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Combined Directed *ortho* and Remote Metalation−Suzuki Cross-Coupling Strategies. Efficient Synthesis of Heteroaryl-Fused Benzopyranones from Biaryl *O*-Carbamates

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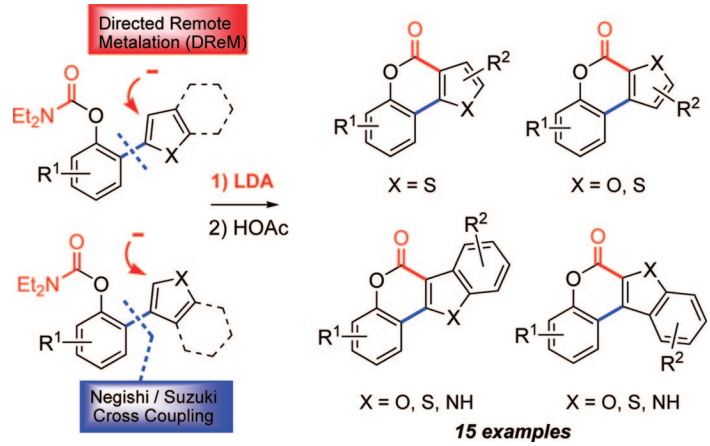

A concise synthesis of heteroaryl dibenzopyranones **9a**,**b**, **10a**,**b**, **11a**−**c**, and **12a**−**c** has been achieved by the LDA-induced migration of heterobiaryl *O*-carbamates **18**, **21**, **25**, and **30** which, in turn, were prepared in good yield using a combined directed *ortho* lithiation (DoM)−transition-metal-catalyzed Suzuki cross-coupling strategy. An efficient and general route to a wide variety of heterocycles including coumestans **19a**,**c** and the previously unknown isothiocoumestan ring system **22b** has been thereby achieved.

Introduction

As a logical sequel to the synthesis of the naphtho[*b*,*d*]benzopyran-6-one types of natural products, defucogilvocarcin and arnottin I,[1] we envisaged the extension of the directed *ortho* and remote metalation−transition-metal-catalyzed cross-coupling strategies used therein to the construction of heteroaryl-annelated benzopyranones (Scheme 1). To this aim, intermediate heterobiaryls **3** and **4** would be generated and subjected to the LDA-mediated DreM processes to afford intermediate amides **5** and **6** which, upon acid-catalyzed cyclization, would afford the benzopyranones with heterocyclic annelation. At the outset, **3** and **4** would be derived by cross-coupling of aryl *O*-carbamate **1** with heteroaromatic **2** partners, with X, Y = Met, Hal substituents dictated by the efficiency of the modern Suzuki−Miyaura, Negishi, and Stille regimens to be adopted.[2] The aryl carbamates **3** and **4** would incorporate suitable protection or substitution (PG) to avoid competition from the anionic *ortho*-Fries rearrangement[3] in the subsequent DreM chemistry. This strategy presents opportunities for the construction of a host of heterocyclic systems **9**−**12** (Scheme 2). Herein we report new methods for the synthesis of thieno[3,2-*c*]coumarin **9b**, furo[2,3-*c*]coumarins **10a**, thieno[2,3-*c*]coumarins **10b**, and all three O, S, and N heteroatom series of the coumestans **11a**−**c** and isocoumestans **12a**−**c**.

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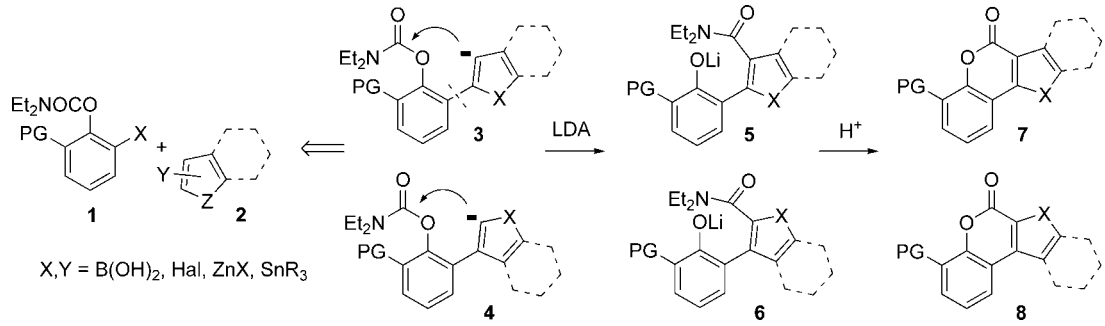
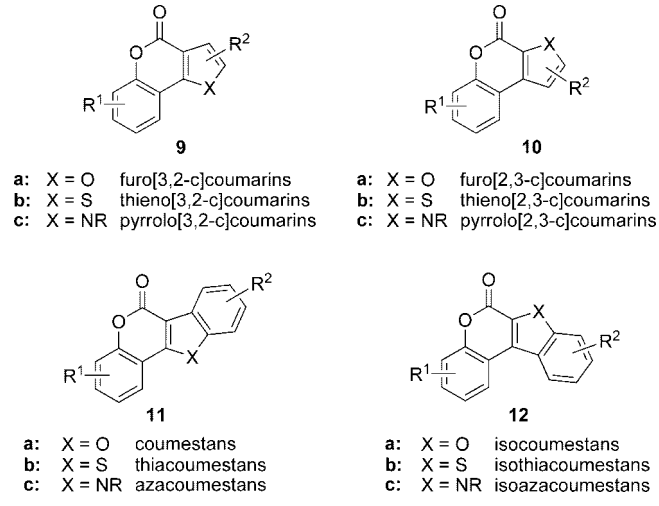
SCHEME 1



Heteroaryl-fused benzopyranones **9**−**12** constitute sizable groups of heterocyclic compounds possessing a diverse range of biological properties. While very few simple heteroaromatic fused coumarins, **9** and **10**, occur in nature, these tricyclic heterocycles are of synthetic interest[4] due to their structural relationship to the coumestan derivatives as well as their biological activity in some instances where studied.[5] The tetracyclic coumestans **11a**, $R^1 = R^2 =$ OH, OMe, a large group of natural products belonging to the isoflavanoid class and isolated mainly from plant sources,[6] have elicited considerable interest due to their rigid stilbene substructure and hence relationship to the potent estrogen diethylstilbesterol as well as tamoxifen (**13**), which is used in breast cancer chemotherapy.[7] In fact, estrogenic[8] and other bioactivities for systems **3a**, both

SCHEME 2



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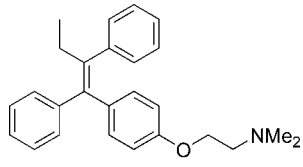
natural and synthetic materials, have been recognized and widely studied.[9] On the other hand, the isocoumestans **12a** do not occur naturally.

The vast synthetic literature for coumestans,[10] as well as continuing efforts for the synthesis[11] and isolation[6c] of this class of compound, is in contrast to the other members of this family (**11b**,**c** and **12a**−**c**) and is undoubtedly an indication of the importance of the biological activities of the coumestans.[8,9] Isocoumestans[12] (**12a**), azacoumestans[13] (**11c**), and isoazacoumestans[14] (**12c**) have received some attention as result of their structural similarity to the coumestans. Interestingly, despite their similarity in structure to their oxygen counterparts, the thia- (**11b**) and isothia- (**12b**) coumestan derivatives have received very little attention. In fact, there is but one method for the preparation of thiacoumestans,[15] whereas the corresponding isothiacoumestan[16] was an unknown ring system until our work. The overall state of synthesis for ring systems **9** and **10** and especially **11a**−**c** and **12a**−**c** and the potential provision of efficient and short routes via the metalation−cross-coupling strategy (Scheme 1) stimulated our efforts.

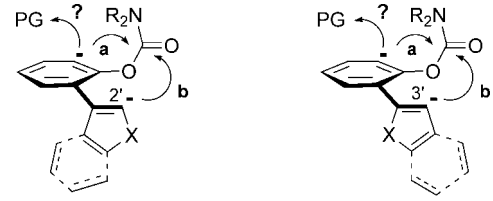


Tamoxifen (13)

Results and Discussion

At the outset, the interesting consideration of the potential deprotonation sites in the heterobiaryl *O*-carbamates **14** and **15** (Scheme 3) was contemplated. In contrast to the biaryl *O*-carbamates,[17] relative rate (*t*-BuOK/DMSO) and pK_a data

SCHEME 3



14 **15**

(polarographic scale)[18] for furans (k_{deprot} C_2/C_3 = 500:1, pK_a = 36) and thiophenes (k_{deprot} $C_2/C_3 = 2.5 \times 10^5$:1, p$K_a$ = ∼35)[19] indicate enhanced $C_{2'}$ acidity, which may allow selective deprotonation in **14** at site **b** over site **a** (pK_a = 37.2),[20] hence overcoming the need for protection (PG) to avoid the anionic *ortho*-Fries rearrangement. The analogous comparison for **15**, pitting $C_{3'}$ versus *ortho*, sites **b** and **a**, respectively, has less potential prognostic input based on the above available data. However, both contemplations may be superseded by the impact of the *O*-carbamate base complexation (complex induced proximity effect (CIPE))[17] and the heterobiaryl rotational isomerism in determining the site of deprotonation.[21]

In preparation for the DreM chemistry toward representative coumestan, thiocoumestan, and azacoumestan derivatives, **3a**−**c**, the intermediate heterobiaryls **7a**−**e** were synthesized by the Suzuki−Miyaura cross-coupling protocol[22] of aryl *O*-carbamoyl *ortho*-boronic acids **5a**,**b** with available benzofuran[23] and benzothiophene[24] iodides **17a**,**b** (Scheme 4 and Table 1, entries 1−4).[22] The exceptional case (entry 5), involving the inversion of coupling partners, was decided by the instability of the *N*-Boc-2-iodoindole derivative. Compounds **16a**,**b** were obtained by metalation−boronation of the readily available corresponding

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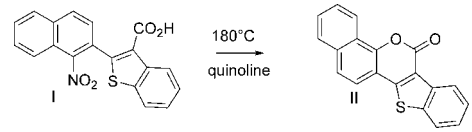

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(21) In pyridyl heterobiaryls, the pyridine ring C−H acidities are invariably higher than those of *O*-carbamate *ortho*-hydrogens as evidenced by DreM processes. See: Wang, W.; Snieckus, V. *J. Org. Chem.* **1992**, *57*, 424.

