Intramolecular Kinetic Isotope Effect. 2-*o,o'*-d_2 + 4b. This reaction was carried out by the procedure described above for 9-*4*-d_1 with the exception that 2-*p,p'*-d_2 was replaced with 2-*o,o'*-d_2. The intensities of the *m/e* 298–300 peaks of the 9/9-*6*-d_1 mixture were used to determine the value of 9/9-*6*-d_1 by an overdetermined least-squares procedure (program MassSpec): (EI, 70eV) *m/z* (intensity) 298 (632), M; 299 (732), M + 1; 300 (91), M + 2. For 9/9-*6*-d_1. ^{1}H NMR ($CDCl_3$): δ 7.79 (H6, d, 1 H), 7.62 (H3, d, 2 H), 7.35 (H4, t, 2 H), 6.92 (H5, m, 2 H), 3.58 (s, 4 H), 1.28 (s, 18 H). ^{13}C NMR ($CDCl_3$): δ 140.1, 139.1, 138.4 (apparent overlapped with δ 139.1, *J* = 25 Hz), 128.9, 128.3, 128.1, 128.0, 99.8, 99.7, 92.7, 75.3, 31.5, 31.3, 27.5.

2-Butynyl (Trimethylsilyl)methyl Ether (20). To a well-stirred mixture of NaH powder (3.37 g, 140.4 mmol) in anhydrous ether (50 mL) was added 2-butyn-1-ol (6.56 g, 93.6 mmol) over a 1-h period; the mixture was then allowed to stir for an additional 3 h. To this gray slurry was added Me_3SiCH_2OTf[38] (18 mL, 90.0 mmol) in anhydrous ether (50 mL) over a 45-min period and the stirring continued for an additional 24 h. The solution was cautiously added to a 1:1 ether/CH_3OH solution until the exothermicity of the reaction ceased. The layers were separated, the aqueous phase was extracted with ether (3 × 75 mL), and the combined extracts were washed with brine and then dried over $MgSO_4$. The ether was removed by evaporation and the residual oil distilled (bp 50 °C (10 Torr)); isolated yield, 11.7 g (80%). ^{1}H NMR ($CDCl_3$): δ 4.02 (q, *J* = 1.9 Hz, 2 H), 3.13 (t, *J* = 1.4 Hz, 2 H), 1.83 (t, *J* = 1.8 Hz, 3 H), 0.02 (s, 9 H). ^{13}C NMR ($CDCl_3$): δ 81.5, 75.7, 63.5, 62.3, 3.1, −3.3. The ^{1}H NMR revealed >95% purity.

Preparation of the Vinyliodonium Triflate 21. A suspension of **2** (1117 mg, 1.55 mmol) in CH_2Cl_2 (30 mL) was prepared in a flame-dried 100-mL Schlenk flask under N_2. To the lemon-yellow suspension was added **20** (266 mg, 1.70 mmol) whereupon the solution turned homogeneous lemon-yellow. After 48 h the mixture became cloudy as a white precipitate formed. The solvent was concentrated to 5 mL. A layer of anhydrous hexane (15 mL) was added. The resulting off-white precipitate was isolated by filtration (632 mg, 63%) and dried under vacuum (0.001 Torr) overnight. Crystals suitable for X-ray structure determination were grown out of a 10:1 ethyl acetate/hexane mixture; the crystals obtained (clear, colorless needles) were dried overnight and then mounted on the diffractometer under a stream of N_2. ^{1}H NMR (CD_2Cl_2): δ 8.15 (d, 2 H), 7.73 (t, 1 H), 7.54 (t, 2 H), 4.28 (s, 2 H), 3.29 (s, 2 H), 2.66 (s, 3 H), 0.09 (s, 9 H). ^{13}C NMR (CD_2Cl_2): δ 155.0, 135.7, 133.4, 132.8, 121.2, 112.7, 71.2, 66.9, 23.2, −3.0. ^{19}F NMR (CD_2Cl_2): δ −73.8, −78.7. Anal. Calcd for $C_{16}H_{21}F_6IO_7S_2Si$: C, 29.19; H, 3.21; F, 17.31; I, 19.28; S, 9.74; Si, 4.27. Found: C, 29.01; H, 3.12; F, 17.28; I, 19.45; S, 9.70; Si, 4.10.

X-ray Analysis of 21. $C_{16}H_{21}F_6IO_7S_2Si$, M_r = 658.4; monoclinic, *C2/c*, *a* = 29.431 (14) Å, *b* = 8.364 (2) Å, *c* = 22.328 (5) Å, β = 108.24 (2)°, *V* = 5220 (3) Å^3, *Z* = 8, D_x = 1.68 g cm^{-3}; λ (Mo Kα) = 0.7107 Å, μ = 1.51 mm^{-1}, *F*(000) = 2608, *T* = 143 K, *R* = 0.056 (*wR* = 0.063) for 3562 unique, observed reflections.

Crystal size 0.12 × 0.12 × 0.50 mm. Siemens P4 diffractometer, unit cell constants from least-squares fit of setting angles for 25 reflections ($2\theta_{av}$ = 20.76°). Data collected (ω scans) to (sin θ)/λ = 0.5947 Å^{-1}, $-36 \le h \le 0$, $-10 \le k \le 0$, $-27 \le l \le 27$. Three standard reflections (200, 020, 002) every 97; Lorentz and polarization corrections; semiempirical absorption correction applied, maximum transmission = 0.720, minimum transmission = 0.689;[39] 4584 unique reflections, 3562 reflections with $F_o > 2.5\sigma(F_o)$ observed.

