Directed *ortho* Metalation Reactions of Aryl *O*-Carbamates; A Regiospecific Synthesis of 2,2-Disubstituted 2*H*-1-Benzopyrans

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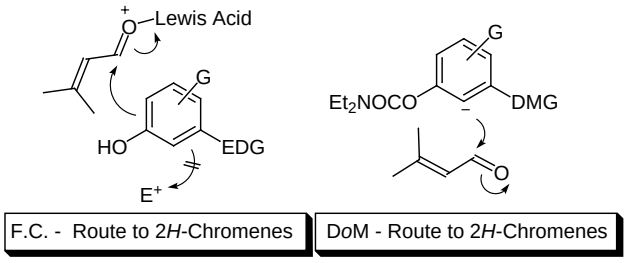
Received 21 June 2000; revised 13 September 2000

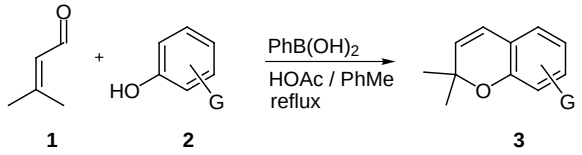
Abstract: A one-pot regiocontrolled synthesis of 2,2-disubstituted 2*H*-1-benzopyrans **5** from aryl *O*-carbamates **4** using the directed *ortho* metalation reaction is described and constitutes an advantageous complement to classical routes for this class of heterocycles.

Key words: 2*H*-1-benzopyran, chromene, directed *ortho* metalation, aryl-*O*-carbamates, carbamoyl migration

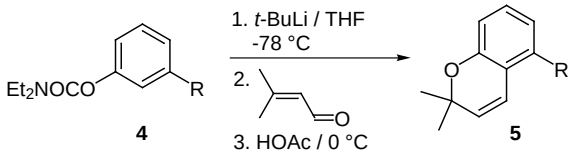
2*H*-Chromenes are key heterocyclic units in a variety of polyoxygenated natural products and bioactive molecules.[1,2] Of the numerous construction motifs for chromenes,[3] the Friedel–Crafts (F. C.) approach (Scheme 1) is by far the most widely used but, as expected, is compromised by poor reactivity for electron-withdrawing substituents and is regiochemically dictated by electrophilic aromatic substitution rules. Recently, we developed a 2*H*-chromene synthesis, **1**+**2** → **3** (Scheme 2), which depends upon this regiochemical control but which may be carried out under relatively mild $PhB(OH)_2$/HOAc conditions compared to the Lewis-acid catalyzed conditions previously reported.[4] As a starting point for the total synthesis of plicadin, a coumestan natural product,[5] we devised a facile synthesis of the chromene **5** (R = $OCONEt_2$) (Scheme 3) which is based on the Directed *ortho* Metalation (D*o*M) reaction of aryl *O*-carbamates.[6] Since, to the best of our knowledge, only two previous reports of chromene construction by D*o*M chemistry have been reported[7] and since this strategy provides derivatives difficult to obtain by classical routes, we undertook to generalize this anionic route to chromenes. Herein we report our results which provide a practical synthetic protocol for 2*H*-chromenes, **4** → **5** (Scheme 3, Table).



