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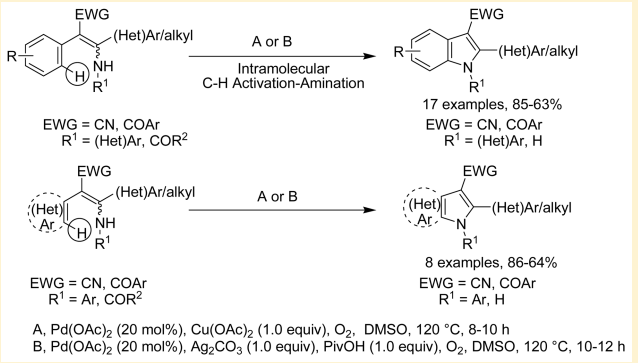
Amine Directed Pd(II)-Catalyzed C−H Activation-Intramolecular Amination of *N*-Het(aryl)/Acyl Enaminonitriles and Enaminones: An Approach towards Multisubstituted Indoles and Heterofused Pyrroles

Somaraju Yugandar, Saidulu Konda, and Hiriyakkanavar Ila*

New Chemistry Unit, Jawaharlal Nehru Centre for Advanced Scientific Research, Jakkur, Bangalore-560064, India

Supporting Information

ABSTRACT: An efficient route to multisubstituted indoles has been developed through intramolecular oxidative C−H activation-amination of readily available 2-(het)aryl-3-(het)-aryl/alkyl-3-(het)aryl/acylaminoacrylonitrile/enaminone precursors in the presence of either palladium acetate/cupric acetate catalytic system under oxygen atmosphere or palladium acetate/silver carbonate in the presence of pivalic acid as additive. The method is compatible with a diverse range of substituents on the aryl ring as well as at the 2- and 3-positions of the indole ring. The versatility of this method was further demonstrated by elaborating it for the synthesis of heterofused pyrroles such as thieno[2,3-*b*]pyrroles, thieno[3,2-*b*]pyrroles, pyrrolo[2,3-*b*]indoles, and pyrrolo[2,3-*b*]pyridines in good yields. Probable mechanisms for the formation of these indoles have been suggested.



INTRODUCTION

The indole ring system represents a key heterocyclic motif[1] that occurs ubiquitously in biologically active natural products[2] as well as in numerous therapeutic agents[3] and in optoelectronic functional materials.[4] Substituted indoles are generally known as "privileged structures" in medicinal chemistry, as they are capable of binding to many receptors with high affinity.[3] The synthesis of indole has been an important area of research for over 100 years, since the first report of Fischer indole synthesis in 1883,[5] and a variety of well-established powerful methods are now available.[5] However, lack of availability of starting materials along with functional group tolerance often limits the scope and generality of a particular indole synthesis. Consequently, the development of efficient, selective, and atom economical methods for the synthesis of indoles from readily available starting materials is highly desirable. Among the reportaire of recent methods, transition metal-catalyzed inter- and intramolecular C−C and/or C−N bond forming reactions are the most powerful and attractive routes for the synthesis of indoles.[5,6] Among the various transition metal-based sources, the palladium compounds have been one of the most widely used catalysts, and, arguably, the palladium-catalyzed intramolecular cyclization of 2-alkynylanilines[6−8] as well as intermolecular coupling of 2-haloanilines with terminal/internal alkynes[9] are among the most frequently used recent methods for the synthesis of 2,3-substituted indoles.[10] Recently, copper-catalyzed intra- and intermolecular amination and C−C bond formation reactions of substituted aryl halides or pseudohalides have also been employed for the synthesis of substituted indoles.[11]

More recently, an increasing number of examples have appeared in the literature involving transition metal-catalyzed oxidative C−H functionalization as a fundamental step for the construction of various heterocycles.[12] This mode of reactivity is particularly attractive because the necessity to install an activating group functionality such as halide in the starting material is eliminated, thus opening a much wider range of more readily accessible precursors.[12] Various catalytic systems based on rhodium, ruthenium, and palladium including copper and iron[12d,f,13] have been developed to effect oxidative C−C and C−heteroatom bond formation.[12] While most of the earlier reported examples involve intermolecular C−H functionalization,[14] only recently, following Buchwald's pioneering report of carbazole synthesis via Pd(II)-catalyzed intramolecular C−H activation/C−N bond formation,[15] has attention been turned to use of these C−H functionalization reactions for the construction of various heterocyclic ring systems.[12c,d,16] Recently, several examples of intramolecular C−H functionalization C−heteroatom bond formation leading to a wide range of benzoheterocycles such as carbazoles,[15,17a,d] indazoles,[18] benzimidazoles,[13a,19] benzoxazoles,[20] benzotriazole,[21] benzo-

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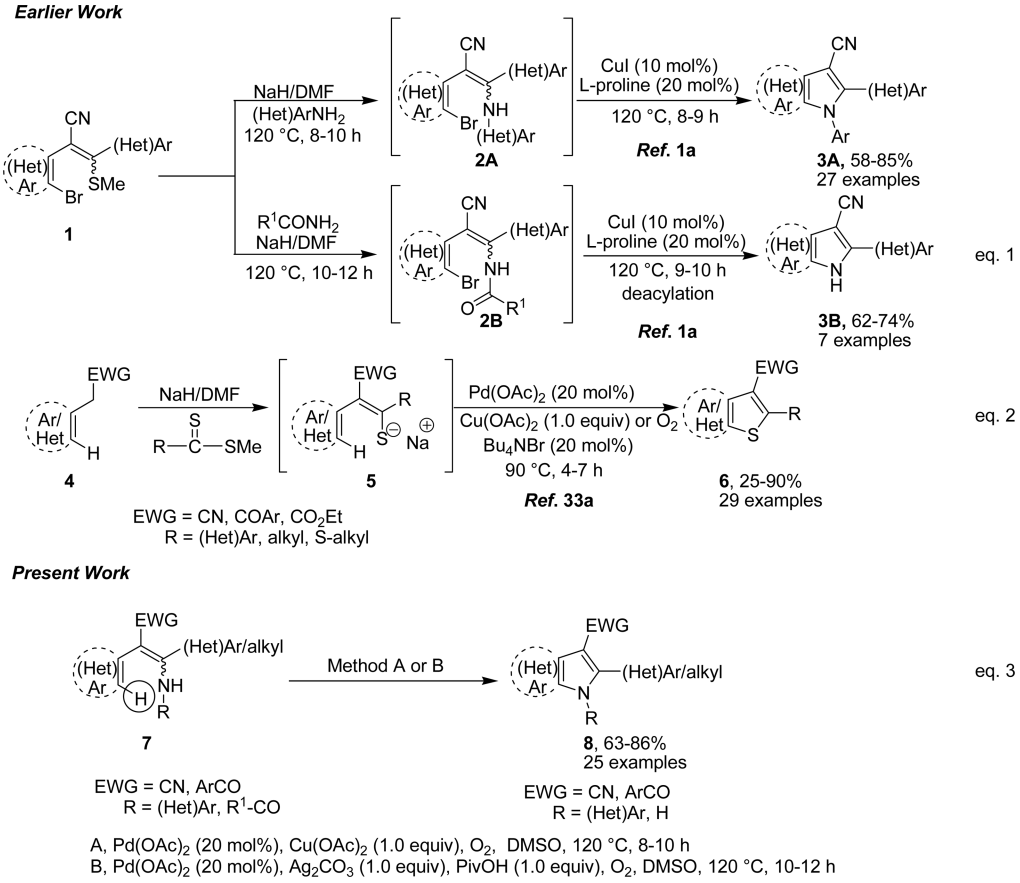
Scheme 1. Synthesis of Substituted Indoles and Benzo[*b*]thiophenes



thiazole,[22] benzothiophene,[23] dibenzofurans,[24] and 2-quinolones[16d] have appeared in the literature.

These methods have also been applied to the indole synthesis, and intramolecular cross dehydrogenative coupling (CDC) has become a promising protocol for the synthesis of indoles from enamines and imines involving C3−C3a bond formation.[25] Thus, Glorius has reported in 2008 an efficient synthesis of indoles via Pd(II)-catalyzed oxidative cyclization of *N*-arylenaminones/esters generated in situ by condensation of simple anilines with 1,3-dicarbonyl compounds.[26] Subsequent to this work, the research groups of Jiao,[27] Cacchi,[13b] Fagnou,[28] Yoshikai,[29a] Zhao,[29b] Liang,[13c] and others[25e,i,29c,g] have explored the use of different metals, oxidants, and reaction conditions to improve the substrate scope. However, despite significant progress in indole synthesis through cross-dehydrative coupling involving C3−C3a bond formation, a practical synthetic method for substituted indoles via catalytic intramolecular CH-activation/C−N bond formation involving construction of N1−C1a bond, parallel to carbazole synthesis, is yet to be realized.[12c,17] There are a few reports in the literature describing indole synthesis via intramolecular C−H-functionalization/C−N bond formation. Thus, Inamoto and co-workers have recently described the synthesis of a few 2-unsubstituted-3-arylindoles via palladium-catalyzed intramolecular oxidative C−H amination of 1,1-bisaryl-2-*N*-tosylenamines.[30] However, the method suffers from lack of generality, low yields, as well as regioselectivity problem, when two aryl groups are unsymmetrically substituted. In another report, Zhao and co-workers have described the synthesis of *N*-substituted-2-methyl-3-cyanoindoles via phenyliodine bis(trifluoroacetate) (PIFA)-mediated intramolecular oxidative cyclization of 2-aryl-3-aryl/alkylamino-2-alkenenitriles.[31,32] However, use of a stoichiometric amount of PIFA and rather a narrow functional group scope (synthesis of only 2-methylindoles and one with 2-(*n*-propyl) group has been reported) are the main disadvantages. Besides, the method suffers from lack of regioselectivity with *m*-substituted (2-aryl)enaminonitriles yielding a mixture of 5- and 7-substituted indoles. Hartwig has recently reported[32a] a complementary strategy for the synthesis of indoles via intramolecular C−H amination of oxime esters involving oxidative addition of Pd(0) species in the N−O bond, which eliminates the need for external oxidant.[32b] However, the generality and scope of the reaction are limited only to a few 3-aryl-2-methylindoles in moderate to good yields along with a regioselectivity problem in some *m*-substituted aryl derivatives.

During the course of our study toward the development of new synthetic methods for biologically important heterocycles utilizing organosulfur intermediates,[33] we have recently reported a novel high yielding route to substituted 1-*N*-(het)aryl/NH-2-(het)aryl/alkyl-3-cyanoindoles **3A** and the related pyrrolofused heterocycles **3B** involving sequential one-pot, base-mediated, and copper-catalyzed inter- and intramolecular amination of 2-[2-bromo(het)aryl]-3-(het)aryl/alkyl-3-(methylthio)acrylonitriles **1** via in situ generated enaminonitrile precursors **2** (Scheme 1, eq 1).[1a] Recently, we have also described an efficient one-pot synthesis of highly functionalized benzo[*b*]thiophenes and their heterofused analogues **6** through palladium-catalyzed intramolecular oxidative C−H functionalization-arylthiolation of in situ generated thioalates **5** from active methylene precursors **4** and dithioesters (Scheme 1, eq

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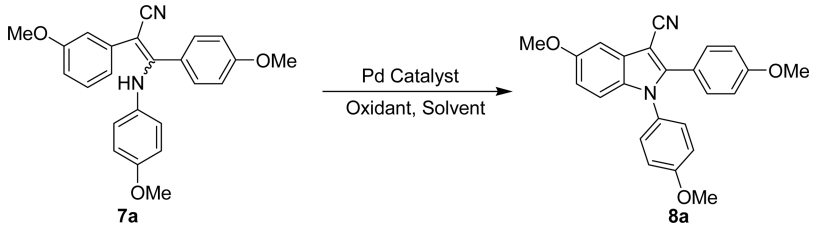
Table 1. Optimization of Reaction Conditions for the Synthesis of Indole 8a from 7a[a]



entry	Pd catalyst (mol %)	oxidant (equiv)	gas, atm	time, h/temp, °C	solvent	% yield **8a**
1	$Pd(OAc)_2$ (20 mol %)	$Cu(OAc)_2$ (1.0)	air	20 h, 120 °C	DMSO	61
2	$Pd(OAc)_2$ (20 mol %)	$Cu(OAc)_2$ (1.0)	O_2	8 h, 120 °C	DMSO	75
3	$PdCl_2$ (20 mol %)	$Cu(OAc)_2$ (1.0)	O_2	12 h, 120 °C	DMSO	60
4	$PdCl_2(PPh_3)_2$ (20 mol %)	$Cu(OAc)_2$ (1.0)	O_2	12 h, 120 °C	DMSO	66
5	$PdCl_2(CH_3CN)_2$ (20 mol %)	$Cu(OAc)_2$ (1.0)	O_2	10 h, 120 °C	DMSO	55
6		$Cu(OAc)_2$ (1.0)	O_2	20 h, 120 °C	DMSO	NR
7	$Pd(OAc)_2$ (20 mol %)	$PhI(OAc)_2$ (1.0)	O_2	15 h, 120 °C	DMSO	48
8	$Pd(OAc)_2$ (20 mol %)	$KHSO_5$ (1.0)	O_2	10 h, 120 °C	DMSO	69
9	$Pd(OAc)_2$ (20 mol %)	AgOAc (1.0)	O_2	24 h, 120 °C	DMSO	62
10	$Pd(OAc)_2$ (20 mol %)	Oxone (1.0)	O_2	24 h, 120 °C	DMSO	trace
11	$Pd(OAc)_2$ (20 mol %)	benzoquinone	O_2	24 h, 120 °C	DMSO	trace
12	$Pd(OAc)_2$ (20 mol %)	$Cu(OAc)_2$ (1.0)	O_2	8 h, 120 °C	DMF	64
13	$Pd(OAc)_2$ (20 mol %)	$Cu(OAc)_2$ (1.0)	O_2	26 h, 110 °C	toluene	51
14	$Pd(OAc)_2$ (10 mol %)	$Cu(OAc)_2$ (1.0)	O_2	14 h, 120 °C	DMSO	65
15	$Pd(OAc)_2$ (20 mol %)	$Cu(OAc)_2{:}H_2O$ (1.0)	O_2	8 h, 120 °C	DMSO	65
16	$Pd(OAc)_2$ (20 mol %)	$Cu(OAc)_2{:}H_2O$ (1.0)	O_2	8 h, 120 °C	DMF	63
17	$Pd(OAc)_2$ (20 mol %)	$Cu(OAc)_2$ (0.5)	O_2	15 h, 120 °C	DMSO	68
18	$Pd(OAc)_2$ (20 mol %)		O_2	12 h, 120 °C	DMSO	65
19	$Pd(OAc)_2$ (20 mol %)	$Cu(OAc)_2$ (1.0), Bu_4NBr (1.0)	O_2	6 h, 120 °C	DMSO	70
20	$Pd(OAc)_2$ (20 mol %)	$Cu(OAc)_2$ (1.0), Na_2CO_3 (2.0), PivOH (1.0)	O_2	15 h, 110 °C	DMSO	58
21	$Pd(OAc)_2$ (20 mol %)	Ag_2CO_3 (1.0), PivOH (1.0)	O_2	10 h, 120 °C	DMSO	81
22	$Pd(OAc)_2$ (20 mol %)	Ag_2CO_3 (0.5), PivOH (0.5)	O_2	17 h, 120 °C	DMSO	67

[a]Reactions were performed with **7a** (0.3 mmol) in 2 mL of solvent.

2).[33a] In continuation of these studies, we now disclose an efficient route to 1-*N*-aryl/NH-2-(het)aryl/alkyl-3-cyano/aroylindoles and their heterofused analogues **8** by palladium-catalyzed intramolecular oxidative C−H functionalization-amination of readily available 2,3-(het)aryl-3-*N*-aryl/acylenaminonitriles and enaminones **7** (Scheme 1, eq 3).[1a] The key feature of this protocol is that it utilizes an aminoaryl group as directing group as well as nucleophilic coupling partner in this intramolecular C−H heterofunctionalization process. Besides, the reaction displays high regioselectivity and good functional group tolerance at various positions of indole skeleton along with high yields in this cyclization reaction.

RESULTS AND DISCUSSION

The desired *N*-arylenaminonitriles **7a−j** and enaminones **7m−n** were prepared in good yields by nucleophilic displacement on the corresponding *β*-(methylthio)acrylonitriles **9a−j**[1a] or the corresponding enones **9m−n** by the appropriate arylamines in the presence of sodium hydride or butyl lithium as the base, respectively (Table 2, see Experimental Section). The corresponding 3-alkyl- and *N*-benzylenaminonitriles **7k−l** and **7o**, on the other hand, were obtained by direct condensation of the respective *α*-(thioacyl) (or acyl)arylacetonitriles **9k−l** and **9o** with appropriate amines in the presence of acetic acid in ethanol (Table 2, see Experimental Section).

We began our investigation on the proposed palladium-catalyzed intramolecular C−H functionalization-amination, using enaminonitrile **7a** as the test substrate for optimizing the reaction conditions, leading to the indole **8a** (Table 1). Our studies revealed that the reaction of **7a** with 20 mol % of $Pd(OAc)_2$, $Cu(OAc)_2$ (1 equiv), in DMSO in air afforded the indole **8a** in 61% yield (Table 1, entry 1). On the other hand, **8a** was obtained in 75% yield, when the same reaction was conducted under the atmosphere of oxygen (entry 2). Among all of the palladium complexes examined, $Pd(OAc)_2$ was found to be most effective catalyst for this transformation (entries 3−5), and in the absence of $Pd(OAc)_2$, formation of indole **8a** was not observed (entry 6), thus demonstrating that the role of $Cu(OAc)_2$ was mainly to reoxidize the reduced palladium species. Similarly, the other reoxidants such as $PhI(OAc)_2$, $KHSO_5$, AgOAc, oxone, and benzoquinone used for similar palladium catalyzed oxidative C−H activation-heterofunctionalization reactions were found to be either less efficient (entries 7−9) or unsuccessful (entries 10 and 11) in this reaction. Similarly, performing the reaction in other solvents like DMF or toluene gave decreased yield of **8a** (entries 12 and 13). Also, a reduced amount of catalytic loading resulted in a significant drop in the conversion (entry 14). Use of $Cu(OAc)_2{\cdot}H_2O$ (1 equiv) as oxidant (15 and 16), or decreasing the amount of $Cu(OAc)_2$ (entry 17) or conducting the reaction in the absence of $Cu(OAc)_2$ under oxygen atmosphere (entry 18), afforded reduced yields of the indole **8a**. Use of Bu_4NBr as additive though facilitated the reaction within 6 h, however, without any improvement in the yield of indole **8a** (entry 19). We also conducted a few optimization experiments in the presence of pivalic acid as additive, which has been reported to exhibit

