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Oxidative Difunctionalization of 2-Amino-4*H*-pyrans in Iodobenzene Diacetate and *N*-Chlorosuccinimide: Reactivity, Mechanistic Insights, and DFT Calculations

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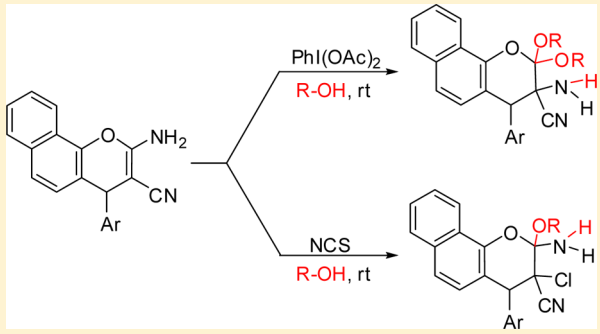
Supporting Information

ABSTRACT: Oxidative difunctionalization of 2-amino-4*H*-pyrans was accomplished with iodobenzene diacetate (IBD) and *N*-chlorosuccinimide (NCS) reagents in alcoholic medium. 2-Amino-4*H*-pyrans undergo geminal dialkoxylation with the migration of an amino group (**1a,b**, **2a−i**, **3a,b**, and **4**) in IBD, whereas with NCS addition of both chlorine and alkoxy groups takes place across the chromene double bond (**6a−i**).



INTRODUCTION

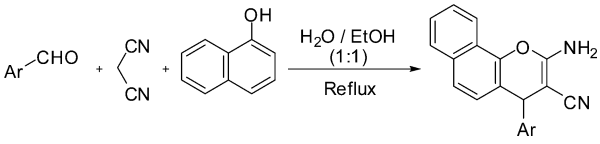
Amino-4*H*-pyrans have long been attractive molecules for medicinal chemists because of their diverse pharmacological profile which includes antibacterial,[1] fungicidal,[2] mollusicidal,[3] anticonvulsant,[4] and antiviral[5] activities. Amino-4*H*-pyrans are isosters of 1,4-dihydropyridines.[6] Annulated aminopyrans, especially heterocyclic analogues of tacrine, are known cholinesterase inhibitors finding applications in treatment of Alzheimer's disease.[7] Among the fused aminopyrans, amino-chromenes receive special attention as antiproliferative and antiarthritic molecules.[8] 4-Aryl-4*H*-chromenes are known apoptosis inducers by tubulin inhibition and vascular disruption.[9] Cyclization of the 7,8 positions of 4-aryl-4*H*-chromenes has been established to lead to more potent anticancer molecules.[10]

As part of an ongoing program on the design and synthesis of new chemical entities incorporating a 4*H*-pyrans, we have recently developed a clean method for synthesis of fused pyrano[2,3-*c*]pyrazoles and evaluated their biological activity.[11] Herein a construction of a series of diversely substituted 4-aryl-4*H*-benzochromenes is envisaged.

RESULTS AND DISCUSSION

At the outset, 2-amino-4-aryl-4*H*-benzo[*h*]chromene-3-carbonitrile analogues[12] were constructed by a catalyst-free protocol via a one-pot, three-component condensation of malononitrile, aromatic aldehyde, and 1-naphthol in water and ethanol (1:1) medium (Scheme 1). The green protocol was found to be of wide scope, and a number of aryl-substituted 2-amino-chromenes were obtained by varying the substitutions on

Scheme 1. Catalyst-Free Construction of 2-Amino-4-aryl-4*H*-benzo[*h*]chromene-3-carbonitrile Analogues



aromatic aldehyde. Synthesis of 2-amino-2′-oxospiro[benzo[*h*]-chromene-4,3′-indoline]-3-carbonitrile was carried out through a reported method[13] as it was not obtained in the green protocol.

Various attempts to utilize both the amine and nitrile functionalities for modifying the chromene skeleton as well construction of heterocycles by employing aforesaid functionalities were unsuccessful.[14] Catalytic oxidative difunctionalization of the chromene double bond was envisaged as a reasonable synthetic transformation for obtaining vicinal substitutions. Hypervalent iodine reagents such as iodobenzene diacetate (IBD) are known for oxidative difunctionalization[15] of flavonoids, indoles, and pyrans, which would be a simple protocol for obtaining diversely substituted amino-4*H*-pyrans.

During the course of the experiments, it was observed that the reaction between 2-amino-4*H*-pyrans and IBD does not proceed with dichloromethane as solvent. When methanol was employed as the solvent, the reaction progressed instantaneously (Scheme 2). An intriguing product was formed, whose

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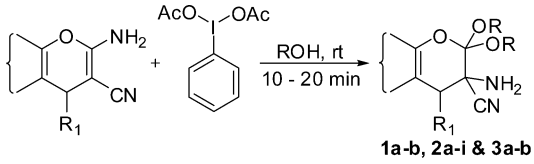
Scheme 2. IBD-Catalyzed Geminal Dialkoxylation with 1,2-Migration of Amino Group



PMR spectrum shows the presence of two signals corresponding to $-OCH_3$ protons at δ 3.8 and 3.4 ppm, respectively, indicating the introduction of two methoxy groups. The amino group, which is at δ 4.7 ppm in the starting material (2-amino-4-phenyl-4*H*-benzo[*h*]chromene-3-carbonitrile), shifted to δ 1.7 ppm in the product. Dialkoxylation suggests the product is not a result of mere oxidative difunctionalization. X-ray crystallography data[16] of the product shows a 1,2-migration of amino group to the C_{12}-carbon bearing nitrile group and geminal dimethoxy groups installed at C_{13}-carbon. From the insights obtained through crystallographic data, the product **2a** (Figure 1) was assigned as 3-amino-2,2-dimethoxy-4-phenyl-

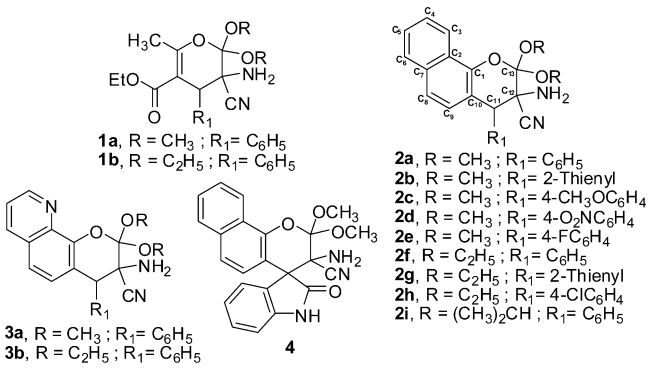


Figure 1. Scope of products from diverse 2-aminopyran analogues.

2,3-dihydro-4*H*-benzo[*h*]chromene-3-carbonitrile. In order to authenticate the phenomena, the dialkoxylation was repeated with ethanol as the solvent. X-ray crystallography data of the product show geminal diethoxy groups at C_{13} with 1,2-migration of the amino group to a C_{12}-carbon-bearing nitrile group. Both compounds **2a** and **2f** crystallized in the centro symmetric space group and are found to be racemic mixtures (1:1) with configurations of *R* and *S* at C_{11} and C_{12}, respectively.