Scheme 1



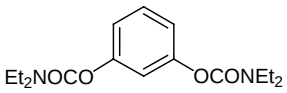
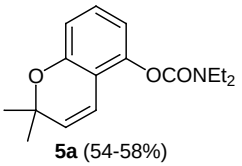
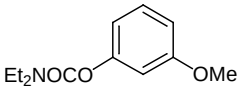
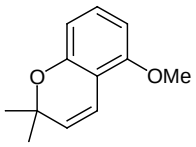
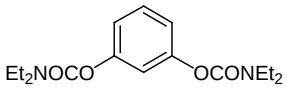
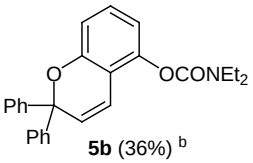
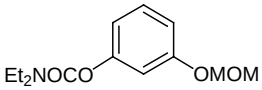
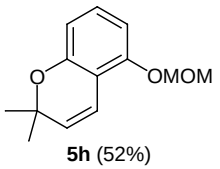
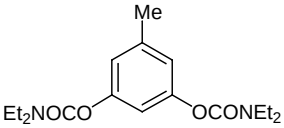
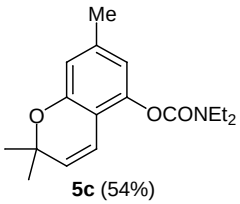
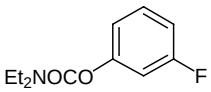
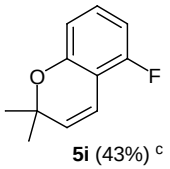
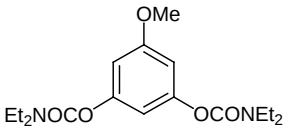
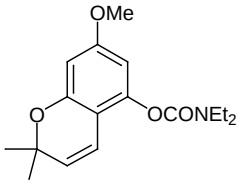
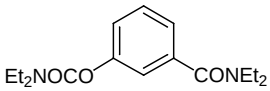
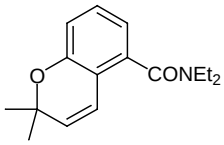
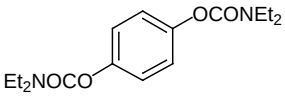
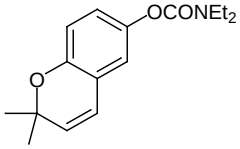
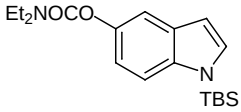
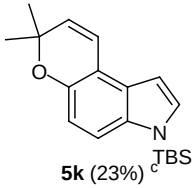
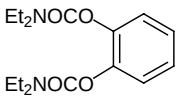
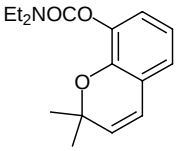
Scheme 2



Scheme 3

In a typical procedure, the resorcinol dicarbamate[8] (entry 1, Table), when subjected to standard metalation with *t*-BuLi at −78 °C for 1 hour, followed by senecialdehyde quench, afforded product **5a** in 54–58% yields after distillation. Similarly, *O*-carbamates bearing other synergistically (1,3-) Directed Metalation Groups (DMGs) (entries 2–4, 7–10) led to 2*H*-chromene derivatives in 21–58% yields. Although clean reactions were observed (no significant side reactions by GC) and chromenes were the only isolable products, yields were not improved by repetitive experiments. Attempts to do so via mediating basicity of the anion by Li-Mg transmetalation[9] were not successful. Nevertheless, for the dicarbamate (entry 1), the reaction was easily scaled to 100 mmol (0.5 M in THF) providing ten-gram quantities of the chromene **5a**. Furthermore, this protocol provides an expeditious route to simple (entries 2–8), unusual (entry 11) and unknown chromenes, bearing selected electron-withdrawing and -donating groups, from a variety of commercially available phenols. With the exception of **5g** and the phenols corresponding to **5a** (**5h**) and **5e**, the prepared chromenes are new compounds. While the phenol of **5e** is conveniently available in higher yields (66%, 1 step) by classical methods,[10] some of the other systems, in particular the 5- substituted derivatives (e. g., **5a**, **b**, **e**, **g**, **i**, **j**) are less efficiently accessible (e. g., phenol derived from **5a**, **5g**, or **5h** was prepared in 28% overall yield).[11] Furthermore, most of the derived chromenes are poised for further D*o*M chemistry.[12]