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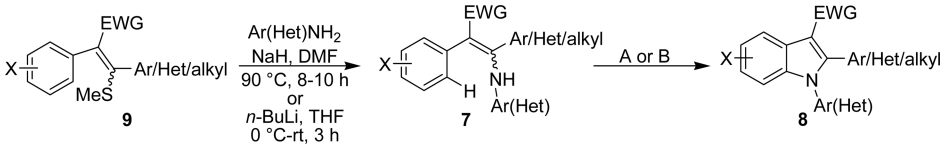
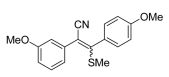
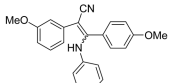
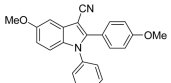
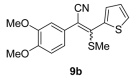
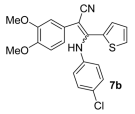
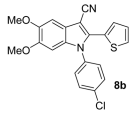
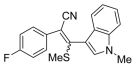
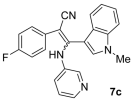
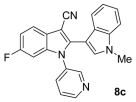
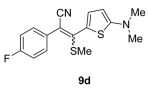
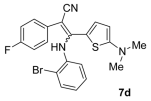
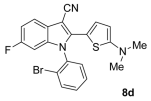
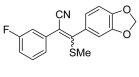
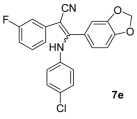
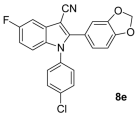
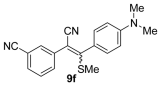
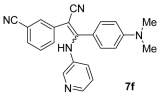
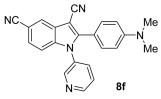
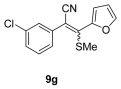
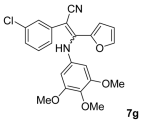
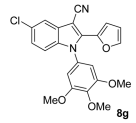
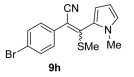
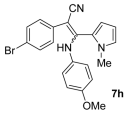
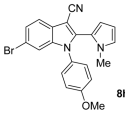
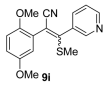
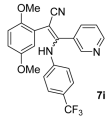
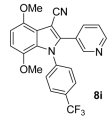
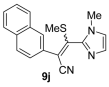
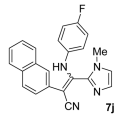
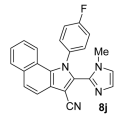
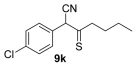
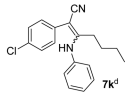
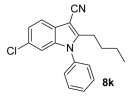
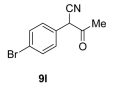
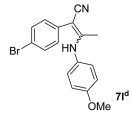
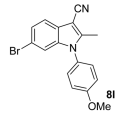
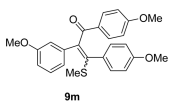
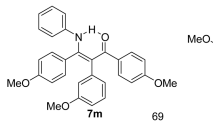
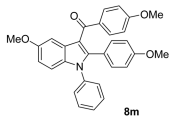
Table 2. Synthesis of 1-*N*-(Het)aryl-2,3-Substituted Indoles 8 from Enaminonitriles/Enaminones 7[e]



entry	substrate 9	substrate	yield (%) 7	product	yield (%) 8
1	 9a	 7a	80	 8a	75[a], 81[b], 73[c]
2	 9b	 7b	87	 8b	70[a], 73[b]
3	 9c	 7c	71	 8c	74[a], 76[b]
4	 9d	 7d	74	 8d	84[a], 85[b]
5	 9e	 7e	65	 8e	72[a], 75[b]
6	 9f	 7f	82	 8f	70[a], 74[b]
7	 9g	 7g	67	 8g	81[a], 83[b]
8	 9h	 7h	73	 8h	76[a], 78[b]
9	 9i	 7i	64	 8i	71[a], 76[b]
10	 9j	 7j	68	 8j	79[a], 80[b]
11	 9k	 7k[d]	70	 8k	72[a], 75[b]
12	 9l	 7l[d]	72	 8l	76[a], 70[b]
13	 9m	 7m	69	 8m	63[a], 60[b]
14	9n	7n	66	8n	73[a], 65[b]
15	9o	7o[d]	62	8o	0[a,b]

[a]Yields of indoles **8** by method A. [b]Yields of indoles **8** by method B. [c]Yield obtained on 3.0 mmol scale. [d]Prepared from α-(thioacyl or acyl)arylacetonitriles. [e]Reaction conditions: Method A, **7** (0.3 mmol), $Pd(OAc)_2$ (20 mol %), $Cu(OAc)_2$ (1.0 equiv) in DMSO (2 mL) heated under O_2 atm at 120 °C for 8−10 h. Method B, **7** (0.3 mmol), $Pd(OAc)_2$ (20 mol), Ag_2CO_3 (1.0 equiv), PivOH (1.0 equiv) in DMSO (2 mL) heated under O_2 atm at 120 °C for 10−12 h.

unprecedented reactivity in a few C−H activation-functionalization reactions.[34] Thus, performing the reaction in the presence of sodium carbonate (2 equiv) and pivalic acid (1 equiv) did not yield any encouraging results, affording the indole **8a** only in 58% yield (entry 20); however, replacement of sodium carbonate by silver carbonate (1 equiv) under similar conditions resulted in a considerable increase in the yield of indole **8a** (entry 21). On the other hand, decreasing the amount of silver carbonate (0.5 equiv) afforded reduced yield of indole **8a** (entry 22). We therefore identified these two optimal conditions (entries 2 and 21) for subsequent studies and conducted most of the experiments under both conditions.

With optimized reaction conditions in hand for the two-step synthesis of indole **8a** from 3-(methylthio)acrylonitrile **9a**, we next attempted one-pot sequence by generating enaminonitrile **7a** in situ from **9a** and 4-methoxyaniline in the presence of either sodium hydride or potasium *t*-butoxide as base and subjecting it to intramolecular C−H amination under optimized reaction conditions. However, indole **8a** could be obtained in maximum yield of only 64% under $Pd(OAc)_2$-catalyzed oxidative cyclization conditions in the presence of silver carbonate and pivalic acid. We therefore performed all subsequent reactions under two-step conditions starting from pure enaminonitriles/enaminones **7** or **11** obtained from **9** and **10**, respectively (Tables 2 and 3).

With the realization of optimized reaction conditions for the synthesis of indole **8a** from enaminonitrile **7a**, we next evaluated the generality and scope of this new protocol for introduction of different substituents at various positions of indole nucleus. These results are summarized in Table 2. Thus, the reaction was found to be amenable with both electron-donating and electron-withdrawing substituents on the 2- aryl ring of enaminonitriles **7a−d**, furnishing the substituted indoles **8a−d** in high yields (Table 2, entries 1−4). Also, it is pertinent

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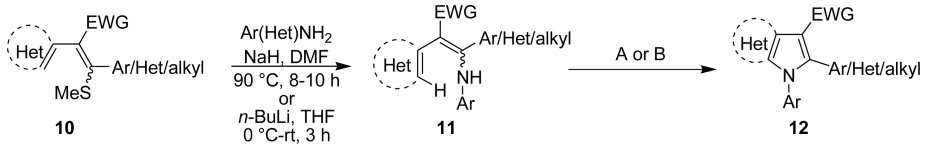
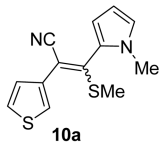
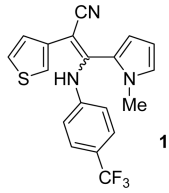
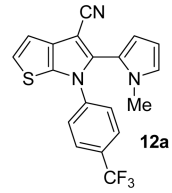
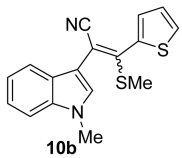
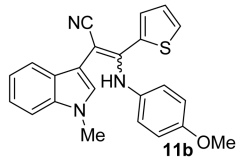
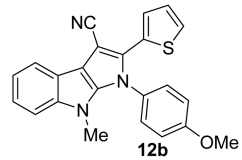
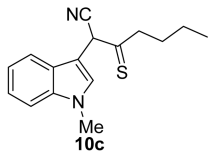
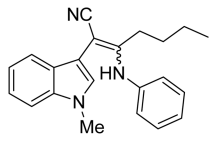
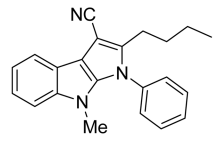
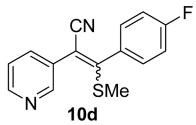
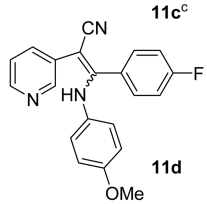
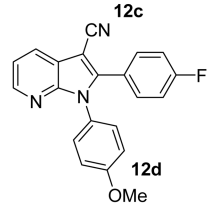
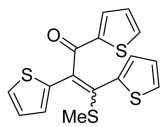
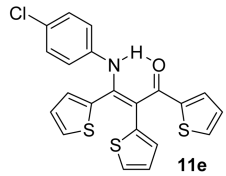
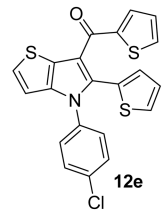
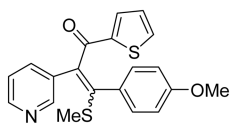
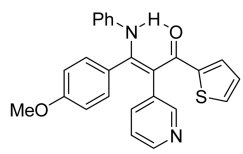
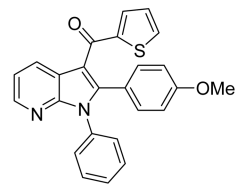
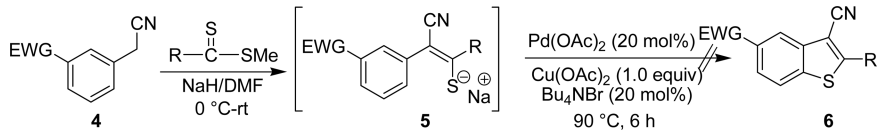
Table 3. Synthesis of Substituted Heterofused Pyrroles 12[d]



entry	substrate **10**	substrate	yield (%) **11**	product	yield (%) **12**
1	 **10a**	 **11a**	72	 **12a**	81[a], 83[b]
2	 **10b**	 **11b**	67	 **12b**	75[a], 74[b]
3	 **10c**	 **11c**[c]	61	 **12c**	70[a]
4	 **10d**	 **11d**	74	 **12d**	86[a], 82[b]
5	 **10e**	 **11e**	60	 **12e**	68[a]
6	 **10f**	 **11f**	68	 **12f**	77[a]

[a]Yields of 12 by method A. [b]Yields of 12 by method B. [c]Prepared from α-(thioacyl)arylacetonitriles. [d]Reaction conditions: Method A, **11** (0.3 mmol), $Pd(OAc)_2$ (20 mol %), $Cu(OAc)_2$ (1.0 equiv) in DMSO (2 mL) heated under O_2 atm at 120 °C for 8−10 h. Method B, **11** (0.3 mmol), $Pd(OAc)_2$ (20 mol), Ag_2CO_3 (1.0 equiv), PivOH (1.0 equiv) in DMSO (2 mL) heated under O_2 atm at 120 °C for 10−12 h.

Scheme 2



4a, EWG = F
b, EWG = CN

5, **6a**, EWG = F; R = 2-thienyl
b, EWG = CN; R = 2-furyl

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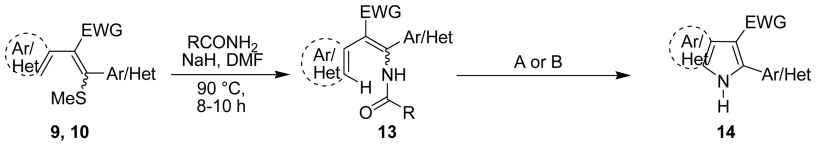
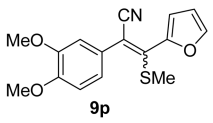
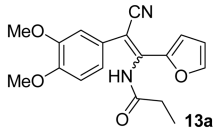
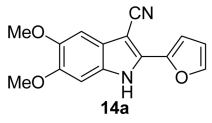
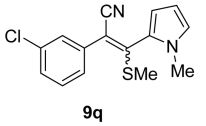
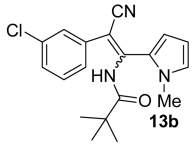
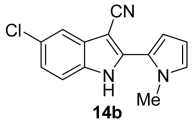
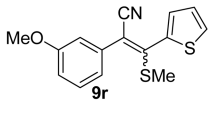
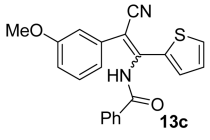
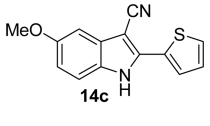
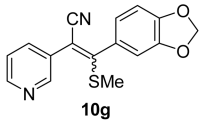
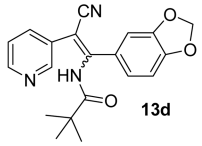
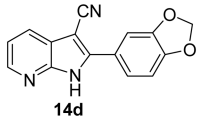
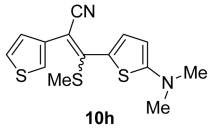
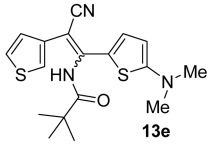
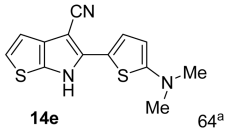
Table 4. Synthesis of 1-Unsubstituted NH-Indoles 14 from *N*-Acylenaminonitriles 13[c]



entry	substrate **9**, **10**	substrate	yield (%) **13**	product	yield (%) **14**
1	 **9p**	 **13a**	68	 **14a**	77[a]
2	 **9q**	 **13b**	71	 **14b**	68[a], 71[b]
3	 **9r**	 **13c**	64	 **14c**	70[a], 74[b]
4	 **10g**	 **13d**	60	 **14d**	73[a], 69[b]
5	 **10h**	 **13e**	67	 **14e**	64[a]

[a]Yields of **14** by method A. [b]Yields of **14** by method B. [c]Reaction conditions: Method A, **13** (0.3 mmol), $Pd(OAc)_2$ (20 mol %), $Cu(OAc)_2$ (1.0 equiv) in DMSO (2 mL) heated under O_2 atm at 120 °C for 8−10 h. Method B, **13** (0.3 mmol), $Pd(OAc)_2$ (20 mol), Ag_2CO_3 (1.0 equiv), PivOH (1.0 equiv) in DMSO (2 mL) heated under O_2 atm at 120 °C for 10−12 h.

to note that enaminonitriles **7e** and **7f** bearing electron-withdrawing substituents (F and CN) *para* to the cyclization position also underwent facile intramolecular C−H arylamination, furnishing the indoles **8e−f** in high yields (Table 2, entries 5 and 6). These results are contrary to our earlier observations during palladium-catalyzed intramolecular C−H functionalization-arylthiolation of the corresponding enethiolates (**5a**,**b**) bearing an electron withdrawing group at 3-position, which failed to furnish the corresponding benzo[*b*]thiophenes **6a**,**b** under optimized conditions (Scheme 2).[33a] The intramolecular C−H arylamination of 3-chloro- and 4-bromo-2-arylenaminonitriles **7g** and **7h** also proceeded smoothly under these conditions, affording the 5-chloro- and 6-bromo-substituted indoles **8g**,**h** in excellent yields (Table 2, entries 7,8). Further, we have found that the reaction displays high regioselectivity in the intramolecular cyclization of 3-substituted 2-arylenaminonitriles (**7a**, **7e−g**) affording only 5-substituted indoles **8a**, **8e−g**, and no trace of the corresponding 7-substituted indoles was detected in the reaction mixture (Table 2, entries 1, 5−7). It should be noted that the previous workers have reported the formation of regioisomeric mixtures of 5- and 7-substituted indoles in the oxidative intramolecular cyclization (C−H amination) of 3-substituted enamine/enaminonitriles.[30,31a] The versatility of this intramolecular C−H amination was further demonstrated by the synthesis of sterically crowded 1,2,3,4,7-pentasubstituted indole **8i** in high yield, when the corresponding **2**-[2,5-bis(methoxy)pheny]-substituted enaminonitrile **7i** was subjected to catalytic oxidative cyclization under similar conditions (Table 2, entry 9). Similarly, the benzofused indole **8j** could also be obtained in good yield from the (*β*-naphthyl)-substituted enaminonitrile **7j** (entry 10). The synthetic potential of this protocol was further evident from efficient introduction of a diverse range of substituted aryl and het(aryl) groups such as (2-thienyl-) (entries 2 and 4), (3-indolyl-) (entry 3), (2-furyl-) (entry 7), (2-*N*-methylpyrrolyl-) (entry 8), (2-imadozolyl-) (entry 10), and (3-pyridyl-) (entry 9) groups at 2-position of the indole ring by intramolecular cycloamination of readily available 3-(het)aryl-substituted enaminonitriles **7a−j**. It should be noted that despite broad application of palladium (or copper)-catalyzed synthesis of 2-substituted indoles from relevant acetylene precursors,[7−10] the related methods for the synthesis of biologically important 2-(het)aryl indoles are scarce in the literature.

The methodology could also be extended for the synthesis of 2-alkylindoles **8k**,**l** in good yields, from the respective 3-alkylenaminonitriles **7k**,**l** (entries 11 and 12). Further, a range of commercially available anilines bearing electron-donating, electron-withdrawing, and sterically constrained substituents

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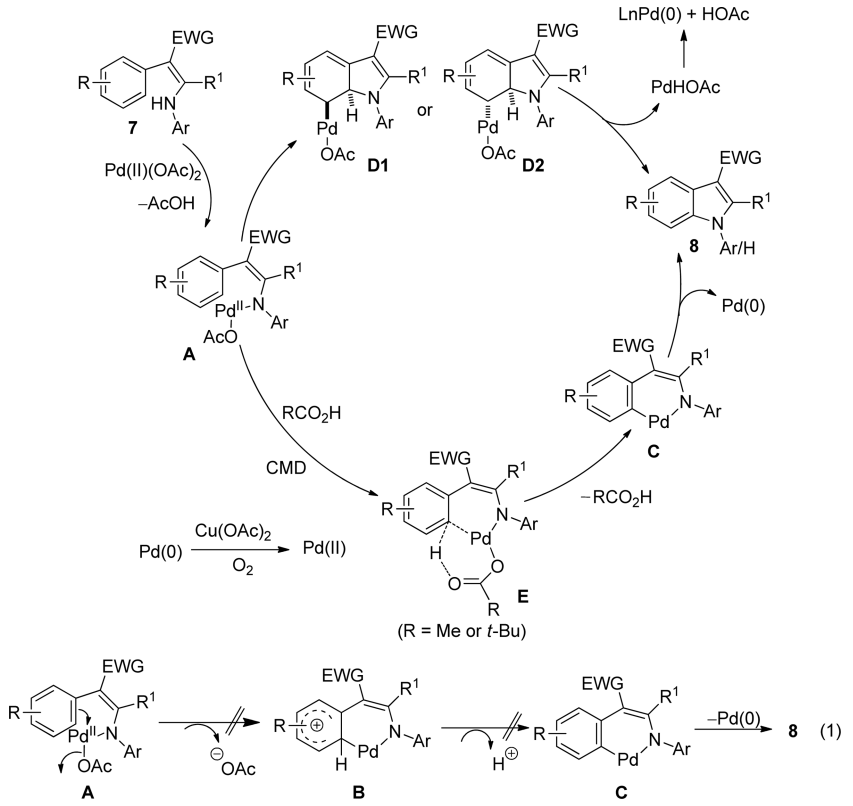
Scheme 3. Plausible Mechanistic Pathways for Formation of Indole 8 from 7



could be installed in *N*-arylindoles **8** (Table 2) as N-coupling partners. Entries 3 and 6 display the synthesis of 1-*N*-(3-pyridyl)indoles **8c** and **8f** by intramolecular cyclization of the enaminonitriles 7**c** and 7**f**, respectively. The scope and utility of this method were further examined by installing other electron-withdrawing groups at 3-position of indole rings. Thus, intramolecular oxidative cyclization of enaminones[35] **7m,n** also proceeded efficiently under optimized conditions affording the substituted 3-aroylindoles **8m,n** in good yields (Table 2, entries 13 and 14).

However, our attempts to synthesize *N*-benzylindole **8o** from the corresponding *N*-benzylenaminonitrile **7o** under optimized reaction conditions, including those of Gaunt,[17b] were not successful, and only starting material was recovered unchanged (Table 2, entry 15).

With the successful implementation of this intramolecular C−H amination methodology for the synthesis of multi-substituted indoles, we next elaborated this protocol for the construction of heterofused pyrroles as depicted in Table 3. It is pertinent to note that despite several examples of transition metal-catalyzed intramolecular C−H activation-heterofunctionalization reactions leading to 5- and 6-membered benzofused heterocycles reported in the literature, examples of a parallel protocol involving intramolecular C−H-heterocyclization on five- or six-membered heterocycles furnishing fused heterocycles are only scarce. We therefore synthesized the desired 2-(het)arylenaminonitrile **11a−d** and the enaminone **11e,f** precursors by reacting the corresponding 3-(methylthio)-enaminonitriles **10a,b**, **10d**, enones **10e,f**, and α-(thioacyl)-arylacetonitrile **10c** with the relevant amines following the procedure similar to that described for enaminonitriles and enones **7** (Table 3, see Experimental Section).