The information obtained from initial screening of the reaction conditions mentioned above led to the establishment of the best parameters for the conversion. The study was extended by varying the 2-aminopyrans as well as readily available alcoholic solvents. The dialkoxylation with 1,2-migration of the amino group is facile in methanol, ethanol, and isopropyl alcohol. However, the reaction does not proceed in ethylene glycol and 2-chloroethanol. Yields and reactivity are better in methanol when compared to both ethanol and isopropyl alcohol. More importantly, the reaction is compatible to various functional groups on the C_{11}-phenyl ring. All of the reactions proceed within a few minutes, and the corresponding products are formed in excellent yields (Table 1).

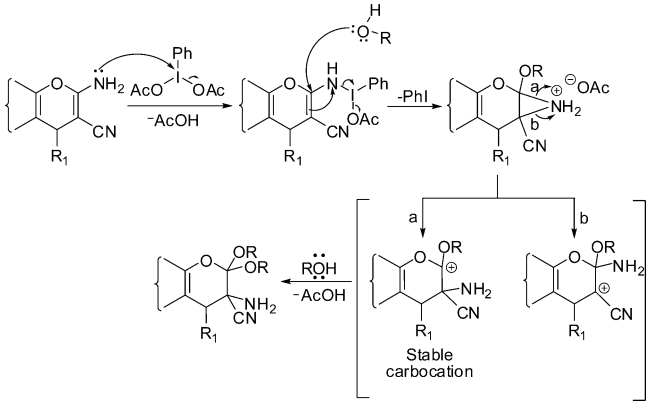
A thorough survey of literature revealed that the unusual geminal dialkoxy addition with migration of amino group has no precedence. Combining aspects of the experimental findings, a plausible mechanism presented in Scheme 3. Initial

Table 1. Dialkoxylation of 2-Amino-4*H*-pyrans with IBD[a]

entry	R	R_1	product	time (min)	yield[b] (%)
1	CH_3	C_6H_5	**1a**	15	80
2	C_2H_5	C_6H_5	**1b**	20	78
3	CH_3	C_6H_5	**2a**	15	78
4	CH_3	2-thienyl	**2b**	15	84
5	CH_3	4-$CH_3OC_6H_4$	**2c**	15	74
6	CH_3	4-$O_2NC_6H_4$	**2d**	10	85
7	CH_3	4-FC_6H_4	**2e**	15	77
8	C_2H_5	C_6H_5	**2f**	20	74
9	C_2H_5	2-thienyl	**2g**	15	78
10	C_2H_5	4-ClC_6H_4	**2h**	15	72
11	$(CH_3)_2CH$	C_6H_5	**2i**	20	70
12	CH_3	C_6H_5	**3a**	20	72
13	C_2H_5	C_6H_5	**3b**	20	70
14	CH_3		**4**	300	60

[a]All of the reactions were carried out using 2-amino-4*H*-pyrans (1 equiv) and IBD (1.1 equiv) in the presence of excess alcohol under rt conditions. [b]Yield of crude product.

Scheme 3. Plausible Mechanism of IBD-Catalyzed Dialkoxylation of 2-Amino-4*H*-pyrans



formation of the aminoiodinane species is followed by immediate attack of alcohol to form the aziridine ring. The aziridine opens to a stable carbocation at the α-carbon. Attack of alcohol as a nucleophile then occurs to yield the geminal dialkoxylation product. Since the reaction is instantaneous, none of the intermediates could be isolated. Density functional theory (DFT) calculations were carried out to see the energy profile of the reaction. From the energy profile in Figure 2 it is evident that the transition state with a barrier of about 20 kcal/mol involves the cleavage of acetic acid from IBD with proton abstraction from methanol solvent molecule followed by nucloephilic attack of the methoxy group leading to azridine ring formation. The exothermicity of the reaction is found to be due to highly stabilized aziridine ring, which further leads to product formation.

In order to understand the role of IBD in transformation, a routine investigation was performed on 2-amino-4-phenyl-4*H*-benzo[*h*]chromene-3-carbonitrile with various iodine-containing oxidizing agents listed in Table 2. Iodine and [hydroxy(tosyloxy)iodo]benzene (HTIB) gave 2-oxo-4-phenyl-2*H*-benzo[*h*]chromene-3-carbonitrile (**5**) as a sole product. 2-Iodoxybenzoic acid (IBX) does not show any effect on 2-aminochromene, whereas in the case of *N*-iodosuccinimide (NIS) product **5** was observed in trace amounts. Perhaps iodine(III)-mediated aziridination of the pyran ring is the

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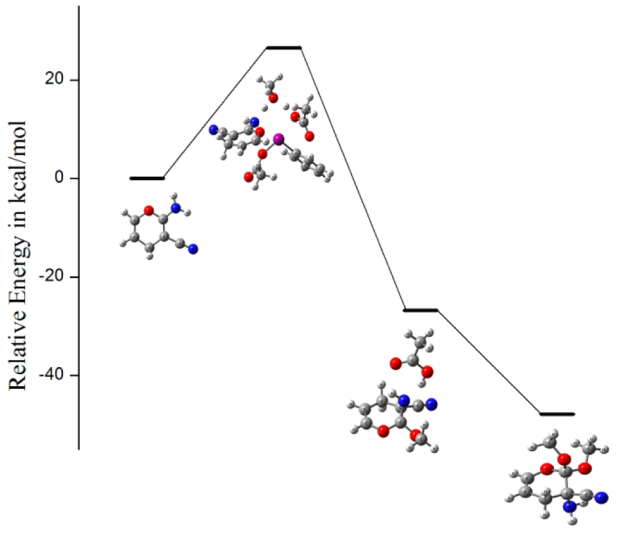
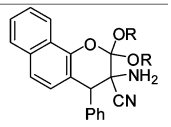
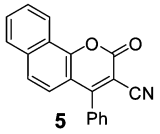
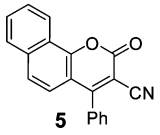
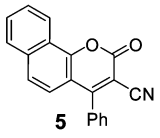


Figure 2. Free energy profile for IBD-catalyzed geminal dialkoxylation with 1,2-amino migration reaction as calculated in the gas phase by the DFT method.

Table 2. Screening of Different Catalytic and Solvent Systems for Difunctionalization of 2-amino-4-phenyl-4*H*-benzo[*h*]chromene-3-carbonitrile[a]

Reagent / Solvent	Time	Product
IBD / R-OH	15 min (R=CH_3) 20 min (R=C_2H_5)	
HTIB / MeOH	2.5 h	 **5**
NIS / MeOH	12 h	 **5**
		(Trace amount)
Iodine / EtOH	10 h	 **5**
IBX / MeOH	24 h	No reaction

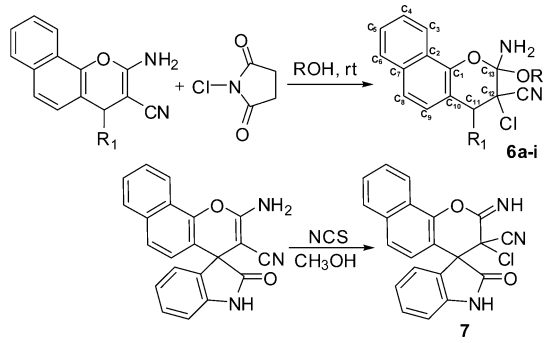
[a]All of the reactions are carried out by stirring under rt conditions and open to air.