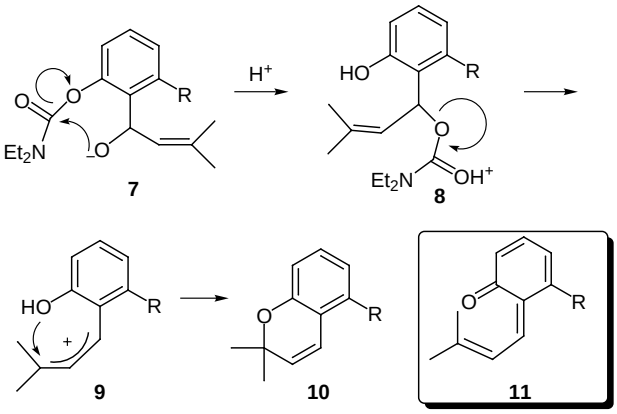
Table Synthesis of 2*H*-Chromenes 5 by Directed *ortho* Metalation

Entry	carbamate	product [a]	Entry	carbamate	product [a]
1	 **4a**	 **5a** (54-58%)	7	 **4g**	 **5g** (40-54%)
2	 **4a**	 **5b** (36%) [b]	8	 **4h**	 **5h** (52%)
3	 **4c**	 **5c** (54%)	9	 **4i**	 **5i** (43%) [c]
4	 **4d**	 **5d** (22%)	10	 **4j**	 **5j** (36%)
5	 **4e**	 **5e** (28%)	11	 **4k**	 **5k** (23%) [c]
6	 **4f**	 **5f** (21%)			

[a] Yields represent isolated yields for purified products.
[b] β-phenylcinnamaldehyde was used as the aldehyde.
[c] Reaction conditions: *s*-BuLi/TMEDA/−78 °C/THF.

In view of the recalcitrance of the *O*-carbamate to both acid- and base-mediated hydrolysis,[13] the ready formation of the chromene by HOAc quench (as a part of the work-up procedure) deserves a comment. Several experiments were carried out in order to gain insight into the low yields of the reaction. No regioisomers of products **5** were observed. The low yields of products are not due to incomplete metalation. This was established by CD_3OD quench experiment (84% incorporation by NMR). Attempts to isolate intermediates corresponding to protio-**7** and deprotio-**8** by MeI or NH_4Cl quench experiments at low temperature gave only final product **5**. Thus, we envisage that the initially formed adduct **7** (Scheme 4) undergoes facile *O*-to-*O*-migration of the carbamoyl moiety which is driven by the phenolate leaving group ability. The resulting intermediate **8** undergoes acid-catalyzed solvolysis to the allylic cation **9**, which is rapidly trapped by the phenolic OH to give product **10**. An alternative pathway, via the *ortho*-quinone methide **11**, formed directly from **8** or via **9,** followed by electrocyclic ring closure, cannot be excluded.[14]

In summary, a D*o*M protocol, **4** → **5**, for 2*H*-chromene derivatives has been developed which takes advantage of the synergistic effect of a 1,3-diDMG arrangement to set the regiochemical consequence by the D*o*M reaction. While the yields are low to modest, this procedure allows



Scheme 4

rapid access to substituted 2*H*-chromenes, which are difficult to prepare by the classical Friedel–Crafts approach and, at times, may complement the latter method.[4]

Further D*o*M chemistry on **5** and related 2*H*-chromene *O*-carbamates is in progress and will be reported in due course.

All experiments were carried out under Ar in dried glassware. THF was freshly distilled from sodium benzophenone ketyl under Ar prior to use. All reagents and chemicals were purchased from Aldrich. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-250 or AC-200 spectrometer. Mps were obtained on a Büchi-20 apparatus and are uncorrected. IR spectra were obtained on a Perkin–Elmer 983 spectrometer. MS were determined on a high resolution Varian MAT-CH7 instrument at 70 eV.