To our delight, these substrates underwent smooth intramolecular C−H activation-cycloamination under previously described optimal conditions,[36] furnishing the various substituted heterofused pyrroles such as thieno[2,3-*b*]pyrrole (**12a**) (entry 1), thieno[3,2-*b*]pyrrole **12e** (entry 5), pyrrolo-[2,3-*b*]indole **12b,c** (Table 3, entries 2 and 3), and 7-azaindoles **12d**, **12f** (entries 4 and 6) in good yields (Table 3).

Encouraged by the above studies, we next undertook the synthesis of few 1-*N*-unsubstituted (NH) indoles **14** via palladium-catalyzed intramolecular C−H amination of the corresponding *N*-acylenaminonitriles **13** as shown in Table 4. The requisite *N*-acylenaminonitrile precursors **13a−e** were synthesized via conjugate displacement on 2-het(aryl)-3-(methylthio)acrylonitriles **9** or **10** by the respective primary amides in the presence of sodium hydride as base (see Experimental Section). Thus, catalytic intramolecular C−H cycloamination of these *N*-acylenamides **13a−e** under previously described conditions proceeded efficiently to afford the corresponding 1-*N*-unsubstituted indoles **14a−c** and heterofused pyrroles **14d,e** in good yields via in situ hydrolysis of the resulting *N*-acylindoles as observed in our previous studies[1a] (Table 4, entries 1−5).[36]

Mechanistic Studies. Although a full mechanistic understanding of the reaction has yet to be established, on the basis of previous mechanisms, analogous to those proposed to similar palladium-catalyzed process along with our observations, we suggest a plausible mechanistic pathway as shown in Scheme 3. Thus, arylamino moiety in the substrates **7** can readily coordinate with Pd(II) catalyst to form palladium(II) aminoaryl/amide complex **A** with concomitant release of acetic acid. Once the palladium is in close proximity to the C−H bond of aryl ring, the initially formed coordinated Pd complex **A** could facilitate *ortho*-palladation process and evolve into

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product indole **8** by different mechanisms (Scheme 3). Thus, the intermediate **A** could be converted to the palladacycle **C** via an intramolecular electrophilic palladation (SE_{Ar}) mechanism[15,20] through intermediate **B** (Scheme 3, eq 1). However, this reaction mechanism appears to be inconsistent with the observation that substrates bearing both electron-withdrawing as well as electron-donating substituents at the 3-position display comparable reactivity, yielding product indoles in good yields regardless of the electronic character of the substituents (Table 2, entries 5−7 vs entries 1,2). These studies suggest that an electrophilic palladation mechanism does not operate. We therefore propose two alternative pathways for this cycloamination reaction as displayed in Scheme 3. Thus, the coordinated Pd(II) complex **A** can undergo intramolecular cyclization through insertion into arene to give intermediate **D1** (Heck like) or **D2** (Wacker like), which would undergo β-hydrogen elimination to give indole **8**.[17a] The third possible pathway may involve σ bond metathesis through irreversible ligand assisted "concerted metalation-deprotonation" (CMD) mechanism[37] involving intermediate **E**. Subsequent reductive elimination gives the product indole **8** through palladacycle intermediate **C**, with concurrent formation of Pd(0), which is then oxidized by cupric actate (or oxygen) to regenerate Pd(II) species. In view of the observation that the reaction proceeds efficiently in the presence of pivalic acid as additive, wherein an anionic pivalate (or acetate)−Pd bond ligand aids in proton abstraction, a σ bond metathesis pathway through CMD mechanism is more likely preferred in this process. However, a possible pathway involving $Cu(OAc)_2$-promoted oxidation of palladacycle intermediate C to more highly oxidized species facilitating reductive elimination of palladium(II) and C−N bond formation cannot be ruled out at the current time.[17b]

The excellent regioselectivity observed in these reactions with the formation of only 5-substituted indoles, in cases where two regioisomeric products could be obtained (Table 2, entries 1, 2, 5, 6, 7, 13, 14, and 15, Table 4, entries 1−3), suggests that this ring-forming reaction may be controlled by steric factors. On the other hand, the observed regioselective cyclization of 2-(3-thienyl)enaminonitriles **11a** (Table 3, entry 1) and **13e** (Table 4, entry 5) at 2-position of the thiophene ring can be rationalized in terms of the stability of the product thieno[2,3-*b*]pyrroles **12a** and **14e** in comparison to the products formed by cyclization at 4-position. Similarly, in the case of the corresponding 3-(3-pyridyl)enaminonitriles **11d**, **13d**, and enaminone **11f** (Table 3, entries 4 and 6, Table 4, entry 4), the observed regioselectivity yielding only 7-azaindoles **12d**, **12f**, and **14d**, respectively, appears to be governed by the proximity of pyridyl nitrogen, which might complex with palladium acetate in the palladacycle **C** (Scheme 3), thus directing the cyclization at 2-position of the pyridine ring instead of at 4-position.

CONCLUSION

In summary, we have developed an efficient palladium-catalyzed intramolecular oxidative C−H functionalization/C−N bond-forming approach for substituted *N*-aryl/NH indoles from readily available *N*-aryl/acylenaminonitriles and enaminones. This C−H functionalization strategy allows the assembly of indoles with a variety of substitution patterns and functional groups under relatively mild conditions, and both electron-donating and electron-withdrawing groups are tolerated in the benzene ring. The reaction displays high regioselectivity and broad substrate scope with functional group diversity in comparison to earlier described similar reactions. Furthermore, this methodology can be extended to other novel pyrrolo fused heteroaromatics, a feature that is noteworthy, because most of the previously reported intramolecular C−H activation/C-heteroatom bond-forming reactions employ substituted benzene precursors, leading to benzoheterocycles, while extension of this strategy for the synthesis of fused heteroaromatics is scarce in the literature. Although a detailed mechanistic study is yet to be undertaken, the reaction represents one of the few examples in which an aryl C−H bond is activated by an aminoaryl directing group, that subsequently acts as the reaction partner in the same process.[16c] Such a kind of intramolecular C−H heterofunctionalization reaction, in which heteroatoms act as directing group as well as internal nucleophiles, are useful and atom economical processes for the construction of heterocyclic scaffolds, because they obviate the necessity of a directing ligand in the substrate, which lessens the advantageous impact of C−H functionalization process over the other methods that employ prefunctionalized C−(pseudo) halogen bond containing substrates. The widespread use of indole skeleton in natural products and designed compounds, combined with its pharmaceutical importance, should render the method broadly useful. Further study to understand precise mechanism as well as to expand the range of substrates is currently underway in our laboratory.

EXPERIMENTAL SECTION

General Information. All reagents were purchased from commercial suppliers and used without further purification. Solvents were dried according to the standard procedures. All of the reactions were monitored by thin layer chromatography using standard TLC silica gel plates and visualized with UV light. Column chromatography was performed using silica gel (100−200 mesh). Nuclear magnetic resonance spectra were recorded on a (400 MHz) FT NMR spectrometer with $CDCl_3$ or DMSO-d_6 as solvent. Chemical shifts were reported in δ ppm using residual solvent protons as internal standard (δ 7.26 for $CDCl_3$ and δ 2.50 for DMSO-d_6 in ^{1}H NMR, δ 77.16 for $CDCl_3$ and δ 39.52 for DMSO-d_6 in ^{13}C NMR). Coupling constants were reported as *J* values in Hertz (Hz). Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), sex (sextet), dd (double doublet), dt (doublet of triplet), td (triplet of doublet), ddd (doublet of doublet of doublet), m (multiplet), and br (broad). Infrared spectra of neat samples were recorded in ATR (attenuated total reflectance) mode using an FT-IR instrument and HRMS on a Q-TOF spectrometer. Melting points were recorded using an electrothermal capillary melting point apparatus and are uncorrected.

*General Procedure for the Synthesis of 3-(Methylthio)-2-het-(aryl)-3-het(aryl)/alkylacrylonitriles/enones **9** and **10**.* The desired acrylonitrile and enone precursors **9a−j**, **9m**,**n** (Table 2), **9p−r** (Table 4), **10a**,**b**, and **10d−h** (Tables 3 and 4) were prepared following a procedure similar to that reported for the corresponding 2-(2-bromohet(aryl-3-(methylthio)acrylonitrile precursors **1**.[38] A solution of the appropriate (het)arylacetonitrile/deoxybenzoin (3.0 mmol) in dry DMF (10 mL) was added to a stirred solution of NaH (144.0 mg, 6.0 mmol, 60% suspension in mineral oil) in DMF at 0 °C. After the reaction mixture was stirred for 30 min, the reaction mixture was cooled to 0 °C, a solution of the corresponding het(aryl)dithioester (3.0 mmol) in DMF (3 mL) was added, and the reaction mixture was further stirred for 1 h at room temperature followed by alkylation with methyl iodide (0.22 mL, 3.6 mmol) at 0 °C. After being stirred for 0.5 h at room temperature (monitored by TLC), the reaction mixture was diluted with saturated NH_4Cl solution (25 mL), extracted with EtOAc (2 × 25 mL), and the combined organic layer was washed with water (2 × 25 mL), brine (25 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude products were purified by column chromatography using EtOAc/hexane as eluent. The spectral and

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analytical data of all of the unknown precursors **9** and **10** are given below.

*2-(3-Methoxyphenyl)-3-(4-methoxyphenyl)-3-(methylthio)-acrylonitrile (**9a**).* Obtained as a 55:45 inseparable mixture of geometrical isomers, yellow semi solid (727.7 mg, 78%): R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2923, 2195, 1519, 1446, 812; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 8.8 Hz, 1.1H), 7.35 (t, J = 8.4 Hz, 0.55H), 7.19−7.17 (m, 0.55H), 7.15−7.12 (m, 1.35H), 7.05 (t, J = 8.0 Hz, 0.55H), 7.00 (d, J = 8.8 Hz, 1.1H), 6.92 (dd, J = 8.4 Hz, 2.4 Hz, 0.55H), 6.82 (d, J = 8.8 Hz, 0.9H), 6.72−6.67 (m, 0.9H), 6.63−6.62 (m, 0.45H), 3.86 (s, 1.65H), 3.85 (s, 1.65H), 3.79 (s, 1.35H), 3.59 (s, 1.35H), 2.08 (s, 1.35H), 1.90 (s, 1.65H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.9, 160.7, 160.0, 159.8, 159.4, 158.3, 135.7, 135.3, 131.4, 130.6, 129.7, 129.4, 128.4, 126.8, 122.0, 121.7, 119.1, 119.0, 114.72, 114.68, 114.5, 114.4, 114.3, 108.9, 108.5, 55.51, 55.48, 55.44, 55.2, 16.9, 16.4; HRMS (ESI) m/z calcd for $C_{18}H_{18}NO_2S$ $[M + H]^+$ 312.1058, found 312.1065.

*2-(3,4-Dimethoxyphenyl)-3-(methylthio)-3-(thiophen-2-yl)-acrylonitrile (**9b**).* Obtained as a 60:40 inseparable mixture of geometrical isomers, yellow solid (789.3 mg, 83%): mp 81−83 °C; R_f 0.5 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2927, 2195, 1519, 1416, 1136; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, J = 5.2 Hz, 1.2 Hz, 0.4H), 7.44 (dd, J = 3.6 Hz, 0.8 Hz, 0.4H), 7.42 (dd, J = 4.8 Hz, 0.8 Hz, 0.6H), 7.18 (dd, J = 8.4 Hz, 2.0 Hz, 0.4H), 7.14−7.12 (m, 0.8H), 6.99−6.95 (m, 1.2H), 6.93−6.90 (m, 1.0H), 6.74 (d, J = 8.4 Hz, 0.6H), 6.63 (d, J = 2.0 Hz, 0.6H), 3.92 (s, 2.4H), 3.84 (s, 1.8H), 3.61 (s, 1.8H), 2.27 (s, 1.8H), 2.04 (s, 1.2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 149.7, 149.6, 149.5, 149.0, 148.8, 147.4, 138.6, 137.7, 130.9, 130.1, 130.0, 129.5, 127.9, 127.8, 126.8, 126.5, 122.6, 122.3, 119.1, 118.8, 112.3, 112.1, 111.5, 111.1, 111.0, 110.1, 56.2, 56.1, 56.0, 55.8, 17.6, 17.1; HRMS (ESI) m/z calcd for $C_{16}H_{16}NO_2S_2$ $[M + H]^+$ 318.0622, found 318.0617.

*2-(4-Fluorophenyl)-3-(1-methyl-1H-indol-3-yl)-3-(methylthio)-acrylonitrile (**9c**).* Obtained as a 65:35 inseparable mixture of geometrical isomers, yellow solid (656.8 mg, 68%): mp 75−77 °C; R_f 0.4 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2933, 2190, 1500, 1210, 833; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 7.6 Hz, 0.65H), 7.63−7.60 (m, 1.3H), 7.50 (s, 0.65H), 7.44−7.37 (m, 1H), 7.34−7.27 (m, 1.35H), 7.27−7.17 (m, 1.35H), 7.16−7.12 (m, 1.35H), 7.09−7.05 (m, 0.35H), 7.01 (s, 0.35H), 6.80−6.76 (m, 0.65H), 3.88 (s, 1.95H), 3.75 (s, 1.05H), 2.20 (s, 1.05H), 1.98 (s, 1.95H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.5 (d, $^1J_{C-F}$ = 248.0 Hz), 161.9 (d, $^1J_{C-F}$ = 247.0 Hz), 153.9, 151.7, 137.5, 137.4, 131.9, 131.79, 131.75, 131.6, 131.5, 131.0, 130.8, 130.73, 130.66, 130.6, 126.4, 125.8, 123.03, 122.99, 121.29, 121.26, 120.7, 120.5, 120.2, 119.8, 115.61, 115.60, 115.4, 110.9, 110.1, 109.89, 109.85, 105.8, 105.5, 33.5, 33.4, 17.14, 17.05; HRMS (ESI) m/z calcd for $C_{19}H_{16}FN_2S$ $[M + H]^+$ 323.1018, found 323.1019.

*3-(5-(Dimethylamino)thiophen-2-yl)-2-(4-fluorophenyl)-3-(methylthio)acrylonitrile (**9d**).* Obtained as a single geometrical isomer, brown solid (849.0 mg, 89%): mp 85−87 °C; R_f 0.6 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2920, 2190, 1485, 1221, 840; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35−7.31 (m, 2H), 7.00−6.95 (m, 2H), 6.91 (d, J = 4.2 Hz, 1H), 5.69 (d, J = 4.2 Hz, 1H), 2.92 (s, 6H), 2.47 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.5, 162.3 (d, $^1J_{C-F}$ = 247.0 Hz), 149.2, 135.3, 131.8, 131.7, 131.6, 131.5, 120.6, 120.5, 116.0, 115.8, 103.6, 102.6, 42.1, 18.8; HRMS (ESI) m/z calcd for $C_{16}H_{16}FN_2S_2$ $[M + H]^+$ 319.0739, found 319.0729.

*3-(Benzo[d][1,3]dioxol-5-yl)-2-(3-fluorophenyl)-3-(methylthio)-acrylonitrile (**9e**).* Obtained as a 70:30 inseparable mixture of geometrical isomers, yellow semi solid (741.8 mg, 79%): R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2935, 2210, 1510, 1262, 869; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42−7.38 (m, 0.7H), 7.35−7.32 (m, 0.3H), 7.17−7.12 (m, 0.7H), 7.10−7.04 (m, 0.3H), 6.98−6.91 (1.7H), 6.88−6.83 (m, 0.6H), 6.82−6.80 (m, 0.6H), 6.79−6.74 (m, 0.6H), 6.67−6.65 (m, 1.5H), 6.05 (s, 0.6H), 6.00 (s, 1.4H), 2.11 (s, 2.1H), 1.96 (s, 0.9); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.7 (d, $^1J_{C-F}$ = 246.0 Hz), 162.6 (d, $^1J_{C-F}$ = 245.0 Hz), 160.7, 159.4, 149.2, 149.1, 148.5, 148.4, 136.5, 136.4, 135.9, 135.8, 130.4, 130.3, 130.1, 130.0, 129.7, 127.8, 125.2, 125.12, 125.09, 124.3, 123.3, 118.6, 118.5, 116.6, 116.4, 116.3, 116.1, 116.0, 115.8, 115.2, 115.0, 109.8, 109.2, 109.0, 108.9, 108.0, 107.95, 107.8, 101.87, 101.85, 16.8, 16.4; HRMS (ESI) m/z calcd for $C_{17}H_{13}FNO_2S$ $[M + H]^+$ 314.0651, found 314.0645.

*3-(1-Cyano-2-(4-(dimethylamino)phenyl)-2-(methylthio)vinyl)-benzonitrile (**9f**).* Obtained as a 75:25 inseparable mixture of geometrical isomers, yellow solid (679.4 mg, 71%): mp 104−106 °C; R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2907, 2230, 2199, 1600, 1515, 1170, 814; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94−7.93 (m, 0.75H), 7.83 (dt, J = 8.0 Hz, 1.2 Hz, 0.75H), 7.62 (dt, J = 8.0 Hz, 1.2 Hz, 0.75H), 7.53 (t, J = 8.0 Hz, 0.75H), 7.43−7.37 (m, 2.25H), 7.29 (d, J = 7.6 Hz, 0.25H), 7.02 (d, J = 8.8 Hz, 0.5H), 6.76 (d, J = 8.8 Hz, 1.5H), 6.55 (d, J = 8.8 Hz, 0.5H), 3.05 (s, 4.5H), 2.99 (s, 1.5H), 2.15 (s, 0.75H), 1.98 (s, 2.25H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.5, 162.7, 151.8, 151.6, 136.9, 136.3, 133.9, 133.6, 133.2, 132.9, 131.7, 131.6, 130.7, 130.6, 129.6, 129.3, 122.4, 119.9, 119.3, 119.1, 118.5, 118.4, 113.0, 112.7, 111.9, 111.8, 104.5, 103.9, 40.2, 40.1, 17.3, 16.9; HRMS (ESI) m/z calcd for $C_{19}H_{18}N_3S$ $[M + H]^+$ 320.1221, found 320.1217.

*2-(3-Chlorophenyl)-3-(furan-2-yl)-3-(methylthio)acrylonitrile (**9g**).* Obtained as a 80:20 inseparable mixture of geometrical isomers, brown semi solid (602.2 mg, 73%): R_f 0.6 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2960, 2208, 1498, 1255, 842; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, J = 2.0 Hz, 0.8 Hz, 0.8H), 7.59−7.58 (m, 0.8H), 7.48−7.45 (m, 0.8H), 7.39−7.34 (m, 1.8H), 7.24−7.18 (m, 0.4H), 7.15−7.14 (m, 0.2H), 7.07−7.04 (m, 1H), 6.61 (dd, J = 3.6 Hz, 0.8 Hz, 0.2H), 6.58 (dd, J = 3.2 Hz, 1.6 Hz, 0.8H), 6.46 (dd, J = 3.6 Hz, 1.6 Hz, 0.2H), 2.39 (s, 0.6H), 2.09 (s, 2.4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.5, 147.7, 147.3, 145.33, 145.27, 145.2, 136.5, 135.9, 134.7, 134.5, 130.0, 129.8, 129.5, 129.2, 128.8, 128.7, 127.7, 127.0, 118.7, 118.5, 117.0, 116.1, 112.6, 112.3, 109.0, 106.8, 17.5, 17.3; HRMS (ESI) m/z calcd for $C_{14}H_{11}ClNOS$ $[M + H]^+$ 276.0250 and 278.0220, found 276.0246 and 278.0212.