driving force for unusual migration of amino group. Such iodine(III)-catalyzed aziridination has literature precedence in some cyclic allylic carbamates.[17]

Notably different results were obtained when the oxidizing reagent was *N*-chlorosuccinimide (NCS). Reacting 2-amino-chromene with NCS in methanol gave addition of a single methoxy group as indicated by the NMR spectrum. However, the chemical shift of the amino group in the product was not drastically different as in the case of the product obtained from IBD reaction, indicating that migration of the amino group may not have occurred. Further, the mass spectrum indicated the presence of chlorine. The structure of the compound **6g** validated by X-ray crystallography[18] gave conclusive evidence that the chromene double bond is oxidatively difunctionalized by the addition of chlorine and methoxy groups, leading to the formation of 2-amino-3-chloro-2-alkoxy-4-aryl-2,3-dihydro-4*H*-benzo[*h*]chromene-3-carbonitrile. Similar to the IBD case, compound **6g** crystallized in the centrosymmetric space group. The compounds **6a–i** are found to be racemic mixtures (1:1) with a configuration of *R*,*R*,*S* at C_{11}, C_{12}, and C_{13}, respectively.

The optimized reaction conditions were employed by studying the reaction scope as well as generality by varying the solvents and the phenyl ring substitutions as shown in Table 3. The reaction proceeds instantaneously in methanol,

Table 3. Difunctionalization of 2-Amino-4*H*-pyrans with NCS[a]



entry	R	R_1	product	time (min)	yield[b] (%)
1	CH_3	C_6H_5	**6a**	10	88
2	CH_3	4-$CH_3C_6H_4$	**6b**	10	80
3	CH_3	4-$CH_3OC_6H_4$	**6c**	10	91
4	CH_3	4-FC_6H_4	**6d**	10	83
5	CH_3	4-$O_2NC_6H_4$	**6e**	10	84
6	CH_3	2-Thienyl	**6f**	10	82
7	C_2H_5	4-ClC_6H_4	**6g**	overnight	82
8	C_2H_5	2-Thienyl	**6h**	overnight	80
9	$(CH_3)_2CH$	C_6H_5	**6i**	overnight	77
10	CH_3		**7**	overnight	70
11		4-BrC_6H_4	**7a**	15	77

[a]All reactions were carried out using 2-amino-4*H*-pyrans (1 equiv) and NCS (1.1 equiv) in the presence of excess alcohol under rt conditions. [b]Yield of crude product.

whereas it takes a longer time when ethanol or isopropyl alcohol is used as a solvent. However, it stops at an intermediate stage in the presence of methanol for 2-amino-2′-oxospiro[benzo[*h*]chromene-4,3′-indoline]-3-carbonitrile to afford 3-chloro-2-imino-2′-oxo-3,4-dihydrospiro[benzo[*h*]-chromene-4,3′-indoline]-3-carbonitrile (**7**) with 70% yield. The reactions with NCS also do not progress in alternative non-nucleophilic solvents.

A plausible mechanism to corroborate with the experimental observations is shown in Scheme 4. As is evident from the proposed mechanism, a stepwise addition of chlorine at *β*-carbon followed by the addition of alcohol across C═NH leaves no scope for NH_2 migration. Since the addition is

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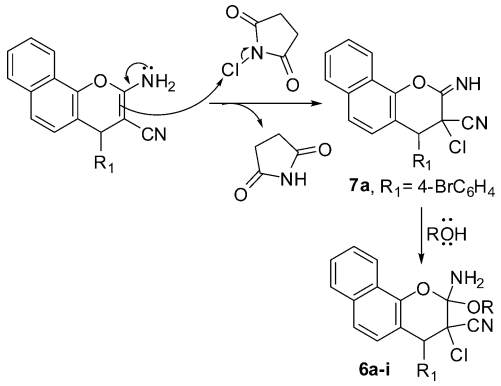
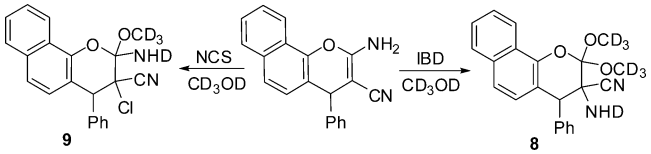
Scheme 4. Proposed Mechanism for Chloroalkoxylation of 2-Amino-4*H*-pyrans in the Presence of NCS and Alcohol



stepwise, the intermediate **7a** (where the reaction was carried out in isopropyl alcohol) could be isolated and characterized.

Difunctionalization of 2-amino-4-phenyl-4*H*-benzo[*h*]-chromene-3-carbonitrile in IBD as well as NCS was revisited by executing the experiments in methanol-d_4 (Scheme 5). In

Scheme 5. Deuterated Methanol Study



both the cases, the crude products obtained after reaction were subjected to spectral analysis. As expected, the PMR spectra show the disappearance of $-OCH_3$ signals. In the case of IBD, PMR spectra of the product (**8**) show a broad singlet for one proton at δ 1.78 ppm, and in the NCS case, spectra of the product (**9**) showed a broad singlet for one proton at δ 2.75 ppm. They were both assigned as −NHD signals. When subjected to D_2O exchange in both cases, the −NHD signals disappeared. The fact that the PMR chemical shifts of the amino group (−NHD) vary in each case suggests that they are not on identical carbons. From a mechanistic analysis of either protocol, a loss of amino proton at initial stages of reaction and a gain of proton from the alcohol is expected. The methanol-d_4 experiments corroborate the proposed mechanism. Further, both products were confirmed by mass spectrometry.

CONCLUSION

In summary, oxidative difunctionalization of the chromene double bond has been studied in alcoholic solvent medium in the presence IBD as well as NCS. Addition of geminal dialkoxy groups and 1,2-migration of $-NH_2$ occur in the case of IBD via an apparent intramolecular aziridination. In marked contrast, the NCS mediated reaction results in an anticipated ddition of chlorine and alkoxy groups across the chromene double bond in a stepwise manner. Deuterated methanol experiments and DFT calculations are supportive of the proposed mechanisms. Studies of scope, application, and limitations of this unusual protocol with amino migration on related systems are currently under investigation.

EXPERIMENTAL SECTION

General Methods. All reactions were performed under rt conditions and open to air. Melting points were determined in open capillary tubes and are uncorrected. ^{1}H NMR (300 MHz, 400 MHz, 500 MHz) and ^{13}C NMR (75, 125 MHz) spectra were recorded in $CDCl_3$ and DMSO-d_6. Chemical shifts are given in δ values referenced to the solvent. All of the yields mentioned in the experimental data are of isolated crude products unless otherwise mentioned.

General Procedure for the Synthesis of 1a,b, 2a−i, 3a,b. To a suspension of 2-amino-4*H*-pyran (1 mmol) in 5 mL of methanol (or ethanol) was added IBD (1.1 mmol) with stirring at rt open to air. The reaction mixture immediately became a clear solution followed by the precipitation of product. The mixture was filtered and washed with the corresponding alcohol to afford the desired product. The structures of the products (**2a** and **2f**) were assigned on the basis of spectral and X-ray crystallographic data.

