256.0373.

*Diethyl 2-[(5-Bromopyridin-2-yl)methylene]malonate (**23**).* The product was isolated as a white solid: mp 59−61 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, J = 2.3 Hz, 1 H), 7.85 (dd, J = 8.2, 2.4 Hz, 1 H), 7.57 (s, 1 H), 7.29 (d, J = 8.3 Hz, 1 H), 4.40 (q, J = 7.2 Hz, 2 H), 4.32 (q, J = 7.1 Hz, 2 H), 1.35 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 164.0, 151.2, 149.8, 139.5, 137.8, 129.9, 127.2, 122.1, 62.1, 61.7, 14.3, 14.2; HRMS (EI) calcd for $C_{13}H_{15}BrNO_4$ 328.0184, found 328.0186.

*Dimethyl 2-[(5-Bromopyridin-2-yl)methylene]malonate (**25**).* The product was isolated as a white solid: mp 96−99 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1 H), 7.86 (dd, J = 8.2, 2.3 Hz, 1 H), 7.61 (s, 1 H), 7.29 (d, J = 8.3 Hz, 1 H), 3.90 (s, 3 H), 3.86 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 164.3, 151.4, 149.5, 139.6, 138.6, 129.0, 127.4, 122.3, 53.1, 52.8; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{11}H_{10}BrNO_4$) 299.9866, found 299.9870.

*Diethyl 2-(Quinolin-2-ylmethylene)malonate (**27**).* The product was isolated as a white solid: mp 69−71 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.18 (d, J = 8.4 Hz, 1 H), 8.00 (d, J = 8.5 Hz, 1 H), 7.81 (m, 2 H), 7.72 (t, J = 5.7 Hz, 1 H), 7.56 (t, J = 5.4 Hz, 1 H), 7.50 (d, J = 8.4 Hz, 1 H), 4.52 (q, J = 7.1 Hz, 2 H), 4.36 (q, J = 7.1 Hz, 2 H), 1.37 (td, J = 7.1, 1.0 Hz, 6 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 166.7, 164.1, 151.2, 148.1, 139.6, 137.0, 130.3, 130.3, 130.1, 128.2, 127.9, 127.7, 123.1, 62.1, 61.6, 14.4; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{17}H_{17}NO_4$) 300.1230, found 299.1158.

*Diethyl 2-[(6-(4-Fluorophenyl)pyridin-2-yl)methylene]malonate (**29**).* The product was isolated as a white solid: mp 103−106 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (m, 2 H), 7.78 (t, J = 7.8 H, 1 H), 7.67 (m, 2 H), 7.34 (d, 1 H), 7.16 (m, 2 H), 4.32 (m, 4 H), 1.36 (t, J = 7.1 Hz, 3 H), 1.18 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 165.6, 164.2, 162.3, 156.8, 151.0, 139.3, 137.9, 135.3, 135.2, 129.5, 129.4, 129.3, 124.8, 121.3, 115.9, 115.6, 62.0, 61.6, 14.3, 14.1; HRMS (EI) calcd for $[M + Na]^+$ ($M = C_{19}H_{18}FNO_4$) 366.1112, found 366.1117.

*Diethyl 2-[(6-(4-Methoxyphenyl)pyridin-2-yl)methylene]-malonate (**30**).* The product was isolated as a white solid: mp 82−84 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, J = 8.9 Hz, 2 H), 7.68 (m, 3 H), 7.27 (d, J = 6.7 Hz, 1 H), 6.99 (d, J = 6.8 Hz, 2 H), 4.32 (m, 4 H), 3.86 (s, 3 H), 1.35 (t, J = 7.1 Hz, 3 H), 1.18 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 164.3, 161.0, 157.4, 150.8, 139.6, 137.6, 131.7, 129.0, 128.9, 124.2, 120.9, 114.1, 61.9, 61.6, 55.5, 14.3, 14.1; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{20}H_{21}NO_5$) 356.1492, found 356.1500.

*Ethyl 2-Benzoyl-3-(pyridin-2-yl)acrylate (**31**).*[24] The product was isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 4.0 Hz, 1 H), 7.86 (d, J = 7.6 Hz, 2 H), 7.81 (s, 1 H), 7.50 (td, J = 7.7, 1.6 Hz, 1 H), 7.38 (t, J = 7.3 Hz, 1 H), 7.29 (t, J = 7.3 Hz, 3 H), 6.94 (dd, J = 7.1, 5.2 Hz, 1 H), 4.14 (q, J = 7.1 Hz, 2 H), 1.09 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.3, 164.6, 150.9, 149.1, 139.7, 136.9, 136.5, 134.3, 132.6, 128.2, 125.9, 123.8, 61.4, 13.9; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{17}H_{15}NO_3$) 282.1125, found 282.1129.

*Methyl 3-Oxo-2-(pyridin-2-ylmethylene)butanoate (**32**).*[25] A 4:1 mixture of isomers were isolated as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, J = 4.1 Hz, 1 H), 7.66 (td, J = 7.7, 1.8 Hz, 1 H), 7.48 (s, 1 H), 7.34 (d, J = 7.7 Hz, 1 H), 7.18 (ddd, J = 7.6, 4.8, 1.0 Hz, 1 H), 3.78 (s, 4 H), 2.46 (s, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.5, 194.7, 168.3, 164.9, 151.3, 151.1, 149.9, 149.5, 138.4, 137.6, 136.9, 136.9, 136.5, 136.2, 126.5, 126.2, 124.7, 124.2, 52.6, 52.3, 31.0, 26.7; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{11}H_{11}NO_3$) 206.0812, found 206.0814.

dx.doi.org/10.1021/jo2025543 | *J. Org. Chem.* 2012, 77, 2743−2755

*(E)-3-(Pyridin-2-yl)acrylonitrile (**34**).*[26] The product was isolated as a gray solid: mp 81−83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 3.0 Hz, 1 H), 7.74 (t, J = 8.0 Hz, 1 H), 7.39 (d, J = 16.0 Hz, 1 H), 7.33 (m, 2 H), 6.59 (d, J = 16.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.1, 150.3, 148.7, 137.0, 125.2, 124.3, 118.0, 100.8; HRMS (EI) calcd for $[M + H]^+$ ($M = C_8H_6N_2$) 131.0604, found 131.0603.

*(E)-2-(2-Nitrovinyl)pyridine (**36**).*[27] The previously mentioned procedure was used in addition to a subsequent step to complete the dehydration. The crude mixture was treated with 10 equiv of Ac_2O, followed by 5 equiv of triethylamine. The reaction was allowed to stir at rt overnight before it was poured into water and extracted with ethyl acetate (3 × 20 mL). Using silica gel column chromatography, the product was isolated as an tan solid: mp 84−87 °C; ^{1}H NMR (300 MHz, acetone) δ 8.63 (d, J = 4.2 Hz, 1 H), 7.96 (d, J = 13.2 Hz, 1 H), 7.86 (d, J = 13.2 Hz, 1 H), 7.75 (td, J = 7.8, 1.8 Hz, 1 H), 7.45 (d, J = 7.8 Hz, 1 H), 7.34 (ddd, J = 7.8, 4.8, 0.6 Hz, 1 H); ^{13}C NMR (75 MHz, acetone) δ 150.7, 149.4, 140.7, 137.4, 137.3, 126.5, 125.9; HRMS (EI) calcd for $[M + H]^+$ ($M = C_7H_6N_2O_2$) 150.0429, found 150.0435.