*2-(4-Bromophenyl)-3-(1-methyl-1H-pyrrol-2-yl)-3-(methylthio)-acrylonitrile (**9h**).* Obtained as a 60:40 inseparable mixture of geometrical isomers, yellow solid (784.4 mg, 79%): mp 103−105 °C; R_f 0.6 (1:2 EtOAc/hexane); IR (neat, cm^{-1}) 2920, 2202, 1482, 1049, 861; ^1H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.8 Hz, 0.8H), 7.51 (d, J = 8.8 Hz, 0.8H), 7.32 (d, J = 8.8 Hz, 1.2H), 6.87 (d, J = 8.8 Hz, 1.2H), 6.80 (t, J = 2.0 Hz, 0.4H), 6.65 (t, J = 2.0 Hz, 0.6H), 6.41 (dd, J = 4.0 Hz, 2.0 Hz, 0.4H), 6.30 (dd, J = 4.0 Hz, 2.0 Hz, 0.6H), 6.22 (dd, J = 3.6 Hz, 2.8 Hz, 0.4H), 6.20 (dd, J = 3.6 Hz, 2.4 Hz, 0.6H), 3.7 (s, 1.2H), 3.13 (s, 1.8H), 2.21 (s, 1.8H), 1.89 (s, 1.2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.4, 149.8, 133.8, 132.7, 132.0, 131.9, 130.8, 129.6, 126.9, 126.5, 125.8, 125.6, 123.1, 122.0, 118.6, 118.5, 114.4, 113.5, 109.9, 109.5, 108.9, 107.1, 34.4, 16.8, 16.2; HRMS (ESI) m/z calcd for $C_{15}H_{14}BrN_2S$ $[M + H]^+$ 333.0061 and 335.0041, found 333.0058 and 335.0037.

*2-(2,5-Dimethoxyphenyl)-3-(methylthio)-3-(pyridin-3-yl)-acrylonitrile (**9i**).* Obtained as a 65:35 inseparable mixture of geometrical isomers, yellow semi solid (627.1 mg, 67%): R_f 0.3 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 2962, 2210, 1513, 1276, 842; ^1H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 1.6 Hz, 0.35H), 8.70 (dd, J = 4.8 Hz, 1.6 Hz, 0.35H), 8.46 (dd, J = 4.8 Hz, 1.6 Hz, 0.65H), 8.39 (d, J = 2.0 Hz, 0.65H), 7.87 (dt, J = 8.0 Hz, 2.0 Hz, 0.35H), 7.49 (dt, J = 8.0 Hz, 2.0 Hz, 0.65H), 7.45 (ddd, J = 8.0 Hz, 4.8 Hz, 0.8 Hz, 0.35H), 7.18 (ddd, J = 8.0 Hz, 4.8 Hz, 0.8 Hz, 0.65H), 6.96−6.91 (m, 1.05H), 6.73 (dd, J = 9.2 Hz, 3.2 Hz, 0.65H), 6.65 (d, J = 9.2 Hz, 0.65H), 6.49 (d, J = 3.2 Hz, 0.65H), 3.87 (s, 1.05H), 3.80 (s, 1.05H), 3.64 (s, 1.95H), 3.58 (s, 1.95H), 2.11 (s, 1.95H), 1.87 (s, 1.05H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.2, 155.3, 153.6, 153.5, 151.3, 151.2, 150.9, 150.1, 150.0, 149.8, 136.84, 136.79, 132.2, 131.7, 123.7, 123.1, 122.7, 117.8, 117.6, 116.7, 116.5, 116.3, 116.1, 113.0, 112.6, 108.3, 107.5, 56.5, 56.1, 56.0, 55.9, 16.6; HRMS (ESI) m/z calcd for $C_{17}H_{17}N_2O_2S$ $[M + H]^+$ 313.1011, found 313.1009.

*3-(1-Methyl-1H-imidazol-2-yl)-3-(methylthio)-2-(naphthalen-2-yl)acrylonitrile (**9j**).* Obtained as a 55:45 inseparable mixture of geometrical isomers, off white solid (750.2 mg, 82%): mp 70−72 °C; R_f 0.3 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 2925, 2208, 1470, 1276, 859; ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 1.6 Hz, 0.45H), 7.93−7.85 (m, 1.55H), 7.78−7.69 (m, 1.55H), 7.67 (d, J = 1.6 Hz,

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0.55H), 7.63 (d, J = 8.4 Hz, 0.55H), 7.56−7.53 (m, 1.0H), 7.48−7.44 (m, 1.35H), 7.25 (d, J = 1.2 Hz, 0.45H), 7.06 (d, J = 0.8 Hz, 0.45H), 6.96 (dd, J = 8.8 Hz, 2.0 Hz, 0.55H), 6.78 (d, J = 1.2 Hz, 0.55H), 3.82 (s, 1.35H), 3.07 (s, 1.65H), 2.20 (s, 1.65H), 1.96 (s, 1.35H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 147.6, 146.5, 141.4, 140.1, 133.3, 133.0, 132.9, 132.8, 130.9, 130.4, 129.9, 129.6, 129.0, 128.6, 128.5, 128.43, 128.41, 128.0, 127.8, 127.6, 127.4, 127.2, 126.9, 126.8, 125.5, 124.4, 122.3, 122.2, 117.51, 117.47, 113.4, 112.3, 33.4, 33.1, 15.6; HRMS (ESI) m/z calcd for $C_{18}H_{16}N_3S$ $[M + H]^+$ 306.1065, found 306.1061.

2-(3-Methoxyphenyl)-1,3-bis(4-methoxyphenyl)-3-(methylthio)-prop-2-en-1-one (**9m**). Obtained as a 65:35 inseparable mixture of geometrical isomers, yellow semi solid (1.02 g, 81%): R_f 0.6 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2835, 1649, 1459, 1243, 835; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.8 Hz, 1.3H), 7.76 (d, J = 8.8 Hz, 0.7H), 7.30 (d, J = 8.8 Hz, 1.3H), 7.29−7.25 (m, 1.05H), 7.16−7.14 (m, 0.7H), 7.02−6.95 (m, 2H), 6.85−680 (m, 1.65H), 6.74−6.67 (m, 2H), 6.66−6.61 (m, 1.3H), 3.86 (s, 1.95H), 3.81 (s, 1.05H), 3.79 (s, 1.95H), 3.77 (s, 1.05H), 3.71 (s, 1.05H), 3.55 (s, 1.95H), 1.844 (s, 1.05H), 1.840 (s, 1.95H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 195.6, 195.3, 163.8, 163.3, 159.62, 159.60, 159.5, 159.4, 141.3, 139.9, 138.8, 138.6, 138.4, 137.8, 132.1, 132.0, 131.9, 131.4, 130.3, 130.1, 129.6, 129.41, 129.35, 128.7, 122.1, 121.8, 114.8, 114.6, 114.2, 114.0, 113.71, 113.67, 113.60, 113.56, 55.6, 55.5, 55.42, 55.40, 55.3, 55.2, 16.3, 16.1; HRMS (ESI) m/z calcd for $C_{25}H_{25}O_4S$ $[M + H]^+$ 421.1474, found 421.1468.

2-(3-Chlorophenyl)-1-(4-chlorophenyl)-3-(1-methyl-1H-indol-3-yl)-3-(methylthio)prop-2-en-1-one (**9n**). Obtained as a 65:35 inseparable mixture of geometrical isomers, yellow solid (933.5 mg, 69%): mp 116−118 °C; R_f 0.6 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2922, 1658, 1585, 1250, 780; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.8 Hz, 0.65H), 7.89−7.87 (m, 0.65H), 7.59 (t, J = 2.0 Hz, 0.65H), 7.54 (d, J = 8.0 Hz, 0.35H), 7.45−7.44 (m, 2.45H), 7.34 (t, J = 7.6 Hz, 0.65H), 7.31−7.29 (m, 1.0H), 7.25−7.19 (m, 1.0H), 7.18 (d, J = 2.0 Hz, 0.65H), 7.16−7.14 (m, 0.35H), 7.10−7.04 (m, 1.65H), 7.01−6.96 (m, 0.65H), 6.95−6.91 (m, 2.3H), 3.78 (s, 1.05H), 3.58 (s, 1.95H), 1.95 (s, 1.95H), 1.84 (s, 1.05H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.1, 195.7, 142.0, 140.1 139.9, 139.5, 137.8, 137.5, 137.1, 136.5, 136.4, 135.7, 135.5, 134.8, 134.3, 134.2, 132.1, 131.5, 130.9, 129.9, 129.8, 129.7, 129.6, 129.3, 128.9, 128.1, 127.9, 127.8, 127.5, 127.3, 126.7, 126.5, 123.0, 122.6, 120.9, 120.7, 120.6, 120.5, 112.4, 110.4, 109.7, 109.6, 33.3, 33.0, 16.5, 16.4; HRMS (ESI) m/z calcd for $C_{25}H_{20}Cl_2NOS$ $[M + H]^+$ 452.0643 and 454.0613, found 452.0639 and 454.0616.

2-(3,4-Dimethoxyphenyl)-3-(furan-2-yl)-3-(methylthio)-acrylonitrile (**9p**). Obtained as a 75:25 inseparable mixture of geometrical isomers, brown semi solid (693.5 mg, 77%): R_f 0.4 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2925, 2204, 1457, 1241, 807; ^1H NMR (400 MHz, $CDCl_3$) δ 7.63−7.62 (m, 0.25H), 7.40 (d, J = 0.8 Hz, 0.75H), 7.18−7.13 (m, 0.75H), 7.01 (d, J = 3.6 Hz, 0.25H), 6.91 (d, J = 8.0 Hz, 0.25H), 6.87 (dd, J = 8.4 Hz, 2.0 Hz, 0.75H), 6.77 (d, J = 8.4 Hz, 0.75H), 6.58 (d, J = 2.0 Hz, 0.75H), 6.55 (d, J = 3.6 Hz, 0.75H), 6.45 (dd, J = 3.6 Hz, 2.0 Hz, 0.75H), 3.92 (s, 0.75H), 3.91 (s, 0.75H), 3.87 (s, 2.25H), 3.69 (s, 2.25H), 2.34 (s, 2.25H), 2.06 (s, 0.75H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 149.6, 149.4, 148.9, 148.8, 148.7, 148.1, 144.7, 144.6, 144.5, 141.8, 127.1, 126.4, 122.5, 121.7, 119.0, 118.7, 115.8, 115.2, 112.2, 111.9, 111.5, 111.1, 110.91, 110.88, 108.4, 56.1, 56.0, 55.9, 55.7, 17.1, 17.0; HRMS (ESI) m/z calcd for $C_{16}H_{16}NO_3S$ $[M + H]^+$ 302.0851, found 302.0845.

2-(3-Chlorophenyl)-3-(1-methyl-1H-pyrrol-2-yl)-3-(methylthio)-acrylonitrile (**9q**). Obtained as a 50:50 inseparable mixture of geometrical isomers, yellow semi solid (682.5 mg, 79%): R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2931, 2202, 1483, 1248, 824; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, J = 3.2 Hz, 2.0 Hz, 0.5H), 7.5 (dt, J = 7.2 Hz, 1.6 Hz, 0.5H), 7.40−7.33 (m, 1H), 7.15−7.10 (m, 1H), 6.96 (dd, J = 2.4 Hz, 2.0 Hz, 0.5H), 6.88 (dt, J = 6.4 Hz, 2.0 Hz, 0.5H), 6.80 (dd, J = 2.4 Hz, 2.0 Hz, 0.5H), 6.67 (dd, J = 3.2 Hz, 2.0 Hz, 0.5H), 6.42 (dd, J = 3.6 Hz, 1.6 Hz, 0.5H), 6.32 (dd, J = 3.6 Hz, 1.6 Hz, 0.5H), 6.23−6.21 (m, 1H), 3.71 (s, 1.5H), 3.14 (s, 1.5H), 2.22 (s, 1.5H), 1.90 (s, 1.5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.2, 150.7, 136.6, 135.4, 134.7, 130.0, 129.8, 129.3, 129.1, 128.1, 128.0, 127.4, 126.8, 126.6, 126.2, 125.9, 125.5, 118.52, 118.45, 114.6, 113.6, 109.9, 109.1, 108.9, 106.6, 34.42, 34.38, 16.8, 16.2; HRMS (ESI) m/z calcd for $C_{15}H_{14}ClN_2S$ $[M + H]^+$ 289.0566 and 291.0537, found 289.0561 and 291.0532.

2-(3-Methoxyphenyl)-3-(methylthio)-3-(thiophen-2-yl)-acrylonitrile (**9r**). Obtained as a 60:40 inseparable mixture of geometrical isomers, yellow semi solid (860.9 mg, 83%): R_f 0.6 (1:2 EtOAc/hexane); IR (neat, cm^{-1}) 2930, 2210, 1470, 1276, 824; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, J = 5.2 Hz, 1.2 Hz, 0.6H), 7.47 (dd, J = 3.6 Hz, 1.2 Hz, 0.6H), 7.42 (dd, J = 4.8 Hz, 1.2 Hz, 0.4H), 7.35 (t, J = 8.0 Hz, 0.6H), 7.19−7.12 (m, 2.2H), 6.98−6.91 (m, 1.4H), 6.85 (ddd, J = 7.6 Hz, 1.6 Hz, 0.8 Hz, 0.4H), 6.78 (ddd, J = 8.4 Hz, 2.8 Hz, 0.8 Hz, 0.4H), 6.74−6.73 (m, 0.4H), 3.84 (s, 1.8H), 3.65 (s, 1.2H), 2.30 (s, 1.2H), 2.04 (s, 1.8H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.8, 159.7, 151.2, 149.6, 138.4, 137.3, 135.6, 135.3, 131.2, 130.3, 129.8, 129.74, 129.68, 127.90, 127.86, 121.80, 121.78, 119.0, 118.7, 115.03, 114.99, 114.7, 114.2, 111.2, 110.0, 55.5, 55.3, 17.7, 17.3; HRMS (ESI) m/z calcd for $C_{15}H_{14}NOS_2$ $[M + H]^+$ 288.0517, found 288.0511.

3-(1-Methyl-1H-pyrrol-2-yl)-3-(methylthio)-2-(thiophen-3-yl)-acrylonitrile (**10a**). Obtained as a 55:45 inseparable mixture of geometrical isomers, brown semi solid (623.9 mg, 80%): R_f 0.6 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2989, 2209, 1483, 1278, 838; ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, J = 2.8 Hz, 1.6 Hz, 0.45H), 7.55 (dd, J = 5.2 Hz, 1.6 Hz, 0.45H), 7.38 (dd, J = 5.2 Hz, 2.8 Hz, 0.45H), 7.11 (dd, J = 5.2 Hz, 2.8 Hz, 0.55H), 6.97 (dd, J = 2.8 Hz, 1.2 Hz, 0.55H), 6.78 (t, J = 2.0 Hz, 0.45H), 6.72 (t, J = 2.0 Hz, 0.55H), 6.37−6.34 (m, 1H), 6.29−6.24 (m, 1.1H), 6.21 (dd, J = 3.2 Hz, 2.4 Hz, 0.45H), 3.66 (s, 1.35H), 3.21 (s, 1.65H), 2.16 (s, 1.65H), 1.94 (s, 1.35H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.5, 146.8, 135.4, 134.0, 128.3, 127.1, 126.4, 126.3, 126.0, 125.72, 125.67, 125.1, 124.5, 118.7, 118.4, 112.92, 112.87, 109.7, 108.7, 106.6, 105.2, 34.3, 34.2, 16.4, 16.1; HRMS (ESI) m/z calcd for $C_{13}H_{13}N_2S_2$ $[M + H]^+$ 261.0520, found 261.0513.

2-(1-Methyl-1H-indol-3-yl)-3-(methylthio)-3-(thiophen-2-yl)-acrylonitrile (**10b**). Obtained as a 60:40 inseparable mixture of geometrical isomers, brown solid (669.5 mg, 72%): mp 85−87 °C; R_f 0.6 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2919, 2201, 1473, 1222, 820; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.0 Hz, 0.4H), 7.53 (dd, J = 5.2 Hz, 1.2 Hz, 0.4H), 7.46−7.45 (m, 0.8H), 7.38−7.29 (m, 1.6H), 7.27−7.17 (m, 2.0H), 7.15 (dd, J = 5.2 Hz, 3.6 Hz, 0.4H), 7.10 (s, 0.6H), 7.09 (dd, J = 4.0 Hz, 1.2 Hz, 0.6H), 7.01−6.97 (m, 0.6H), 6.88 (dd, J = 4.8 Hz, 3.2 Hz, 0.6H), 3.86 (s, 1.2H), 3.74 (s, 1.8H), 2.35 (s, 1.8H), 2.05 (s, 1.2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 146.7, 143.3, 139.0, 138.8, 136.9, 136.7, 131.1, 131.0, 130.8, 130.0, 129.6, 129.1, 127.7, 127.6, 126.0, 125.3, 122.8, 122.5, 120.64, 120.58, 120.3, 119.5, 119.2, 109.8, 109.7, 109.6, 108.5, 106.2, 104.0, 33.4, 33.2, 17.9, 17.4; HRMS (ESI) m/z calcd for $C_{17}H_{15}N_2S_2$ $[M + H]^+$ 311.0677, found 311.0676.

3-(4-Fluorophenyl)-3-(methylthio)-2-(pyridin-3-yl)acrylonitrile (**10d**). Obtained as a single geometrical isomer, off-white solid (502.1 mg, 62%): mp 80−82 °C; R_f 0.5 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 2932, 2206, 1498, 1418, 1229, 810; ^1H NMR (400 MHz, $CDCl_3$) δ 8.38 (dd, J = 4.8 Hz, 1.6 Hz, 1H), 8.26 (d, J = 1.6 Hz, 1H), 7.43 (dt, J = 8.0 Hz, 2.4 Hz, 1H), 7.19−7.16 (m, 2H), 7.14−7.11 (m, 1H), 7.05−7.01 (m, 2H), 2.09 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.5 (d, $^1J_{C-F}$ = 251.0 Hz), 159.9, 150.2, 148.9, 136.4, 131.8, 131.7, 130.5, 129.94, 129.91, 123.3, 117.8, 116.9, 116.6, 106.3, 16.4; HRMS (ESI) m/z calcd for $C_{15}H_{12}FN_2S$ $[M + H]^+$ 271.0705, found 271.0701.

3-(Methylthio)-1,2,3-tri(thiophen-2-yl)prop-2-en-1-one (**10e**). Obtained as a 55:45 inseparable mixture of geometrical isomers, brown semi solid (676.6 mg, 65%): R_f 0.5 (1:9 EtOAc/hexane); IR (neat, cm^{-1}) 2839, 1652, 1592, 1258, 831; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 3.6 Hz, 0.45H), 7.70 (d, J = 4.8 Hz, 0.45H), 7.54−7.48 (m, 1.45H), 7.40 (d, J = 5.2 Hz, 0.55H), 7.264−7.265 (m, 0.55H), 7.17−7.13 (m, 1.45H), 7.07−7.04 (m, 1.1H), 7.01 (dd, J = 4.8 Hz, 3.6 Hz, 0.55H), 6.97−6.93 (m, 0.9H), 6.87−6.80 (m, 1.55H), 2.17 (s, 1.65H), 1.97 (s, 1.35H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.8, 187.3, 143.9, 143.6, 141.0, 138.1, 137.8, 135.9, 135.04, 135.0, 134.88, 134.86, 134.7, 134.3, 131.0, 130.6, 130.17, 130.15, 129.8,

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129.1, 128.9, 128.8, 128.5, 128.0, 127.7, 127.6, 127.5, 127.2, 126.8, 126.7, 17.3, 16.7; HRMS (ESI) m/z calcd for $C_{16}H_{13}OS_4$ $[M + H]^+$ 348.9849, found 348.9849.