_O_-Aryl Carbamates 4; General Procedure[8]

To a stirred suspension of the corresponding phenol (1 mmol) and K_2CO_3 (1.5 mmol) in MeCN (0.5 M) was added *N*,*N*-diethylcarbamoyl chloride (1.5 mmol). (Note: for bis-carbamates of entries 1–6, 3 mmol of both K_2CO_3 and *N*,*N*-diethylcarbamoyl chloride are required). The reaction mixture was heated to reflux until the reaction was completed (TLC). The mixture was cooled, poured into H_2O (5 mL) and the aqueous layer was extracted with Et_2O (3 × 5 mL). The combined Et_2O extracts were washed with 10% NaOH (2 × 5 mL), H_2O (2 × 5 mL), brine (2 × 5 mL), dried (Na_2SO_4), concentrated in vacuo, and the crude residue was purified as specified below.

1,3-Bis(*N*,*N*-diethylcarbamoyl) benzene (4a)[15]

Distillation: bp 235–240 °C (bath temp)/0.02 mmHg; yellow oil; yield: 86–89%.

IR (neat): ν = 2976, 2934, 1706, 876, 752 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.16–1.26 (m, 12H), 3.33–3.42 (m, 8H), 6.95–6.98 (m, 3H), 7.27–7.34 (m, 1H).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 152.7, 150.9, 128.0, 117.2, 114.6, 41.2, 40.8, 13.1, 12.2.

EIMS: *m/z* (%) = 308 (M$^+$, 100), 209 (6), 100 (35).

HRMS: calcd. for $C_{16}H_{24}N_2O_4$: 308.1736. Found: 308.1747.

3-Methylphenyl-1,3-bis(*N*,*N*-diethylcarbamate) (4c)

Column chromatography: EtOAc/hexanes (1:1); colorless oil; yield: quant.

IR (neat): ν = 2968, 1720, 1618, 1414, 1152 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.15–1.35 (m, 12H), 2.33 (s, 3H), 3.30–3.50 (m, 8H), 6.79 (br s, 3H).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 153.9, 151.6, 139.6, 119.0, 112.6, 42.1, 41.8, 21.2, 14.1, 13.3.

EIMS: *m/z* (%) = 322 (M$^+$, 17), 101 (8), 100 (100), 72 (63).

HRMS: calcd. for $C_{17}H_{26}N_2O_4$: 322.1894. Found: 322.1887.

5-Methoxyphenyl-1,3-bis(*N*,*N*-diethylcarbamate) (4d)

Column chromatography: EtOAc/hexanes (1:4); colorless oil; yield: 95%.

IR (neat): ν = 2975, 2936, 1722, 1609, 1467, 1415, 1055, 1001 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.10–1.30 (m, 12H), 3.25–3.50 (m, 8H), 3.78 (s, 3H), 6.54 (d, 2H, *J* = 2.0 Hz), 6.58 (d, 1H, *J* = 2.0 Hz).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 160.3, 153.5, 152.3, 108.0, 104.6, 55.4, 42.0, 41.7, 14.0, 13.2.

EIMS: *m/z* (%) = 338 (M$^+$, 28), 127 (10), 101 (10), 100 (100), 72 (71).

HRMS: calcd. for $C_{17}H_{26}N_2O_5$: 338.1842. Found: 338.1850.

1,4-Bis(*N*,*N*-diethylcarbamoyl) benzene (4e)[16]

Column chromatography: EtOAc/hexanes (1:4); colorless solid; mp 103–105 °C (hexanes/EtOAc); yield: 91%.

IR (neat): ν = 2979, 2938, 1723, 1503, 1472, 1416, 1278, 1190, 955 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.10–1.41 (m, 12H), 3.22–3.59 (m, 8H), 7.09 (s, 4H).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 153.8, 148.1, 121.9, 41.9, 41.6, 13.9, 13.1.

1,2-Bis(*N*,*N*-diethylcarbamoyl) benzene (4f)[17]

Column chromatography: EtOAc/hexanes (1:4); colorless solid; mp 38–41 °C (hexanes/EtOAc); yield: 86%.

IR (neat): ν = 2985, 2935, 1723, 1496, 1410, 1255, 1151, 1097, 960 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.02–1.38 (m, 12H), 3.19–3.54 (m, 8H), 7.17 (s, 4H).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 153.1, 143.1, 125.5, 123.3, 41.9, 41.6, 17.8, 13.0.