*Dimethyl 2-(Thiazol-2-ylmethylene)malonate (**37**).* The product was isolated as a tan solid: mp 54−56 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 3.1 Hz, 1 H), 7.80 (s, 1 H), 7.55 (d, J = 3.1 Hz, 1 H), 3.94 (s, 4 H), 3.87 (s, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 164.0, 159.9, 145.6, 132.3, 127.4, 123.6, 53.2, 53.1; HRMS (EI) calcd for $[M + Na]^+$ ($M = C_9H_9NO_4S$) 250.0144, found 250.0147.

General Procedure for Preparation of the 2-(Pyrido[1,2-*a*]indol-10-yl)malonates 1a−13c, 17c, 19c, and 21c−24c. To a flame-dried 6-dram vial containing a stir bar, the corresponding 2-(pyridin-2-ylmethylene)malonate (0.5 mmol), and the benzyne precursor (1.75 equiv) was added anhydrous THF (5 mL), followed by TBAT (2.2 equiv). The mixture was then allowed to stir for 24 h at ambient temperature before it was poured into a separatory funnel containing a saturated aq solution of NH_4Cl (20 mL) and ethyl acetate (20 mL). The organic layer was removed, and the aqueous layer was extracted again with ethyl acetate (2 × 20 mL). The combined organic layers were dried with Na_2SO_4 and concentrated in vacuo to yield a crude mixture, which was purified by column chromatography using gradient solvent combinations of either hexanes and ethyl acetate, or hexanes and dichloromethane. In some cases, subsequent preparative TLC with chloroform was required in order to remove residual impurities left over from the TBAT.

*Diethyl 2-(Pyrido[1,2-a]indol-10-yl)malonate (**4**).* The product was isolated as a yellow oil (110.5 mg, 68%): ^{1}H NMR (300 MHz, acetone) δ 8.33 (d, J = 7.2 Hz, 1 H), 7.88 (m, 2 H), 7.58 (d, J = 9.3 Hz, 1 H), 7.43, (t, J = 7.2 Hz, 1 H), 7.31 (t, J = 7.5 Hz, 1 H), 6.97 (dd, J = 6.6, 2.7 Hz, 1 H), 6.52 (t, J = 6.6 Hz, 1 H), 5.24 (s, 1 H), 4.24 (m 4 H), 1.27 (t, J = 7.2 Hz, 6 H); ^{13}C NMR (75 MHz, acetone) δ 168.8, 135.0, 129.4, 128.2, 124.5, 123.3, 123.0, 120.1, 119.5, 118.0, 110.4, 108.2, 94.8, 61.9, 49.3, 14.3; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{19}H_{19}NO_4$) 326.1387, found 326.1394.

*Dimethyl 2-(Pyrido[1,2-a]indol-10-yl)malonate (**6**).* The product was isolated as a yellow oil (109.9 mg, 74%): ^{1}H NMR (400 MHz, acetone-d_6) δ 8.69 (d, J = 7.1 Hz, 1 H), 8.12 (d, J = 8.3 Hz, 1 H), 7.88 (d, J = 8.1 Hz, 1 H), 7.66 (dd, J = 9.4, 1.0 Hz, 1 H), 7.37 (ddd, J = 8.1, 7.0, 1.0 Hz, 1 H), 7.29 (ddd, J = 8.1, 7.0, 1.1 Hz, 1 H), 7.05 (ddd, J = 9.4, 6.4, 1.0 Hz, 1 H), 6.63 (t, J = 6.8 Hz, 1 H), 5.42 (s, 1 H), 3.69 (s, 6 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 169.7, 135.6, 130.3, 128.9, 125.9, 123.9, 123.9, 120.8, 120.2, 118.4, 111.6, 109.1, 95.8, 52.8, 49.1; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{17}H_{15}NO_4$) 298.1074, found 298.1081.

*Di-tert-butyl 2-(Pyrido[1,2-a]indol-10-yl)malonate (**8**).* The product was isolated as a yellow oil (76.2 mg, 40%): 1 H NMR (400 MHz, acetone-d_6) δ 8.68 (d, J = 7.1 Hz, 1 H), 8.10 (d, J = 8.3 Hz, 1 H), 7.93 (d, J = 8.1 Hz, 1 H), 7.68 (dd, J = 9.4, 1.1 Hz, 1 H), 7.37 (ddd, J = 8.1, 7.0, 1.0 Hz, 1 H), 7.28 (ddd, J = 8.1, 7.0, 1.1 Hz, 1 H), 7.02 (ddd, J = 9.4, 6.3, 1.0 Hz, 1 H), 6.60 (t, J = 7.0 Hz, 1 H), 5.13 (s, 1 H), 1.45 (s, 18 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 168.3, 135.5, 130.2, 129.1, 125.8, 123.4, 123.3, 120.8, 120.6, 119.0, 111.5, 108.8, 96.7, 81.9, 52.1, 28.2; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{23}H_{28}NO_4$) 382.2013, found 382.2021.

*Dibenzyl 2-(Pyrido[1,2-a]indol-10-yl)malonate (**10**).* The product was isolated as a yellow oil (161.6 mg, 72%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (d, J = 7.1 Hz, 1 H), 7.81−7.87 (m, 2 H), 7.50 (d, J = 9.4 Hz, 1 H), 7.37 (t, J = 7.5 Hz, 1 H), 7.33−7.11 (m, 1 H), 6.91 (dd, J = 9.4, 6.4 Hz, 1 H), 6.51 (t, J = 6.7 Hz, 1 H), 5.34 (s, 1 H), 5.19 (q, J = 12.3 Hz, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.5, 135.6, 135.1, 129.4, 128.6, 128.4, 128.4, 128.2, 124.5, 123.4, 123.1, 120.2, 119.5, 117.9, 110.4, 108.3, 94.3, 67.6, 49.3; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{29}H_{23}NO_4$) 450.1700, found 450.1707.

*Diethyl 2-(7-Methylpyrido[1,2-a]indol-10-yl)malonate (**12**).* The product was isolated as a yellow oil (100.3 mg, 59%): ^{1}H NMR (400 MHz, acetone-d_6) δ 8.50 (s, 1 H), 8.07 (d, J = 8.2 Hz, 1 H), 7.87 (d, J = 8.0 Hz, 1 H), 7.62 (d, J = 9.5 Hz, 1 H), 7.33 (t, J = 7.3 Hz, 1 H), 7.25 (t, J = 7.3 Hz, 1 H), 6.93 (d, J = 9.4 Hz, 1 H), 5.33 (s, 1 H), 4.15−4.18 (m, 4 H), 1.19 (t, J = 7.0 Hz, 6 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 160.2, 134.7, 130.0, 128.9, 127.1, 123.3, 122.9, 120.5, 120.3, 118.34, 118.25, 111.4, 95.5, 61.9, 49.7, 18.2, 14.5; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{20}H_{22}NO_4$) 340.1543, found 340.1552.