*3-(4-Methoxyphenyl)-3-(methylthio)-2-(pyridin-3-yl)-1-(thiophen-2-yl)prop-2-en-1-one (**10f**).* Obtained as a 55:45 inseparable mixture of geometrical isomers, yellow solid (1.1 g, 66%): mp 85−87 °C; R_f 0.6 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 2917, 1629, 1602, 1504, 1406, 828; ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 0.45H), 8.54 (d, J = 4.8 Hz, 0.45H), 8.31−8.30 (m, 1.1H), 7.87 (dt, J = 7.6 Hz, 2.0 Hz, 0.45H), 7.72 (dd, J = 3.6 Hz, 1.2 Hz, 0.55H), 7.69 (dd, J = 4.8 Hz, 1.2 Hz, 0.55H), 7.47−7.46 (m, 0.55H), 7.43 (dt, J = 8.0 Hz, 1.6 Hz, 0.9H), 7.34−7.32 (m, 1.1H), 7.27−7.24 (m, 1.1H), 7.14 (dd, J = 4.8 Hz, 4.0 Hz, 0.45H), 7.06 (dd, J = 7.6 Hz, 4.8 Hz, 0.9H), 6.90 (t, J = 4.8 Hz, 0.45H), 6.81 (d, J = 8.8 Hz, 1.1H), 6.76 (d, J = 8.8 Hz, 0.9H), 3.79 (s, 1.65H), 3.74 (s, 1.35H), 1.88 (s, 1.35H), 1.87 (s, 1.65H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.7, 188.2, 160.0, 150.6, 150.5, 148.9, 148.0, 145.9, 144.6, 144.2, 143.5, 136.7, 136.6, 135.4, 134.9, 134.7, 134.6, 134.4, 134.0, 133.8, 133.4, 131.7, 131.4, 129.0, 128.6, 128.4, 127.9, 127.5, 123.3, 123.2, 114.4, 114.0, 55.4, 55.3, 16.3; HRMS (ESI) m/z calcd for $C_{20}H_{18}NO_2S_2$ $[M + H]^+$ 368.0779, found 368.0773.

*3-(Benzo[d][1,3]dioxol-5-yl)-3-(methylthio)-2-(pyridin-3-yl)-acrylonitrile (**10g**).* Obtained as a 70:30 inseparable mixture of geometrical isomers, off-white solid (973.7 mg, 69%): mp 94−96 °C; R_f 0.3 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 2924, 2199, 1483, 1249, 876; ^1H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 0.7H), 8.60 (d, J = 4.4 Hz, 0.7H), 8.38 (d, J = 4.0 Hz, 0.3H), 8.28 (d, J = 1.6 Hz, 0.3H), 7.89 (dt, J = 8.0 Hz, 2.0 Hz, 0.7H), 7.51 (dt, J = 8.0 Hz, 2.0 Hz, 0.3H), 7.38 (dd, J = 8.0 Hz, 4.8 Hz, 0.7H), 7.16 (dd, J = 8.0 Hz, 4.8 Hz, 0.3H), 7.0 (dd, J = 8.0 Hz, 2.0 Hz, 0.7H), 6.94−6.92 (m, 1.3H), 6.72 (d, J = 8.0 Hz, 0.3H), 6.68−6.63 (m, 0.7H), 6.06 (s, 1.4H), 5.99 (s, 0.6H), 2.13 (s, 0.9H), 1.97 (s, 2.1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.0, 160.8, 150.2, 150.1, 149.6, 149.4, 149.3, 148.7, 148.6, 148.5, 136.6, 136.2, 130.8, 130.3, 129.3, 127.4, 124.2, 123.4, 123.3, 118.3, 118.1, 109.7, 109.1, 108.9, 105.6, 105.5, 101.9, 16.8, 16.4; HRMS (ESI) m/z calcd for $C_{16}H_{13}N_2O_2S$ $[M + H]^+$ 297.0698, found 297.0698.

*3-(5-(Dimethylamino)thiophen-2-yl)-3-(methylthio)-2-(thiophen-3-yl)acrylonitrile (**10h**).* Obtained as a 58:42 inseparable mixture of geometrical isomers, red solid (755.2 mg, 82%): mp 62−64 °C; R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2927, 2187, 1485, 1323, 913; ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, J = 3.2 Hz, 1.2 Hz, 0.48H), 7.51−7.48 (m, 1H), 7.34 (dd, J = 2.8 Hz, 1.2 Hz, 0.52H), 7.32 (dd, J = 4.8 Hz, 2.8 Hz, 0.52H), 7.16 (dd, J = 5.2 Hz, 2.8 Hz, 0.48H), 6.94 (d, J = 4.0 Hz, 0.48H), 6.90 (dd, J = 5.2 Hz, 1.2 Hz, 0.52H), 5.92 (d, J = 4.0 Hz, 0.48H), 5.74 (d, J = 4.0 Hz, 0.52H), 3.03 (s, 2.88H), 2.95 (s, 3.12H), 2.43 (s, 1.56H), 2.15 (s, 1.44H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.4, 164.1, 149.3, 148.2, 135.94, 135.91, 134.5, 133.3, 128.4, 127.9, 125.6, 125.4, 125.3, 122.9, 121.1, 120.8, 120.2, 103.3, 102.7, 100.6, 97.9, 42.3, 42.2, 18.7, 18.6; HRMS (ESI) m/z calcd for $C_{14}H_{15}N_2S_3$ $[M + H]^+$ 307.0397, found 307.0400.

*General Procedure for the Synthesis of N-Aryl/acylenaminonitrile/enaminones **7a−j, 11a,b, 11d−f, 13a−e**.* A solution of 3-(methylthio)acrylonitrile **9** or **10** (1.0 mmol) in dry DMF (3 mL) was added to a stirred suspension of het(aryl)amine or the corresponding aryl/alky amide (1.1 mmol) and NaH (28.8 mg, 1.2 mmol, 60% suspension in mineral oil) in DMF (5 mL) at room temperature, followed by heating at 90 °C for 8−10 h (monitored by TLC). It was then poured into saturated NH_4Cl (25 mL) solution, extracted with EtOAc (2 × 25 mL), washed with water (2 × 25 mL), brine (20 mL), dried (Na_2SO_4), and the solvent was evaporated under reduced pressure to give crude products, which were purified by column chromatography using EtOAc/hexane as eluent.

*2-(3-Methoxyphenyl)-3-(4-methoxyphenyl)-3-(4-methoxyphenylamino)acrylonitrile (**7a**).* Obtained as a 75:25 inseparable mixture of geometrical isomers, pale yellow solid (308.8 mg, 80%): mp 83−85 °C; R_f 0.5 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3310, 2928, 2196, 1491, 1249, 855; ^1H NMR (400 MHz, DMSO-d_6) δ 9.17 (br s, 0.25H), 8.84 (br s, 0.75H), 7.50, (d, J = 8.8 Hz, 1.5H), 7.21 (t, J = 8.0 Hz, 0.75H), 7.15 (d, J = 8.8 Hz, 0.75H), 7.05 (t, J = 8.0 Hz, 0.25H), 6.99−6.94 (m, 2.25H), 6.87−6.79 (m, 1.75H), 6.75−6.72 (m, 1.25H), 6.69 (d, J = 9.2 Hz, 1.5H), 6.62 (d, J = 9.2 Hz, 1.5H), 6.56 (d, J = 8.0 Hz, 0.25H), 6.44 (t, J = 2.0 Hz, 0.25H), 3.79 (s, 2.25H), 3.70 (s, 0.75H), 3.67 (s, 2.25H), 3.66 (s, 0.75H), 3.60 (s, 2.25H), 3.52 (s, 0.75H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.3, 160.9, 160.5, 159.4, 156.5, 156.2, 156.0, 155.4, 135.7, 135.5, 133.7, 133.2, 132.4, 131.9, 131.6, 130.5, 129.2, 125.6, 124.3, 124.2, 123.3, 122.3, 122.1, 120.8, 114.6, 114.4, 114.3, 114.2, 114.1, 114.0, 113.5, 112.4, 87.4, 85.3, 55.53, 55.49, 55.46, 55.41, 55.4, 55.1; HRMS (ESI) m/z calcd for $C_{24}H_{23}N_2O_3$ $[M + H]^+$ 387.1709, found 387.1704.

*3-(4-Chlorophenylamino)-2-(3,4-dimethoxyphenyl)-3-(thiophen-2-yl)acrylonitrile (**7b**).* Obtained as a 75:25 inseparable mixture of geometrical isomers, yellow solid (344.5 mg, 87%): mp 201−201 °C; R_f 0.3 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3307, 2919, 2196, 1518, 1249, 855; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 3.2 Hz, 0.75H), 7.47 (dd, J = 4.8 Hz, 0.4 Hz, 0.75H), 7.36 (d, J = 4.0 Hz, 0.25H), 7.13−7.08 (m, 3H), 7.04, (dd, J = 8.4 Hz, 2.0 Hz, 0.75H), 6.95 (d, J = 2.0 Hz, 0.75H), 6.87−6.81 (m, 1.5H), 6.75−6.70 (m, 0.75H), 6.62 (d, J = 8.8 Hz, 1.5H), 6.58 (d, J = 2.0 Hz, 0.25H), 6.32 (br s, 0.75H), 3.88 (s, 2.25H), 3.85 (s, 0.75H), 3.78 (s, 2.25H), 3.63 (s, 0.75H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 149.7, 149.3, 148.8, 148.6, 146.7, 145.6, 140.0, 139.3, 135.9, 134.4, 132.4, 132.0, 130.3, 130.0, 129.3, 129.2, 128.8, 128.4, 128.0, 127.7, 125.9, 125.6, 122.3, 122.2, 121.19, 121.15, 121.10, 120.1, 112.7, 111.9, 111.5, 111.2, 92.6, 90.9, 56.14, 56.07, 55.98, 55.78; HRMS (ESI) m/z calcd for $C_{21}H_{18}ClN_2O_2S$ $[M + H]^+$ 397.0778 and 399.0748, found 397.0772 and 399.0753.

*2-(4-Fluorophenyl)-3-(1-methyl-1H-indol-3-yl)-3-(pyridin-3-ylamino)acrylonitrile (**7c**).* Obtained as a 85:15 inseparable mixture of geometrical isomers, yellow solid (261.2 mg, 71%): mp 176−178 °C; R_f 0.6 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 3280, 2953, 2190, 1599, 1463, 1120; ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 2.8 Hz, 1H), 8.06 (dd, J = 4.4 Hz, 1.2 Hz, 1H), 7.77 (s, 0.85H), 7.63 (s, 0.15H), 7.49−7.41 (m, 3H), 7.34−7.31 (m, 1H), 7.23−7.19 (m, 1.15H), 7.09−7.04 (m, 2.85H), 7.01−6.98 (m, 1H), 6.92 (d, J = 4.8 Hz, 0.85H), 6.90 (d, J = 4.4 Hz, 0.15H), 6.48 (br s, 0.15H), 6.42 (br s, 0.85H), 3.87 (s, 2.55H), 3.86 (s, 0.45H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.1 (d, $^1J_{C-F}$ = 247.0 Hz), 148.6, 147.6, 147.3, 143.9, 142.5 (d, $^1J_{C-F}$ = 237.0 Hz), 142.2, 141.4, 138.6, 138.2, 138.1, 138.0, 137.5, 137.3, 133.3, 133.0, 130.7, 130.6, 130.5, 130.0, 129.9, 128.9, 127.2, 126.1, 126.0, 125.6, 125.4, 123.4, 123.03, 122.98, 122.4, 121.4, 120.8, 120.7, 116.7, 116.4, 115.6, 115.4, 110.21, 110.16, 1.09.9, 108.0, 106.3, 89.1, 88.2, 33.7, 33.5; HRMS (ESI) m/z calcd for $C_{23}H_{18}FN_4$ $[M + H]^+$ 369.1515, found 369.1513.

*3-(2-Bromophenylamino)-3-(5-(dimethylamino)thiophen-2-yl)-2-(4-fluorophenyl)acrylonitrile (**7d**).* Obtained as a 75:25 inseparable mixture of geometrical isomers, orange solid (326.3 mg, 74%): mp 52−54 °C; R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 3305, 2928, 2186, 1461, 1273, 834; ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 4.4 Hz, 0.75H), 7.52 (dd, J = 8.0 Hz, 1.6 Hz, 0.25H), 7.41 (dd, J = 8.0 Hz, 1.6 Hz, 0.75H), 7.34−7.30 (m, 1.75H), 7.11−7.06 (m, 0.25H), 7.0−6.92 (m, 1.5H), 6.91−6.87 (m, 1.5H), 6.82−6.78 (m, 0.25H), 6.76−6.70 (m, 2H), 6.57 (br s, 0.25H), 6.14 (br s, 0.75H), 5.89 (d, J = 4.0 Hz, 0.75H), 5.59 (d, J = 4.4 Hz, 0.25H) 3.00 (s, 4.5H), 2.88 (s, 1.5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.2, 163.8, 161.9 (d, $^1J_{C-F}$ = 247.0 Hz), 161.7 (d, $^1J_{C-F}$ = 246.0 Hz), 147.1, 145.7, 140.1, 139.3, 135.2, 134.5, 132.9, 132.6, 131.6, 131.5, 130.6, 130.5, 130.0, 129.8, 129.7, 128.2, 128.0, 126.9, 123.3, 123.2, 122.6, 120.8, 120.7, 120.0, 118.7, 116.9, 116.0, 115.8, 115.7, 115.6, 114.3, 113.8, 103.0, 102.2, 88.1, 87.2, 42.3, 42.2; HRMS (ESI) m/z calcd for $C_{21}H_{18}BrFN_3S$ $[M + H]^+$ 442.0389 and 444.0368, found 442.0387 and 444.0369.

*3-(Benzo[d][1,3]dioxol-5-yl)-3-(4-chlorophenylamino)-2-(3-fluorophenyl)acrylonitrile (**7e**).* Obtained as a single geometrical isomer, yellow solid (254.8 mg, 65%): mp 85−87 °C; R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 3265, 2191, 1487, 1245, 819; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.33 (m, 1H), 7.9 (s, 1H), 7.21−7.16 (m, 2H), 7.08 (d, J = 8.8 Hz, 2H), 7.01−6.96 (m, 2H), 6.84 (d, J = 8.0 Hz, 1H), 6.57 (d, J = 8.8 Hz, 2H), 6.50 (br s, 1H), 6.02 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.4 (d, $^1J_{C-F}$ = 246.0 Hz), 154.1, 150.2, 148.3, 138.9, 135.9, 135.8, 131.2, 131.1, 129.3, 128.9, 126.7, 125.0, 124.17, 124.15, 123.0, 122.0, 115.7, 115.4, 115.2, 115.0, 109.8, 109.0, 101.9, 89.5; HRMS (ESI) m/z calcd for $C_{22}H_{15}ClFN_2O_2$ $[M + H]^+$ 393.0806 and 395.0777, found 393.0800 and 395.0780.

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*3-(1-Cyano-2-(4-(dimethylamino)phenyl)-2-(pyridin-3-ylamino)-vinyl)benzonitrile (**7f**).* Obtained as a single geometrical isomer, pale yellow solid (299.3 mg, 82%): mp 175−177 °C; R_f 0.3 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 3243, 2985, 2232, 2192, 1606, 1366, 1193, 817; ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 4.4 Hz, 1H), 8.07 (d, J = 2.4 Hz, 1H), 7.73 (s, 1H), 7.68 (d, J = 7.6 Hz, 1H), 7.49 (d, J = 8.8 Hz, 2H), 7.46−7.40 (m, 2H), 7.03−6.99 (m, 1H), 6.92−6.90 (m, 1H), 6.66 (d, J = 8.8 Hz, 2H), 6.42 (br s, 1H), 3.03 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.1, 154.7, 150.7, 149.8, 138.7, 136.3, 135.6, 135.1, 131.3, 131.0, 130.3, 128.8, 126.4, 125.7, 118.7, 113.8, 113.7, 111.5, 111.4, 40.3; HRMS (ESI) m/z calcd for $C_{23}H_{20}N_5$ $[M + H]^+$ 366.1719, found 366.1710.

*2-(3-Chlorophenyl)-3-(furan-2-yl)-3-(3,4,5-trimethoxyphenylamino)acrylonitrile (**7g**).* Obtained as a 75:25 inseparable mixture of geometrical isomers, yellow solid (274.7 mg, 67%): mp 105−107 °C; R_f 0.4 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3282, 2946, 2188, 1463, 1120, 759; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 0.75H), 7.36 (s, 0.5H), 7.28−7.26 (m, 2H), 7.20−7.08 (m, 2.25H), 6.99 (s, 0.25H), 6.89 (br s, 0.25H), 6.59 (d, J = 1.2 Hz, 0.75H), 6.44 (br s, 0.75H), 6.37 (d, J = 3.2 Hz, 0.5H), 5.98 (s, 0.5H), 5.92 (s, 1.5H), 3.77 (s, 0.75H), 3.71 (s, 2.25H), 3.68 (s, 1.5H), 3.66 (s, 4.5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.6, 153.5, 147.1, 145.3, 144.7, 144.6, 144.1, 142.4, 136.3, 135.8, 135.5, 135.4, 134.7, 134.6, 134.4, 130.0, 129.7, 128.7, 128.5, 127.6, 127.2, 126.9, 126.2, 121.4, 119.7, 116.8, 112.7, 112.4, 98.5, 98.4, 87.7, 84.9, 61.1, 56.11, 56.08; HRMS (ESI) m/z calcd for $C_{22}H_{20}ClN_2O_4$ $[M + H]^+$ 411.1112 and 413.1082, found 411.1108 and 413.1081.

*2-(4-Bromophenyl)-3-(4-methoxyphenylamino)-3-(1-methyl-1H-pyrrol-2-yl)acrylonitrile (**7h**).* Obtained as a 90:10 inseparable mixture of geometrical isomers, yellow solid (297.1 mg, 73%): mp 155−157 °C; R_f 0.6 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3293, 2939, 2192, 1508, 1240, 823; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.4 Hz, 0.2H), 7.37 (d, J = 8.8 Hz, 0.2H), 7.27 (d, J = 8.4 Hz, 1.8H), 6.98 (br s, 0.9H), 6.77 (d, J = 8.8 Hz, 1.8H), 6.73−6.71 (m, 2H), 6.65−6.63 (m, 2H), 6.58 (t, J = 2.0 Hz, 0.9H), 6.48 (d, J = 8.0 Hz, 0.2H), 6.44 (br s, 0.1H), 6.23−6.19 (m, 0.1H), 6.10−6.05 (m, 1.8H), 3.73 (s, 2.7H), 3.72 (s, 0.3H), 3.43 (s, 0.3H), 3.19 (s, 2.7H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 156.4, 156.0, 147.4, 145.7, 133.8, 133.5, 133.3, 133.0, 132.6, 131.6, 130.0, 129.4, 127.1, 126.2, 123.8, 122.8, 121.8, 121.2, 120.9, 120.6, 119.6, 116.6, 116.4, 115.0, 114.7, 114.5, 109.7, 109.4, 86.8, 84.2, 55.6, 55.5, 35.0, 34.6; HRMS (ESI) m/z calcd for $C_{21}H_{19}BrN_3O$ $[M + H]^+$ 408.0711 and 410.0691, found 408.0707 and 410.0688.

*2-(2,5-Dimethoxyphenyl)-3-(pyridin-3-yl)-3-(4-(trifluoromethyl)-phenylamino)acrylonitrile (**7i**).* Obtained as a single geometrical isomer, yellow solid (272.0 mg, 64%): mp 77−79 °C; R_f 0.5 (3:2 EtOAc/hexane); IR (neat, cm^{-1}) 3253, 2925, 2179, 1604, 1245, 823; ^1H NMR (400 MHz, $CDCl_3$) δ 8.8 (s, 1H), 8.68 (d, J = 4.0 Hz, 1H), 8.05 (dt, J = 8.0 Hz, 1.6 Hz, 1H), 7.39 (dd, J = 8.0 Hz, 4.8 Hz, 1H), 7.31 (d, J = 8.4 Hz, 2H), 7.02 (dd, J = 2.0 Hz, 1.2 Hz, 1H), 6.93−6.92 (m, 2H), 6.83 (br s, 1H), 6.60 (d, J = 8.8 Hz, 2H), 3.80 (s, 3H), 3.77 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 154.5, 151.6, 151.0, 150.7, 150.6, 143.4, 137.7, 129.5, 126.4 (q, J_{C-F} = 4.0 Hz), 125.2, 124.8, 123.7, 121.8, 120.5, 120.4, 116.34, 116.25, 113.8, 90.4, 56.8, 56.0; HRMS (ESI) m/z calcd for $C_{23}H_{19}F_3N_3O_2$ $[M + H]^+$ 426.1429, found 426.1426.