3-Methoxyphenyl-*N*,*N*-diethylcarbamate (4g)

Distillation: bp 115–117 °C/0.05 mmHg; colorless oil; yield: 96%.

IR (neat): ν = 2963, 2836, 1719, 1417, 969 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.13–1.15 (m, 6H), 3.31–3.51 (m, 4H), 3.79 (s, 3H), 6.68–6.76 (m, 3H), 7.27 (t, 1H, *J* = 8.0 Hz).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 159.9, 152.1, 128.9, 113.4, 110.4, 107.3, 54.7, 41.7, 41.4, 13.7, 12.8.

EIMS: *m/z* (%) = 223 (M$^+$, 42), 178 (4), 127 (20), 100 (100), 91 (50), 72 (100).

HRMS: calcd. for $C_{12}H_{17}NO_3$: 223.1208. Found: 223.1214.

3-Fluorophenyl-*N*,*N*-diethylcarbamate (4i)

Distillation: bp 120–125 °C / 0.2 mmHg (Kugelrohr); colorless oil; yield: 84%.

IR (neat): ν = 3091, 2978, 2937, 1720, 1607, 1422, 1257, 1155, 965 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.02–1.38 (m, 6H), 3.18–3.55 (m, 4H), 6.64–7.11 (m, 3H), 7.18–7.39 (m, 1H).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 162.5 (d, *J* = 247.2 Hz), 153.3, 152.2 (d, *J* = 10.7 Hz), 129.6 (d, *J* = 9.1 Hz), 117.2 (d, *J* = 3.1 Hz), 111.6 (d, *J* = 21.4 Hz), 109.4 (d, *J* = 23.7 Hz), 42.0, 41.7, 13.8, 12.9.

EIMS: *m/z* (%) = 211 (M^+, 2), 112 (11), 100 (42), 72 (100).

HRMS: calcd. for $C_{11}H_{14}FNO_2$: 211.1009. Found: 211.1001.

3-[(Diethylamino)carbonyl]phenyl-*N,N*-diethylcarbamate (4j)
Distillation: bp 130−135 °C / 0.03 mmHg; colorless oil; yield: 80%.

IR (neat): ν = 2973, 2844, 1710 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.12−1.29 (m, 12H), 3.26−3.52 (m, 8H), 7.10−7.36 (m, 4H).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 170.0, 153.6, 151.3, 138.1, 129.0, 122.5, 122.1, 119.8, 42.0, 41.2, 40.7, 39.8, 13.4.

Anal: calcd. for $C_{16}H_{24}N_2O_3$: C, 65.73; H, 8.27; N, 9.58. Found: C, 65.54; H, 8.29; N, 9.74.

Chromenes 5; General Procedure
To a cooled (−78 °C) solution of **4** (1 mmol) in THF (0.5 M) was added *t*-BuLi solution (1.1 mmol) while keeping the internal temp <−75 °C (20 min addition time). The mixture was stirred for 15 min, 3-methylbut-2-enal (1.3 mmol) was added over 15 min (internal temp <−74 °C), and the mixture was stirred for 1 h at −78 °C. The mixture was allowed to warm to r.t., stirred for 1 h, cooled to 0 °C, and sequentially treated with HOAc (1.3 mmol) and brine solution (2 mL), and stirred for 1 h at r.t. The organic phase was separated, the aqueous phase was extracted with Et_2O (3 × 5 mL), and the combined organic extracts were evaporated in vacuo. Excess aldehyde was removed under high vacuum (0.1 mmHg), the residue was dissolved in Et_2O (10 mL), dried (Na_2SO_4), concentrated in vacuo, and the crude residue was purified as specified below.

2,2-Dimethyl-2*H*-5-chromenyl-*N,N*-diethylcarbamate (5a)
Distillation: bp 120−130 °C / 0.2 mmHg (Kugelrohr); yellow oil; yield: 54−58%.