*Ethyl 3-amino-3-cyano-2,2-dimethoxy-6-methyl-4-phenyl-2,3-dihydro-4H-pyran-5-carboxylate (**1a**):* yield 0.277 g (80%); mp 144−145 °C; IR (neat, cm^{-1}) 3379, 3315, 2982, 2232, 1705, 1646, 1116, 708; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39−7.28 (m, 5H), 4.34 (s, 1H), 3.91−3.80 (m, 2H), 3.71 (s, 3H), 3.53 (s, 3H), 2.33 (d, J = 1.7 Hz, 3H), 1.6 (s, 2H), 0.68 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 157.3, 136.4, 129.1, 128.5, 127.8, 120.7, 110.8, 105.7, 59.9, 56.1, 52.9, 50.9, 48.3, 18.2, 13.3. MS (ESI) m/z 369 (M + Na)$^+$; HRMS ESI (M + Na)$^+$ m/z calcd for $C_{18}H_{22}N_2O_5Na$ (M + Na)$^+$ 369.1420, found 369.1413.

*Ethyl 3-amino-3-cyano-2,2-diethoxy-6-methyl-4-phenyl-2,3-dihydro-4H-pyran-5-carboxylate (**1b**):* yield 0.292 g (78%); mp 149−151 °C; IR (neat, cm^{-1}) 3399, 3328, 2978, 2230, 1702, 1636, 1095, 710; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39−7.26 (m, 5H), 4.35 (s, 1H), 4.14−3.64 (m, 6H), 2.31 (d, J = 1.5 Hz, 3H), 1.60 (s, 2H), 1.35−1.26 (m, 6H), 0.67 (t, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 157.5, 136.6, 129.2, 128.4, 127.4, 120.8, 110.7, 105.4, 61.0, 59.9, 59.3, 56.3, 48.2, 18.3, 15.4, 15.0, 13.3; MS (ESI) m/z 397 (M + Na)$^+$; HRMS ESI (M + Na)$^+$ m/z calcd for $C_{20}H_{26}N_2O_5Na$ (M + Na)$^+$ 397.1733, found 397.1726.

*3-Amino-2,2-dimethoxy-4-phenyl-2,3-dihydro-4H-benzo[h]-chromene-3-carbonitrile (**2a**):* yield 0.281 g (78%); mp 188−190 °C; IR (neat, cm^{-1}) 3394, 3325, 2229, 1113, 720; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30−8.24 (m, 1H), 7.79−7.73 (m, 1H), 7.55−7.29 (m, 8H), 6.90 (d, J = 8.3 Hz, 1H), 4.82 (s, 1H), 3.96 (s, 3H), 3.48 (s, 3H), 1.72 (brs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.2, 135.8, 133.6, 131.2, 128.7, 128.5, 127.6, 126.5, 126.1, 124.3, 121.9, 121.0, 120.9, 115.8, 111.2, 56.8, 53.6, 50.8, 50.6; MS (ESI): m/z 383 (M + Na)$^+$; HRMS ESI (M + Na)$^+$ m/z calcd for $C_{22}H_{20}N_2O_3Na$ (M + Na)$^+$ 383.1366, found 383.1358.

*3-Amino-2,2-dimethoxy-4-(thiophene-2-yl)-2,3-dihydro-4H-benzo[h]chromene-3-carbonitrile (**2b**):* yield 0.307 g (84%); mp 176−178 °C; IR (neat, cm^{-1}) 3399, 3317, 2225, 1120, 715; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28−8.22 (m, 1H), 7.79−7.72 (m, 1H), 7.54−7.44 (m, 2H), 7.42−7.35 (m, 2H), 7.19 (d, J = 3.0 Hz, 1H), 7.12−7.08 (m, 1H), 7.02 (d, J = 8.3 Hz, 1H), 5.14 (s, 1H), 3.95 (s, 3H), 3.48 (s, 3H), 1.90 (brs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.6, 137.8, 133.8, 129.9, 127.6, 127.0, 126.7, 126.6, 126.2, 126.1, 124.1, 121.9, 121.1, 120.6, 115.6, 111.2, 57.1, 53.5, 50.8, 46.7; MS (ESI) m/z 389 (M + Na)$^+$; HRMS ESI (M + Na)$^+$ m/z calcd for $C_{20}H_{18}N_2O_3NaS$ (M + Na)$^+$ 389.0930, found 389.0923.

*3-Amino-2,2-dimethoxy-4-(4-methoxyphenyl)-2,3-dihydro-4H-benzo[h]chromene-3-carbonitrile (**2c**):* yield 0.288 g (74%); mp 188−189 °C; IR (neat, cm^{-1}) 3394, 3330, 2231, 1512, 1115, 772; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28−8.23 (m, 1H), 7.77−7.72 (m, 1H), 7.55−7.15 (m, 5H), 6.97−6.87 (m, 3H), 4.76 (s, 1H), 3.94 (s, 3H), 3.83 (s, 3H), 3.47 (s, 3H), 1.71 (brs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 145.1, 133.6, 132.2, 127.6, 126.5, 126.1, 124.3, 121.9, 121.0, 116.0, 114.1, 111.3, 56.9, 55.3, 53.5, 50.8, 49.9; MS (ESI) m/z 413 (M + Na)$^+$; HRMS ESI (M + Na)$^+$ m/z calcd for $C_{23}H_{22}N_2O_4Na$ (M + Na)$^+$ 413.1471, found 413.1461.

*3-Amino-2,2-dimethoxy-4-(4-nitrophenyl)-2,3-dihydro-4H-benzo[h]chromene-3-carbonitrile (**2d**):* yield 0.344 g (85%); mp 198−199 °C; IR (neat, cm^{-1}) 3384, 3314, 2233, 1520, 1351, 1110,

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801; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35−8.23 (m, 3H), 7.78 (d, J = 7.4 Hz, 1H), 7.70−7.48 (m, 4H), 7.40 (d, J = 8.3 Hz, 1H), 6.74 (d, J = 8.3 Hz, 1H), 4.92 (s, 1H), 3.95 (s, 3H), 3.49 (s, 3H), 1.68 (brs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.0, 145.3, 143.6, 133.7, 132.2, 127.7, 127.0, 126.5, 125.8, 124.2, 123.6, 122.4, 121.0, 120.0, 114.4, 111.1, 56.4, 53.5, 51.0, 50.6; MS (ESI) m/z 428 (M + Na)$^+$; HRMS ESI (M + Na)$^+$ m/z calcd for $C_{22}H_{19}N_3O_5Na$ (M + Na)$^+$ 428.1216, found 428.1208.

*3-Amino-2,2-dimethoxy-4-(4-fluorophenyl)-2,3-dihydro-4H-benzo[h]chromene-3-carbonitrile (**2e**):* yield 0.291 g (77%); mp 164−166 °C; IR (neat, cm^{-1}) 3383, 3321, 2230, 1111, 819; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33−8.26 (m, 1H), 7.82−7.76 (m, 1H), 7.60−7.30 (m, 5H), 7.13 (t, J = 8.3 Hz, 2H), 6.88 (d, J = 9.0 Hz, 1H), 4.84 (s, 1H), 3.97 (s, 3H), 3.48 (s, 3H), 1.66 (brs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.5, 161.2, 145.2, 133.6, 132.8, 131.6, 127.6, 126.7, 126.2, 125.9, 124.3, 122.0, 121.0, 120.8, 115.8, 115.6, 111.2, 56.7, 53.5, 50.8, 49.9; MS (ESI) m/z 401 (M + Na)$^+$; HRMS ESI (M + Na)$^+$ m/z calcd for $C_{22}H_{19}N_2O_3FNa$ (M + Na)$^+$ 401.1271, found 401.1263.