*3-(4-Fluorophenylamino)-3-(1-methyl-1H-imidazol-2-yl)-2-(naphthalen-2-yl)acrylonitrile (**7j**).* Obtained as a 50:50 inseparable mixture of geometrical isomers, yellow solid (250.2 mg, 68%): mp 153−155 °C; R_f 0.5 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 3123, 2197, 1505, 1228, 830; ^1H NMR (400 MHz, $CDCl_3$) δ 8.0 (s, 0.5H), 7.84−7.79 (m, 1.5H), 7.72 (dd, J = 5.6 Hz, 3.2 Hz, 0.5H), 7.65 (dd, J = 6.4 Hz, 2.8 Hz, 0.5H), 7.59 (t, J = 8.4 Hz, 1H), 7.51−7.50 (m, 1.5H), 7.42 (dd, J = 6.0 Hz, 3.2 Hz, 1H), 7.37 (br s, 0.5H), 7.21 (s, 0.5H), 7.10 (s, 0.5H), 6.95−6.87 (m, 3H), 6.82−6.75 (m, 1H), 6.74−6.70 (m, 1H), 6.58 (dd, J = 8.4 Hz, 4.4 Hz, 1H), 3.63 (s, 1.5H), 3.15 (s, 1.5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.7 (d, $^1J_{C-F}$ = 243.0 Hz), 159.5 (d, $^1J_{C-F}$ = 243.0 Hz), 143.9, 142.7, 140.2, 139.4, 135.8, 135.76, 135.73, 135.69, 133.7, 133.5, 132.9, 132.1, 130.7, 130.6, 130.3, 129.9, 129.4, 128.4, 128.2, 128.1, 128.0, 127.9, 127.6, 127.1, 127.0, 126.7, 126.5, 125.5, 125.3, 123.6, 123.0, 122.84, 122.76, 121.63, 121.55, 120.1, 119.5, 116.31, 116.28, 116.09, 116.05, 92.5, 89.9, 33.9, 33.5; HRMS (ESI) m/z calcd for $C_{23}H_{18}FN_4$ $[M + H]^+$ 369.1515, found 369.1522.

*3-(1-Methyl-1H-pyrrol-2-yl)-2-(thiophen-3-yl)-3-(4-(trifluoromethyl)phenylamino)acrylonitrile (**11a**).* Obtained as a single geometrical isomer, yellow solid (268.5 mg, 72%): mp 130−132 °C; R_f 0.4 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 3399, 2981, 2202, 1518, 1112, 838; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (dd, J = 3.2 Hz, 1.6 Hz, 1H), 7.41−7.37 (m, 3H), 7.23 (dd, J = 4.8 Hz, 1.2 Hz, 1H), 6.76 (dd, J = 3.6 Hz, 1.6 Hz, 1H), 6.74−6.73 (m, 1H), 6.71 (br s, 1H), 6.50 (d, J = 8.4 Hz, 2H), 6.26 (dd, J = 3.6 Hz, 2.4 Hz, 1H), 3.42 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 143.8, 142.7, 133.7, 127.6, 127.5, 126.8 (q, J_{C-F} = 4.0 Hz), 124.7, 124.5, 124.2, 123.8, 122.9, 120.9, 117.4, 116.7, 109.8, 88.0, 35.0; HRMS (ESI) m/z calcd for $C_{19}H_{15}F_3N_3S$ $[M + H]^+$ 374.0939, found 374.0936.

*3-(4-Methoxyphenylamino)-2-(1-methyl-1H-indol-3-yl)-3-(thiophen-2-yl)acrylonitrile (**11b**).* Obtained as a 90:10 inseparable mixture of geometrical isomers, yellow solid (257.9 mg, 67%): mp 72−74 °C; R_f 0.5 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3307, 2924, 2196, 1491, 1249, 855; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, J = 3.6 Hz, 1.2 Hz, 0.9H), 7.53 (d, J = 8.0 Hz, 0.9H), 7.40 (dd, J = 5.2 Hz, 1.2 Hz, 0.9H), 7.35 (d, J = 8.4 Hz, 1H), 7.29 (s, 0.9H), 7.27−7.23 (m, 0.9H), 7.19−7.16 (m, 0.2H), 7.09−7.04 (m, 1.8H), 7.02−6.98 (m, 0.1H), 6.96−6.95 (m, 0.1H), 6.91 (s, 0.1H), 6.82−6.80 (m, 0.2H), 6.77 (s, 0.1H), 6.73−6.70 (m, 0.3H), 6.66 (s, 3.7H), 6.38 (s, 0.9H), 3.81 (s, 2.7H), 3.73 (s, 0.3H), 3.71 (s, 0.3H), 3.70 (s, 2.7H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 156.0, 146.6, 137.3, 135.4, 134.0, 131.6, 129.5, 129.2, 127.3, 125.5, 123.0, 122.6, 122.1, 120.5, 120.2, 114.4, 110.0, 107.4, 81.9, 55.5, 33.2; HRMS (ESI) m/z calcd for $C_{23}H_{20}N_3OS$ $[M + H]^+$ 386.1327, found 386.1315.

*3-(4-Fluorophenyl)-3-(4-methoxyphenylamino)-2-(pyridin-3-yl)-acrylonitrile (**11d**).* Obtained as a single geometrical isomer, off-white solid (255.3 mg, 74%): mp 85−87 °C; R_f 0.3 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 3310, 2922, 2199, 1490, 1142, 855; ^1H NMR (400 MHz, $CDCl_3$) δ 8.74 (br s, 1H), 8.45−8.43 (m, 1H), 7.78 (d, J = 7.6 Hz, 1H), 7.60−7.56 (m, 2H), 7.31−7.29 (m, 1H), 7.08 (t, J = 8.8 Hz, 2H), 6.71 (br s, 1H), 6.63−6.62 (m, 4H), 3.69 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.2 (d, $^1J_{C-F}$ = 251.0 Hz), 156.7, 155.6, 149.6, 148.5, 136.2, 132.9, 132.8, 132.5, 132.3, 132.2, 129.6, 125.1, 123.9, 121.3, 116.3, 116.1, 114.5, 84.1, 55.6; HRMS (ESI) m/z calcd for $C_{21}H_{17}FN_3O$ $[M + H]^+$ 346.1356, found 346.1349.

*N-(2-Cyano-2-(3,4-dimethoxyphenyl)-1-(furan-2-yl)vinyl)-propionamide (**13a**).* Obtained as a 85:15 inseparable mixture of geometrical isomers, brown solid (221.6 mg, 68%): mp 165−167 °C; R_f 0.5 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 3238, 2216, 1668, 1488, 1276; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 2.0 Hz, 0.85H), 7.37 (d, J = 1.6 Hz, 0.15H), 7.34 (br s, 0.15H), 7.16 (d, J = 3.6 Hz, 0.85H), 7.04 (dd, J = 8.4 Hz, 2.0 Hz, 0.85H), 6.98 (br s, 0.85H), 6.95 (d, J = 2.0 Hz, 0.85H), 6.93−6.88 (m, 1H), 6.82 (d, J = 8.4 Hz, 0.15H), 6.73 (d, J = 2.0 Hz, 0.15H), 6.56 (dd, J = 3.6 Hz, 2.0 Hz, 0.85H), 6.36 (dd, J = 3.6 Hz, 1.6 Hz, 0.15H), 6.27 (d, J = 3.6 Hz, 0.15H), 3.90 (s, 2.55H), 3.88 (s, 0.45H), 3.85 (s, 2.55H), 3.74 (s, 0.45H), 2.45 (q, J = 7.6 Hz, 0.3H), 2.24 (q, J = 7.6 Hz, 1.7H), 1.25 (t, J = 7.6 Hz, 0.45H), 1.10 (t, J = 7.6 Hz, 2.55H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 172.2, 149.9, 149.8, 149.6, 149.1, 148.3, 147.3, 144.5, 144.4, 136.7, 135.6, 124.9, 124.8, 122.1, 121.6, 119.3, 118.3, 115.6, 112.9, 112.6, 112.5, 112.0, 111.7, 111.5, 111.4, 99.9, 56.2, 56.1, 56.03, 56.0, 30.2, 29.8, 9.4, 9.3; HRMS (ESI) m/z calcd for $C_{18}H_{19}N_2O_4$ $[M + H]^+$ 327.1345, found 327.1340.

*N-(2-(3-Chlorophenyl)-2-cyano-1-(1-methyl-1H-pyrrol-2-yl)vinyl)-pivalamide (**13b**).* Obtained as a single geometrical isomer, yellow solid (242.1 mg, 71%): mp 140−142 °C; R_f 0.6 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 3238, 2972, 2210, 1670, 1582, 1206; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 1.2 Hz, 1H), 7.39−7.37 (m, 2H), 7.34−7.30 (m, 1H), 7.28 (br s, 1H), 6.82 (t, J = 2.0 Hz, 1H), 6.61 (dd, J = 3.6 Hz, 1.6 Hz, 1H), 6.23 (dd, J = 4.0 Hz, 2.8 Hz, 1H), 3.66 (s, 3H), 1.14 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 175.4, 141.0, 135.2, 134.9, 130.8, 128.9, 128.3, 128.1, 126.8, 126.7, 119.5, 115.4, 109.4,

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99.1, 40.1, 35.1, 27.2; HRMS (ESI) m/z calcd for $C_{19}H_{21}ClN_3O$ $[M + H]^+$ 342.1373 and 344.1344, found 342.1370 and 344.1349.

*N-(2-Cyano-2-(3-methoxyphenyl)-1-(thiophen-2-yl)vinyl)-benzamide (**13c**).* Obtained as a 60:40 inseparable mixture of geometrical isomers, yellow semi solid (230.4 mg, 64%): R_f 0.5 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3242, 2980, 2212, 1673, 1477, 1089, 708; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (br s, 0.4H), 7.92 (d, J = 7.6 Hz, 0.6H), 7.84−7.83 (m, 1H), 7.77 (br s, 0.6H), 7.68 (d, J = 7.2 Hz, 1.2H), 7.62−7.57 (m, 0.8H), 7.55−7.49 (m, 1.8H), 7.44−7.38 (m, 1.2H), 7.30−7.21 (m, 0.8H), 7.15 (dd, J = 4.8 Hz, 4.0 Hz, 0.8H), 7.09−7.01 (m, 1.8H), 6.95−6.90 (m, 0.8H), 6.87−6.86 (m, 1.2H), 3.71 (s, 1.2H), 3.70 (s, 1.8H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.9, 165.6, 160.3, 159.9, 142.3, 141.7, 137.1, 136.2, 133.8, 133.4, 133.2, 133.1, 132.9, 132.8, 132.7, 131.4, 131.1, 130.5, 130.0, 129.7, 129.0, 128.9, 128.1, 127.6, 127.5, 122.0, 120.7, 119.5, 119.3, 118.1, 115.6, 115.3, 114.6, 113.4, 104.3, 102.0, 55.3; HRMS (ESI) m/z calcd for $C_{21}H_{17}N_2O_2S$ $[M + H]^+$ 361.1011, found 361.0999.

*N-(1-(Benzo[d][1,3]dioxol-5-yl)-2-cyano-2-(pyridin-3-yl)vinyl)-pivalamide (**13d**).* Obtained as a 90:10 inseparable mixture of geometrical isomers, pale yellow solid (209.4 mg, 60%): mp 153−155 °C; R_f 0.3 (3:2 EtOAc/hexane); IR (neat, cm^{-1}) 3242, 2942, 2219, 1665, 1519, 1276; ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1.8H), 8.39 (s, 0.1H), 8.28 (s, 0.1H), 7.82−7.77 (m, 1H), 7.54−7.50 (m, 1H), 7.37 (br s, 0.9H), 7.18 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 6.99 (s, 0.9H), 6.88 (d, J = 8.0 Hz, 0.9H), 6.67 (s, 0.2H), 6.58 (s, 0.1H), 6.03 (s, 1.8H), 5.95 (s, 0.2H), 1.20 (s, 0.9H), 1.12 (s, 8.1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 176.6, 175.7, 150.7, 150.6, 150.5, 150.2, 149.9, 149.5, 149.1, 148.7, 148.3, 136.5, 136.3, 130.3, 128.1, 126.3, 124.3, 124.1, 123.7, 119.0, 117.8, 109.1, 108.9, 108.8, 108.4, 102.0, 101.9, 98.3, 97.4, 40.1, 40.0, 27.3, 27.1; HRMS (ESI) m/z calcd for $C_{20}H_{20}N_3O_3$ $[M + H]^+$ 350.1505, found 350.1516.

*N-(2-Cyano-1-(5-(dimethylamino)thiophen-2-yl)-2-(thiophen-3-yl)vinyl)pivalamide (**13e**).* Obtained as a 60:40 inseparable mixture of geometrical isomers, yellow semi solid (240.5 mg, 67%): R_f 0.5 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3239, 2216, 1668, 1488, 1208, 809; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 4.4 Hz, 0.6H), 7.38−7.34 (m, 1H), 7.32−7.29 (m, 1H), 7.26−7.24 (m, 0.4H), 7.12 (dd, J = 5.2 Hz, 1.2 Hz, 0.6H), 7.07 (br s, 0.6H), 7.02 (dd, J = 4.8 Hz, 0.8 Hz, 0.4H), 6.85 (d, J = 4.4 Hz, 0.4H), 5.87 (d, J = 5.4 Hz, 0.6H), 5.68 (d, J = 4.0 Hz, 0.4H), 3.00 (s, 3.6H), 2.91 (s, 2.4H), 1.35 (s, 3.6H), 1.20 (s, 5.4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 177.1, 176.5, 164.2, 163.4, 141.7, 141.5, 134.5, 133.9, 133.5, 133.3, 128.3, 127.2, 126.3, 126.1, 125.9, 124.1, 120.9, 119.9, 119.4, 119.1, 103.1, 102.4, 93.5, 91.4, 42.3, 42.1, 39.94, 39.9, 27.5, 27.4; HRMS (ESI) m/z calcd for $C_{18}H_{22}N_3OS_2$ $[M + H]^+$ 360.1204, found 360.1208.

*General Procedure for the Synthesis of N-Aryl/benzylenaminonitriles **7k**, **7o**, and **11c**.* A solution of of α-(thioacylaryl)acetonitriles **9k**, **9o**, and **10c** (1.0 mmol) (prepared by condensation of respective (het)arylacetonitriles and dithioesters in the presence of sodium hydride in DMF[1a,33g] and used as such without purification) and corresponding amines (1.2 mmol) in acetic acid (0.068 mL, 1.2 mmol) and ethanol (20 mL) was heated at 70 °C with stirring for 6−8 h (monitored by TLC). The reaction mixture was evaporated under reduced pressure, poured into saturated $NaHCO_3$ solution (20 mL), and extracted with EtOAc (2 × 25 mL). The combined organic layer was washed with water (2 × 25 mL), brine (25 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude products were purified by column chromatography using EtOAc/hexane as eluent.

*2-(4-Chlorophenyl)-3-(phenylamino)hept-2-enenitrile (**7k**).* Obtained as a 90:10 inseparable mixture of geometrical isomers, yellow solid (217.0 mg, 70%): mp 45−47 °C; R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 3305, 2928, 2186, 1569, 834; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (m, 6H), 7.18−7.11 (m, 1.2H), 6.96 (d, J = 7.6 Hz, 1.8H), 6.78 (br s, 0.1H), 6.43 (br s, 0.9H), 2.69 (t, J = 8.0 Hz, 1.8H), 2.39 (t, J = 8.0 Hz, 0.2H), 1.55−1.52 (m, 1.8H), 1.35−1.30 (m, 2H), 1.09−1.01 (m, 0.2H), 0.83 (t, J = 7.2 Hz, 2.7H), 0.62 (t, J = 7.2 Hz, 0.3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.9, 158.7, 138.9, 133.3, 132.8, 132.0, 131.3, 130.4, 129.6, 129.5, 129.4, 129.0, 126.2, 125.8, 125.4, 124.5, 121.4, 84.1, 31.5, 30.5, 29.8, 27.7, 22.4, 22.2, 13.7, 13.4; HRMS (ESI) m/z calcd for $C_{19}H_{20}ClN_2$ $[M + H]^+$ 311.1315 and 313.1286, found 311.1310 and 313.1285.

*3-(Benzylamino)-3-(4-(dimethylamino)phenyl)-2-(3-methoxyphenyl)acrylonitrile (**7o**).* Obtained as a single geometrical isomer, yellow solid (712.3 mg, 62%): mp 85−87 °C; R_f 0.3 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3282, 2946, 2188, 1504, 1229; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.25 (m, 5H), 7.12 (d, J = 8.8 Hz, 2H), 6.90 (d, J = 2.0 Hz, 1H), 6.89 (d, J = 2.0 Hz, 1H), 6.86 (t, J = 2.0 Hz, 1H), 6.57 (d, J = 8.8 Hz, 2H), 4.67 (br s, 3H), 3.76 (s, 3H), 2.96 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.4, 161.8, 160.4, 150.7, 139.8, 135.5, 130.5, 129.1, 128.7, 127.8, 127.3, 122.7, 120.6, 119.2, 115.5, 113.8, 112.0, 55.4, 47.3, 40.3; HRMS (ESI) m/z calcd for $C_{25}H_{26}N_3O$ $[M + H]^+$ 384.2076, found 384.2080.

*2-(1-Methyl-1H-indol-3-yl)-3-(phenylamino)hept-2-enenitrile (**11c**).* Obtained as a single geometrical isomer, off-white solid (200.6 mg, 61%): mp 85−87 °C; R_f 0.6 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 3250, 2917, 2182, 1603, 1245, 823; ^1H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.31−7.25 (m, 3H), 7.18 (s, 1H), 7.17−7.12 (m, 2H), 6.98 (d, J = 7.6 Hz, 2H), 6.45 (br s, 1H), 3.81 (s, 3H), 2.80 (t, J = 7.6 Hz, 2H), 1.56−151 (m, 2H), 1.36 (sextet, J = 7.2 Hz, 2H), 0.85 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.8, 139.5, 137.2, 129.3, 129.1, 126.2, 125.3, 124.6, 122.5, 122.2, 120.2, 119.9, 109.9, 106.3, 33.1, 30.7, 30.3, 22.4, 13.8; HRMS (ESI) m/z calcd for $C_{22}H_{24}N_3$ $[M + H]^+$ 330.1970, found 330.1966.

*2-(4-Bromophenyl)-3-(4-methoxyphenylamino)but-2-enenitrile (**7l**).* Enaminonitrile **7l** was prepared following the reported procedure[31a] by condensation of α-acetyl-(4-bromophenyl)acetonitrile (237.0 mg, 1.0 mmol) with 4-methoxyaniline (135.3 mg, 1.1 mmol) in the presence of acetic acid (0.068 mL, 1.2 mmol) in refluxing ethanol (20 mL). Obtained as a 90:10 inseparable mixture of geometrical isomers, off-white solid (246.2 mg, 72%): mp 158−160 °C; R_f 0.6 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3256, 2926, 2179, 1510, 1245, 823; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.4 Hz, 1.8H), 7.46 (d, J = 8.4 Hz, 0.2H), 7.32 (d, J = 8.4 Hz, 1.8H), 7.17 (d, J = 8.4 Hz, 0.2H), 7.07 (d, J = 8.8 Hz, 0.2H), 6.95 (d, J = 8.8 Hz, 1.8H), 6.90−6.88 (m, 0.3H), 6.85 (d, J = 8.8 Hz, 1.8H), 6.57 (br s, 0.9H), 3.82 (s, 0.3H), 3.80 (s, 2.7H), 2.19 (s, 2.7H), 1.91 (s, 0.3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.3, 155.6, 132.8, 132.5, 131.8, 131.3, 130.8, 127.4, 121.4, 114.7, 81.8, 55.7, 18.7; HRMS (ESI) m/z calcd for $C_{17}H_{16}BrN_2O$ $[M + H]^+$ 343.0446 and 345.0426, found 343.0440 and 345.0422.