SCHEME 4

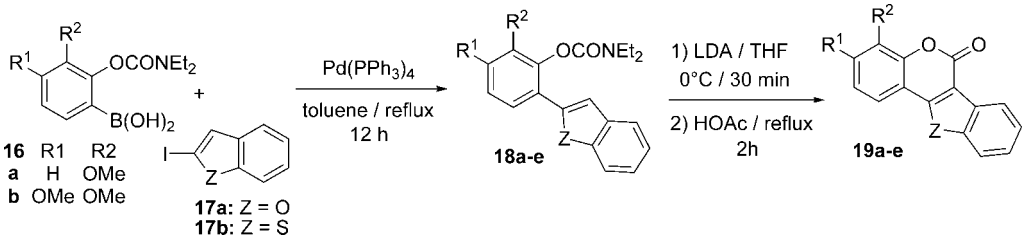
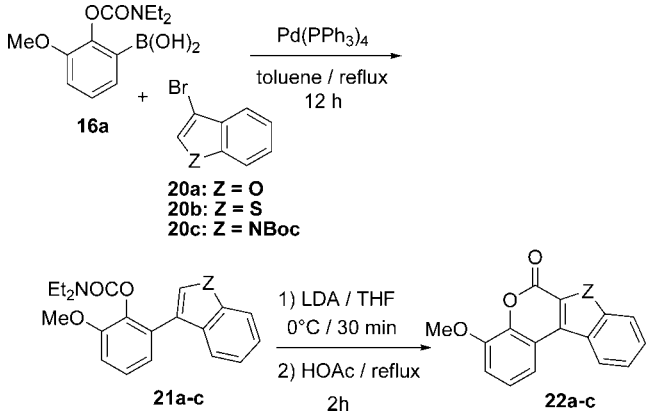


TABLE 1. Synthesis of Coumestans 19a,c, Thiacoumestans 19b,d, and Azacoumestan 19e

entry	**18/19**	R^1	R^2	Z	yield **18**, %	yield **19**, %
1	**a**	H	OMe	O	79	79
2	**b**	H	OMe	S	79	96
3	**c**	OMe	OMe	O	94	75
4	**d**	OMe	OMe	S	93	77
5[a]	**e**	H	OMe	*N*-Boc	54	83[c]

[a] Cross-coupling performed with aryliodide/indole 2-boronic acid in DME as solvent (reflux). [b] DME was used as solvent in the cross-coupling step. [c] Final product was isolated as Z = NH; boc cleavage occurs on cyclization.

SCHEME 5



aryl *O*-carbamates and used in unpurified form (see Experimental Section).

When subjected to treatment with LDA (2.5 equiv) at 0 °C → rt followed by extractive workup and subjection of the crude reaction mixture to refluxing HOAc, compounds **18a−e** were smoothly converted into the corresponding coumestan, thiacoumestan, and azacoumestan derivatives **19a−e** in good to excellent yields (Table 1, entries 1−5).[25] As expected for the azacoumestan **8e** (entry 5), *N*-Boc cleavage occurs under the acetic acid cyclization conditions.

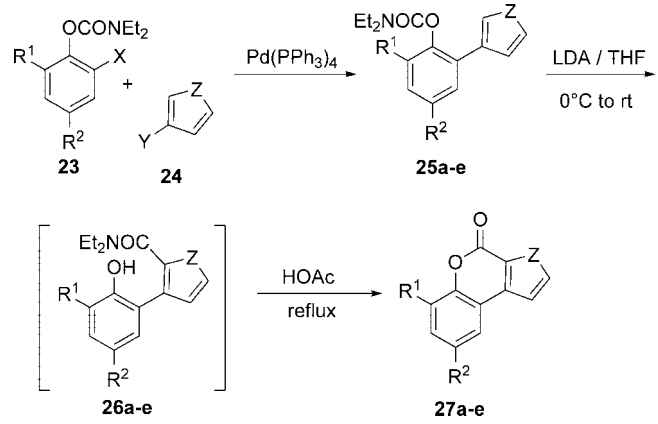
DreM-carbamoyl migration precursors **11a−c** for single test case of isocoumestan, isothiacoumestan, and isoazacoumestan derivatives were likewise prepared from the *O*-carbamate boronic acid **5a** and heterocyclic **10a−c** partners (Scheme 5 and Table 2, entries 1−3). With two exceptions (entry 5 and 6), and for unknown reasons, good yields of heterobiaryl products were observed.[26] Using identical LDA conditions, the

TABLE 2. Synthesis of Isocoumestans, Isothiacoumestans, and Isoazacoumestans 22a−c

entry	Z	**20**	yield **21**, %	yield **22**, %
1[a]	O	**a**	34	34
2[a]	S	**b**	86	86
3	*N*-Boc	**c**	60	60[b]

[a] DME used as solvent. [b] Product (**22c**) isolated as Z = NH; boc cleavage occurs on cyclization.

SCHEME 6



isocoumestan **12a**, isothiocoumestan **12b**, and isoazacoumestan **12c** were similarly prepared in good yields (Table 2, entries 1−3) using the standard LDA conditions on the intermediary heterobiaryls **11a−c**. To the best of our knowledge, the preparation of **12b** constitutes the first synthesis of the 6*H*-thianaphthenyl[2,3-*c*]benzo[*e*]pyran-6-one ring system.[16]

Synthesis of Coumarins (1a−c) and Isocoumarins (2a−c). Synthesis of the tricyclic coumarin derivatives (**1a−c**, **2a−c**) began with a study of the coupling reactions of appropriate *O*-carbamates **23a−e** with functionalized π-excessive aromatics **24** (Scheme 6 and Table 3), and it was demonstrated that the Negishi methodology proved satisfactory for the preparation of 2-(3-furyl)-*O*-arylcarbamates (entry 2 vs 5), whereas the Suzuki protocol was more efficient for the synthesis of 2-(3-thienyl)-*O*-arylcarbamates (entry 1 vs 3 and 4).[27]

Carbamoyl migration of the heteroarylcarbamates **25a−e** (Scheme 6) proceeded rapidly under the standard conditions

(22) (a) Miyaura, N.; Yamagi, T.; Suzuki, A. *Synth. Commun.* **1981**, *11*, 513. (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. Toluene was found to be a superior solvent as opposed to the normally used DME (Siddiqui, M. A.; Snieckus, V. *Tetrahedron Lett.* **1988**, *29*, 5463) the latter resulting in significant amounts of carbamate hydrolysis.

(23) Mann, I. S.; Widdowson, D. A.; Clough, J. M. *Tetrahedron* **1991**, *47*, 7981.

(24) Gaertner, R. *J. Am. Chem. Soc.* **1952**, *74*, 4950.

(25) The unsubstituted aryl *O*-carbamate, **18**, R1 = R2 = H, was shown to undergo the anionic *ortho*-Fries rearrangement into the corresponding salicylamide in 59% yield when treated with LDA under the conditions of Table 1, thus indicating a comparably higher aromatic ring thermodynamic acidity under these conditions and necessitating the PG strategy (see Scheme 3): Coelho, A. L.; Snieckus, V. Unpublished results.

(26) The corresponding Negishi coupling using inverted partners, iodocarbamate corresponding to **5a** and zinc bromides corresponding to **10a** and **10b**, produced heterobiaryls **11a** and **11b** in 31 and 0% (intractable mixture) respectively. See: James, C. A. Ph.D thesis, University of Waterloo, 1998.

TABLE 3. Synthesis of Furocoumarin and Thienocoumarin Derivatives 17a−e

entry	R^1	R^2	X	Y	Z	25/27	yield 25, %	yield 27, %
1[a]	TMS	H	$B(OH)_2$	Br	S	**a**	47	62
2[b]	H	OMe	ZnCl	Br	S	**b**	40	38
3[a]	H	H	Br	$B(OH)_2$	S	**c**	90	48
4[a]	OMe	H	I	$B(OH)_2$	S	**d**	80	43
5[b]	OMe	H	I	ZnBr	O	**e**	84	45

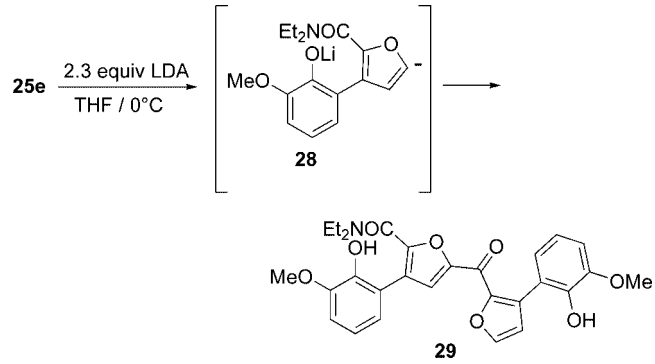
[a] Na_2CO_3 (2 M)/DME reflux. [b] THF/reflux.

(2−3 equiv of LDA/THF/0 °C), being complete in ca. 10 min, which is presumably the result of the enhanced acidity of the heteroaryl α-position.[28] Although the intermediate hydroxyamides could be isolated, cyclization during purification on silica gel to the extent of 5−10% was commonly observed. Thus, conveniently, direct cyclization was carried out on the crude intermediates leading to the corresponding thieno- (**27a−d**) and furocoumarins (**27e**) in moderate yields over two steps. Interestingly, for the conversion **25a** → **27a**, the TMS substituent, installed as a PG against the anionic *ortho*-Fries rearrangement, survives the HOAc cyclization conditions, which may be of potential value in electrophile-induced *ipso*-desilylation chemistry.[29]

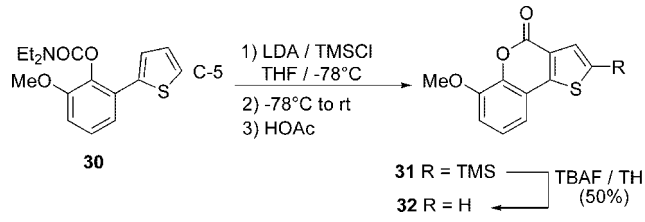
In an effort to understand the reason for the modest yields of the migration products **27a−e**, the 2-(3-furyl)-*O*-carbamate **25e** was reinvestigated in detail. Careful examination of the reaction mixture from the LDA reaction revealed the expected dibenzopyranone **27e** (40% yield) as well as the difuryl ketone **29** in 20% yield (Scheme 7). Formation of **29** can be rationalized by an intermolecular condensation of the furyl C_5-anionic intermediate **28** resulting from initial carbamoyl migration followed by deprotonation. The presence of an electron-withdrawing group on the furan ring is expected to enhance the acidity of heteroaryl protons,[30] hence offering competitive $C_{5'}$ relative to $C_{2'}$ deprotonation events. A PG solution to this problem was successfully tested in the synthesis of the thienocoumarin series (Scheme 8).