IR (neat): ν = 2977, 1722, 1638, 1611, 1460, 1418, 1277, 1225, 1156, 1116, 1060, 758 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.17−1.29 (m, 6H), 1.43 (s, 6H), 3.37−3.47 (m, 4H), 5.62 (d, 1H, *J* = 10.0 Hz), 6.38 (d, 1H, *J* = 10.0 Hz), 6.63 (d, 1H, *J* = 8.1 Hz), 6.64 (d, 1H, *J* = 8.1 Hz), 7.06 (t, 1H, *J* = 8.1 Hz).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 153.2, 146.8, 130.3, 127.9, 116.0, 114.3, 114.0, 112.9, 75.4, 41.8, 41.4, 27.4, 13.9, 12.9.

EIMS: *m/z* (%) = 275 (M^+, 55), 260 (100), 175 (8), 161 (26).

HRMS: calcd. for $C_{16}H_{21}NO_3$: 275.1521. Found: 275.1518.

2,2-Diphenyl-2*H*-5-chromenyl-*N,N*-diethylcarbamate (5b)
Column chromatography: EtOAc/hexanes (1:4); colorless solid; yield: 36%.

IR (neat): ν = 3063, 3033, 2926, 1721, 1607, 1482, 1446, 1237, 987, 754 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.17−1.31 (m, 6H), 3.33−3.51 (m, 4H), 6.16 (d, 1H, *J* = 9.8 Hz), 6.61 (d, 1H, *J* = 9.8 Hz), 6.79−7.15 (m, 3H), 7.20−7.45 (m, 10H).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 152.6, 152.3, 144.9, 129.5, 128.8, 128.1, 127.4, 127.0, 126.5, 123.3, 121.1, 121.0, 116.4, 82.5, 42.1, 41.7, 14.1, 13.3.

HRMS: calcd. for $C_{26}H_{25}NO_3$: 399.1834. Found: 399.1842.

2,2,7-Trimethyl-2*H*-5-chromenyl-*N,N*-diethylcarbamate (5c)
Column chromatography: EtOAc/hexanes (1:4); yellow oil; yield: 54−55%.

IR (neat): ν = 2976, 2933, 1720, 1627, 1566, 1416, 1266, 1152, 1118, 1072 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.15−1.35 (m, 6H), 1.42 (s, 6H), 2.25 (s, 3H), 3.30−3.50 (m, 4H), 5.56 (d, 1H, *J* = 9.9 Hz), 6.34 (d, 1H, *J* = 9.9 Hz), 6.48 (s, 2H).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 153.9, 153.4, 146.9, 139.0, 129.7, 116.4, 115.0, 114.0, 112.0, 75.9, 42.1, 41.8, 27.8, 21.4, 14.3, 13.3.

EIMS: *m/z* (%) = 289 (M^+, 23), 275 (18), 274 (100), 175 (18), 174 (29), 100 (98), 85 (16), 72 (40).

HRMS: calcd. for $C_{17}H_{23}NO_3$: 289.1679. Found: 289.1685.

7-Methoxy-2,2,-dimethyl-2*H*-5-chromenyl-*N,N*-diethylcarbamate (5d)
Column chromatography: EtOAc/hexanes (1:4); yellow oil; yield: 22%.

IR (neat) ν = 2974, 2935, 1722, 1624, 1574, 1415, 1268, 1150, 1118, 1071 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.15−1.30 (m, 6H), 1.42 (s, 6H), 3.35−3.50 (m, 4H), 3.75 (s, 3H), 5.49 (d, 1H, *J* = 9.9 Hz), 6.25 (s, 2H), 6.31 (d, 1H, *J* = 9.9 Hz).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 160.2, 154.5, 153.7, 148.0, 127.9, 116.3, 108.2, 101.0, 99.6, 76.4, 55.4, 42.2, 41.9, 27.9. 14.3, 13.3.

EIMS: *m/z* (%) = 305 (M^+, 23), 291 (12), 290 (68), 190 (10), 100 (100), 72 (63).