*General Procedure for the Synthesis of N-Arylenaminones **7m,n** and **11e,f**.* A solution of 3-(methylthio)enones **9m,n** and **10e,f** (1.0 mmol) in dry THF (5 mL) was added to a stirred solution of arylamine (1.1 mmol) and n-BuLi (0.75 mL, 1.6 M solution in hexane, 1.2 mmol) in THF (10 mL) at 0 °C, and the reaction mixture was further stirred for 2−3 h at room temperature (monitored by TLC). It was then poured into saturated NH_4Cl (25 mL) solution, extracted with EtOAc (2 × 25 mL), washed with water (2 × 25 mL), brine (20 mL), dried (Na_2SO_4), and the solvent was evaporated under reduced pressure to give crude products, which were purified by column chromatography using EtOAc/hexane as eluent.

*2-(3-Methoxyphenyl)-1,3-bis(4-methoxyphenyl)-3-(phenylamino)prop-2-en-1-one (**7m**).* Obtained as yellow solid (320.8 mg, 69%): mp 45−47 °C; R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 3264, 2993, 1639, 1424, 1244, 832; ^1H NMR (400 MHz, $CDCl_3$) δ 13.89 (s, 1H), 7.20 (d, J = 8.8 Hz, 2H), 7.09 (t, J = 8.0 Hz, 2H), 6.95 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 8.8 Hz, 2H), 6.84 (d, J = 8.0 Hz, 1H), 6.71 (d, J = 8.0 Hz, 2H), 6.66−6.59 (m, 4H), 6.50 (dd, J = 8.0 Hz, 2.0 Hz, 1H), 6.43 (d, J = 7.6 Hz, 1H), 6.37 (s, 1H), 3.73 (s, 3H), 3.70 (s, 3H), 3.49 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 193.5, 161.4, 160.4, 159.5, 158.8, 141.0, 140.0, 135.3, 131.3, 130.4, 128.7, 128.3, 126.8, 126.5, 124.1, 123.8, 118.9, 113.5, 112.7, 111.8, 55.28, 55.24, 55.21; HRMS (ESI) m/z calcd for $C_{30}H_{28}NO_4$ $[M + H]^+$ 466.2018, found 466.2020.

*2-(3-Chlorophenyl)-1-(4-chlorophenyl)-3-(4-methoxyphenylamino)-3-(1-methyl-1H-indol-3-yl)prop-2-en-1-one (**7n**).* Obtained as a single geometrical isomer, yellow solid (347.1 mg, 66%): mp 138−140 °C; R_f 0.3 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3372, 2918, 1656,

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1455, 1246, 927; ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.19 (s, 1H), 7.20 (d, J = 8.0 Hz, 1H), 7.15 (d, J = 8.4 Hz, 1H), 7.12−7.08 (m, 5H), 6.93−6.90 (m, 1H), 6.87−6.85 (m, 1H), 6.84−6.79 (m, 3H), 6.77 (t, J = 8.0 Hz, 1H), 6.68−6.66 (m, 1H), 6.55 (d, J = 8.8 Hz, 2H), 6.42 (s, 1H), 3.66 (s, 3H), 3.57 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 191.3, 158.8, 156.7, 142.2, 141.4, 136.3, 134.6, 133.2, 133.1, 132.9, 131.5, 131.3, 129.6, 128.4, 127.8, 126.0, 125.5, 124.5, 122.3, 120.7, 120.5, 114.0, 110.7, 109.3, 108.4, 55.4, 33.0; HRMS (ESI) m/z calcd for $C_{31}H_{25}Cl_2N_2O_2$ $[M + H]^+$ 527.1293 and 529.1264, found 527.1287 and 529.1262.

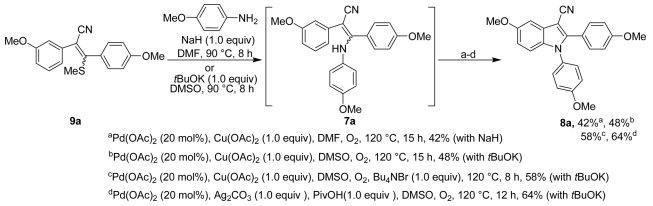
*3-(4-Chlorophenylamino)-1,2,3-tri(thiophen-2-yl)prop-2-en-1-one (**11e**).* Obtained as a single geometrical isomer, pale green solid (255.6 mg, 60%): mp 143−145 °C; R_f 0.6 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 3391, 1606, 1485, 1262, 844; ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.04 (s, 1H), 7.41 (dd, J = 4.8 Hz, 0.8 Hz, 1H), 7.28−7.25 (m, 2H), 7.11 (d, J = 8.8 Hz, 0.8 Hz, 2H), 6.92−6.88 (m, 2H), 6.84 (dd, J = 4.8 Hz, 4.0 Hz, 1H), 6.79−6.77 (m, 2H), 6.74 (d, J = 8.8 Hz, 2H), 6.66 (dd, J = 4.0 Hz, 1.2 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 183.8, 156.8, 146.1, 139.9, 138.3, 134.0, 132.5, 132.2, 131.6, 131.0, 130.4, 129.0, 128.9, 127.9, 127.5, 126.9, 126.6, 124.7, 102.9; HRMS (ESI) m/z calcd for $C_{21}H_{15}ClNOS_3$ $[M + H]^+$ 428.0004 and 429.9975, found 427.9997 and 429.9968.

*3-(4-Methoxyphenyl)-3-(phenylamino)-2-(pyridin-3-yl)-1-(thiophen-2-yl)prop-2-en-1-one (**11f**).* Obtained as a single geometrical isomer, yellow solid (280.1 mg, 68%): mp 48−50 °C; R_f 0.5 (3:2 EtOAc/hexane); IR (neat, cm^{-1}) 3265, 1630, 1571, 1495, 1244, 912; ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.11 (s, 1H), 8.37−8.35 (m, 2H), 7.35 (d, J = 5.2 Hz, 2H), 7.122−7.06 (m, 3H), 7.00−6.96 (m, 1H), 6.85 (d, J = 8.4 Hz, 2H), 6.77−6.73 (m, 3H), 6.60 (d, J = 8.8 Hz, 2H), 6.40 (d, J = 3.6 Hz, 1H), 3.68 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 183.0, 163.3, 159.7, 154.3, 147.7, 146.9, 141.2, 139.3, 135.1, 131.2, 131.0, 128.9, 127.3, 125.9, 124.7, 123.9, 123.0, 114.4, 113.8, 106.9, 55.2; HRMS (ESI) m/z calcd for $C_{25}H_{21}N_2O_2S$ $[M + H]^+$ 413.1324, found 413.1318.

*General Procedure for Palladium-Catalyzed Intramolecular C−H Functionalization-amination of Enaminonitriles/Enaminones **7**, **11**, and **13**: Synthesis of Substituted N-Het(aryl)/NH-3-cyano/aroyl Indoles **8a−n**, **14a−e**, and the Corresponding Heterofused Pyrroles **12a−f**. Method A.* A suspension of enaminonitrile/enaminone **7**, **11**, or **13** (0.3 mmol), $Pd(OAc)_2$ (13.4 mg, 20 mol %), and $Cu(OAc)_2$ (54.3 mg, 0.3 mmol) in dry DMSO (2 mL) was evacuated and backfilled with oxygen (3 cycles) and then stirred at 120 °C for 8−10 h (monitored by TLC). The reaction mixture was cooled to room temperature, diluted with distilled water (20 mL), and extracted with EtOAc (2 × 30 mL). The organic layer was washed with brine (10 mL), dried (Na_2SO_4), and the solvent was evaporated under reduced pressure to give crude products, which were purified by column chromatography using EtOAc/hexane as eluent.

Method B. A suspension of enaminonitrile/enaminone **7**, **11**, or **13** (0.3 mmol), $Pd(OAc)_2$ (13.4 mg, 20 mol %), Ag_2CO_3 (82.7 mg, 0.3 mmol), and PivOH (30.6 mg, 0.3 mmol) in dry DMSO (2 mL) was evacuated and backfilled with oxygen (3 cycles) and then stirred at 120 °C for 10−12 h (monitored by TLC). The reaction mixture was worked up as described for method A, and the crude indoles thus obtained were purified by column chromatography using EtOAc/hexane as eluent.

*One-Pot Synthesis of N-Substituted Indole **8a** from 2-(3-Methoxyphenyl)-3-(4-methoxyphenyl)-3-(methylthio)acrylonitrile **9a**.* A solution of 2-(3-methoxyphenyl)-3-(4-methoxyphenyl)-3-(methylthio)acrylonitrile **9a** (311.0 mg, 1.0 mmol) in dry DMF or DMSO (3 mL) was added to a stirred suspension of 4-methoxy aniline (123.0 mg, 1.0 mmol) and NaH (24.0 mg, 1.0 mmol, 60% suspension in mineral oil) or *t*BuOK (112.2 mg, 1.0 mmol) in DMF or DMSO (5 mL) at room temperature, followed by heating at 90 °C for 8 h (monitored by TLC). After being cooled to room temperature, $Pd(OAc)_2$ (44.9 mg, 20 mol %), oxidant (1.0 equiv), and additive (1.0 equiv) were added to the reaction mixture, evacuated, and backfilled with oxygen (3 cycles) and then stirred at 120 °C for 8−15 h (monitored by TLC). The reaction mixture was cooled to room temperature, diluted with distilled water (20 mL), and extracted with EtOAc (2 × 30 mL). The organic layer was washed with brine (10 mL), dried (Na_2SO_4), and the solvent was evaporated under reduced pressure to give crude products, which were purified by column chromatography using EtOAc/hexane as eluent.



*5-Methoxy-1,2-bis(4-methoxyphenyl)-1H-indole-3-carbonitrile (**8a**).*[1a] Obtained from enaminonitrile **7a**,white solid (85.8 mg, 75%): mp 140−142 °C; R_f 0.4 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2936, 2208, 1514, 1479, 803; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J = 8.8 Hz, 2H), 7.22 (d, J = 2.4 Hz, 1H), 7.13 (d, J = 9.2 Hz, 2H), 7.08 (d, J = 8.8 Hz, 1H), 6.93 (d, J = 9.2 Hz, 2H), 6.89 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 6.85 (d, J = 8.8 Hz, 2H), 3.90 (s, 3H), 3.85 (s, 3H), 3.80 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.4, 159.5, 156.5, 147.4, 132.9, 131.3, 129.7, 129.2, 128.5, 121.4, 117.3, 114.9, 114.6, 114.3, 112.5, 100.6, 85.9, 56.0, 55.7, 55.4; HRMS (ESI) m/z calcd for $C_{24}H_{21}N_2O_3$ $[M + H]^+$ 385.1552, found 385.1547.

*1-(4-Chlorophenyl)-5,6-dimethoxy-2-(thiophen-2-yl)-1H-indole-3-carbonitrile (**8b**).*[1a] Obtained from enaminonitrile **7b**, white solid (87.30 mg, 73%): mp 194−196 °C; R_f 0.6 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2988, 2209, 1483, 1278, 874; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.8 Hz, 2H), 7.35−7.34 (m, 2H), 7.27 (d, J = 8.8 Hz, 2H), 7.18 (s, 1H), 7.03 (dd, J = 4.8 Hz, 3.6 Hz, 1H), 6.50 (s, 1H), 3.99 (s, 3H), 3.81 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 149.2, 147.9, 138.8, 135.7, 135.1, 132.4, 130.4, 130.2, 129.9, 129.6, 128.5, 127.6, 120.8, 116.8, 100.6, 94.2, 86.9, 56.6, 56.5; HRMS (ESI) m/z calcd for $C_{21}H_{16}ClN_2O_2S$ $[M + H]^+$ 395.0621 and 397.0592, found 395.0597 and 397.0560.

*6-Fluoro-2-(1-methyl-1H-indol-3-yl)-1-(pyridin-3-yl)-1H-indole-3-carbonitrile (**8c**).*[1a] Obtained from enaminonitrile **7c**, pale yellow solid (83.10 mg, 76%): mp 190−192 °C; R_f 0.4 (2:3 EtOAc/hexane); IR (neat, cm^{-1}) 2956, 2189, 1465, 1225, 845; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69−8.67 (m, 1H), 8.30 (dd, J = 4.8 Hz, 1.6 Hz, 1H), 7.95 (dd, J = 8.0 Hz, 1.2 Hz, 1H), 7.45−7.36 (m, 6H), 7.33 (dd, J = 8.0 Hz, 4.8 Hz, 1H), 7.07−7.02 (m, 2H), 3.78 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.0 (d, $^1J_{C-F}$ = 240.0 Hz), 149.0 (d, $^2J_{C-F}$ = 110.0 Hz), 137.5, 137.4, 137.1, 134.6, 134.0, 130.8, 125.6, 124.4, 124.2, 122.9, 120.6, 120.51, 120.50 (d, $^2J_{C-F}$ = 100.0 Hz), 120.0, 116.3, 112.0, 111.8, 110.0, 102.9, 98.0, 97.8, 88.0, 33.4; HRMS (ESI) m/z calcd for $C_{23}H_{16}FN_4$ $[M + H]^+$ 367.1359, found 367.1348.

*1-(2-Bromophenyl)-2-(5-(dimethylamino)thiophen-2-yl)-6-fluoro-1H-indole-3-carbonitrile (**8d**).* Obtained from enaminonitrile **7d**, yellow solid (117.6 mg, 85%): mp 175−177 °C; R_f 0.4 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2956, 2215, 1615, 1322, 727; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (dd = J = 8.0 Hz, 1.2 Hz, 1H), 7.36−7.32 (m, 2H), 7.14−7.11 (m, 2H), 7.05−7.01 (m, 2H), 6.93 (t, J = 8.0 Hz, 1H), 5.77 (d, J = 4.8 Hz, 1H), 3.07 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.5, 160.7 (d, $^1J_{C-F}$ = 240.0 Hz), 143.4, 143.3, 137.5, 137.3, 136.1, 134.4, 131.70, 131.66, 131.2, 129.2, 124.7, 124.4, 119.74, 119.65, 117.4, 112.3, 111.5, 111.2, 102.4, 98.0, 97.7, 82.8, 42.4; HRMS (ESI) m/z calcd for $C_{21}H_{16}BrFN_3S$ $[M + H]^+$ 440.0232 and 442. 0212, found 440.0229 and 442.0211.

*2-(Benzo[d][1,3]dioxol-5-yl)-1-(4-chlorophenyl)-5-fluoro-1H-indole-3-carbonitrile (**8e**).* Obtained from enaminonitrile **7e**, white solid (87.3 mg, 75%): mp 175−177 °C; R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2922, 2183, 1486, 1218, 917; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47−7.44 (m, 3H), 7.17 (d, J = 8.8 Hz, 2H), 7.14 (t, J = 4.0 Hz, 1H), 7.03 (td, J = 8.2 Hz, 2.4 Hz, 1H), 6.88 (dd, J = 8.4 Hz, 2.0 Hz, 1H), 6.80 (d, J = 8.0 Hz, 1H), 6.76 (d, J = 2.0 Hz, 1H), 6.00 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.8 (d, $^1J_{C-F}$ = 239.0 Hz), 148.7 (d, $^2J_{C-F}$ = 82.0 Hz), 148.2, 135.1 (d, $^3J_{C-F}$ = 21.0 Hz), 134.0, 130.3, 129.7, 129.2, 128.4 (d, $^4J_{C-F}$ = 11.0 Hz), 124.7, 121.8, 115.9, 113.3, 113.0, 112.5, 112.4, 109.4 (d, $^2J_{C-F}$ = 90.0 Hz), 105.1 (d, $^3J_{C-F}$ = 25.0 Hz), 101.8, 87.7; HRMS (ESI) m/z calcd for

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$C_{22}H_{13}ClFN_2O_2$ $[M + H]^+$ 391.0650 and 393.0620, found 391.0645 and 393.0614.

*2-(4-(Dimethylamino)phenyl)-1-(pyridin-3-yl)-1H-indole-3,5-dicarbonitrile (**8f**).* Obtained from enaminonitrile **7f**, pale yellow solid (80.5 mg, 74%): mp 245−247 °C; R_f 0.5 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 2907, 2222, 2210, 1482, 1233, 827; ^1H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, J = 4.0 Hz, 1H), 8.60 (br s, 1H), 8.11 (s, 1H), 7.58 (dt, J = 3.6 Hz, 1.6 Hz, 1H), 7.50 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.46 (dd, J = 8.0 Hz, 4.8 Hz, 1H), 7.24 (s, 1H), 7.19 (d, J = 8.8 Hz, 2H), 6.60 (d, J = 8.8 Hz, 2H), 2.99 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.4, 151.0, 150.2, 149.0, 139.1, 135.5, 133.5, 131.1, 128.2, 127.3, 124.5, 124.4, 119.4, 115.5, 113.5, 111.9, 111.8, 106.8, 86.9, 40.1; HRMS (ESI) m/z calcd for $C_{23}H_{18}N_5$ $[M + H]^+$ 364.1562, found 364.1562.

*5-Chloro-2-(furan-2-yl)-1-(3,4,5-trimethoxyphenyl)-1H-indole-3-carbonitrile (**8g**).* Obtained from enaminonitrile **7g**, off-white solid (101.5 mg, 83%): mp 245−247 °C; R_f 0.5 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 2969, 2207, 1479, 1253, 825; ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 2.0 Hz, 1H), 7.54 (d, J = 1.6 Hz, 1H), 7.22 (dd, J = 8.6 Hz, 1.6 Hz, 1H), 7.03 (d, J = 8.6 Hz, 1H), 6.55 (s, 2H), 6.42 (dd, J = 3.6 Hz, 1.8 Hz, 1H), 6.19 (d, J = 3.6 Hz, 1H), 3.97 (s, 3H), 3.82 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 154.3, 144.6, 143.5, 139.3, 137.76, 136.83, 132.0, 129.1, 128.7, 125.3, 119.1, 115.6, 112.8, 112.6, 112.0, 105.6, 84.2, 61.3, 56.6; HRMS (ESI) m/z calcd for $C_{22}H_{18}ClN_2O_4$ $[M + H]^+$ 409.0955 and 411.0926, found 409.0951 and 411.0924.

*6-Bromo-1-(4-methoxyphenyl)-2-(1-methyl-1H-pyrrol-2-yl)-1H-indole-3-carbonitrile (**8h**).* Obtained from enaminonitrile **7h**, pale yellow solid (101.5 mg, 78%): mp 165−167 °C; R_f 0.6 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2831, 2206, 1479, 1253, 803; ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.4 Hz, 1H), 7.46 (d, J = 8.6 Hz, 2H), 7.17 (d, J = 8.6 Hz, 2H), 6.93 (dd, J = 8.4 Hz, 2.4 Hz, 1H), 6.81 (t, J = 2.0 Hz, 1H), 6.79 (d, J = 2.4 Hz, 1H), 6.49 (dd, J = 4.4 Hz, 1.2 Hz, 1H), 6.06 (dd, J = 4.4 Hz, 2.4 Hz, 1H), 4.11 (s, 3H), 3.78 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.0, 158.9, 149.1, 140.0, 134.9, 132.9, 130.2, 127.4, 124.1, 122.8, 121.6, 118.1, 117.8, 115.7, 109.2, 56.0, 38.3; HRMS (ESI) m/z calcd for $C_{21}H_{17}BrN_3O$ $[M + H]^+$ 406.0555 and 408.0535, found 406.0547 and 408.0529.