For the synthesis of the thienocoumarins **31** and **32** (Scheme 8), the thienyl aryl *O*-carbamate **30** was prepared by the Negishi tactic, optimized for the *ortho*-iodoaryl *O*-carbamate−thienylzinc bromide coupling rather than vice versa (see Experimental Section), and the results are consistent with the

SCHEME 7



SCHEME 8



previously observed trend for related systems (Table 3). Initial attempts to effect carbamoyl migration on **30** under the standard conditions or with excess LDA and at elevated temperatures (THF, reflux) afforded only starting material. On the basis of the conjecture presented for the result observed for **25e**, circumvention of the problem was devised by the use of a TMS as an in situ generated C_5 PG.[31] Thus treatment of carbamate **30** with 2 equiv of TMSCl and 5 equiv of LDA at −78 °C followed by warming to rt resulted in the desired migration, as verified by subsequent acidic cyclization of the unisolated crude phenol amide to a mixture of compounds **21** and **22** (79% combined yield). TBAF-mediated desilylation afforded the thienocoumarin **22** in moderate yield.

Conclusion

In summary, we have provided a combined DreM−carbamoyl migration−transition-metal-catalyzed cross-coupling strategy for the preparation of series of coumestan (Schemes 4 and 5, and Tables 1 and 2) and coumarin (Schemes 6 and 7, and Table 3) heterocycles. A comparison of available, efficient methods for the synthesis of these ring shows favorable positions of the demonstrated methodology. Although substitution on aryl and especially on heteroaryl rings has not been surveyed in the overall procedures, consideration of functional groups which are compatible with metalation conditions in the synthesis of cross-coupling partners (use of the silicon PG tactic, Scheme 8) and the acknowledged mild conditions in the Suzuki−Miyaura and Negishi procedures allow projection of considerable scope for the construction of the **9−12** classes of heterocycles. For example, synthesis of furo[3,2-*c*]coumarin (**9a**), pyrrolo[3,2-*c*]coumarin (**9c**), pyrrolo[2,3-*c*]coumarin (**10c**), as well inverted azacoumestan, diazacoumestan, and isodiazacoumestan[10e] ring systems may be anticipated according to the methodology described herein.

(27) The choice of Negishi vs Suzuki coupling tactics was also determined by other aspects of reactivity. For example, the Negishi protocol to prepare **25d** invariably gave mixtures of the desired 2-(3-thienyl)carbamate along with the corresponding 2-(2-thienyl)carbamate as determined by GC injection of an authentic sample prepared by an independent method (**30**, Scheme 8; see Experimental Section). Suzuki conditions to prepare **25e** afforded the desired product in only 16% yield (see Experimental Section). That the coupling reactions proceed in higher yields with the metal in the heteroaromatic species is in keeping with the finding of others that high electron density in the coupling partner bearing the leaving group retards the reaction (see Fitton, P.; Rick, E. A. *J. Organomet. Chem.* **1971**, *28*, 287. For a general review of mechanistic aspects of cross-coupling, see: Armatore, C.; Jutand, A. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-i., Ed.; John Wiley & Sons Inc.: Hoboken, NJ, 2002; pp 943−972). Practical considerations also dictated the choice of one protocol over the other; for example, in the Negishi method for the preparation of **25d** (employing **23**, X = ZnCl, and **24**, Y = Br), a significant amount of starting arylcarbamate was present in the reaction mixture, making purification difficult due to its copolarity with the product. In this case, incorporating the metal group in the heteroaromatic partner (**24**, Y = ZnX) avoided this issue.

(28) Reutov, O. A.; Beletskaya, I. P.; Butin, K. P. *CH Acids*; Pergamon Press: Oxford, 1978; pp 67−119.

(29) Zhao, Z.; Snieckus, V. *Org. Lett.* **2005**, *7*, 2523–2526.

(30) Rajappa, S. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Ed.; Pergamon: Oxford, 1984; Vol 4, p 770.

(31) Silicon PGs are useful in DoM and other strong base-mediated chemistry. See: Hartung, C. G.; Snieckus, V. In *Modern Arene Chemistry*; Astruc, D., Ed.; Wiley-VCH: New York, 2002; pp 330−367.

Experimental Section

General Methods and Procedures have been reported elsewhere.[32]

2-*N*,*N*-Diethylcarbamato-3-trimethylsilylphenylboronic acid (23a). According to general procedure B, a solution of *N*,*N*-diethyl *O*-(2-trimethylsilyl)phenylcarbamate[33] (5.07 g, 19.1 mmol) and TMEDA (3.75 mL, 24.9 mmol) in THF (50 mL) at −78 °C was sequentially treated with *s*-BuLi (19.1 mL, 1.30 mol/L) and $B(OMe)_3$ (5.0 mL, 4.00 mmol). Acidification of the reaction mixture with 10% HCl (pH 5−6) followed by standard workup afforded **23a** (5.40 g, 94%) as a colorless solid which was used without further purification.

2-*N*,*N*-Diethylcarbamato-3-methoxyphenylboronic acid (16a). According to general procedure B, a solution of *N*,*N*-diethyl *O*-(2-methoxy)phenylcarbamate (4.95 g, 22.2 mmol) and TMEDA (3.70 mL, 24.5 mmol) in THF (40 mL) at −78 °C was sequentially treated with *s*-BuLi (19.0 mL, 1.35 mol/L) and $B(OMe)_3$ (4.9 mL, 4.30 mmol). Acidification of the reaction mixture with 10% HCl (pH 5−6) followed by standard workup afforded **16a** (5.20 g) as a colorless solid which was used without further purification.

***N*,*N*-Diethyl *O*-(2-iodo-6-methoxy)phenylcarbamate (23d).** According to general procedure B, a solution of *N*,*N*-diethyl *O*-(2-methoxy)phenylcarbamate (2.52 g, 11.3 mmol) and TMEDA (2.00 mL, 13.3 mmol) in THF (20 mL) at −78 °C was sequentially treated with *s*-BuLi (9.80 mL, 1.35 mol/L) and a solution of I_2 (3.60 g, 14.2 mmol) in THF (10 mL). Standard workup followed by column chromatography afforded the title compound as a colorless wax (3.43 g, 87%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.31 (m, 1H), 6.86−6.84 (m, 2H), 3.74 (s, 3H), 3.48−3.36 (m, 4H), 1.30 (t, J = 6.8 Hz, 3H), 1.19 (t, J = 6.8 Hz, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 152.1 (e) (×2), 141.0 (e), 129.7 (o), 127.1 (o), 112.1 (o), 92.2 (e), 55.8 (o), 42.0 (e), 41.8 (e), 14.0 (o), 13.0 (o). The material was used as is without further purification.

***N*,*N*-Diethyl *O*-[2-(3-thienyl)]phenylcarbamate (25c).** According to general procedure G, a mixture of *N*,*N*-diethyl *O*-(2-bromo)phenylcarbamate (1.78 g, 6.55 mmol), 3-thiopheneboronic acid (1.03 g, 8.05 mmol), $Pd(PPh_3)_4$ (0.140 g, 0.121 mmol), and Na_2CO_3 (10.0 mL, 2 mol/L) in DME (100 mL) was heated at reflux for 5 h. Standard workup followed by column chromatography afforded 1.62 g (90%) of the title compound as a colorless oil: IR (neat) ν (max) 2976, 2933, 1716, 1686, 1490, 1458, 1418 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.45 (dd, J = 7.5, 1.8 Hz, 1H), 7.36−7.16 (m, 6H), 3.33 (m, 4H), 1.11 (t, J = 7.2 Hz, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 154.0 (e), 148.5 (e), 138.0 (e), 130.2 (o), 129.9 (e), 128.4 (o), 128.2 (o), 125.2 (o), 124.9 (o), 123.4 (o), 122.8 (o), 42.0 (e), 41.7 (e), 14.0 (o), 13.2 (o); MS (EI (70 eV)) *m*/*e* (rel intensity) 275 (M^+, 68), 222 (2.9), 176 (8.8), 147 (23), 115 (18), 100 (100), 72 (78); HRMS (EI (70 eV)) *m*/*e* calcd for $C_{15}H_{17}NO_2S$ 275.0980, found 275.0982.

***N*,*N*-Diethyl 3-(2-hydroxyphenyl)thiophene-2-carboxamide (26d).** According to general procedure H, a solution of carbamate **25d** (0.484 g, 1.76 mmol) in THF (10 mL) was added via canula to a solution of LDA (2.11 mmol) in THF (10 mL). After 10 min, the reaction mixture was quenched with saturated NH_4Cl, and subsequent standard workup followed by column chromatography (4:1 hexane/EtOAc) afforded the title compound (0.244 g, 50%) as a foam which was used without further purification: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.37 (s, 1H, exch), 7.42 (d, J = 5.1 Hz, 1H), 7.25 (m, 1H), 7.15 (dd, J = 7.6, 1.7 Hz, 1H), 7.02 (dd, J = 8.0, 1.0 Hz, 1H), 6.97 (d, J = 5.1 Hz, 1H), 6.92 (app dt, J = 7.4, 1.8 Hz, 1H), 3.49 (m, 4H), 1.25−1.07 (m, 6H).