*3-Amino-2,2-diethoxy-4-phenyl-2,3-dihydro-4H-benzo[h]-chromene-3-carbonitrile (**2f**):* yield 0.287 g (74%); mp 194−195 °C; IR (neat, cm^{-1}) 3391, 3324, 2231, 1098, 710; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.25−8.20 (m, 1H), 7.77−7.71 (m, 1H), 7.53−7.27 (m, 8H), 6.89 (d, J = 9.0 Hz, 1H), 4.82 (s, 1H), 4.35−4.23 (m, 2H), 4.02−3.90 (m, 1H), 3.76−3.64 (m, 1H), 1.61 (brs, 2H), 1.46 (t, J = 7.5 Hz, 3H), 1.08 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.5, 136.1, 133.6, 131.2, 128.7, 128.4, 127.5, 126.6, 126.5, 126.0, 124.3, 121.6, 121.2, 121.1, 115.7, 111.1, 61.5, 59.1, 57.0, 50.6, 15.7, 14.9; MS (ESI) m/z 411 (M + Na)$^+$; HRMS ESI (M + Na)$^+$ m/z calcd for $C_{24}H_{24}N_2O_3Na$ (M + Na)$^+$ 411.1679, found 411.1669.

*3-Amino-2,2-diethoxy-4-(thiophene-2-yl)-2,3-dihydro-4H-benzo-[h]chromene-3-carbonitrile (**2g**):* yield 0.307 g (78%); mp 152−154 °C; IR (neat, cm^{-1}) 3391, 3320, 2230, 1115, 704; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 7.0 Hz, 1H), 7.56−7.48 (m, 2H), 7.45−7.37 (m, 2H), 7.27−7.20 (m, 1H), 7.15−7.10 (m, 1H), 7.04 (d, J = 8.0 Hz, 1H), 5.21 (s, 1H), 4.36−4.27 (m, 2H), 4.01−3.93 (m, 1H), 3.75−3.67 (m, 1H), 1.98 (brs, 2H), 1.46 (t, J = 7.0 Hz, 3H), 1.06 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.9, 138.1, 133.8, 129.8, 127.6, 127.0, 126.6, 126.5, 126.3, 126.0, 124.1, 121.7, 121.3, 120.8, 115.6, 111.1, 61.6, 59.2, 57.3, 46.6, 15.7, 14.9; MS (ESI) m/z 417 (M + Na)$^+$; HRMS ESI (M + Na)$^+$ m/z calcd for $C_{22}H_{22}N_2O_3NaS$ (M + Na)$^+$ 417.1243, found 417.1233.

*3-Amino-2,2-diethoxy-4-(4-chlorophenyl)-2,3-dihydro-4H-benzo-[h]chromene-3-carbonitrile (**2h**):* yield 0.303g (72%); mp 179−180 °C; IR (neat, cm^{-1}) 3394, 3328, 2231, 1106, 806; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 7.0 Hz, 1H), 7.57−7.27 (m, 7H), 6.87 (d, J = 9.0 Hz, 1H), 4.84 (s, 1H), 4.34−4.26 (m, 2H), 4.01−3.93 (m, 1H), 3.75−3.67 (m, 1H), 1.74 (brs, 2H), 1.44 (t, J = 7.0 Hz, 3H), 1.05 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.5, 134.6, 134.4, 133.6, 132.5, 128.8, 127.5, 126.6, 126.2, 126.1, 124.3, 121.8, 121.1, 120.8, 115.2, 111.0, 61.4, 59.2, 56.8, 50.0, 15.6, 14.8; MS (ESI) m/z 445 (M + Na)$^+$; HRMS ESI (M + Na)$^+$ m/z calcd for $C_{24}H_{23}N_2O_3ClNa$ (M + Na)$^+$ 445.1289, found 445.1282.

*3-Amino-2,2-diisopropoxy-4-phenyl-2,3-dihydro-4H-benzo[h]-chromene-3-carbonitrile (**2i**):* yield 0.291 g (70%); mp 192−193 °C; IR (neat, cm^{-1}) 3395, 3334, 2229, 1115, 716; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24−8.17 (m, 1H), 7.82−7.75 (m, 1H), 7.61−7.30 (m, 8H), 6.93 (d, J = 8.6 Hz, 1H), 5.07−4.95 (m, 1H), 4.92 (s, 1H), 4.62−4.49 (m, 1H), 1.67 (brs, 2H), 1.55 (d, J = 6.0 Hz, 3H), 1.46 (d, J = 6.2 Hz, 3H), 1.31 (d, J = 6.2 Hz, 3H), 0.75 (d, J = 6.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.0, 136.3, 133.6, 131.2, 128.7, 128.3, 127.6, 126.7, 126.4, 126.0, 124.4, 121.1, 121.0, 115.5, 111.3, 69.5, 66.0, 58.4, 50.5, 24.3, 23.7, 23.1; MS (ESI) m/z 439 (M + Na)$^+$; HRMS ESI (M + Na)$^+$ m/z calcd for $C_{26}H_{28}N_2O_3Na$ (M + Na)$^+$ 439.1992, found 439.1983.

*3-Amino-2,2-dimethoxy-4-phenyl-2,3-dihydro-4H-pyrano[3,2-h]-quinoline-3-carbonitrile (**3a**):* yield 0.260 g (72%); mp 228−229 °C; IR (neat, cm^{-1}) 3396, 3323, 2228, 1114, 776; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.00 (dd, J = 2.2, 1.5 Hz, 1H), 8.10 (dd, J = 2.2, 1.5 Hz, 1H), 7.54−7.28 (m, 7H), 7.00 (d, J = 9.0 Hz, 1H), 4.88 (s, 1H), 3.94 (s, 3H), 3.51 (s, 3H), 1.83 (brs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 145.6, 139.0, 135.5, 131.1, 128.6, 128.2, 127.1, 121.6, 120.8, 119.9, 111.5, 56.1, 53.2, 50.9, 50.8; MS (ESI) m/z 362 (M + H)$^+$; HRMS ESI (M + H)$^+$ m/z calcd for $C_{21}H_{20}N_3O_3$ (M + H)$^+$ 362.1499, found 362.1492.

*3-Amino-2,2-diethoxy-4-phenyl-2,3-dihydro-4H-pyrano[3,2-h]-quinoline-3-carbonitrile (**3b**):* yield 0.272 g (70%); mp 174−176 °C; IR (neat, cm^{-1}) 3399, 3330, 2231, 1122, 717; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.96 (d, J = 3.9 Hz, 1H), 8.17 (d, J = 8.3 Hz, 1H), 7.68−7.24 (m, 7H), 6.97 (d, J = 8.6 Hz, 1H), 4.87 (s, 1H), 4.39−4.19 (m, 2H), 4.04−3.90 (m, 1H), 3.84−3.70 (m, 1H), 1.93 (brs, 2H), 1.42 (t, J = 6.9 Hz, 3H), 1.04 (t, J = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 146.0, 139.1, 135.9, 135.5, 131.2, 128.6, 128.4, 128.3, 127.3, 121.5, 121.0, 120.6, 120.0, 111.3, 61.4, 59.2, 56.4, 51.0, 15.5, 14.7; MS (ESI) m/z 390 (M + H)$^+$; HRMS ESI (M + H)$^+$ m/z calcd for $C_{23}H_{24}N_3O_3$ (M + H)$^+$ 390.1812, found 390.1805.