*4,7-Dimethoxy-2-(pyridin-3-yl)-1-(4-(trifluoromethyl)phenyl)-1H-indole-3-carbonitrile (**8i**).* Obtained from enaminonitrile **7i**, off-white solid (95.3 mg, 76%): mp 98−100 °C; R_f 0.6 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 2950, 2218, 1466, 1245, 840; ^1H NMR (400 MHz, $CDCl_3$) δ 8.57 (br s, 1H), 8.46 (br s, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.34−7.28 (m, 3H), 6.67 (d, J = 8.8 Hz, 1H), 6.61 (d, J = 8.8 Hz, 1H), 4.0 (s, 3H), 3.53 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.5, 150.4, 147.7, 143.9, 141.9, 141.2, 137.5, 131.0, 130.7, 129.6, 128.0, 125.5 (q, J_{C-F} = 4.0 Hz), 125.1, 123.7, 119.3, 116.2, 106.9, 102.7, 88.3, 56.3, 56.2; HRMS (ESI) m/z calcd for $C_{23}H_{17}F_3N_3O_2$ $[M + H]^+$ 424.1273, found 424.1267.

*1-(4-Fluorophenyl)-2-(1-methyl-1H-imidazol-2-yl)-1H-benzo[g]-indole-3-carbonitrile (**8j**).* Obtained from enaminonitrile **7j**, off-white solid (87.6 mg, 80%): mp 174−176 °C; R_f 0.5 (2:3 EtOAc/hexane); IR (neat, cm^{-1}) 2985, 2209, 1483, 1278, 838; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 8.0 Hz, 1H), 7.89 (d, J = 8.8 Hz, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.48−7.40 (m, 3H), 7.28−7.24 (m, 1H), 7.19 (t, J = 8.4 Hz, 2H), 7.09 (d, J = 8.8 Hz, 1H), 7.07 (s, 1H), 6.98 (s, 1H), 3.73 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.1 (d, $^1J_{C-F}$ = 249.0 Hz), 135.2, 134.60, 134.57, 132.7, 131.8, 130.9 (d, $^4J_{C-F}$ = 9.0 Hz), 130.1, 129.7, 126.0 (d, $^2J_{C-F}$ = 92.0 Hz), 125.2, 124.6, 122.7, 122.3, 120.9, 118.3, 116.8 (d, $^3J_{C-F}$ = 23.0 Hz), 115.1, 92.0, 34.0; HRMS (ESI) m/z calcd for $C_{23}H_{16}FN_4$ $[M + H]^+$ 367.1359, found 367.1353.

*2-Butyl-6-chloro-1-phenyl-1H-indole-3-carbonitrile (**8k**).* Obtained from enaminonitrile **7k**, yellow semisolid (69.4 mg, 75%): R_f 0.6 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2832, 2209, 1479, 1253, 825; ^1H NMR (400 MHz, $CDCl_3$) δ 7.63−7.58 (m, 4H), 7.33−7.31 (m, 2H), 7.24 (dd, J = 8.8 Hz, 2.0 Hz, 1H), 7.0 (d, J = 1.6 Hz, 1H), 2.81 (t, J = 7.6 Hz, 2H), 1.55−1.47 (m, 2H), 1.34−1.22 (m, 2H), 0.80 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.3, 138.0, 135.7, 130.3, 129.8, 129.7, 128.1, 125.6, 123.3, 120.0, 115.9, 111.3, 86.4, 31.1, 26.2, 22.3, 13.6; HRMS (ESI) m/z calcd for $C_{19}H_{18}ClN_2$ $[M + H]^+$ 309.1159 and 311.1129, found 309.1158 and 311.1129.

*6-Bromo-1-(4-methoxyphenyl)-2-methyl-1H-indole-3-carbonitrile (**8l**).* Obtained from enaminonitrile **7l**, white solid (87.6 mg, 76%): mp 128−130 °C; R_f 0.5 (2:3 EtOAc/hexane); IR (neat, cm^{-1}) 2989, 2219, 1515, 1245, 840; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.4 Hz, 1H), 7.36 (dd, J = 8.4 Hz, 1.4 Hz, 1H), 7.22 (d, J = 8.8 Hz, 2H), 7.18 (d, J = 1.4 Hz, 1H), 7.08 (d, J = 8.8 Hz, 2H), 3.91 (s, 3H), 2.41 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.5, 147.2, 138.5, 129.0, 128.1, 125.8, 120.3, 117.1, 115.9, 115.5, 114.3, 86.5, 55.8, 12.7; HRMS (ESI) m/z calcd for $C_{17}H_{14}BrN_2O$ $[M + H]^+$ 341.0290 and 343.0269, found 341.0283 and 343.0263.

*(5-Methoxy-2-(4-methoxyphenyl)-1-phenyl-1H-indol-3-yl)(4-methoxyphenyl)methanone (**8m**).* Obtained from enaminone **7m**, off-white solid (87.3 mg, 63%): mp 128−130 °C; R_f 0.3 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2921, 1732, 1488, 1261, 830; ^1H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.8 Hz, 2H), 7.53 (d, J = 2.4 Hz, 1H), 7.40−7.34 (m, 3H), 7.19−7.18 (m, 2H), 7.12 (d, J = 8.8 Hz, 1H), 6.94 (d, J = 8.8 Hz, 2H), 6.88 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 6.63 (d, J = 8.8 Hz, 2H), 6.52 (d, J = 8.8 Hz, 2H), 3.85 (s, 3H), 3.75 (s, 3H), 3.66 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 192.4, 163.0, 162.4, 159.5, 156.3, 144.9, 137.7, 133.4, 132.7, 132.0, 131.9, 129.6, 129.5, 128.6, 128.5, 128.0, 127.8, 114.0, 113.9, 113.4, 113.1, 56.0, 55.5, 55.3; HRMS (ESI) m/z calcd for $C_{30}H_{26}NO_4$ $[M + H]^+$ 464.1862, found 464.1856.

*(5-Chloro-1-(4-methoxyphenyl)-2-(1-methyl-1H-indol-3-yl)-1H-indol-3-yl)(4-chlorophenyl)methanone (**8n**).* Obtained from enaminone **7n**, yellow solid (115.0 mg, 73%): mp 152−154 °C; R_f 0.6 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2917, 1762, 1585, 1250, 902; ^1H NMR (400 MHz, $CDCl_3$) δ 8.81−8.79 (m, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.42−7.41 (m, 1H), 7.39−7.29 (m, 4H), 7.23−7.16 (m, 5H), 7.08 (d, J = 8.8 Hz, 2H), 6.88 (dd, J = 8.4 Hz, 2.4 Hz, 1H), 6.77 (d, J = 2.4 Hz, 1H), 3.72 (s, 3H), 3.69 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.5, 169.5, 157.6, 150.0, 142.8, 141.4, 138.6, 136.8, 134.9, 133.6, 133.5, 129.1, 129.0, 128.4, 128.1, 127.1, 126.2, 123.0, 122.9, 121.6, 121.0, 113.1, 109.63, 109.59, 109.0, 55.2, 32.9; HRMS (ESI) m/z calcd for $C_{31}H_{23}Cl_2N_2O_2$ $[M + H]^+$ 525.1137 and 527.1107, found 525.1131 and 527.1106.

*5-(1-Methyl-1H-pyrrol-2-yl)-6-(4-(trifluoromethyl)phenyl)-6H-thieno[2,3-b]pyrrole-4-carbonitrile (**12a**).* Obtained from enaminonitrile **11a**, off-white solid (91.7 mg, 83%): mp 95−97 °C; R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2932, 2217, 1416, 1322, 847; ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 5.2 Hz, 1H), 7.07 (d, J = 5.2 Hz, 1H), 6.71 (dd, J = 2.4 Hz, 1.6 Hz, 1H), 6.31(dd, J = 3.6 Hz, 1.6 Hz, 1H), 6.19 (dd, J = 3.6 Hz, 2.4 Hz, 1H), 3.32 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 141.5, 137.6, 136.9, 130.8, 130.1, 129.8, 127.1 (q, J_{C-F} = 4.0 Hz), 125.2, 124.0, 120.9, 120.6, 117.3, 115.7, 114.4, 109.2, 90.8, 34.6; HRMS (ESI) m/z calcd for $C_{19}H_{13}F_3N_3S$ $[M + H]^+$ 372.0782, found 372.0770.

*1-(4-Methoxyphenyl)-8-methyl-2-(thiophen-2-yl)-1,8-dihydropyrrolo[2,3-b]indole-3-carbonitrile (**12b**).* Obtained from enaminonitrile **11b**, pale yellow solid (91.7 mg, 75%): mp 118−120 °C; R_f 0.6 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2930, 2186, 1508, 1236, 824; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94−7.92 (m, 1H), 7.36 (d, J = 8.8 Hz, 2H), 7.30 (dd, J = 3.6 Hz, 1.2 Hz, 1H), 7.28−7.25 (m, 2H), 7.24−7.21 (m, 2H), 7.02 (d, J = 8.8 Hz, 2H), 6.98 (dd, J = 5.2 Hz, 3.6 Hz, 1H), 3.91 (s, 3H), 3.31 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.0, 140.9, 140.4, 134.6, 131.1, 130.8, 128.3, 128.1, 127.2, 127.0, 122.2, 120.4, 119.4, 117.7, 114.9, 114.3, 109.4, 107.4, 84.2, 55.8, 30.2; HRMS (ESI) m/z calcd for $C_{23}H_{18}N_3OS$ $[M + H]^+$ 384.1171, found 384.1166.

*2-Butyl-8-methyl-1-phenyl-1,8-dihydropyrrolo[2,3-b]indole-3-carbonitrile (**12c**).* Obtained from enaminonitrile **11c**, pink solid (68.6 mg, 70%): mp 145−147 °C; R_f 0.5 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 2956, 2220, 1464, 1245, 840; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88−7.86 (m, 1H), 7.60−7.59 (m, 3H), 7.45−7.43 (m, 2H), 7.25−7.18 (m, 3H), 3.25 (s, 3H), 2.71 (t, J = 7.6 Hz, 2H), 1.45 (quintet, J = 7.6 Hz, 2H), 1.26 (sextet, J = 7.6 Hz, 2H), 0.80 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 143.4, 140.3, 139.0, 136.0, 130.0, 129.9, 128.7, 121.5, 120.0, 119.6, 119.0, 117.6, 109.3, 105.8, 83.7, 32.0,

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30.2, 26.1, 22.2, 13.7; HRMS (ESI) m/z calcd for $C_{22}H_{22}N_3$ $[M + H]^+$ 328.1814, found 328.1809.

*2-(4-Fluorophenyl)-1-(4-methoxyphenyl)-1H-pyrrolo[2,3-b]-pyridine-3-carbonitrile (**12d**).* Obtained from enaminonitrile **11d**, white solid (68.6 mg, 86%): mp 122−124 °C; R_f 0.5 (2:3 EtOAc/hexane); IR (neat, cm^{-1}) 2982, 2209, 1483, 1278, 874; ^1H NMR (400 MHz, $CDCl_3$) δ 8.44 (dd, J = 4.8 Hz, 1.2 Hz, 1H), 8.13 (dd, J = 7.8 Hz, 1.2 Hz, 1H), 7.44−7.40 (m, 2H), 7.31 (dd, J = 7.8 Hz, 4.8 Hz, 1H), 7.18 (d, J = 8.8 Hz, 2H), 7.08 (t, J = 8.4 Hz, 2H), 6.96 (d, J = 8.8 Hz, 2H), 3.84 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.4 (d, $^1J_{C-F}$ = 250.0 Hz), 159.6, 148.5, 146.9, 132.0, 131.9, 129.4, 127.9, 127.7, 124.53, 124.50, 120.3, 119.0, 116.2, 116.0, 115.6, 114.8, 85.0, 55.5; HRMS (ESI) m/z calcd for $C_{21}H_{15}FN_3O$ $[M + H]^+$ 344.1199, found 344.1199.

*(4-(4-Chlorophenyl)-5-(thiophen-2-yl)-4H-thieno[3,2-b]pyrrol-6-yl)(thiophen-2-yl)methanone (**12e**).* Obtained from enaminone **11e**, pale yellow solid (86.4 mg, 68%): mp 166−168 °C; R_f 0.5 (1:9 EtOAc/hexane); IR (neat, cm^{-1}) 2922, 1728, 1488, 1261, 883; ^1H NMR (400 MHz, $CDCl_3$) δ 7.57−7.54 (m, 2H), 7.38 (d, J = 8.8 Hz, 2H), 7.271−7.269 (m, 1H), 7.24−7.21 (m, 3H), 6.94−6.91 (m, 2H), 6.84 (dd, J = 5.2 Hz, 3.6 Hz, 1H), 6.82 (d, J = 5.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 182.4, 144.5, 144.3, 136.8, 134.2, 133.9, 133.03, 133.0, 131.5, 131.4, 129.7, 128.7, 128.3, 127.5, 127.0, 126.7, 125.5, 110.9; HRMS (ESI) m/z calcd for $C_{21}H_{13}ClNO\,S_3$ $[M + H]^+$ 425.9848 and 427.9818, found 425.9844 and 427.9816.

*(2-(4-Methoxyphenyl)-1-phenyl-1H-pyrrolo[2,3-b]pyridin-3-yl)-(thiophen-2-yl)methanone (**12f**).* Obtained from enaminone **11f**, pale yellow solid (94.7 mg, 77%): mp 126−128 °C; R_f 0.5 (1:9 EtOAc/hexane); IR (neat, cm^{-1}) 2835, 1650, 1504, 1243, 833; ^1H NMR (400 MHz, $CDCl_3$) δ 8.37 (br s, 1H), 7.35 (d, J = 5.2 Hz, 2H), 7.122−7.05 (m, 3H), 6.99 (t, J = 7.6 Hz, 1H), 6.85 (d, J = 8.4 Hz, 2H), 6.77−6.73 (m, 3H), 6.60 (d, J = 8.8 Hz, 2H), 6.40 (d, J = 3.6 Hz, 1H), 3.68 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 182.0, 162.3, 158.7, 153.3, 146.7, 145.9, 140.2, 138.3, 134.1, 130.2, 130.0, 127.9, 126.3, 124.9, 123.7, 122.9, 122.0, 113.4, 112.8, 105.9, 54.2; HRMS (ESI) m/z calcd for $C_{25}H_{19}N_2O_2S$ $[M + H]^+$ 411.1167, found 411.1160.

*2-(Furan-2-yl)-5,6-dimethoxy-1H-indole-3-carbonitrile (**14a**).* Obtained from *N*-acylenaminonitrile **13a**, brown solid (62.0 mg, 77%): mp 145−147 °C; R_f 0.5 (2:3 EtOAc/hexane); IR (neat, cm^{-1}) 3201, 2832, 2219, 1486, 1211, 992; ^1H NMR (400 MHz, $CDCl_3$) δ 8.78 (br s, 1H), 7.51 (s, 1H), 7.17 (d, J = 3.2 Hz, 1H), 7.11 (s, 1H), 6.90 (s, 1H), 6.60 (s, 1H), 3.96 (s, 3H), 3.93 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 148.9, 147.4, 144.7, 142.8, 134.1, 129.0, 121.4, 116.6, 112.8, 109.7, 100.6, 94.8, 81.7, 56.42, 56.40; HRMS (ESI) m/z calcd for $C_{15}H_{13}N_2O_3$ $[M + H]^+$ 269.0926, found 269.0925.

*5-Chloro-2-(1-methyl-1H-pyrrol-2-yl)-1H-indole-3-carbonitrile (**14b**).* Obtained from *N*-acylenaminonitrile **13b**, off-white solid (54.1 mg, 71%): mp 200−202 °C; R_f 0.6 (1:4 EtOAc/hexane); IR (neat, cm^{-1}) 3292, 2209, 1427, 1278, 798; ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (br s, 1H), 7.72 (d, J = 2.0 Hz, 1H), 7.34 (d, J = 8.4 Hz, 1H), 7.28 (d, J = 2.0 Hz, 1H), 6.88 (t, J = 2.0 Hz, 1H), 6.58 (dd, J = 4.0 Hz, 1.6 Hz, 1H), 6.28 (dd, J = 4.0 Hz, 2.8 Hz, 1H), 3.86 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 139.2, 133.2, 129.7, 128.6, 127.2, 124.9, 122.6, 119.1, 116.2, 113.0, 112.7, 109.6, 85.0, 35.9; HRMS (ESI) m/z calcd for $C_{14}H_{11}ClN_3$ $[M + H]^+$ 256.0642 and 258.0612, found 256.0633 and 258.0604.

*5-Methoxy-2-(thiophen-2-yl)-1H-indole-3-carbonitrile (**14c**).*[1a] Obtained from *N*-acylenaminonitrile **13c**, off-white solid (56.3 mg, 74%): mp 191−193 °C; R_f 0.4 (2:3 EtOAc/hexane); IR (neat, cm^{-1}) 3233, 2981, 2214, 1464, 1219, 819; ^1H NMR (400 MHz, $CDCl_3$) δ 8.70 (br s, 1H), 7.74 (d, J = 3.2 Hz, 1H), 7.46 (d, J = 4.8 Hz, 1H), 7.30 (d, J = 8.8 Hz, 1H), 7.18 (t, J = 4.4 Hz, 1H), 7.13 (d, J = 2.0 Hz, 1H), 6.93 (dd, J = 8.4 Hz, 2.0 Hz, 1H), 3.88 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 156.4, 139.3, 131.5, 129.8, 129.6, 128.7, 127.4, 127.3, 116.8, 115.4, 112.6, 100.8, 83.7, 56.0; HRMS (ESI) m/z calcd for $C_{14}H_{11}N_2OS$ $[M + H]^+$ 255.0592, found 255.0589.

*2-(Benzo[d][1,3]dioxol-5-yl)-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile (**14d**).* Obtained from *N*-acylenaminonitrile **13d**, off-white solid (57.7 mg, 73%): mp 280−282 °C; R_f 0.5 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 3237, 2989, 2218, 1464, 1254, 819; ^1H NMR (400 MHz, DMSO-d_6) δ 13.07 (br s, 1H), 8.39 (dd, J = 4.8 Hz, 1.6 Hz, 1H), 8.06 (dd, J = 8.0 Hz, 1.2 Hz, 1H), 7.58 (dd, J = 8.4 Hz, 2.0 Hz, 1H), 7.54 (d, J = 2.0 Hz, 1H), 7.30 (dd, J = 8.0 Hz, 4.0 Hz, 1H), 7.18 (d, J = 8.0 Hz, 1H), 6.16 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 149.1, 148.0, 147.7, 145.6, 145.1, 126.8, 122.6, 122.2, 120.8, 118.2, 116.4, 109.1, 107.2, 101.9, 79.4; HRMS (ESI) m/z calcd for $C_{15}H_{10}N_3O_2$ $[M + H]^+$ 264.0773, found 264.0766.

*5-(5-(Dimethylamino)thiophen-2-yl)-6H-thieno[2,3-b]pyrrole-4-carbonitrile (**14e**).* Obtained from *N*-acylenaminonitrile **13e**, pale yellow solid (52.5 mg, 64%): mp 165−167 °C; R_f 0.6 (2:3 EtOAc/hexane); IR (neat, cm^{-1}) 3204, 2829, 2216, 1486, 1211, 811; ^1H NMR (400 MHz, $CDCl_3$) δ 8.54 (br s, 1H), 7.39 (d, J = 5.2 Hz, 1H), 7.36 (d, J = 4.2 Hz, 1H), 7.23 (d, J = 5.2 Hz, 1H), 5.83 (d, J = 4.2 Hz, 1H), 3.01 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.7, 152.4, 146.0, 131.6, 129.3, 129.1, 119.0, 117.1, 116.4, 102.6, 93.7, 42.5; HRMS (ESI) m/z calcd for $C_{13}H_{12}N_3S_2$ $[M + H]^+$ 274.0473, found 274.0479.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02902.

Copies of ^1H NMR and ^{13}C NMR spectra for all new compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: hila@jncasr.ac.in.

Notes

The authors declare no competing financial interest.

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