4*H*-Thieno[2,3-*c*]benzo[*e*]pyran-4-one (27c). According to general procedure D, a solution of phenol amide **26c** (0.062 g, 0.230 mmol) in HOAc (5 mL) was heated at reflux for 10 min at which point the HOAc was removed in vacuo. Standard workup followed by recrystallization (hexane/Et_2O) afforded the title compound as colorless fine needles (0.039 g, 85%): mp 122−124 °C (hexane/Et_2O); IR (KBr) ν (max) 2924, 1722, 1656, 1611, 1589, 1533, 1498, 1452 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.92 (d, J = 5.1 Hz, 1H), 7.85−7.81 (m, 1H), 7.64 (d, J = 5.1 Hz, 1H), 7.51 (dd, J = 8.4, 1.6 Hz, 1H), 7.46−7.27 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 157.2 (e), 152.6 (e), 145.0 (e), 136.8 (o), 130.1 (o), 124.5 (o), 123.8 (o), 123.4 (e), 122.3 (o), 117.5 (o), 117.3 (e); MS (EI (70 eV)) *m*/*e* (rel intensity) 202 (M^+, 100), 174 (29), 145 (15), 120 (3.8), 102 (9.0), 87 (7.1). Anal. Calcd for $C_{11}H_6O_2S$: C, 65.33; H, 2.99; S, 15.85. Found: C, 65.38; H, 3.01; S, 15.66.

***N*,*N*-Diethyl *O*-[2-(3-thienyl)-6-trimethylsilyl]phenylcarbamate (25a).** According to general procedure G, a mixture of 2-*N*,*N*-diethylcarbamato-3-trimethylsilylphenylboronic acid (**23a**) (1.89 g, 6.15 mmol), 3-bromothiophene (0.84 g, 4.90 mmol), $Pd(PPh_3)_4$ (0.300 g, 0.260 mmol), and Na_2CO_3 (10 mL, 2.0 mol/L) in DME was heated at reflux for 1 h. Standard workup followed by column chromatography (9:1 hexane/EtOAc) and recrystallization (hexane) afforded the title compound (0.796 g, 47%) as colorless plates: mp 60−63 °C (hexane); IR (CH_2Cl_2) ν (max) 2977, 1713, 1599, 1522, 1475 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.44 (dd, J = 7.2, 1.8 Hz, 1H), 7.39 (dd, J = 7.6, 1.8 Hz, 1H), 7.30−7.28 (m, 2H), 7.23 (dd, J = 7.6, 7.2 Hz, 1H), 7.16 (dd, J = 3.9, 2.5 Hz, 1H), 3.36 (q, J = 7.2 Hz, 2H), 3.17 (m, 2H), 1.09 (t, J = 7.2 Hz, 3H), 0.95 (t, J = 7.2 Hz, 3H), 0.30 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 151.4 (e), 136.6 (e), 132.1 (o), 131.1 (e), 129.8 (o), 128.5 (e), 126.6 (o), 123.2 (o), 122.5 (o), 120.6 (o), 39.1 (e), 19.0 (e), 11.7 (o), 10.6 (o); MS (EI (70 eV)) *m*/*e* (rel intensity) 347 (M^+, 1.4), 332 (15), 217 (3.9), 100 (100), 72 (49). Anal. Calcd for $C_{18}H_{25}NO_2SSi$: C, 62.21; H, 7.25; N, 4.03. Found: C, 62.19; H, 7.31; N, 4.01.

6-Trimethylsilyl-4*H*-thieno[2,3-*c*]benzo[*e*]pyran-4-one (27a). According to general procedure H, a solution of aryl carbamate **23a** (0.411 g, 1.18 mmol) in THF (5 mL) was added to a solution of LDA (1.42 mmol) in THF (3 mL) at 0 °C, and the reaction mixture was allowed to warm to rt over 2 h. Standard workup afforded the crude phenol amide, which was cyclized according to general procedure D. Standard workup followed by column chromatography (6:1 hexane/EtOAc) and recrystallization (hexane/Et_2O) afforded the title compound (0.202 g, 62%) as colorless needles: mp 135−136 °C (hexane/Et_2O); IR (CH_2Cl_2) ν (max) 3022, 2941, 1719, 1593, 1530, 1453, 1413 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.89 (d, J = 5.2 Hz, 1H), 7.85 (dd, J = 7.7, 1.6 Hz, 1H), 7.64 (d, J = 5.2 Hz, 1H), 7.59 (dd, J = 7.2, 1.6 Hz, 1H), 7.33 (app t, J = 7.2 Hz, 1H), 0.44 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 157.1 (e), 145.3 (e), 136.4 (o), 135.7 (o), 129.2 (e), 124.7 (o), 124.4 (e), 124.2 (o), 122.4 (o), 116.6 (e), −0.12 (o); MS (EI (70 eV)) *m*/*e* (rel intensity) 274 (M^+, 24), 259 (100), 231 (23), 203 (6.3), 187 (3.5), 171 (7.0), 122 (11). Anal. Calcd for $C_{14}H_{14}O_2SSi$: C, 61.28; H, 5.14; S, 11.68. Found: C, 61.43; H, 5.34; N, 11.72.

***N*,*N*-Diethyl *O*-[2-(3-thienyl)-6-methoxy)phenylcarbamate (25d). Procedure 1:** According to general procedure G, a mixture of *N*,*N*-diethyl *O*-(2-iodo-6-methoxy)phenylcarbamate (**23d**) (0.271 g, 0.776 mmol), 3-thiopheneboronic acid (0.151 g, 1.18 mmol), $Pd(PPh_3)_4$ (48.8 mg, 0.042 mmol), and Na_2CO_3 (10 mL) in DME was heated at reflux for 16 h. Standard workup followed by column chromatography (5:1 hexane/EtOAc) and distillation afforded the title compound (0.190 g, 80%) as a colorless oil: bp 155−162 °C/0.15−0.2 mmHg (Kugelrohr); IR (neat) ν (max) 3098, 2974, 2935, 1717, 1608, 1581, 1530, 1467 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.38 (dd, J = 2.9, 1.3 Hz, 1H), 7.29 (dd, J = 5.0, 3.0 Hz, 1H), 7.25 (dd, J = 5.0, 1.3 Hz, 1H), 7.15 (app t, J = 7.9 Hz, 1H), 7.04 (dd, J = 7.8, 1.6 Hz, 1H), 6.88 (dd, J = 8.0, 1.5 Hz, 1H), 3.81 (s, 3H), 3.35 (m, 4H), 1.13 (t, J = 7.1 Hz, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 153.7 (e), 152.3 (e), 137.8 (e), 137.6 (e), 130.9 (e), 128.2 (o), 125.6 (o), 124.7 (o), 122.8 (o), 121.5 (o), 111.1 (o), 56.0 (o), 42.0 (e), 41.8 (e), 13.8 (o), 13.2 (o); MS (EI (70 eV)) *m*/*e* (rel intensity) 305 (M^+, 41), 290 (4.5), 205 (14), 221 (14), 100 (100),

(32) See: James, C. A.; Snieckus, V. *J. Org. Chem.* **2009**, *74*, 10.1021/jo9001454. Note that the ^{13}C JMOD spectra were acquired with the parameter $D3$ = 0.006 s (default = 0.008 s) to account for the larger (ca. 200 Hz) coupling constant of the C atom directly bound to the heteroatom of compounds containing a p-excessive heterocycle.

(33) Sibi, M. P.; Snieckus, V. *J. Org. Chem.* **1983**, *48*, 1935.

72 (45). Anal. Calcd for $C_{16}H_{19}NO_3S$: C, 62.93; H, 6.27; N, 4.59. Found: C, 63.14; H, 6.47; N, 4.55.

Procedure 2: According to general procedure G, a mixture of 2-*N*,*N*-diethylcarbamato-3-methoxyphenylboronic acid (**16a**) (0.640 g, 2.397 mmol), 3-bromothiophene (0.307 g, 1.88 mmol), $Pd(PPh_3)_4$ (0.108 g, 0.094 mmol), and Na_2CO_3 (10 mL) in DME (20 mL) was heated at reflux for 16 h. Standard workup followed by column chromatography (5:1 hexane/EtOAc) and distillation afforded the title compound as a colorless oil (0.377 g, 66%).

Procedure 3: According to general procedure E, a solution of 3-bromothiophene in THF (10 mL) was sequentially treated with *n*-BuLi (3.30 mL, 1.78 mol/L), a solution of $ZnBr_2$ (1.60 g, 7.11 mmol) in THF (10 mL), *N*,*N*-diethyl *O*-(2-iodo-6-methoxy)phenylcarbamate (0.882 g, 2.53 mmol), and $Pd(PPh_3)_4$ (0.105 g, 0.091 mmol), and the reaction mixture was allowed to stir at rt for 12 h. Standard workup followed by column chromatography and distillation (bp 155−162 °C/0.2 mmHg) afforded the title compound as an inseparable mixture contaminated with the corresponding 2-thienyl isomer as identified by GC. Total mass: 0.678 g (42% 3-thienyl, 33% 2-thienyl by NMR).

Procedure 4: According to general procedure F, a solution of *N*,*N*-diethyl *O*-(2-methoxy)phenylcarbamate (1.26 g, 5.64 mmol) in THF (15 mL) was sequentially treated with *s*-BuLi (8.06 mL, 1.05 mol/L), $ZnCl_2$ (8.98 mL, 1.0 mol/L), and a solution of 3-bromothiophene (1.84 g, 11.3 mmol) and $Pd(PPh_3)_4$ (150 mg, 0.130 mmol) in THF (20 mL). The reaction mixture was allowed to heat at reflux for 48 h, and standard workup followed by column chromatography afforded the title compound, 0.646 g (38%).