HRMS: calcd. for $C_{17}H_{23}NO_4$: 305.1627. Found: 305.1621.

2,2-Dimethyl-2*H*-6-chromenyl-*N,N*-diethylcarbamate (5e)
Column chromatography: EtOAc/hexanes (1:4); yellow oil; yield: 28%.

IR (neat): ν = 3053, 2982, 2937, 1720, 1636, 1475, 1411, 1257, 1167, 967 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.12−1.31 (br m, 6H), 1.42 (s, 6H), 3.28−3.50 (br m, 4H), 5.61 (d, 1H, *J* = 9.8 Hz), 6.26 (d, 1H, *J* = 9.8 Hz), 6.72 (d, 1H, *J* = 8.7 Hz), 6.75 (d, 1H, *J* = 2.4 Hz), 6.83 (dd, 1H, *J* = 8.4, 2.5 Hz).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 154.5, 149.8, 144.8, 131.2, 121.9, 121.7, 121.5, 119.2, 116.4, 76.1, 42.1, 41.7, 27.7, 14.1, 13.3.

EIMS: *m/z* (%) = 275 (M^+,16), 260 (67), 189 (24), 161 (19), 132 (37), 100 (100).

HRMS: calcd. for $C_{16}H_{21}NO_3$: 275.1521. Found: 275.1532.

2,2-Dimethyl-2*H*-8-chromenyl-*N,N*-diethylcarbamate (5f)
Column chromatography: EtOAc/hexanes (1:4); colorless oil; yield: 21%.

IR (neat) ν = 3068, 2980, 2925, 1726, 1459, 1417, 1272, 1150 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.08−1.28 (br m, 6H), 1.40 (s, 6H), 3.32−3.53 (br m, 4H), 5.60 (d, 1H, *J* = 9.9 Hz), 6.32 (d, 1H, *J* = 9.8 Hz), 6.74−7.03 (m, 3H).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 154.0, 144.9, 139.9, 130.9, 123.0, 122.9, 122.6, 122.1, 120.0, 72.6, 42.3, 28.0, 14.0, 13.5.

EIMS: *m/z* (%) = 275 (M^+,8), 260 (100), 189 (11), 161 (18), 132 (4).

HRMS: calcd. for $C_{16}H_{21}NO_3$: 275.1521. Found: 275.1508.

5-Methoxy-2,2-dimethyl-2*H*-chromene (5g)[18]
Column chromatography: Et_2O/hexanes (1:9); colorless oil; yield: 40−54%.

IR (neat): ν = 2971, 2838, 1635, 1620 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.40 (s, 6H), 3.78 (s, 3H), 5.55 (d, 1H, *J* = 10.0 Hz), 6.37 (d, 1H, *J* = 8.2 Hz), 6.42 (d, 1H, *J* = 8.2 Hz), 6.65 (d, 1H, *J* = 10.0 Hz), 7.05 (t, 1H, *J* = 8.2 Hz).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 155.2, 153.7, 128.8, 128.7, 116.8, 110.6, 109.5, 102.9, 75.6, 55.5, 27.7.

5-(Methoxymethoxy)-2,2-dimethyl-2*H*-chromene (5h)
Column chromatography: EtOAc/hexanes (1:9); colorless solid; yield: 52%.

IR (neat): ν = 3072, 3045, 2974, 2930, 1639, 1606, 1579, 1245, 1157, 1053, 758 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.43 (s, 6H), 3.49 (s, 3H), 5.18 (s, 2H), 5.59 (d, 1H, *J* = 9.9 Hz), 6.48 (d, 1H, *J* = 8.1 Hz), 6.60 (d, 1H, *J* = 8.3 Hz), 6.68 (d, 1H, *J* = 10.0 Hz), 7.02 (t, 1H, *J* = 8.4 Hz).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 153.7, 152.9, 129.3, 128.9, 116.8, 111.5, 110.4, 106.6, 94.8, 75.7, 56.1, 27.8.