*Dimethyl 2-(7-Methylpyrido[1,2-a]indol-10-yl)malonate (**14**).* The product was isolated as a yellow oil (98.0 mg, 63%): ^{1}H NMR (300 MHz, acetone-d_6) δ 8.51 (dd, J = 2.4, 1.2 Hz, 1 H), 8.08 (d, J = 8.2 Hz, 1 H), 7.85 (dd, J = 8.1, 0.9 Hz, 1 H), 7.60 (d, J = 9.5 Hz, 1 H), 7.33 (ddd, J = 8.2, 7.0, 1.2 Hz, 1 H), 7.25 (ddd, J = 8.2, 7.0, 1.3 Hz, 1 H), 6.94 (dd, J = 9.5, 1.5 Hz, 1 H), 5.40 (s, 2 H), 3.69 (s, 8 H), 2.30 (s, 4 H); ^{13}C NMR (75 MHz, acetone-d_6) δ 169.8, 134.7, 130.0, 128.9, 127.3, 123.5, 122.9, 120.6, 120.2, 118.4, 118.1, 111.5, 95.3, 52.8, 49.2, 18.2; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{18}H_{17}NO_4$) 312.1230, found 312.1234.

*Dimethyl 2-(7-Methoxypyrido[1,2-a]indol-10-yl)malonate (**16**).* The product was isolated as a yellow oil (67.1 mg, 41%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88−7.76 (m, 3 H), 7.54 (d, J = 10.0 Hz, 1 H), 7.37 (ddd, J = 8.0, 6.9, 0.8 Hz, 1 H), 7.29 (ddd, J = 8.0, 6.9, 1.0 Hz, 1 H), 6.86 (dd, J = 9.9, 2.1 Hz, 1 H), 5.24 (s, 1 H), 3.88 (s, 3 H), 3.75 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.3, 146.9, 132.6, 129.7, 128.0, 122.7, 120.2, 119.8, 119.4, 118.7, 110.3, 105.4, 94.3, 56.4, 52.9, 48.9; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{18}H_{17}NO_5$) 328.1179, found 328.1176.

*Diethyl 2-(7-Fluoropyrido[1,2-a]indol-10-yl)malonate (**18**).* The product was isolated as a yellow oil (66.8 mg, 39%): ^{1}H NMR (400 MHz, acetone-d_6) δ 8.80 (d, J = 3.1 Hz, 1 H), 8.12 (d, J = 8.2 Hz, 1 H), 7.93 (d, J = 8.2 Hz, 1 H), 7.78 (dd, J = 10.0, 5.5 Hz, 1 H), 7.35 (m, 2 H), 7.09 (ddd, J = 10.0, 7.9, 2.1 Hz, 1 H), 5.40 (s, 1 H), 4.18 (m, 4 H), 1.20 (t, J = 7.1 Hz, 6 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 169.0, 123.6, 121.3, 120.7, 120.2, 120.1, 118.3, 116.5, 116.2, 111.9, 111.8, 111.5, 62.0, 49.6, 14.4; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{19}H_{18}FNO_4$) 344.1293, found 344.1295.

*Diethyl 2-(7-Chloropyrido[1,2-a]indol-10-yl)malonate (**20**).* The product was isolated as a yellow oil (77.0 mg, 43%): ^{1}H NMR (300 MHz, acetone-d_6) δ 8.87 (s, 1 H), 8.19 (d, J = 7.7 Hz, 1 H), 7.92 (d, J = 8.3 Hz, 1 H), 7.74 (dd, J = 9.9, 0.85 Hz, 1 H), 7.37 (m, 2 H), 7.02 (dd, J = 9.9, 1.8 Hz, 1 H), 5.39 (s, 1 H), 4.18 (m, 4 H), 1.20 (t, J = 7.1 Hz, 6 H); ^{13}C NMR (75 MHz, acetone-d_6) δ 168.9, 133.5, 130.3, 129.1, 124.5, 124.0, 123.8, 121.7, 120.6, 119.8, 116.6, 111.9, 97.8, 62.1, 49.6, 14.4; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{19}H_{18}ClNO_4$) 360.0997, found 360.1002.

*Dimethyl 2-(7-Chloropyrido[1,2-a]indol-10-yl)malonate (**22**).* The product was isolated as a yellow oil (74.4 mg, 45%): ^{1}H NMR (300 MHz, acetone-d_6) δ 8.88 (dd, J = 1.8, 0.9 Hz, 1 H), 8.20 (d, J = 7.7 Hz, 1 H), 7.90 (d, J = 8.2 Hz, 1 H), 7.72 (dd, J = 9.9, 0.9 Hz, 1 H), 7.44−7.30 (m, 2 H), 7.03 (dd, J = 9.9, 1.8 Hz, 1 H), 5.46 (s, 3 H), 3.70 (s, 6 H); ^{13}C NMR (75 MHz, acetone-d_6) δ 168.8, 132.8, 129.6, 128.4, 124.0, 123.5, 123.2, 121.1, 119.8, 118.9, 116.0, 111.2, 96.8, 52.2, 48.3; HRMS (EI) calcd for $[M + H]^+$ ($M = C_{17}H_{14}ClNO_4$) 332.0684, found 332.0688.

*Diethyl 2-(7-Bromopyrido[1,2-a]indol-10-yl)malonate (**24**).* The product was isolated as a yellow oil (94.8 mg, 47%): ^{1}H NMR (300 MHz, acetone-d_6) δ 8.95 (s, 1 H), 8.21 (d, J = 8.3 Hz, 1 H), 7.92 (d, J = 7.7 Hz, 1 H), 7.68 (dd, J = 9.8, 0.8 Hz, 1 H), 7.36 (m, 2 H),

dx.doi.org/10.1021/jo2025543 | J. Org. Chem. 2012, 77, 2743−2755

7.09 (dd, J = 9.9, 1.7 Hz, 1 H), 5.39 (s, 1 H), 4.17 (m, 4 H), 1.20 (t, J = 7.1 Hz, 6 H); ^{13}C NMR (75 MHz, acetone-d_6) δ 168.9, 133.4, 130.2, 128.9, 126.4, 126.1, 124.1, 121.7, 120.6, 119.9, 111.9, 103.0, 97.8, 62.0, 49.6, 14.4; HRMS (EI) calcd for $[M + H]^+$ (M = $C_{19}H_{18}BrNO_4$) 404.0492, found 404.0492.

*Dimethyl 2-(7-Bromopyrido[1,2-a]indol-10-yl)malonate (**26**).* The product was isolated as a yellow oil (95.4 mg, 51%): ^{1}H NMR (400 MHz, acetone-d_6) δ 8.95 (d, J = 0.7 Hz, 1 H), 8.21 (d, J = 8.4 Hz, 1 H), 7.89 (d, J = 8.1 Hz, 1 H), 7.66 (d, J = 9.8 Hz, 1 H), 7.43−7.30 (m, 2 H), 7.10 (dd, J = 9.8, 1.6 Hz, 1 H), 5.45 (s, 1 H), 3.70 (s, 7 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 169.5, 133.5, 130.2, 128.9, 126.6, 126.2, 124.2, 121.8, 120.4, 119.8, 111.9, 103.0, 97.5, 52.9, 49.0; HRMS (EI) calcd for $[M + H]^+$ (M = $C_{17}H_{15}BrNO_4$) 376.0179, found 376.0173.