6-Methoxy-4*H*-thieno[2,3-*c*]benzo[*e*]pyran-4-one (27d). According to general procedure H, a solution of carbamate **25d** (0.232 g, 0.761 mmol) in THF (5 mL) was added to a solution of LDA (1.52 mmol) in THF (5 mL) at 0 °C. The reaction mixture was allowed to stir for 10 min, and standard workup afforded the crude hydroxy amide which was cyclized according to general procedure D (5 mL of HOAc). Standard workup followed by column chromatography (4:1 hexane/EtOAc) and recrystallization (EtOH) furnished the title compound (0.0457 g, 27%) as colorless needles: mp 158−160 °C (EtOH); IR (KBr) ν (max) 3085, 2975, 2936, 1721, 1605, 1580, 1466, 1420 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.91 (d, J = 5.3 Hz, 1H), 7.60 (d, J = 5.3 Hz, 1H), 7.37 (dd, J = 7.9, 1.5 Hz, 1H), 7.25 (dd, J = 8.0, 7.9 Hz, 1H), 7.02 (dd, J = 8.0, 1.4 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 156.6 (e), 147.8 (e), 145.1 (e), 142.1 (e), 136.7 (o), 124.4 (o), 122.7 (o), 118.0 (e), 115.2 (o), 112.0 (o), 56.1 (o); MS (EI (70 eV)) *m*/*e* (rel intensity) 232 (M^+, 100), 217 (13), 203 (4.5), 189 (34), 161 (13), 145 (4.5), 133 (12), 116 (4.5), 89 (16), 63 (10). Anal. Calcd for $C_{12}H_8O_3S$: C, 62.06; H, 3.47. Found: C, 62.10; H, 3.60.

***N*,*N*-Diethyl *O*-[2-(3-thienyl)-4-methoxy]phenylcarbamate (25b).** According to general procedure F, carbamate *N*,*N*-diethyl *O*-(4-methoxy)phenylcarbamate (3.04 g, 13.6 mmol) was sequentially treated with *s*-BuLi (11.2 mL, 1.47 mol/L), TMEDA (2.50 mL, 16.36 mmol), a solution of $ZnCl_2$ (16.4 mL, 1.0 mol/L in Et_2O), 3-bromothiophene (2.67 g, 16.4 mmol), and $Pd(PPh_3)_4$ (0.250 g, 0.216 mmol) in THF (40 mL), and the reaction mixture was heated at reflux for 48 h. Standard workup followed by column chromatography (8:1 → 5:1 hexane/EtOAc) and recrystallization (hexane/Et_2O) afforded the title compound (1.66 g, 40%) as colorless needle-prisms: mp 66−68 °C (hexane/Et_2O); IR (KBr) ν (max) 2974, 2935, 2866, 1715, 1609, 1584, 1534, 1499, 1470 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.35−7.30 (m, 2H), 7.22−7.20 (m, 1H), 7.08 (J = 8.8 Hz, 1H), 6.96 (d, J = 3.1 Hz, 1H), 6.85 (dd, J = 8.8, 3.1 Hz, 1H), 3.80 (s, 3H), 3.30 (m, 4H), 1.10 (t, J = 7.1 Hz, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 156.8 (e), 154.4 (e), 142.1 (e), 138.0 (e), 130.6 (e), 128.2 (o), 124.9 (o), 124.0 (o), 122.9 (o), 115.1 (o), 113.4 (o), 55.6 (o), 41.9 (e), 41.6 (e), 14.0 (o), 13.2 (o); MS (EI (70 eV)) *m*/*e* (rel intensity) 305 (M^+, 17), 232 (3.0), 205 (4.1), 177 (3.6), 134 (6.8), 100 (100), 72 (43). Anal. Calcd for $C_{16}H_{19}NO_3S$: C, 62.93; H, 6.27; N, 4.59; S, 10.50. Found: C, 63.17; H, 6.38; N, 4.47; S, 10.61.

***N*,*N*-Diethyl 3-(2-hydroxy-4-methoxyphenyl)-2-thiophenecarboxamide (26b).** According to general procedure H, a solution of carbamate **25b** (0.270 g, 0.884 mmol) in THF (5 mL) was added to a solution of LDA (2.6 mmol) in THF (10 mL) at 0 °C, and the mixture was allowed to stir for 3 h. Standard workup followed by column chromatography (3:1 hexane/EtOAc) afforded the title compound as a foam (0.159 g, 59%): ^1H NMR (250 MHz, $CDCl_3$) δ 7.41 (d, J = 5.0 Hz, 1H), 6.98 (d, J = 5.0 Hz, 1H), 6.96 (d, J = 8.8 Hz, 1H), 6.83 (dd, J = 8.8, 3.0 Hz, 1H), 3.76 (s, 3H), 3.40−3.29 (m, 4H), 1.08 (m, 6H).

8-Methoxy-4*H*-thieno[2,3-*c*]benzo[*e*]pyran-4-one (27b). According to general procedure D, a solution of hydroxy amide **26b** (0.0490 g, 0.160 mmol) in HOAc (5 mL) was heated at reflux for 10 min. Standard workup followed by recrystallization (hexane/Et_2O) afforded the title compound (0.0300 g, 81%) as colorless needles: mp 120−122 °C (hexane/Et_2O); IR (KBr) ν (max) 3020, 1712, 1594, 1536, 1466 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.92 (d, J = 5.3 Hz, 1H), 7.62 (d, J = 5.3 Hz, 1H), 7.38 (d, J = 9.1 Hz, 1H), 7.27 (d, J = 2.5 Hz, 1H), 7.07 (dd, J = 9.1, 2.5 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 156.2 (e), 147.0 (e), 144.8 (e), 136.6 (o), 124.8 (e), 122.3 (o), 118.5 (o), 117.8 (e), 117.1 (o), 106.9 (o), 55.9 (o); MS (EI (70 eV)) *m*/*e* (rel intensity) 232 (M^+, 100), 217 (73), 189 (14), 161 (14), 145 (3.3), 133 (10), 116 (5.6), 89 (14), 63 (13). Anal. Calcd for $C_{12}H_8O_3S$: C, 62.06; H, 3.47. Found: C, 62.20; H, 3.61.

***N*,*N*-Diethyl *O*-[2-(2-thienyl)-6-methoxy]phenylcarbamate (30).** According to general procedure E, a solution of 2-bromothiophene (1.65 g, 10.1 mmol) in THF (20 mL) was sequentially treated with *n*-BuLi (6.30 mL, 11.2 mmol), $ZnBr_2$ (3.35 g, 14.9 mmol), *N*,*N*-diethyl *O*-(2-iodo-6-methoxy)phenylcarbamate (1.56 g, 4.46 mmol), and $Pd(PPh_3)_4$ (0.150 g, 0.130 mmol), and the reaction mixture was allowed to stir at rt for 12 h. Standard workup followed by column chromatgraphy (5:1 hexane/EtOAc) and distillation afforded the title compound as a colorless oil (1.29 g, 95%): bp 145−150 °C/0.5−0.6 mmHg; IR (neat) ν (max) 2974, 2939, 1722, 1605, 1580, 1526, 1466, 1419 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.33−7.30 (m, 2H), 7.23 (dd, J = 8.1, 1.9 Hz, 1H), 7.16 (dd, J = 8.1, 7.8 Hz, 1H), 7.05 (dd, J = 5.1, 3.7 Hz, 1H), 6.88 (dd, J = 7.8, 1.9 Hz, 1H), 3.84 (s, 3H), 3.48−3.36 (m, 4H), 1.21 (m, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 153.3 (e), 152.5 (e), 138.3 (e), 137.2 (e), 128.8 (e), 126.8 (o), 125.8 (o), 125.7 (o), 120.5 (o), 111.1 (o), 56.0 (o), 42.1 (e), 41.9 (e), 13.9 (o), 13.2 (o); MS (EI (70 eV)) *m*/*e* (rel intensity) 305 (M^+, 71), 290 (1.6), 262 (15), 223 (46), 205 (6.8), 100 (100), 72 (45). Anal. Calcd for $C_{16}H_{19}NO_3S$: C, 62.93; H, 6.27; N, 4.59. Found: C, 62.86; H, 6.26; N, 4.51.

6-Methoxy-2-trimethylsilyl-4*H*-thieno[3,2-*c*]benzo[*e*]pyran-4-one (31) and 6-Methoxy-4*H*-thieno[3,2-*c*]benzo[*e*]pyran-4-one (32). Procedure 1: To a solution of carbamate **30** (0.450 g, 1.33 mmol) and TMSCl (0.18 mL, 1.42 mmol) in THF (10 mL) at −78 °C was added a solution of LDA (6.87 mmol) in THF (10 mL) dropwise via canula. The reaction mixture was allowed to warm to rt over 12 h. Standard workup followed by cyclization according to general procedure D (20 mL of HOAc) afforded the crude cyclized compounds. Standard workup followed by column chromatography (3:1 hexane/EtOAc) afforded the silylated lactone **31** (0.255 g, 63%) as a colorless oil and the desilylated lactone **32** (0.493 g, 16%) as colorless plates. Silylated lactone **31**: IR (neat) ν (max) 2954, 2840, 1733, 1608, 1534, 1487, 1468 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.26 (dd, J = 7.9, 1.9 Hz, 1H), 7.20 (app t, J = 7.9 Hz, 1H), 7.00 (dd, J = 7.9. 1.7 Hz, 1H), 3.97 (s, 3H), 0.39 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 157.0 (e), 152.5 (e), 147.8 (e), 142.7 (e), 133.5 (o), 126.6 (e), 124.4 (o), 117.8 (e), 115.1 (o), 112.1 (o), 56.2 (o), −0.42 (o); MS (EI (70 eV)) *m*/*e* (rel intensity) 304 (M^+, 82), 289 (53), 274 (12), 244 (21), 206 (100), 192 (20), 177 (27), 163 (47), 134 (34), 109 (26); HRMS (EI (70 eV)) *m*/*e* calcd for $C_{15}H_{16}O_3SSi$ 304.0590, found 304.0598. Desilylated lactone **32**: mp 168−169 °C (hexane/CH_2Cl_2); IR (CH_2Cl_2) ν (max) 3029, 2990, 1735, 1592, 1473, 1423 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.64 (d, J = 5.3 Hz, 1H), 7.41 (d, J = 5.3 Hz,

1H), 7.25 (m, 1H), 7.20 (app t, $J = 7.9$ Hz, 1H), 7.00 (dd, $J = 7.1$, 2.4 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 156.6 (e), 148.5 (e), 147.8 (e), 140.9 (e), 126.8 (o), 126.0 (o), 125.4 (e), 124.5 (o), 117.6 (e), 114.8 (o), 112.1 (o), 56.2 (o); MS (EI (70 eV)) *m/e* (rel intensity) 232 (M^+, 91), 217 (8.0), 203 (8.4), 189 (23), 159 (18), 133 (10), 121 (71), 119 (100). Anal. Calcd for $C_{12}H_8O_3S$: C, 62.06; H, 3.47. Found: C, 62.10; H, 3.29.