EIMS: *m/z* (%) = 220 (M^+,6), 205 (100), 175 (52), 161 (57).

HRMS: calcd. for $C_{13}H_{16}O_3$: 220.1099. Found: 220.1106.

5-Fluoro-2,2-dimethyl-2*H*-chromene (5i)
Column chromatography: EtOAc/hexanes (1:9); colorless oil; yield: 43%.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.44 (s, 6H), 5.63 (d, 1H, *J* = 9.9 Hz), 6.52−6.60 (m, 3H), 6.96−7.08 (m, 1H).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 158.6 (d, *J* = 251.5 Hz), 154.1 (d, *J* = 15.1 Hz), 130.6 (d, *J* = 2.3 Hz), 128.8 (d, *J* = 9.9 Hz), 125.6, 115.1 (d, *J* = 4.6 Hz), 112.1 (d, *J* = 3.0 Hz), 107.2 (d, *J* = 21.4 Hz), 76.3, 27.8.

EIMS: *m/z* (%) = 178 (M^+,1), 163 (100), 115 (13).

HRMS: calcd. for $C_{11}H_{11}FO$: 178.0794. Found: 178.0787.

***N*,*N*-Diethyl-2,2-dimethyl-2*H*-5-chromenecarboxamide (5j)**
Column chromatography: EtOAc/hexanes (1:9); colorless oil; yield: 36%.

IR (neat): ν = 3056, 2976, 2931, 1630, 1443, 1379, 1295, 1115, 767 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.16−1.30 (m, 6H), 1.43 (s, 6H), 3.09−3.20 (m, 4H), 5.65 (d, 1H, *J* = 9.8 Hz), 6.28 (d, 1H, *J* = 9.8 Hz), 6.73 (d, 1H, *J* = 7.9 Hz), 6.82 (d, 1H, *J* = 7.9 Hz), 7.10 (t, 1H, *J* = 7.9 Hz).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 169.9, 152.9, 134.4, 131.8, 128.9, 119.0, 117.9, 117.6, 116.7, 74.2, 42.9, 38.9, 27.8, 14.0, 12.9.

EIMS: *m/z* (%) = 259 (M^+,4), 244 (37), 173 (100), 144 (19), 115 (23).

HRMS: calcd. for $C_{16}H_{21}NO_2$: 259.1572. Found: 259.1560.

3-[1-(*tert*-Butyl)-1,1-dimethylsilyl]-7,7-dimethyl-3,7-dihydropyrano[3,2-*e*]indole (5k)
Column chromatography: EtOAc/hexanes (1:9); colorless solid; mp 63−65 °C (hexanes/EtOAc); yield: 23%.

^1H NMR (200 MHz, $CDCl_3$): δ = 0.56 (s, 6H), 0.91 (s, 9H), 1.44 (s, 6H), 5.61 (d, 1H, *J* = 9.8 Hz), 6.57 (d, 1H, *J* = 3.0 Hz), 6.60 (d, 1H, *J* = 8.9 Hz), 6.62 (d, 1H, *J* = 9.8 Hz), 7.14 (d, 1H, *J* = 3.4 Hz), 7.22 (d, 1H, *J* = 8.9 Hz).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 146.5, 136.3, 132.0, 129.3, 128.3, 120.1, 113.8, 111.8, 111.6, 101.6, 75.4, 27.6, 26.3, 19.4, −4.0.

EIMS: *m/z* (%) = 313 (M^+,13), 298 (100), 183 (24), 120 (10).

HRMS: calcd. for $C_{19}H_{27}NOSi$: 313.1862. Found: 313.1873.

Acknowledgement

We are grateful to NSERC Canada and Monsanto for support under the Industrial Research Chair tenure at Waterloo (1992−98) and the continuing NSERC support of our synthetic programs at Queen's University.

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Article Identifier:
1437-210X,E;2001,0,01,0140,0144,ftx,en;M00800SS.pdf