*Diethyl 2-(Indolo[1,2-a]quinolin-7-yl)malonate (**28**).* The product was isolated as a yellow oil (51.8 mg, 32%): ^{1}H NMR (400 MHz, acetone-d_6) δ 8.76 (d, J = 8.5 Hz, 1 H), 8.63 (d, J = 8.5 Hz, 1 H), 8.01 (d, J = 7.6 Hz, 1 H), 7.82 (dd, J = 7.7, 1.2 Hz, 1 H), 7.72 (t, J = 8.0 Hz, 1 H), 7.67 (d, J = 9.6 Hz, 1 H), 7.50−7.34 (m, 4 H), 5.44 (s, 1 H), 4.27−4.11 (m, 1 H), 1.21 (t, J = 7.1 Hz, 1 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 169.1, 137.4, 135.5, 133.5, 130.2, 130.2, 130.0, 125.4, 125.1, 124.3, 123.2, 122.8, 121.2, 118.5, 116.6, 115.3, 101.6, 62.2, 49.5, 14.5; HRMS (EI) calcd for $[M + H]^+$ (M = $C_{23}H_{21}NO_4$) 376.1543, found 376.1551.

*Methyl 3-Oxo-2-(pyrido[1,2-a]indol-10-yl)butanoate (**33**).* The product was isolated as a yellow oil (171.1 mg, 61%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.41 (s, 1 H), 8.34 (d, J = 7.1 Hz, 1 H), 7.91 (d, J = 8.3 Hz, 1 H), 7.58 (d, J = 8.0 Hz, 1 H), 7.40 (t, J = 7.5 Hz, 1 H), 7.31 (t, J = 7.6 Hz, 1 H), 7.20 (d, J = 9.3 Hz, 1 H), 6.92 (dd, J = 8.8, 6.8 Hz, 1 H), 6.51 (t, J = 6.7 Hz, 1 H), 3.65 (s, 3 H), 1.84 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 174.2, 134.7, 129.2, 124.6, 123.1, 122.5, 119.9, 119.5, 118.1, 110.5, 107.9, 97.8, 93.9, 52.0, 20.1; HRMS (EI) calcd for $[M + H]^+$ (M = $C_{17}H_{15}NO_3$) 282.1125, found 282.1130.

*2-(Pyrido[1,2-a]indol-10-yl)acetonitrile (**35**).* To a flame-dried 6-dram vial containing a stir bar, compound **35** (0.5 mmol), and the benzyne precursor (1.5 equiv) was added anhydrous MeCN (5 mL), followed by CsF (2.25 equiv). The mixture was then allowed to stir for 24 h at 65 °C before it was poured into a separatory funnel containing a saturated aq solution of NH_4Cl (20 mL) and ethyl acetate (20 mL). The organic layer was removed, and the aqueous layer was extracted again with ethyl acetate (2 × 20 mL). The combined organic layers were dried with Na_2SO_4 and concentrated in vacuo to yield a crude mixture, which was purified by column chromatography using gradient solvent combinations of hexanes and dichloromethane. The reaction afforded 9.1 mg (9%) product **35** as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 7.1 Hz, 1 H), 7.91 (d, J = 8.3 Hz, 1 H), 7.83 (d, J = 8.1 Hz, 1 H), 7.48 (m, 2 H), 7.36 (t, J = 7.6 Hz, 1 H), 7.03 (dd, J = 9.3, 6.4 Hz, 1 H), 6.56 (t, J = 6.7 Hz, 1 H), 4.08 (s, 3 H), 1.56 (s, 8 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5, 134.1, 127.8, 124.8, 123.7, 123.4, 120.6, 118.2, 117.9, 116.5, 110.7, 108.3, 90.6, 13.1; HRMS (EI) calcd for $[M + H]^+$ (M = $C_{14}H_{10}N_2$) 207.0917, found 207.0920.

*Diethyl 2-(2,3-Dimethoxypyrido[1,2-a]indol-10-yl)malonate (**39**).* The product was isolated as a yellow oil (129.9 mg, 64%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, J = 8.0 Hz, 1 H), 7.69 (s, 1 H), 7.60 (d, J = 8.0 Hz, 1 H), 7.38 (s, 1 H), 6.89 (t, J = 8.0 Hz, 1 H), 6.53 (t, J = 8.0 Hz, 1 H), 5.33 (s, 1 H), 4.18 (q, J = 8.0 Hz, 4 H), 1.21 (t, J = 6.0 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 149.0, 147.5, 134.4, 125.0, 124.2, 122.7, 121.2, 118.1, 108.5, 101.4, 95.5, 94.7, 61.8, 56.5, 56.2, 49.7, 14.5; HRMS (EI) calcd for $[M + Na]^+$ (M = $C_{21}H_{22}NO_6$) 408.1418, found 408.1420.

*Diethyl 2-(Benzo[e]pyrido[1,2-a]indol-12-yl)malonate (**41**).* The product was isolated as a yellow oil (124.1 mg, 66%): ^{1}H NMR (400 MHz, acetone-d_6) δ 8.82 (d, J = 7.1 Hz, 1 H), 8.73 (d, J = 8.3 Hz, 1 H), 8.23 (d, J = 9.0 Hz, 1 H), 8.04 (d, J = 7.8 Hz, 1 H), 7.72 (dd, J = 13.0, 9.2 Hz, 2 H), 7.62 (t, J = 7.8 Hz, 1 H), 7.54 (t, J = 7.4 Hz, 1 H), 7.09 (ddd, J = 9.3, 6.4, 0.8 Hz, 1 H), 6.79 (t, J = 6.6 Hz, 1 H), 5.95 (s, 1 H), 4.21 (q, J = 7.1 Hz, 1 H), 1.18 (t, J = 7.1 Hz, 1 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 169.5, 135.0, 132.8, 129.9, 128.9, 126.6, 126.4, 125.5, 124.8, 123.5, 122.6, 122.2, 119.0, 112.3, 110.6, 99.0, 62.2, 51.1, 14.5; HRMS (EI) calcd for $[M + H]^+$ (M = $C_{23}H_{21}NO_4$) 376.1543, found 376.1554.

*Diethyl 2-(1-Methoxypyrido[1,2-a]indol-10-yl)malonate (**43**).* The product was isolated as a yellow oil (133.4 mg, 75%): ^{1}H NMR (400 MHz, acetone-d_6) δ 8.59 (d, J = 7.1 Hz, 1 H), 7.68 (d, J = 8.4 Hz, 1 H), 7.58 (d, J = 9.4 Hz, 1 H), 7.19 (t, J = 8.1 Hz, 1 H), 6.97 (ddd, J = 9.4, 6.3, 0.8 Hz, 1 H), 6.83 (d, J = 7.7 Hz, 1 H), 6.61 (dd, J = 9.9, 3.6 Hz, 1 H), 6.06 (s, 1 H), 4.18 (qd, J = 7.1, 1.4 Hz, 1 H), 3.99 (s, 1 H), 1.20 (t, J = 7.1 Hz, 1 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 169.8, 155.1, 134.6, 130.9, 125.6, 122.7, 121.5, 120.1, 119.8, 109.4, 104.7, 103.6, 96.0, 61.9, 55.9, 50.5, 14.5; HRMS (EI) calcd for $[M + H]^+$ (M = $C_{20}H_{21}NO_5$) 356.1492, found 356.1492.

*Dimethyl 2-(1,3-Dimethoxypyrido[1,2-a]indol-10-yl)malonate (**45**).* The product was isolated as a yellow oil (130.8 mg, 73%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 7.1 Hz, 1 H), 7.50 (d, J = 9.4 Hz, 1 H), 6.93−6.74 (m, 2 H), 6.56−6.37 (m, 2 H), 6.00 (s, 1 H), 3.96 (s, 3 H), 3.91 (s, 3 H), 3.75 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 156.1, 154.8, 133.2, 129.8, 123.6, 120.8, 119.2, 113.9, 108.6, 95.3, 94.5, 85.3, 55.9, 55.7, 52.8, 49.2, 49.2; HRMS (EI) calcd for $[M + H]^+$ (M = $C_{19}H_{19}NO_6$) 358.1285, found 358.1289.