6-Methoxy-4*H*-thieno[3,2-*c*]benzo[*e*]pyran-4-one (32). To a solution of silyl lactone **31** (0.241 g, 0.792 mmol) in THF (10 mL) was added TBAF (1.70 mL, 1.70 mmol in THF) at 0 °C, and the reaction mixture was allowed to stir for 20 min. Standard workup followed by column chromatography (2:1 hexane/EtOAc) followed by recrystallization (hexane/CH_2Cl_2) afforded the title compound (0.0915 g, 50%) as colorless fine needles. Spectral data were consistent with those obtained in the preparation above.

***N*,*N*-Diethyl *O*-[2-(3-furyl)-6-methoxy]phenylcarbamate (25e). Procedure 1:** According to general procedure E, a solution of 3-bromofuran (0.70 mL, 7.79 mol) in THF (15 mL) was sequentially treated with *n*-BuLi (4.60 mL, 1.68 mol/L), a solution of $ZnBr_2$ (2.09 g, 9.27 mmol) in THF (10 mL), *N*,*N*-diethyl *O*-(2-iodo-6-methoxy)phenylcarbamate (1.38 g, 3.95 mmol), and $Pd(PPh_3)_4$ (0.150 g, 0.129 mmol), and the reaction mixture was allowed to stir at rt for 4 h. Standard workup followed by column chromatography (5:1 hexane/EtOAc) and distillation afforded the title compound as a colorless oil (0.958 g, 84%): bp 150−156 °C/1.5 mmHg (Kugelrohr); IR (neat) ν (max) 2974, 2937, 2840, 1719, 1619, 1576, 1468 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.68 (dd, $J = 1.4$, 0.9 Hz, 1H), 7.44 (app t, $J = 1.7$ Hz, 1H), 7.17 (app t, $J = 7.9$ Hz, 1H), 7.06 (dd, $J = 7.9$, 1.6 Hz, 1H), 6.87 (dd, $J = 7.9$, 1.6 Hz, 1H), 6.66 (dd, $J = 1.7$, 0.9 Hz, 1H), 3.83 (s, 3H), 3.82−3.37 (m, 4H), 1.26 (t, $J = 7.1$ Hz, 3H), 1.19 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 153.5 (e), 152.3 (e), 142.5 (o), 140.2 (o), 137.7 (e), 127.0 (e), 125.7 (o), 121.5 (e), 120.2 (o), 110.7 (o), 110.1 (o), 55.9 (o), 42.0 (e), 41.8 (e), 13.9 (o), 13.2 (o); MS (EI (70 eV)) *m/e* (rel intensity) 289 (M^+, 75), 190 (7.5), 160 (10), 100 (100), 72 (47). Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.29; H, 6.71; N, 4.71.

Procedure 2: According to general procedure G, a mixture of 3-bromofuran (0.869 g, 5.914 mmol), (*N*,*N*-diethylcarbamato-3-methoxy)phenylboronic acid (2.11 g, 7.91 mmol), $Pd(PPh_3)_4$ (0.137 g, 0.119 mmol), and Na_2CO_3 (20 mL, 2 mol/L) in DME (40 mL) was heated at reflux for 12 h. Standard workup followed by column chromatography (5:1 hexane/EtOAc) afforded the title compound as a colorless oil (0.272 g, 16%). Spectral data were consistent with those obtained in the preparation above.

***N*,*N*-Diethyl 3-(2-hydroxy-3-methoxyphenyl)furan-2-carboxamide (28) and Ketone (29).** According to general procedure H, a solution of carbamate **25e** (0.127 g, 0.438 mmol) in THF (5 mL) was added to a solution of LDA (0.992 mmol) in THF (5 mL) at 0 °C. The reaction mixture was allowed to stir for 15 min at which point standard workup followed by column chromatography (1:1 hexane/EtOAc) afforded the desired product as a foam (57.0 mg, 45%) along with ketone **29** (22.4 mg, 20%) as a gum.

Carboxamide 28: IR (CH_2Cl_2) ν (max) 3584−3038, 2976, 1631, 1605, 1572, 1489, 1440 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.13 (s, 1H), 7.48 (d, $J = 1.8$ Hz, 1H), 6.87 (s, 3H), 6.55 (d, $J = 1.8$ Hz, 1H), 3.90 (s, 3H), 3.48 (q, $J = 7.3$ Hz, 2H), 3.37 (q, $J = 7.3$ Hz, 2H), 1.23−1.25 (m, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 162.3 (e), 149.5 (e), 144.4 (e), 142.4 (e), 142.1 (o), 126.2 (e), 122.6 (o), 121.2 (e), 119.8 (o), 115.0 (o), 111.1 (o), 56.02 (o), 43.3 (e), 48.8 (e), 14.3 (o), 12.5 (o); MS (EI (70 eV)) *m/e* (rel intensity) 290 (M + H, 100), 217 (48), 202 (19), 173 (4.7), 160 (4.7), 129 (5.9), 95 (22); HRMS (EI (70 eV)) *m/e* calcd for $C_{16}H_{20}NO_4$ 290.1392, found 290.1385.

Ketone 29: IR (neat) ν (max) 3520−3126, 2957, 1721, 1632, 1574, 1441 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.68 (d, $J = 1.8$ Hz, 1H), 7.65 (s, 1H), 7.02−6.87 (m, 6H), 6.79 (d, $J = 1.8$ Hz, 1H), 6.56 (s, 1H), 3.92 (s, 3H), 3.91 (s, 3H), 3.48 (q, $J = 7.3$ Hz, 2H), 3.37 (q, $J = 7.3$ Hz, 2H), 1.29−1.16 (m, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 170.1 (e), 161.3 (e), 149.3 (e), 149.0 (e), 147.9 (e), 146.4 (e), 146.0 (e), 145.2 (o), 144.1 (e), 143.9 (e), 131.9 (e), 126.7 (e), 124.4 (e), 123.6 (o), 122.9 (o), 122.4 (o), 120.0 (o), 120.0 (o), 119.5 (e), 116.1 (o), 111.4 (o), 111.2 (o), 56.1 (o), 56.1 (o), 43.6 (e), 40.9 (e), 14.3 (o), 12.5 (o); MS (EI (70 eV)) *m/e* (rel intensity) 506 (M^+, 100), 492 (8.3), 434 (18), 386 (18), 371 (36), 316 (22), 293 (17); HRMS (EI (70 eV)) *m/e* calcd for $C_{28}H_{28}NO_8$ 506.1815, found 506.1768.

6-Methoxy-4*H*-furano[2,3-*c*]benzo[*e*]pyran-4-one (27e). Procedure 1: *Direct Cyclization:* According to general procedure H, a solution of carbamate **25e** (0.250 g, 0.864 mmol) in THF (5 mL) was added to a solution of LDA (3.05 mmol) in THF (7 mL), and the reaction mixture was allowed to stir for 10 min. Standard workup followed by cyclization of the crude hydroxy amide according to general procedure D (8 mL HOAc) and purification by column chromatography (2:1 hexane/EtOAc) and recrystallization (hexane/CH_2Cl_2) afforded the title compound as fine colorless plates (36.1 mg, 19%): mp 154.5−155 °C (hexane/CH_2Cl_2); IR (KBr) ν (max) 355, 2986, 1746, 1607, 1568, 1488, 1422 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.19 (d, $J = 1.8$ Hz, 1H), 7.47 (dd, $J = 7.8$, 1.4 Hz, 1H), 7.33 (d, $J = 1.8$ Hz, 1H), 7.30 (app t, $J = 8.0$ Hz, 1H), 7.19 (dd, $J = 8.1$, 1.3 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 152.0 (e), 148.5 (e), 142.6 (e), 138.5 (e), 134.1 (e), 125.5 (o), 117.7 (e), 116.4 (o), 112.8 (o), 108.9 (o), 107.6 (o), 56.4 (o); MS (EI (70 eV)) *m/e* (rel intensity) 216 (100), 210 (34), 188 (5.0), 173 (31), 145 (26), 102 (20); HRMS (EI (70 eV)) *m/e* calcd for $C_{12}H_8O_4$ 216.0423, found 216.0424.

Procedure 2: *Stepwise*: According to general procedure D, a solution of hydroxyamide **26e** (38.0 mg, 0.131 mmol) in HOAc (5 mL) was heated at reflux for 10 min. Standard workup followed by column chromatography afforded the title compound as a colorless solid (26.0 mg, 68%). Spectral data were consistent with those obtained in the preparation above.

***N*,*N*-Diethyl *O*-[2-(3-thianaphthenyl)-6-methoxy]phenylcarbamate (21b).** According to general procedure G, a mixture of 3-bromothianaphthene[34] (0.560 g, 2.63 mmol), (*N*,*N*-diethylcarbamato-3-methoxy)phenylboronic acid (**16a**) (1.05 g, 3.93 mmol), $Pd(PPh_3)_4$ (0.160 g, 0.139 mmol), and Na_2CO_3 (20 mL, 2 mol/L) was heated at reflux for 12 h. Standard workup followed by column chromatography (5:1 hexane/EtOAc) and distillation afforded the title compound (0.803 g, 86%) as a colorless oil: bp 160−165 °C/0.3 mmHg (Kugelrohr); IR (neat) ν (max) 3066, 2974, 2935, 1718, 1608, 1581, 1469 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.86 (m, 1H), 7.68 (m, 1H), 7.42 (s, 1H), 7.32 (m, 1H), 7.25 (dd, $J = 8.0$, 7.5 Hz, 1H), 7.04−7.00 (m, 2H), 3.88 (s, 3H), 3.19 (m, 2H), 3.08 (m, 2H), 1.00 (t, $J = 6.5$ Hz, 3H), 0.74 (t, $J = 6.5$ Hz, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 153.5 (e), 152.6 (e), 139.7 (e), 138.7 (e), 133.0 (e), 130.5 (e), 125.7 (o), 124.7 (o), 124.2 (o), 124.2 (o), 124.0 (o), 123.4 (o), 122.7 (o), 122.4 (o), 112.0 (o), 56.1 (o), 41.9 (e), 41.7 (e), 13.3 (o); MS (EI (70 eV)) *m/e* (rel intensity) 355 (M^+, 33), 299 (3.1), 255 (3.2), 227 (5.6), 184 (6.2), 177 (6.2), 100 (100), 72 (36); HRMS (EI (70 eV)) *m/e* calcd for $C_{20}H_{21}NO_3S$ 355.1243, found 355.1252.