Experimental Procedure for the Synthesis of 3-Amino-2,2-dimethoxy-2′-oxo-2,3-dihydrospiro[benzo[*h*]chromene-4,3′-indoline]-3-carbonitrile (4). To a suspension of 2-amino-2′-oxospiro[benzo[*h*]chromene-4,3′-indoline]-3-carbonitrile (0.339 g, 1 mmol) in 5 mL of methanol was added IBD (0.354 g, 1.1 mmol) with stirring at room temperature open to air. The resulting clear solution was allowed to stir at rt for 5 h. The solvent methanol from the mixture was removed under vacuum followed by partitioning of the reaction mixture between dichloromethane (2 × 15 mL) and water (10 mL). The organic layers collected were dried over anhydrous sodium sulfate and concentrated. The crude reaction mixture was subjected to column chromatography on silica gel (ethyl acetate/hexane 3:7) to afford the required product **4**. Isolated yield of pure product: 0.240 g (60%); mp 170−171 °C; IR (neat, cm^{-1}) 3274, 2230, 1720, 1471, 1123, 752; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.32 (d, J = 7.6 Hz, 1H), 7.77 (d, J = 7.6 Hz, 1H), 7.60−7.51 (m, 2H), 7.41 (d, J = 8.6 Hz, 1H), 7.29−7.25 (m, 2H), 7.00−6.93 (m, 2H), 6.68 (d, J = 7.6 Hz, 1H), 3.89 (s, 3H), 3.59 (s, 3H), 2.78 (brs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.0, 145.6, 140.9, 134.0, 130.8, 129.8, 128.4, 127.7, 127.1, 126.5, 124.9, 124.5, 123.3, 122.8, 121.2, 118.7, 114.1, 111.9, 110.3, 59.1, 58.1, 53.6, 50.4; MS (ESI) m/z 424 (M + Na)$^+$; HRMS ESI (M + Na)$^+$ m/z calcd for $C_{23}H_{19}N_3O_4Na$ (M + Na)$^+$ 424.1267, found 424.1266.

Experimental Procedure for the Synthesis of 2-Oxo-4-phenyl-2*H*-benzo[*h*]chromene-3-carbonitrile (5). To a suspension of 2-amino-4-phenyl-4*H*-benzo[*h*]chromene-3-carbonitrile (0.298 g, 1 mmol) in 5 mL of ethanol was added iodine (0.279 g, 1.1 mmol), and the resulting mixture was refluxed for 12 h. The solid formed was filtered and washed with cooled ethanol to afford the required product **5** as yellow solid: yield 0.160 g (54%); mp 215−217 °C; IR (neat, cm^{-1}) 3439, 3332, 2924, 2223, 1720, 1536, 1355, 758; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, J = 7.9 Hz, 1H), 7.90 (d, J = 7.1 Hz, 1H), 7.80−7.61 (m, 6H), 7.57−7.50 (m, 2H), 7.30 (d, J = 8.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.2, 152.1, 148.7, 136.4, 136.2, 131.1, 128.5, 128.3, 128.0, 125.7, 123.8, 123.3, 122.7, 121.9, 113.4, 113.1; MS (ESI) m/z 298 (M + H)$^+$; HRMS ESI (M + H)$^+$ m/z calcd for $C_{20}H_{12}NO_2$ (M + H)$^+$ 298.0862, found 298.0859.

General Procedure for the Synthesis of 6a−i. To a suspension of 2-amino-4*H*-pyran (1 mmol) in 5 mL of methanol (or ethanol) was added NCS (1.1 mmol) with stirring at room temperature open to air. The resulting clear solution was stirred at room temperature until the product precipitated. The reaction mixture was filtered and washed with the corresponding alcohol to separate the desired product. The structures of the products (**6a−i**) were assigned on the basis of the spectral data. Further, the product **6g** was confirmed by X-ray crystallographic data.

*2-Amino-3-chloro-2-methoxy-4-phenyl-2,3-dihydro-4H-benzo-[h]chromene-3-carbonitrile (**6a**):* yield 0.320 g (88%); mp 133−135 °C; IR (neat, cm^{-1}) 3404, 3331, 2229, 1967, 1389, 1089, 723; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35−8.29 (m, 1H), 7.83−7.77 (m, 1H), 7.64−7.34 (m, 8H), 6.81 (d, J = 8.6 Hz, 1H), 4.89 (s, 1H), 3.41 (s, 3H), 2.76 (brs, 2H); ^{13}C NMR δ (75 MHz, $CDCl_3$): 145.5, 136.2, 133.7, 131.4, 128.7, 128.4, 128.0, 127.6, 126.9, 126.4, 125.9, 124.5, 122.2, 121.4, 117.3, 116.0, 104.5, 68.8, 54.8, 52.9, 49.9; MS (ESI): m/z

365 $(M + H)^+$, 348 $(M - NH_2)^+$; HRMS ESI $(M + H)^+$ m/z calcd for $C_{21}H_{18}N_2O_2Cl$ $(M + H)^+$ 365.1051, found 365.1053.

*2-Amino-3-chloro-2-methoxy-4-(4-methylphenyl)-2,3-dihydro-4H-benzo[h]chromene-3-carbonitrile (**6b**):* yield 0.302 g (80%); mp 135−137 °C; IR (neat, cm^{-1}) 3421, 3345, 2231, 1901, 1391, 1084, 720; ^1H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 8.9 Hz, 1H), 7.79 (d, J = 7.9 Hz, 1H), 7.58−7.18 (m, 7H), 6.83 (d, J = 8.9 Hz, 1H), 4.86 (s, 1H), 3.40 (s, 3H), 2.74 (brs, 2H), 2.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.4, 138.6, 133.7, 133.2, 131.2, 129.2, 128.8, 127.6, 126.8, 126.3, 126.0, 124.5, 122.2, 121.3, 117.5, 116.1, 104.5, 68.9, 54.4, 52.6, 49.8, 21.2; MS (ESI): m/z 379 $(M + H)^+$, 362 $(M - NH_2)^+$; HRMS ESI $(M + H)^+$ m/z calcd for $C_{22}H_{20}N_2O_2Cl$ $(M + H)^+$ 379.1207, found 379.1209.

*2-Amino-3-chloro-2-methoxy-4-(4-methoxyphenyl)-2,3-dihydro-4H-benzo[h]chromene-3-carbonitrile (**6c**):* yield 0.319 g (81%); mp 134−136 °C; IR (neat, cm^{-1}) 3417, 3345, 2230, 1899, 1383, 1088, 762; ^1H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 6.9 Hz, 1H), 7.79 (d, J = 6.9 Hz, 1H), 7.61−7.28 (m, 5H), 6.95 (d, J = 8.0 Hz, 2H), 6.84 (d, J = 9.2 Hz, 1H), 4.84 (s, 1H), 3.85 (s, 3H), 3.40 (s, 3H), 2.75 (brs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 145.4, 133.7, 132.4, 128.1, 127.6, 126.9, 126.3, 125.9, 124.5, 122.2, 121.4, 117.6, 116.2, 113.8, 104.5, 69.1, 55.3, 54.7, 52.2, 49.8; MS (ESI): m/z 395 $(M + H)^+$, 376 $(M - NH_2)^+$; HRMS ESI $(M + H)^+$ m/z calcd for $C_{22}H_{20}N_2O_3Cl$ $(M + H)^+$ 395.1157, found 395.1162.