General Procedure for Preparation of the Pyridin-2-ylmethanimines. The commercially available aldehyde (2.34 mmol) was added to a 5−10 mL round-bottom flask equipped with a magnetic stir bar. The flask was sealed and purged with argon, and water (0.6 mL) was added. To the resulting suspension or solution was added the corresponding amine (1−3 equiv), and the mixture was stirred at room temperature overnight. Then, the reaction mixture was subjected to an aqueous work-up using ethyl acetate or diethyl ether as the organic phase. The organic layer was separated and dried over anhydrous $MgSO_4$, and the solvent was removed to afford the pure imine.

*tert-Butyl(pyridin-2-yl-methylene)amine (**46**).*[28] This compound was obtained as a yellow liquid (322.2 mg, 85%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 4.0 Hz, 1 H), 8.36 (s, 1 H), 8.02 (d, J = 7.9 Hz, 1 H), 7.73 (t, J = 7.7 Hz, 1 H), 7.29 (ddd, J = 7.5, 4.9, 1.2 Hz, 1 H), 1.31 (s, 9 H).

*Isopropyl(pyridin-2-yl-methylene)amine (**49**).*[29] This compound was obtained as a brown liquid (250.2 mg, 72%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 4.5 Hz, 1 H), 8.38 (s, 1 H), 7.98 (d, J = 7.9 Hz, 1 H), 7.72 (t, J = 7.7 Hz, 1 H), 7.34−7.25 (m, 1 H), 3.70−3.57 (m, 1 H), 1.27 (d, J = 6.3 Hz, 6 H).

*Cyclohexyl(pyridin-2-yl-methylene)amine (**51**).*[30] This compound was obtained as a brown liquid (440.1 mg, 99%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (d, J = 4.9 Hz, 1 H), 8.39 (s, 1 H), 7.98 (d, J = 7.9 Hz, 1 H), 7.72 (t, J = 6.8 Hz, 1 H), 7.29 (ddd, J = 7.4, 4.9, 1.2 Hz, 1 H), 3.29 (tt, J = 10.3, 4.0 Hz, 1 H), 1.91−1.49 (m, 7 H), 1.46−1.14 (m, 3 H).

*Adamantyl(pyridin-2-yl-methylene)amine (**53**).* This compound was obtained as a yellow solid (516.1 mg, 92%): mp 40−42 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, J = 3.1 Hz, 1 H), 8.34 (s, 1 H), 8.01 (d, J = 6.9 Hz, 1 H), 7.71 (t, J = 7.1 Hz, 1 H), 7.32−7.23 (m, 1 H), 2.16 (s, 3 H), 1.82 (s, 6 H), 1.71 (q, J = 12.5 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.4, 155.8, 149.4, 136.7, 124.5, 121.1, 58.3, 43.2, 36.7, 29.7; HRMS (EI) calcd for $C_{16}H_{20}N_2$ 241.1699, found 241.1700.

*Allyl(pyridin-2-yl-methylene)amine (**55**).*[31] This compound was obtained as a dark brown oil (270.4 mg, 79%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.65 (d, J = 4.8 Hz, 1 H), 8.40 (s, 1 H), 8.18−7.88 (m, 1H), 7.75 (t, J = 7.7 Hz, 1 H), 7.45−7.28 (m, 1 H), 6.24−5.95 (m, 1H), 5.37−5.04 (m, 2 H), 4.32 (dd, J = 5.8, 1.4 Hz, 2 H).

*Propargyl(pyridin-2-yl-methylene)amine (**57**).* This compound was obtained as a brown liquid (262.3 mg, 78%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, J = 1.7 Hz, 1 H), 8.66 (d, J = 3.8 Hz, 1 H), 7.98 (d, J = 7.9 Hz, 1 H), 7.75 (t, J = 6.9 Hz, 1 H), 7.37−7.29 (m, 1 H), 4.64−4.51 (m, 2 H), 2.55 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 154.4, 149.7, 136.8, 125.2, 121.7, 78.5, 76.4, 47.3; HRMS (EI) calcd for $C_9H_8N_2$ 145.0760, found 145.0761.

*1-(Benzo[1,3]dioxol-5-yl)-N-(pyridin-2-yl-methylene)-methanamine (**58**).* This compound was obtained as a pale yellow solid (505.8 mg, 90%): mp 75−77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 4.8 Hz, 1 H), 8.43 (s, 1 H), 8.03 (d, J = 7.9 Hz, 1 H), 7.72

dx.doi.org/10.1021/jo2025543 | J. Org. Chem. 2012, 77, 2743−2755

(t, J = 7.7 Hz, 1 H), 7.35−7.26 (m, 1 H), 6.83 (s, 1 H), 6.78 (s, 2 H), 5.92 (s, 2 H), 4.76 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 154.6, 149.5, 147.9, 146.8, 136.7, 132.6, 124.9, 121.5, 121.5, 108.9, 108.9, 108.4, 101.1, 101.1, 101.0, 64.8; HRMS (EI) calcd for $C_{14}H_{12}N_2O_2$ 241.0972, found 241.0978.

*N-(Pyridin-2-ylmethylene)-2-(thiophen-2-yl)ethanamine (**60**).* This compound was obtained as a yellow oil (409.3 mg, 87%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64 (ddd, J = 4.8, 1.6, 0.9 Hz, 1 H), 8.33 (s, 1 H), 8.00 (d, J = 7.9 Hz, 1 H), 7.75 (td, J = 7.8, 1.7 Hz, 1 H), 7.32 (ddd, J = 7.4, 4.8, 1.2 Hz, 1 H), 7.13 (dd, J = 5.1, 1.2 Hz, 1 H), 6.92 (dd, J = 5.1, 3.4 Hz, 1 H), 6.85 (dd, J = 3.4, 0.9 Hz, 1 H), 3.95 (td, J = 7.1, 1.3 Hz, 2 H), 3.27 (t, J = 7.1 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 154.6, 149.6, 142.3, 136.8, 131.7, 126.9, 125.4, 125.0, 123.9, 121.6, 62.8, 31.5; HRMS (EI) calcd for $C_{12}H_{12}N_2S$ 217.0794, found 217.0797.

*(E)-1-[3-(Pyridin-2-ylmethyleneamino)propyl]pyrrolidin-2-one (**62**).* This compound was obtained as a yellow oil (226.5 mg, 41%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (d, J = 3.8 Hz, 1 H), 8.34 (s, 1 H), 7.90 (d, J = 7.9 Hz, 1 H), 7.70 (ddt, J = 9.4, 7.7, 1.8 Hz, 1 H), 7.32−7.22 (m, 1H), 3.64 (t, J = 6.9 Hz, 2 H), 3.36 (q, J = 6.8 Hz, 4 H), 2.31 (t, J = 8.1 Hz, 2 H), 2.02−1.86 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.1, 162.5, 154.4, 149.6, 136.7, 124.9, 121.6, 59.0, 47.3, 40.8, 31.2, 28.5, 18.0; HRMS (EI) calcd for $C_{13}H_{18}N_3O$ 232.1444, found 232.1447.