Migration Product of 21b: *N*,*N*-Diethyl 3-(2-hydroxy-3-methoxyphenyl)thianaphthene-2-carboxamide. According to general procedure H, a solution of carbamate **21b** (0.281 g, 0.792 mmol) in THF (10 mL) was added to a solution of LDA (2.46 mmol) in THF (5 mL) at 0 °C. The reaction mixture was allowed to stir for 15 min, and standard workup followed by column chromatography (3:2 hexane/EtOAc) afforded the title compound (0.190 g, 68%) as a foam: IR (CH_2Cl_2) ν (max) 3329, 2973, 1621, 1538, 1474, 1439 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.87−7.83 (m, 1H), 7.57−7.53 (m, 1H), 7.36 (app dt,, $J = 7.1$, 1.7 Hz, 1H), 7.35 (app dt, $J = 7.0$, 1.7 Hz, 1H), 6.97−6.90 (m, 3H), 3.93 (s, 3H), 1.90−1.22 (m, 4H), 1.00−0.98 (m, 3H), 0.94−0.91 (m, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.1 (e), 147.7 (e), 143.6 (e), 138.8 (e), 138.4 (e), 133.5 (e), 131.6 (e), 124.8 (o), 125.1 (o), 124.3

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(o), 123.6 (o), 122.3 (o), 122.1 (o), 121.0 (e), 119.9 (o), 111.0 (o), 56.1 (o), 43.1 (e), 39.2 (o), 13.6 (o), 12.0 (o); MS (EI (70 eV)) *m/e* (rel intensity) 356 (M^+, 100), 340 (16), 283 (58), 268 (17), 195 (7.5); HRMS (EI (70 eV)) *m/e* calcd for $C_{20}H_{22}NO_3S$ 356.1321, found 356.1326.

4-Methoxy-4*H*-thianaphtheno[2,3-*c*]benzo[*e*]pyran-6-one (22b). According to general procedure D, a solution of the corresponding hydroxy amide (0.190 g, 0.536 mmol) in HOAc (10 mL) was heated at reflux for 10 min. Standard workup followed by recrystallization (CH_2Cl_2/hexane) afforded the title compound (0.143 g, 95%) as light yellow needles: mp 206−207 °C (dec) (CH_2Cl_2/hexane); IR (KBr) ν (max) 3013, 2928, 2824, 1720, 1605, 1585, 1449 cm^{-1}; ^1H NMR (500 MHz, DMF-d_7) δ 8.89 (d, J = 7.95 Hz, 1H), 8.34−8.29 (m, 2H), 7.78−7.71 (m, 2H), 7.41 (app t, J = 8.3 Hz, 1H), 7.39 (d, J = 7.4 Hz, 1H), 4.03 (s, 3H); ^{13}C NMR (62.9 MHz, DMF-d_7) δ 157.7 (e), 148.6 (e), 143.7 (e), 142.8 (e), 139.4 (e), 135.6 (e), 129.3 (e), 127.1 (e), 126.8 (o), 126.5 (e), 125.6 (o), 124.5 (o), 119.1 (e), 115.9 (o), 113.3 (o), 56.6 (o); MS (EI (70 eV)) *m/e* (rel intensity) 282 (M^+, 100), 239 (26), 224 (3.1), 211 (14), 195 (6.2), 183 (20), 139 (26). Anal. Calcd for $C_{16}H_{10}O_3S$: C, 68.07; H, 3.57. Found: C, 67.84; H, 3.70.

***N*,*N*-Diethyl *O*-[2-(3-benzofuranyl)-6-methoxy]phenylcarbamate (21a). Procedure 1:** According to general procedure G, a mixture of 3-bromobenzofuran[35] (1.11 g, 5.19 mmol), 2-*N*,*N*-diethylcarbamato-3-methoxyphenylboronic acid (**16a**) (1.82 g, 6.82 mmol), $Pd(PPh_3)_4$ (0.120 g, 0.104 mmol), and Cs_2CO_3 (20 mL, 2 mol/L) was heated at reflux for 12 h. Standard workup followed by purification by column chromatography (5:1 → 4:1 hexane/EtOAc) and distillation afforded the title compound (0.591 g, 34%) as a colorless oil: bp 155−160 °C/0.3 mmHg (Kugelrohr); IR (neat) 3028, 2975, 2936, 2839, 1718, 1611, 1578, 1453, 1417 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.34 (s, 1H), 7.69 (m, 1H), 7.52 (m, 1H), 7.16 (dd, J = 7.8, 1.7 Hz, 1H), 6.96 (dd, J = 7.8, 1.7 Hz, 1H), 3.85 (s, 3H), 3.27 (q, J = 7.3 Hz, 4H), 1.08 (t, J = 7.3 Hz, 3H), 0.99 (t, J = 7.3 Hz, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 155.1 (e), 153.6 (e), 152.6 (e), 142.7 (o), 138.5 (e), 127.2 (e), 126.4 (e), 125.8 (o), 124.2 (o), 122.7 (o), 121.9 (o), 120.8 (o), 117.3 (e), 111.7 (o), 111.3 (o), 56.0 (o), 42.0 (e), 41.8 (e), 13.7 (o), 13.2 (o); MS (EI (70 eV)) *m/e* (rel intensity) 339 (M^+, 100), 324 (1.9), 285 (1.9), 267 (3.7), 239 (8.6), 239 (9.0), 196 (5.6), 168 (10), 100 (77), 72 (23); HRMS (EI (70 eV)) *m/e* calcd for $C_{20}H_{21}NO_4$ 339.1471, found 339.1484.

***N*,*N*-Diethyl 3-(2-hydroxy-3-methoxyphenyl)benzofuran-2-carboxamide.** According to general procedure H, a solution of carbamate **21a** (0.280 g, 0.827 mmol) in THF (10 mL) was added to a solution of LDA (2.67 mmol) in THF (5 mL) at 0 °C. The reaction mixture was allowed to stir for 15 min, and standard workup followed by column chromatography (2:1 hexane/EtOAc) afforded the title compound (0.229 g, 82%) as a foam: IR (CH_2Cl_2) ν (max) 3518, 3057, 292937, 1614, 1573, 1470 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 8.69 (s, 1H, exch), 7.54−7.59 (m, 2H), 7.38 (ddd, J = 8.2, 7.4, 1.2 Hz, 1H), 7.27−7.21 (m, 1H), 7.01−6.90 (m, 3H), 3.89 (s, 3H), 3.49 (q, J = 7.1 Hz, 2H), 3.37 (q, J = 7.1 Hz, 2H), 1.18 (t, J = 7.1 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 162.5 (e), 153.6 (e), 149.4 (e), 144.4 (e), 144.0 (e), 128.2 (e), 126.2 (o), 123.2 (o), 123.0 (o), 122.4 (o), 121.9 (o), 119.8 (o), 118.9 (e), 111.4 (o), 55.9 (o), 43.2 (e), 40.4 (e), 14.0 (o), 12.4 (o); HRMS (EI (70 eV)) *m/e* calcd for $C_{20}H_{22}NO_4$ 340.1549, found 340.1558.

4-Methoxy-6*H*-benzofurano[2,3-*c*]benzo[*e*]pyran-6-one (22a). According to general procdure D, a solution of the corresponding hydroxy amide (0.229 g, 0.676 mmol) in HOAc (10 mL) was heated at reflux for 10 min. Standard workup followed by recrystallization (CH_2Cl_2/hexane) afforded the title compound (0.154 g, 86%) as a light yellow powder: mp 222−228 °C dec (CH_2Cl_2/hexane); IR (KBr) ν (max) 3073, 3011, 2934, 1731, 1614, 1564, 1468, 1444 cm^{-1}; ^1H NMR (250 MHz, acetone-d_6) δ 8.60 (d, J = 7.9 Hz, 1H), 8.06 (dd, J = 8.0, 1.0 Hz, 1H), 7.95 (d, J = 8.5 Hz, 1H), 7.81 (app dt, J = 7.9, 1.2 Hz, 1H), 7.64 (app dt, J = 7.6, 0.76 Hz, 1H), 7.50 (dd, J = 8.2, 8.0 Hz, 1H), 7.39 (dd, J = 8.2, 1.0 Hz); ^{13}C NMR (50 MHz, DMF-d_7) δ 157.8 (e), 153.3 (e), 148.4 (e), 142.3 (e), 139.5 (e), 130.8 (o), 128.1 (e), 126.1 (o), 125.8 (o), 124.3 (o), 123.1 (e), 118.0 (e), 116.6 (o), 113.7 (o), 113.2 (o), 56.6 (o); MS (EI (70 eV)) *m/e* (rel intensity) 266 (M^+, 18), 223 (8.7), 195 (8.7), 167 (19), 152 (16), 139 (95), 125 (12), 113 (100). Anal. Calcd for $C_{16}H_{10}O_4$: C, 72.18; H, 3.79. Found: C, 72.33; H, 3.71.

***N*-*tert*-Butoxycarbonylindole-2-boronic acid (17c).** To a solution of *N*-*tert*-butoxycarbonylindole[36] (1.03 g, 4.75 mmol) in THF (20 mL) at −78 °C was added *t*-BuLi (4.00 mL, 1.66 mol/L) dropwise over 10 min. The reaction mixture was allowed to stir for 1 h, and $B(OMe)_3$ (1.35 mL, 11.9 mmol) was added quickly. The solution was allowed to warm to rt over 6 h, quenched with saturated NH_4Cl, and subjected to standard workup to afford the crude boronic acid (0.853 g), which was unstable and used without further purification: ^1H NMR (250 MHz, $CDCl_3$) δ 8.02 (d, J = 8.5 Hz, 1H), 7.61 (d, J = 7.4 Hz, 1H), 7.50 (s, 1H), 7.42 (s, 2H, exch), 7.36 (app dt, J = 7.3, 1.3 Hz, 1H), 7.26 (app dt partially obscured by solvent), 1.74 (s, 9H).