*2-Amino-3-chloro-2-methoxy-4-(4-fluorophenyl)-2,3-dihydro-4H-benzo[h]chromene-3-carbonitrile (**6d**):* yield 0.317 g (83%); mp 120−122 °C; IR (neat, cm^{-1}) 3429, 3356, 2234, 1903, 1392, 1088, 762; ^1H NMR (300 MHz, $CDCl_3$) δ 8.35−8.29 (m, 1H), 7.83−7.78 (m, 1H), 7.68−7.32 (m, 5H), 7.12 (t, J = 8.3 Hz, 2H), 6.79 (d, J = 8.3 Hz, 1H), 4.89 (s, 1H), 3.41 (s, 3H), 2.76 (brs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.6, 161.3, 145.5, 133.8, 133.0, 132.1, 127.6, 127.0, 126.5, 125.6, 124.5, 122.4, 121.4, 117.0, 115.9, 115.5, 104.5, 68.7, 54.1, 52.3, 49.8; MS (ESI): m/z 383 $(M + H)^+$, 366 $(M - NH_2)^+$; HRMS ESI $(M + H)^+$ m/z calcd for $C_{21}H_{17}N_2O_2ClF$ $(M + H)^+$ 383.0957, found 383.0958.

*2-Amino-3-chloro-2-methoxy-4-(4-nitrophenyl)-2,3-dihydro-4H-benzo[h]chromene-3-carbonitrile (**6e**):* yield 0.343 g (84%); mp 142−144 °C; IR (neat, cm^{-1}) 3426, 3349, 2233, 1936, 1347, 1086, 762; ^1H NMR (500 MHz, $CDCl_3$) δ 8.34−8.25 (m, 3H), 7.86−7.39 (m, 6H), 6.69 (d, J = 8.8 Hz, 1H), 5.04 (s, 1H), 3.41 (s, 3H), 2.78 (brs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.3, 145.7, 143.7, 133.9, 132.3, 127.7, 127.3, 126.8, 125.1, 124.6, 123.6, 123.1, 122.8, 121.4, 115.7, 115.6, 104.5, 67.9, 54.3, 52.8, 50.0; MS (ESI) m/z 410 $(M + H)^+$, 393 $(M\text{-}NH_2)^+$; HRMS ESI $(M + H)^+$ m/z calcd for $C_{21}H_{17}N_3O_4Cl$ $(M + H)^+$ 410.0902, found 410.0903.

*2-Amino-3-chloro-2-methoxy-4-(thiophene-2-yl)-2,3-dihydro-4H-benzo[h]chromene-3-carbonitrile (**6f**):* yield 0.303 g (82%); mp 126−128 °C; IR (neat, cm^{-1}) 3430, 3343, 2225, 1969, 1347, 1085, 764; ^1H NMR (300 MHz, $CDCl_3$) δ 8.34−8.28 (m, 1H), 7.84−7.78 (m, 1H), 7.63−7.51 (m, 2H), 7.45 (d, J = 9.0 Hz, 1H), 7.41 (d, J = 5.2 Hz, 1H), 7.22 (d, J = 3.7 Hz, 1H), 7.14−7.09 (m, 1H), 6.97 (d, J = 8.3 Hz, 1H), 5.18 (s, 1H), 3.41 (s, 3H), 2.76 (brs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.9, 138.1, 133.9, 129.6, 127.6, 127.0, 126.4, 126.3, 125.6, 124.4, 122.3, 121.4, 117.0, 116.1, 104.5, 68.7, 50.4, 49.9, 48.5; MS (ESI) m/z 371 $(M + H)^+$, 354 $(M\text{-}NH_2)^+$; HRMS ESI $(M + H)^+$ m/z calcd for $C_{19}H_{16}N_2O_2ClS$ $(M + H)^+$ 371.0615, found 371.0621.

*2-Amino-3-chloro-2-ethoxy-4-(4-chlorophenyl)-2,3-dihydro-4H-benzo[h]chromene-3-carbonitrile (**6g**):* yield 0.337 g (82%); mp 155−157 °C; IR (neat, cm^{-1}) 3412, 3336, 2055, 1900, 1348, 1087, 764; ^1H NMR (300 MHz, $CDCl_3$) δ 8.29 (d, J = 7.9 Hz, 1H), 7.80 (d, J = 6.9 Hz, 1H), 7.60−7.28 (m, 7H), 6.78 (d, J = 7.9 Hz, 1H), 4.90 (s, 1H), 4.05 (quin, 1H), 3.62 (quin, 1H), 2.77 (brs, 2H), 0.98 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.8, 134.9, 134.8, 133.7, 132.8, 128.7, 128.2, 127.6, 127.0, 126.4, 125.6, 124.6, 122.3, 121.5, 116.6, 116.0, 104.3, 68.7, 58.5, 54.1, 52.3, 14.9; MS (ESI) m/z 413 $(M + H)^+$, 396 $(M\text{-}NH_2)^+$; HRMS ESI $(M + H)^+$ m/z calcd for $C_{22}H_{19}N_2O_2Cl_2(M + H)^+$ 413.0818, found 413.0820.

*2-Amino-3-chloro-2-ethoxy-4-(thiophene-2-yl)-2,3-dihydro-4H-benzo[h]chromene-3-carbonitrile (**6h**):* yield 0.307 g (80%); mp 119−121 °C; IR (neat, cm^{-1}) 3427, 3350, 1392, 1086, 752; ^1H NMR (300 MHz, $CDCl_3$) δ 8.28 (d, J = 5.2 Hz, 1H), 7.80 (d, J = 5.1 Hz, 1H), 7.61−7.51 (m, 2H), 7.46−7.38 (m, 2H), 7.23−7.19 (m, 1H), 7.15−7.08 (m, 1H), 6.97 (d, J = 8.4 Hz, 1H), 5.20 (s, 1H), 4.06 (quin, 1H), 3.62 (quin, 1H), 2.77 (brs, 2H), 0.98 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.1, 138.2, 133.9, 129.5, 127.5, 127.0, 126.9, 126.3, 126.2, 125.6, 124.4, 122.1, 121.5, 117.0, 116.2, 104.4, 68.9, 58.5, 48.4, 14.9; MS (ESI) m/z 385 $(M + H)^+$; HRMS ESI $(M + H)^+$ m/z calcd for $C_{20}H_{18}N_2O_2SCl$ $(M + H)^+$ 385.0772, found 385.0783.