*(N^1E,N^2E)-N^1,N^2-Bis(pyridin-2-ylmethylene)ethane-1,2-diamine (**64**).* This compound was obtained as a yellow solid (298.9 mg, 54%): mp 61−63 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 4.1 Hz, 2 H), 8.40 (s, 2 H), 7.96 (d, J = 7.9 Hz, 2 H), 7.71 (td, J = 7.7, 1.8 Hz, 2 H), 7.28 (ddd, J = 7.5, 4.9, 1.3 Hz, 2 H), 4.05 (s, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 154.5, 149.6, 136.7, 124.9, 121.5, 61.5; HRMS (EI) calcd for $C_{14}H_{15}N_4$ 239.1291, found 239.1297.

*tert-Butyl-(5-bromopyridin-2-ylmethylene)amine (**66**).* This compound was obtained as a brown solid (545.2 mg, 97%): mp 35−37 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, J = 1.6 Hz, 1 H), 8.29 (s, 1 H), 7.93 (d, J = 8.4 Hz, 1 H), 7.84 (dd, J = 8.5, 1.8 Hz, 1 H), 1.30 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.5, 154.2, 150.5, 139.4, 122.3, 121.9, 58.3, 29.7; HRMS (EI) calcd for $C_{10}H_{13}BrN_2$ 241.0335, found 241.0336.

*tert-Butyl-(5-fluoropyridin-2-ylmethylene)amine (**68**).* This compound was obtained as a yellow oil (193.8 mg, 46%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.45 (d, J = 2.8 Hz, 1 H), 8.32 (s, 1 H), 8.05 (dd, J = 8.8, 4.8 Hz, 1 H), 7.43 (td, J = 8.2, 2.6 Hz, 1 H), 1.29 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2 ($^1J_{CF}$ 257 Hz), 155.2, 152.1 ($^3J_{CF}$ 4 Hz), 137.5 ($^2J_{CF}$ 24 Hz), 123.6 ($^2J_{CF}$ 19 Hz), 122.3 ($^3J_{CF}$ 4 Hz), 58.0, 29.8; HRMS (EI) calcd for $C_{10}H_{13}FN_2$ 181.1136, found 181.1137.

*tert-Butyl-(6-bromopyridin-2-ylmethylene)amine (**70**).* This compound was obtained as colorless crystals (515.2 mg, 91%): mp 50−52 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (s, 1 H), 8.00 (dd, J = 7.6, 0.9 Hz, 1 H), 7.57 (t, J = 7.5 Hz, 1 H), 7.46 (dd, J = 7.8, 0.9 Hz, 1 H), 1.27 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 155.4, 141.4, 139.0, 128.9, 119.5, 58.4, 29.7; HRMS (EI) calcd for $C_{10}H_{13}BrN_2$ 241.0355, found 241.0339.

*tert-Butyl[6-(4-methoxyphenyl)pyridin-2-ylmethylene]amine (**71**).* This compound was obtained as a cream colored solid (305.2 mg, 97%): mp 81−83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1 H), 8.06−7.92 (m, 3 H), 7.73 (t, J = 7.7 Hz, 1 H), 7.64 (d, J = 7.8 Hz, 1 H), 7.00 (d, J = 8.6 Hz, 2 H), 3.85 (s, 3 H), 1.35 (d, J = 2.5 Hz, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 157.4, 156.7, 155.5, 137.2, 131.9, 128.3, 120.6, 118.3, 114.3, 57.9, 55.5, 29.8; HRMS (EI) calcd for $C_{17}H_{21}N_2O$ 269.1648, found 269.1653.

*tert-Butyl(quinolin-2-ylmethylene)amine (**72**).* This compound was obtained as a yellow solid (417.8 mg, 84%): mp 54−56 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1 H), 8.20 (q, J = 8.7 Hz, 2 H), 8.12 (d, J = 8.4 Hz, 1 H), 7.84 (d, J = 8.1 Hz, 1 H), 7.73 (t, J = 7.7 Hz, 1 H), 7.56 (t, J = 7.5 Hz, 1 H), 1.36 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 155.8, 147.8, 136.5, 129.8, 129.5, 128.8, 127.8, 127.2, 118.4, 58.2, 29.8; HRMS (EI) calcd for $C_{14}H_{16}N_2$ 213.1386, found 213.1391.

*tert-Butyl(thiazol-2-ylmethylene)amine (**74**).* This compound was obtained as a pale yellow liquid (198.3 mg, 69%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1 H), 7.87 (d, J = 2.8 Hz, 1 H), 7.35 (d, J = 3.1 Hz, 1 H), 1.28 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9, 143.9, 123.8, 121.2, 58.5, 29.6; HRMS (EI) calcd for $C_8H_{12}N_2S$ 169.0794, found 169.0795.

(E)-4-Methoxy-N-(pyridin-2-ylmethylene)aniline (76).[32] This compound was obtained as a yellow oil (441.2 mg, 89%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, J = 5.0 Hz, 1 H), 8.63 (s, 1 H), 8.19 (d, J = 7.8 Hz, 1 H), 7.80 (td, J = 7.8, 1.8 Hz, 1 H), 7.34 (d, J = 8.7 Hz, 3 H), 6.95 (d, J = 8.8 Hz, 2 H), 3.84 (s, 3 H).

General Procedure for Preparation of the *N*-Methyl-*N*-phenylpyrido[1,2-*a*]indol-10-amines. To a dry 4-dram vial equipped with a magnetic stir bar and screw cap, CsF (228 mg., 1.5 mmol, 6 equiv) was added under an inert atmosphere of nitrogen. Then, the corresponding imine (0.25 mmol), THF (5 mL), and the aryne precursor (0.75 mmol, 3 equiv) were added, and the vial was tightly sealed. The reaction mixture was vigorously stirred at 100 °C for 16 h. After cooling, the reaction mixture was diluted with ethyl acetate, filtered, and concentrated under reduced pressure. The crude reaction mixture was then purified by column chromatography using hexanes or ethyl acetate/hexane mixtures with the addition of 1% triethylamine as the eluent to afford pure product.

*N-(tert-Butyl)-N-phenylpyrido[1,2-a]indol-10-amine (**48**).* This compound was obtained a yellow oil (56.1 mg, 72%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 (d, J = 7.1 Hz, 1 H), 7.83 (dd, J = 10.4, 8.2 Hz, 2 H), 7.48 (dt, J = 9.4, 1.2 Hz, 1 H), 7.40−7.34 (m, 1 H), 7.26 (ddd, J = 8.1, 7.0, 1.2 Hz, 2 H), 6.80 (ddd, J = 9.4, 6.3, 1.0 Hz, 1 H), 6.38 (ddd, J = 7.4, 6.4, 1.2 Hz, 1 H), 1.26 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.5, 134.5, 128.7, 128.3, 127.9, 124.3, 123.1, 122.4, 119.9, 119.4, 119.0, 117.6, 117.8, 112.6, 110.4, 107.9, 57.6, 30.4; HRMS (EI) calcd for $C_{22}H_{22}N_2$ 314.1625, found 314.1633.