***N*,*N*-Diethyl *O*-[2-(*N*-*tert*-butoxycarbonyl-2-indolyl)-6-methoxy]phenylcarbamate (18e).** According to general procedure G, a mixture of *N*,*N*-diethyl *O*-(2-iodo-6-methoxy)phenylcarbamate (0.710 g, 2.03 mmol), *N*-*tert*-butoxycarbonylindole-2-boronic acid (0.6081 g, 2.332 mmol), $Pd(PPh_3)_4$ (0.100 g, 0.0865 mmol), and Na_2CO_3 (10 mL, 2 mol/L) in DME (20 mL) was heated for 1.5 h. Standard workup followed by column chromatography (5:1 hexane/EtOAc) and recrystallization (hexane/CH_2Cl_2) afforded the title compound (0.477 g, 54%) as colorless needle-plates: mp 123−124 °C (hexane/CH_2Cl_2); IR (CH_2Cl_2) ν (max) 2920, 1727, 1577, 1474, 1418 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 8.24 (d, J = 8.4 Hz, 1H), 7.51 (dd, J = 7.0, 0.8 Hz, 1H), 7.29 (ddd, J = 8.4, 7.4, 1.5 Hz, 1H), 7.19 (ddd, J = 7.6, 7.4, 1.2 Hz, 1H), 7.17 (app t, J = 8.0 Hz, 1H), 7.00−6.95 (m, 2H), 6.58 (d, J = 0.5 Hz, 1H), 3.82 (s, 3H), 3.19−3.11 (m, 4H), 1.27 (s, 9H), 0.94−0.88 (m, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 152.7 (e), 151.9 (e), 149.7 (e), 138.6 (e), 136.8 (e), 135.1 (e), 130.1 (e), 128.9 (e), 125.2 (o), 123.9 (o), 122.3 (o), 121.8 (o), 120.3 (o), 114.8 (o), 112.1 (o), 110.2 (o), 82.6 (e), 56.0 (o), 42.1 (e), 41.4 (e), 27.3 (o), 13.4 (o), 12.7 (o); MS (EI (70 eV)) *m/e* (rel intensity) 438 (M^+, 15), 338 (16), 265 (14), 238 (5.0), 195 (3.5), 100 (100), 72 (25). Anal. Calcd for $C_{25}H_{30}N_2O_5$: C, 68.47; H, 6.90; N, 6.39. Found: C, 68.43; H, 6.86; N, 6.45.

4-Methoxy-6*H*-indolo[3,2-*c*]benzo[*e*]pyran-6-one (19e). To a solution of LDA (0.811 mmol) in THF (5 mL) at −78 °C was added a solution of carbamate **18e** (0.107 g, 0.244 mmol) in THF (4 mL) via canula. The resulting solution was allowed to warm to rt over 12 h, and subsequent standard workup afforded the crude hydroxy amide which was cyclized according to general procedure D (10 mL of HOAc). After heating at reflux for 1 h, the cooled solution was diluted with H_2O (10 mL) and cooled in an ice bath. The mixture was filtered, and the precipitate was washed with cold HOAc/H_2O (1:1), affording the title compound (0.0538 g, 83%): mp 289−296 °C dec; IR (KBr) ν (max) 3365, 3070, 2981, 1685, 1623, 1593, 1515, 1465 cm^{-1}; ^1H NMR (500 MHz, DMSO) δ 12.98 (s, 1H), 8.03 (d, J = 7.6 Hz, 1H), 7.75 (d, J = 7.9 Hz, 1H), 7.65 (d, J = 8.1 Hz, 1H), 7.42−7.40 (m, 1H), 7.39 (d, J = 7.9 Hz, 1H), 7.33 (app t, J = 7.6 Hz, 1H), 7.29 (d, J = 8.1 Hz, 1H), 3.94 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ poor solubility did not allow acquisition of a satisfactory ^{13}C spectrum; MS (EI (70 eV)) *m/e* (rel intensity) 265 (M^+, 100), 222 (14), 194 (6.2), 166 (6.0), 141 (30), 100 (54); HRMS (EI (70 eV)) *m/e* calcd for $C_{16}H_{11}NO_3$ 265.0739, found 265.0752.

***N*-*tert*-Butoxycarbonyl-3-bromoindole (20c).** A solution of *N*-*tert*-butoxycarbonylindole (1.06 g, 4.89 mmol) and NBS (0.920 g, 5.17 mmol) in CH_2Cl_2 (50 mL) was heated at reflux for 2 h, and the cooled reaction mixture was diluted with H_2O (50 mL). The layers were separated, and the organic phase was washed (10%

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KOH, H_2O), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography (95:5 hexane/Et_2O), affording the title compound (1.41 g, 98%) as a colorless oil which solidified on standing: mp 54−55 °C (MeOH); IR (KBr) ν (max) 3063, 2979, 1734, 1681, 1447 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 8.14 (d, J = 7.7 Hz, 1H), 7.63 (s, 1H), 7.53−7.49 (m, 1H), 7.39−7.22 (m, 2H), 1.65 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 148.8 (e), 134.6 (e), 129.3 (e), 125.3 (o), 124.7 (o), 123.2 (o), 119.5 (o), 115.1 (o), 97.9 (e), 84.2 (e), 28.1 (o); MS (EI (70 eV)) *m/e* (rel intensity) 297 (53), 295 (53), 241 (61), 239 (61), 224 (7.5), 222 (7.5), 197 (100), 195 (100), 169 (2.5), 167 (2.5). Anal. Calcd for $C_{13}H_{14}NO_2Br$: C, 52.72; H, 4.76; N, 4.73. Found: C, 53.00; H, 4.85; N, 4.79.

***N,N*-Diethyl *O*-[2-(*N*-*tert*-butoxycarbonyl-3-indolyl)-6-methoxy]phenylcarbamate (21c).** According to general procedure G, a mixture of *N*-*tert*-butoxycarbonyl-3-bromoindole (0.988 g, 3.34 mmol), 2-*N*,*N*-diethylcarbamato-3-methoxyphenylboronic acid (**16a**) (1.35 g, 5.06 mmol), $Pd(PPh_3)_4$ (0.190 g, 0.164 mmol), and Na_2CO_3 (10 mL, 2 mol/L) in toluene (125 mL) was heated at reflux for 12 h. Standard workup followed by purification by column chromatography afforded the title compound as a viscous oil (0.883 g, 60%) which solidified on standing: mp 96−97 °C (hexane/CH_2Cl_2); IR (KBr) ν (max) 2977, 1725, 1612, 1576, 1458 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.20 (d, J = 8.2 Hz, 1H), 7.68 (s, 1H), 7.64 (dd, J = 7.0, 1.5 Hz, 1H), 7.32 (ddd, J = 7.9, 7.3, 1.5 Hz, 1H), 7.22 (ddd, J = 7.6, 7.3, 1.5 Hz, 1H), 7.24 (app t, J = 7.9 Hz, 1H), 7.13 (dd, J = 7.9, 1.8 Hz, 1H), 6.97 (dd, J = 7.9, 1.8 Hz, 1H), 3.87 (s, 3H), 3.25 (q, J = 7.0 Hz, 4H), 1.66 (s, 9H), 1.09−1.02 (m, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 152.7 (e), 151.9 (e), 149.7 (e), 138.6 (e), 136.8 (e), 135.1 (e), 130.1 (e), 128.9 (e), 125.2 (o), 123.9 (o), 122.3 (o), 120.3 (o), 114.8 (o), 112.1 (o), 110.2 (o), 82.6 (e), 56.0 (o), 42.3 (e), 41.4 (e), 27.3 (o), 13.4 (o), 12.7 (o); MS (EI (70 eV)) *m/e* (rel intensity) 438 (M^+, 7.5), 382 (1.2), 338 (22), 265 (3.1), 238 (3.3), 195 (1.6), 100 (100), 72 (18). Anal. Calcd for $C_{25}H_{30}N_2O_5$: C, 68.47; H, 6.90; N, 6.39. Found: C, 68.60; H, 6.85; N, 6.50.

4-Methoxy-6*H*-indolo[2,3-*c*]benzo[*e*]pyran-6-one (22c). To a solution of LDA (0.845 mmol) in THF (5 mL) at −78 °C was added a solution of carbamate **21c** (0.112 g, 0.255 mmol) in THF (5 mL) dropwise via canula, and the resulting solution was allowed to warm to rt over 12 h. Standard workup afforded the crude hydroxy amide which was cyclized according to general procedure D (10 mL of HOAc). After heating at reflux for 1 h, the cooled solution was diluted with H_2O (10 mL) and cooled in an ice bath. The mixture was filtered, and the precipitate was washed with cold HOAc/H_2O (1:1), affording the title compound (54.4 mg, 80%) as a colorless fine solid: mp 274−278 °C dec; IR (KBr) ν (max) 3246, 1707, 1539, 1377 cm^{-1}; ^1H NMR (250 MHz, DMSO) δ 12.73 (s, 1H), 8.43 (d, J = 8.2 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.66−7.49 (m, 2H), 7.44−7.30 (m, 2H), 7.18 (d, J = 8.2 Hz, 1H), 3.94 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 155.0 (e), 147.3 (e), 139.7 (e), 139.5 (e), 127.2 (o), 124.9 (o), 122.6 (o), 121.6 (o), 121.6 (e), 121.3 (e), 120.0 (e), 119.0 (e), 115.1 (o), 113.4 (o), 110.2 (o), 55.9 (o); MS (EI (70 eV)) *m/e* (rel intensity) 265 (M^+, 100), 222 (21), 195 (3.7), 166 (3.1), 133 (5.6); HRMS (EI (70 eV)) *m/e* calcd for$C_{16}H_{11}NO_3$ 265.0739, found 265.0739.

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Supporting Information Available: Experimental details for compounds not included in main text. ^1H NMR and ^{13}C data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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