*2-Amino-3-chloro-2-isopropoxy-4-phenyl-2,3-dihydro-4H-benzo-[h]chromene-3-carbonitrile (**6i**):* yield 0.301 g (77%); mp 112−113 °C; IR (neat, cm^{-1}) 3394, 3325, 2229, 1113, 720; ^1H NMR (300 MHz, $CDCl_3$) δ 8.32−8.26 (m, 1H), 7.81−7.75 (m, 1H), 7.59−7.35 (m, 8H), 6.80 (d, J = 8.6 Hz, 1H), 4.89 (s, 1H), 4.80−4.70 (m, 1H), 2.77 (brs, 2H), 1.24 (d, J = 6.2 Hz, 3H), 0.63 (d, J = 6.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.1, 136.5, 133.6, 131.6, 128.9, 128.6, 128.4, 127.5, 126.8, 126.2, 125.9, 124.6, 121.9, 121.6, 117.0, 116.2, 104.5, 69.3, 66.3, 54.6, 52.7, 23.9, 22.6; MS (ESI) m/z 393 $(M + H)^+$, 376 $(M - NH_2)^+$; HRMS ESI $(M + H)^+$ m/z calcd for $C_{23}H_{22}N_2O_2Cl$ $(M + H)^+$ 393.1364, found 393.1369.

Experimental Procedure for the Synthesis of 3-Chloro-2-imino-2′-oxo-3,4-dihydrospiro[benzo[*h*]chromene-4,3′-indoline]-3-carbonitrile (7). To a suspension of 2-amino-2′-oxospiro-[benzo[*h*]chromene-4,3′-indoline]-3-carbonitrile (0.339 g, 1 mmol) in 5 mL of methanol was added NCS (0.146 g, 1.1 mmol) with stirring at room temperature. The resulting clear brown solution was then allowed to stir overnight. The precipitate formed was filtered and dried to afford the desired product **7** as brown solid: yield 0.261 g (70%); mp 242−244 °C; IR (neat, cm^{-1}) 3426, 3349, 2233, 1936, 1347, 1086, 762; ^1H NMR (300 MHz, DMSO-d_6) δ 11.08 (brs, 1H), 9.13 (brs, 1H), 8.33 (d, J = 7.5 Hz, 1H), 7.88−7.80 (m, 1H), 7.67−7.45 (m, 5H), 7.21 (t, J = 7.7 Hz, 1H), 7.14 (d, J = 7.7 Hz, 1H), 6.71 (d, J = 8.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6) δ 172.0, 151.6, 145.6, 142.8, 133.5, 130.3, 126.8, 126.6, 126.1, 123.0, 122.9, 122.3, 122.0, 120.3, 112.1, 111.4, 110.5, 58.8, 48.7; MS (ESI) m/z 374 $(M + H)^+$; HRMS ESI $(M + H)^+$ m/z calcd for $C_{21}H_{13}N_3O_2Cl$ $(M + H)^+$ 374.0690, found 374.0696.

Experimental Procedure for the Synthesis of 4-(4-Bromophenyl)-3-chloro-2-imino-2,3-dihydro-4*H*-benzo[*h*]chromene-3-carbonitrile (7a). To a suspension of 2-amino-4-(4-bromophenyl)-4*H*-benzo[*h*]chromene-3-carbonitrile (0.376 g, 1 mmol) in 5 mL of isopropyl alcohol was added NCS (0.146 g, 1.1 mmol) and the mixture stirred at room temperature for 15 min. The reaction mixture became a clear solution followed by the precipitation of solid product. The precipitate was filtered and dried to afford the desired product **7a** as a white solid: yield 0.316 g (77%); mp 164−165 °C; IR (neat, cm^{-1}) 3283, 2536, 2109, 1692, 1259, 907, 762; ^1H NMR (300 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.29 (d, J = 7.5 Hz, 1H), 7.88 (d, J = 6.7 Hz, 1H), 7.70−7.59 (m, 3H), 7.47 (d, J = 8.3 Hz, 2H), 7.17 (d, J = 8.3 Hz, 1H), 7.07 (d, J = 8.3 Hz, 2H), 4.78 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.2, 134.3, 133.9, 132.5, 130.6, 128.0, 127.7, 127.3, 125.6, 125.0, 123.9, 122.8, 121.0, 114.0, 56.2, 54.7; MS (ESI) m/z 411 $(M)^+$; HRMS ESI $(M + H)^+$ m/z calcd for $C_{20}H_{13}N_2OClBr$ $(M + H)^+$ 410.9899, found 410.9920.

Experimental Procedure for the Synthesis of Compounds 8 and 9. Synthesis of compounds **8** and **9** are similar to that of the compounds **2a** and **6a**, respectively. However, the deuterated methanol (CD_3OD) was used as solvent instead of methanol.

*Compound **8**.* To a suspension of 2-amino-4-phenyl-4*H*-benzo[*h*]-chromene-3-carbonitrile (0.089 g, 0.3 mmol) in 1 mL of methanol-d_4 was added IBD (0.106g, 0.33 mmol) with stirring at room temperature. A clear solution immediately formed followed by the precipitation of product. The mixture was filtered to afford the desired product: yield 0.078 g (72%); mp 189−191 °C; IR (neat, cm^{-1}) 3395, 3326, 2536, 2127, 2076, 1384, 1130, 765; ^1H NMR (300 MHz, $CDCl_3$) δ 8.34−8.28 (m, J = 7.5 Hz, 1H), 7.82−7.76 (m, 1H), 7.59−7.27 (m, 8H), 6.92 (d, J = 8.3 Hz, 1H), 4.86 (s, 1H), 1.78 (brs, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.2, 137.4, 135.8, 133.6, 131.3, 130.2, 128.7, 128.5, 127.6, 126.5, 126.4, 126.1, 124.3, 121.8, 121.0,

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120.9, 115.8, 111.2, 56.7, 50.6; MS (ESI) m/z 367 $(M)^+$; HRMS ESI $(M)^+$ m/z calcd for $C_{22}H_{13}D_7N_2O_3$ $(M)^+$ 367.1907, found 367.1925.

Compound **9**. To a suspension of 2-amino-4-phenyl-4*H*-benzo[*h*]-chromene-3-carbonitrile (0.089 g, 0.3 mmol) in 1 mL of methanol-d_4 was added NCS (0.044 g, 0.33 mmol) and the mixture stirred at room temperature until the product precipitated. The reaction mixture was then filtered to afford the desired product: yield 0.088 g (80%); mp 126−128 °C; IR (neat, cm^{-1}) 3405, 3332, 2544, 2245, 2075, 1383, 1130, 764; ^1H NMR (300 MHz, $CDCl_3$) δ 8.34−8.29 (m, 1H), 7.82−7.77 (m, 1H), 7.61−7.28 (m, 8H), 6.81 (d, J = 9.0 Hz, 1H), 4.89 (s, 1H), 2.75 (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.5, 136.2, 133.7, 131.4, 128.7, 128.5, 128.0, 127.6, 126.9, 126.4, 125.9, 124.5, 122.2, 121.3, 117.3, 116.1, 104.4, 68.7, 54.7, 52.9; MS (ESI) m/z 369 $(M + H)^+$, 351 $(M - HD)^+$. Anal. Calcd for $C_{21}H_{13}D_4N_2O_2Cl$: C, 68.38; H, 5.74; N, 7.59. Found: C, 68.27; H, 5.71; N, 7.64.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Atom coordinates and absolute energies, ^1H and ^{13}C NMR spectra for all compounds, and X-ray data for compounds **2a**, **2f**, and **6g** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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