*N-(Isopropyl)-N-phenylpyrido[1,2-a]indol-10-amine (**50**).* This compound was obtained as a yellow solid (49.9 mg, 66%): mp 129−132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 7.0 Hz, 1 H), 7.94 (d, J = 7.3 Hz, 1 H), 7.60 (d, J = 7.9 Hz, 1 H), 7.35−7.29 (m, 1 H), 7.11 (t, J = 7.8 Hz, 1 H), 6.88−6.82 (m, 1 H), 6.64 (dd, J = 18.4, 7.8 Hz, 1 H), 6.50 (t, J = 6.6 Hz, 1 H), 4.63−4.46 (m, 1 H), 1.25 (d, J = 6.5 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 134.8, 129.2, 128.4, 128.3, 124.4, 123.0, 122.4, 120.0, 119.5, 117.8, 116.4, 113.2, 110.4, 108.1, 107.0, 49.7, 21.5; HRMS (EI) calcd for $C_{21}H_{20}N_2$ 301.1699, found 301.1699.

*N-Cyclohexyl-N-phenylpyrido[1,2-a]indol-10-amine (**52**).* This compound was obtained as a yellow oil (61.1 mg, 75%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 7.0 Hz, 1 H), 7.94 (d, J = 7.1 Hz, 1 H), 7.62 (d, J = 8.1 Hz, 1 H), 7.32 (d, J = 7.6 Hz, 3 H), 7.11 (t, J = 7.9 Hz, 2 H), 6.88−6.81 (m, 1 H), 6.65 (t, J = 7.1 Hz, 1 H), 6.60 (d, J = 8.2 Hz, 2 H), 6.50 (t, J = 6.6 Hz, 1 H), 4.08 (t, J = 11.4 Hz, 1 H), 2.21 (d, J = 12.1 Hz, 2 H), 1.76 (d, J = 13.3 Hz, 2 H), 1.58 (d, J = 16.9 Hz, 1 H), 1.44 (q, J = 13.2 Hz, 2 H), 1.34−1.07 (m, 3 H), 0.98−0.87 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 134.6, 129.2, 128.3, 128.2, 124.3, 123.0, 122.4, 120.0, 119.6, 117.9, 116.3, 113.1, 110.4, 108.1, 107.7, 58.5, 32.0, 26.3, 25.8; HRMS (EI) calcd for $C_{24}H_{24}N_2$ 341.2012, found 341.2013.

*N-Adamantyl-N-phenylpyrido[1,2-a]indol-10-amine (**54**).* This compound was obtained as a yellow solid (61.2 mg, 62%): mp 128−130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 7.0 Hz, 1 H), 7.86 (dd, J = 13.5, 8.2 Hz, 2 H), 7.49 (d, J = 9.4 Hz, 1 H), 7.38 (t, J = 7.1 Hz, 1 H), 7.32−7.23 (m, 2 H), 7.16−7.00 (m, 4 H), 6.85 (dd, J = 8.4, 6.3 Hz, 1 H), 6.74 (t, J = 6.9 Hz, 1 H), 6.44 (t, J = 6.2 Hz, 1 H), 2.19 (s, 6 H), 2.09 (s, 3 H), 1.65 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.3, 135.1, 129.5, 128.2, 127.9, 124.2, 123.0, 122.3, 119.7, 119.2, 118.1, 112.2, 110.3, 107.9, 58.1, 42.5, 36.7, 30.5. HRMS (EI) calcd for $C_{28}H_{28}N_2$ 393.2325, found 393.2324.

*N-Allyl-N-phenylpyrido[1,2-a]indol-10-amine (**56**).* This compound was obtained as an orange oil (40.2 mg, 54%) and was highly unstable in various solvents and neat. Because of the low stability, a clean ^{13}C NMR spectrum of this compound could not be obtained: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, J = 7.1 Hz, 1 H), 7.92 (d, J = 7.1 Hz, 1 H), 7.57 (d, J = 8.4 Hz, 1 H), 7.32 (d, J = 4.9 Hz, 2 H), 7.13 (t, J = 8.0 Hz, 2 H), 6.88−6.79 (m, 1 H), 6.70 (s, 3 H), 6.50 (s, 1 H), 6.12−5.97 (m, 1H), 5.31 (dd, J = 17.2, 1.7 Hz, 1 H), 5.14 (dd, J = 10.3,

dx.doi.org/10.1021/jo2025543 | J. Org. Chem. 2012, 77, 2743−2755

1.6 Hz, 1 H), 4.40 (dt, J = 5.5, 1.6 Hz, 2 H); HRMS (EI) calcd for $C_{21}H_{18}N_2$ 298.1470, found 298.1466.

*N-(Benzo[1,3]dioxol-5-ylmethyl)-N-phenylpyrido[1,2-a]indol-10-amine (**59**).* This compound was obtained as an orange oil (76.6 mg, 78%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, J = 7.1 Hz, 1 H), 7.92 (d, J = 8.3 Hz, 1 H), 7.60 (d, J = 7.3 Hz, 1 H), 7.36−7.28 (m, 2 H), 7.23 (d, J = 9.3 Hz, 1 H), 7.11 (t, J = 8.0 Hz, 2 H), 6.94 (s, 1 H), 6.89 (d, J = 8.6 Hz, 1 H), 6.83 (dd, J = 8.7, 6.8 Hz, 1 H), 6.72 (d, J = 7.9 Hz, 1 H), 6.68 (d, J = 7.9 Hz, 3 H), 6.47 (t, J = 6.7 Hz, 1 H), 5.90 (s, 2 H), 4.96 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.5, 147.9, 146.5, 133.9, 132.1, 129.1, 128.1, 125.7, 124.5, 123.1, 122.4, 120.2, 120.1, 118.7, 117.2, 113.5, 112.1, 110.6, 108.4, 108.0, 107.8, 101.1, 101.0, 101.0, 56.8; HRMS (EI) calcd for $C_{26}H_{19}N_2O_2$ 392.1519, found 392.1527.

*N-Phenyl-N-[2-(thiophen-2-yl)ethyl]pyrido[1,2-a]indol-10-amine (**61**).* This compound was obtained as an orange oil (65.2 mg, 70%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 7.1 Hz, 1 H), 7.97 (d, J = 7.0 Hz, 1 H), 7.61−7.54 (m, 1 H), 7.39−7.32 (m, 2 H), 7.25 (d, J = 8.6 Hz, 1 H), 7.18 (t, J = 8.0 Hz, 2 H), 7.12 (d, J = 5.1 Hz, 1 H), 6.95−6.90 (m, 1 H), 6.90−6.84 (m, 1 H), 6.81 (s, 1 H), 6.72 (t, J = 8.1 Hz, 3 H), 6.52 (t, J = 6.7 Hz, 1 H), 4.12−4.03 (m, 2 H), 3.31−3.20 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 141.8, 132.7, 130.5, 129.4, 128.2, 127.1, 126.2, 125.0, 124.5, 123.6, 123.2, 122.6, 120.2, 118.6, 117.0, 112.9, 110.6, 108.2, 54.1, 28.8; HRMS (EI) calcd for $C_{24}H_{20}N_2S$ 369.1420, found 369.1414.

*1-[3-(Phenyl(pyrido[1,2-a]indol-10-yl)amino)propyl]pyrrolidin-2-one (**63**).* This compound was obtained as an orange oil (57.8 mg, 60%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 7.1 Hz, 1 H), 7.94 (d, J = 7.5 Hz, 1 H), 7.54 (d, J = 6.9 Hz, 1 H), 7.32 (t, J = 6.0 Hz, 2 H), 7.25 (d, J = 9.7 Hz, 1 H), 7.13 (t, J = 7.8 Hz, 2 H), 6.87 (dd, J = 9.3, 6.4 Hz, 1 H), 6.67 (dd, J = 21.0, 7.7 Hz, 3 H), 6.50 (t, J = 6.8 Hz, 1 H), 3.31 (t, J = 7.4 Hz, 2 H), 3.81 (t, J = 7.7 Hz, 2 H), 3.22 (t, J = 7.0 Hz, 2 H), 2.33 (t, J = 8.2 Hz, 2 H), 1.92 (t, J = 7.6 Hz, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 149.3, 132.6, 129.3, 128.1, 126.2, 124.5, 123.2, 122.6, 120.2, 118.6, 117.0, 116.9, 112.9, 110.7, 110.6, 108.2, 49.7, 47.2, 40.7, 31.2, 26.4, 18.0; HRMS (EI) calcd for $C_{25}H_{26}N_3O$ 384.2070, found 384.2063.

*N^1,N^2-Diphenyl-N^1,N^2-di(pyrido[1,2-a]indol-10-yl)ethane-1,2-diamine (**65**).* This compound was obtained as a yellow solid (69.2 mg, 51%): mp 268−271 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, J = 7.1 Hz, 2 H), 7.98- 7.85 (m, 2 H), 7.60−7.45 (m, 2 H), 7.40−7.28 (m, 4 H), 7.17 (d, J = 9.2 Hz, 2 H), 6.96 (dd, J = 8.6, 7.1 Hz, 4 H), 6.80 (dd, J = 9.0, 6.6 Hz, 2 H), 6.59 (t, J = 7.3 Hz, 2 H), 6.48 (dd, J = 11.2, 7.4 Hz, 6 H), 4.15 (s, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.2, 132.6, 129.2, 128.2, 126.1, 124.5, 123.2, 122.6, 120.1, 118.4, 116.9, 112.8, 110.7, 110.6, 108.1, 50.3; HRMS (EI) calcd for $C_{38}H_{30}N_4$ 542.2465, found 542.2472.

*7-Bromo-N-(tert-butyl)-N-phenylpyrido[1,2-a]indol-10-amine (**67**).* This compound was obtained as an orange oil in a 34% yield (NMR yield based on the addition of 1,4-dimethoxybenzene as an internal standard): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1 H), 7.85 (d, J = 8.1 Hz, 1 H), 7.71 (d, J = 8.1 Hz, 1 H), 7.33 (dt, J = 18.6, 8.6 Hz, 3 H), 7.05 (t, J = 8.0 Hz, 2 H), 6.87 (t, J = 8.2 Hz, 3 H), 6.69 (t, J = 7.2 Hz, 1 H), 1.52 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.3, 132.5, 128.7, 128.4, 127.8, 125.5, 124.4, 123.5, 120.9, 119.8, 119.3, 118.7, 118.0, 114.1, 110.4, 102.5, 57.6, 30.4; HRMS (EI) calcd for $C_{22}H_{21}BrN_2$ 392.0883, found 392.0892.

*7-Fluoro-N-(tert-butyl)-N-phenylpyrido[1,2-a]indol-10-amine (**69**).* This compound was obtained as an orange solid in a 22% yield (NMR yield based on the addition of 1,4-dimethoxybenzene as an internal standard): mp 104−105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 3.3 Hz, 1 H), 7.80 (d, J = 8.0 Hz, 1 H), 7.72 (d, J = 7.7 Hz, 1 H), 7.34 (ddd, J = 24.9, 12.8, 6.3 Hz, 3 H), 7.05 (t, J = 8.0 Hz, 2 H), 6.88 (d, J = 8.1 Hz, 2 H), 6.81 (t, J = 7.9 Hz, 1 H), 6.68 (t, J = 7.3 Hz, 1 H), 1.53 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.6, 150.3, 149.4, 132.4, 128.9, 128.4, 123.0, 120.5, 120.0, 119.4, 118.9, 118.8, 118.0, 115.7, 115.4, 113.7, 110.4, 110.3, 109.9, 57.6, 30.4 (extra peaks due to ^{13}C-^{19}F coupling); HRMS (EI) calcd for $C_{22}H_{21}FN_2$ 333.1762, found 333.1754.

*N-(tert-Butyl)-N-phenylindolo[1,2-a]quinolin-7-amine (**73**).* This compound was obtained as a yellow oil (68.3 mg, 75%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 8.3 Hz, 1 H), 8.50 (d, J = 8.5 Hz, 1 H), 7.76 (d, J = 7.8 Hz, 1 H), 7.63 (t, J = 8.5 Hz, 2 H), 7.44 (t, J = 7.6 Hz, 1 H), 7.40−7.30 (m, 3 H), 7.08 (dd, J = 14.5, 8.9 Hz, 3 H), 6.90 (d, J = 8.1 Hz, 2 H), 6.69 (t, J = 7.2 Hz, 1 H), 1.59 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 137.0, 134.7, 131.7 129.8, 129.1 129.0, 128.5, 124.8 124.2, 123.0, 122.2, 119.9, 118.42, 117.8, 117.5, 116.8, 115.7, 114.5, 57.5, 30.4; HRMS (EI) calcd for $C_{26}H_{24}N_2$ 365.2012, found 365.2003.

*N-(tert-Butyl)-N-phenylthiazolo[3,2-a]indol-9-amine (**75**).* This compound was obtained as a colorless solid (21.7 mg, 27%): mp 102−103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 4.2 Hz, 1 H), 7.60 (d, J = 7.8 Hz, 2 H), 7.21 (t, J = 7.4 Hz, 1 H), 7.15 (t, J = 7.6 Hz, 1 H), 7.08 (dt, J = 16.6, 8.2 Hz, 4 H), 6.77 (t, J = 6.9 Hz, 1 H), 6.53 (d, J = 4.2 Hz, 1 H), 1.51 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 136.3, 132.2, 128.4, 128.2, 121.8, 121.5, 119.6, 119.1, 118.7, 114.9, 110.3, 108.8, 108.7, 58.4, 30.5; HRMS (EI) calcd for $C_{20}H_{20}N_2S$ 321.1420, found 321.1421.

*N-(tert-Butyl)-1-methoxy-N-(3-methoxyphenyl)pyrido[1,2-a]-indol-10-amine (**77**).* This compound was obtained as a yellow oil (75.0 mg, 80%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 7.2 Hz, 1 H), 7.48 (d, J = 8.3 Hz, 1 H), 7.27 (d, J = 10.3 Hz, 1 H), 7.20 (t, J = 8.0 Hz, 1 H), 6.92 (t, J = 8.2 Hz, 1 H), 6.80−6.69 (m, 2 H), 6.47−6.33 (m, 3H), 6.18 (dd, J = 7.8, 2.0 Hz, 1 H), 3.84 (s, 3 H), 3.66 (s, 3 H), 1.52 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 154.2, 151.4, 133.0, 129.2, 128.4, 124.0, 121.7, 120.6, 30.0, 119.9, 118.1, 111.4, 111.3, 108.4, 104.7, 103.3, 102.5, 100.4, 57.8, 55.4, 55.1; HRMS (EI) calcd for $C_{24}H_{27}N_2O_2$ 375.2067, found 375.2060.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all novel compounds, as well as NOESY and COSY data for compounds **41**, **43**, **45**, and **77**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully acknowledge the National Science Foundation and the National Institutes of Health Kansas University Center of Excellence in Chemical Methodology and Library Development (P50 GM069663) for their generous financial support. We would also like to thank Dr. Feng Shi and Anton Dubrovskiy for their help in preparing benzyne precursors.

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