Structure solved by direct methods. Full-matrix (298 parameters total, data/parameters = 12.0) weighted [$w = (\sigma^2(F) + gF^2)^{-1}$, $g = 1.3 \times 10^{-4}$] least-squares refinement on *F*. H atoms in idealized positions (C–H = 0.96 Å, $U(H) = 1.2 \times U_{iso}(C)$). Non-H atoms refined with anisotropic thermal parameters. At convergence ($(\Delta/\sigma)_{max}$ = 0.012, $(\Delta/\sigma)_{mean}$ = 0.002 for last 3 cycles) *R* = 0.056, *wR* = 0.063, *S* = 1.11, $(\Delta\rho)_{max}$ = 1.4 e Å^{-3} (near I1 (0.75 Å)), $(\Delta\rho)_{min}$ = −0.62 e Å^{-3}. Neutral atom scattering factors and anomalous dispersion corrections were used;[40] all calculations were performed using the SHELXTL program library.[39]

Attempts to Desilylate 21.[28] A suspension of 18-crown-6 (240 mg, 0.911 mmol) and anhydrous KF (240 mg, 4.13 mmol) in $CDCl_3$ (3 mL) was prepared in a flame-dried 15-mL Schlenk flask under N_2. To the suspension was added **21** (204 mg, 0.310 mmol), and the white slurry was stirred for 18 h. The volatile components were vacuum transferred (0.001 Torr) into a flame-dried 15-mL Schlenk flask. The only products identifiable by ^{1}H and ^{13}C NMR were iodobenzene and the propargyl ether **20**. IR analysis of the nonvolatile and volatile components showed no evidence for an allene (no asymmetric C=C=C stretch in the 2000–1900 cm^{-1} region).

Similar results were obtained when $KF \cdot 2H_2O$ (94 mg, 1.00 mmol) and Bu_4NCl (1139 mg, 4.1 mmol)[27] in CD_3CN (5 mL) were treated with **21** (724 mg, 1.10 mmol). No evidence for an allene was seen in the IR when Bu_4NF (TBAF) (720 μL, 0.720 mmol, 1.0 M) was stirred with a solution of **21** (233 mg, 0.354 mmol) in THF (2.5 mL) for a month.

Acknowledgment. We acknowledge Don Dick and David K. Morita for collecting the mass spectrum of 9/9-*6*-d_1 and helping with the GC analyses. We also thank Jonathan Filley, Christophe Lawrie, and David Collum (Cornell) for helpful discussions. This work was funded by Department of Energy Grant DE-FG02-84ER13299-A008.

Supplementary Material Available: Tables of X-ray crystal and structural data for **21** (9 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(38) The alternative reagent Me_3SiCH_2I affords the undesired alkyl and silyl ethers; see: Chakraborty, T. K.; Reddy, G. V. *J. Chem. Soc., Chem. Commun.* **1989**, 251.

(39) Sheldrick, G. M. SHELXTL, Unix Ver. 4.2; Siemens Analytical X-Ray Instruments, Inc.; Madison, WI, 1991.

(40) *International Tables for X-Ray Crystallography*; Kynoch: Birmingham, England, 1974; Vol. IV.

A Novel Synthesis of 2-Aminochromones via Phosgeniminium Salts

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A novel method for the synthesis of antiplatelet 2-aminochromones making use of the reaction of 2′-hydroxyacetophenone–BF_2 complexes with phosgeniminium chlorides has been developed. Aqueous hydrolysis of the intermediate β-chlorovinylogous amide–BF_2 complex affords the 2-aminochromone in good yield, without the need for chromatographic purification.

Interest in the 2-aminochromone class of compounds relates to its novel antiplatelet activity.[1,2] Research in this area may lead to novel agents useful for the treatment of unstable angina or as adjuncts to conventional thrombo-

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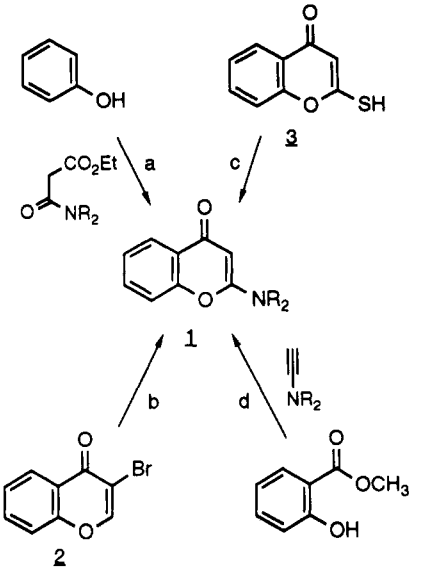
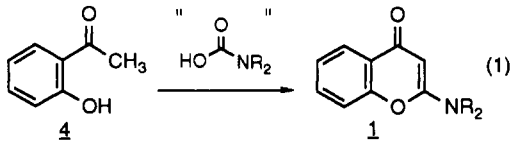
Scheme I



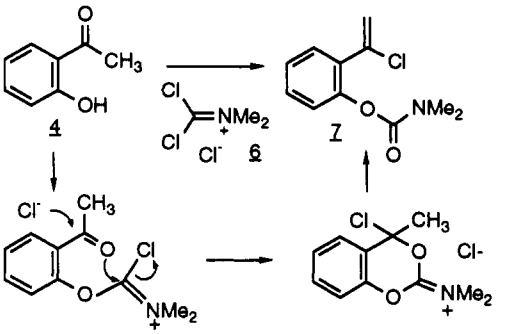
lysis.[3] Several methods have been developed for the synthesis of 2-aminochromones 1 (Scheme I). Vilsmeier condensation of a β-amido ester with phenol (path a)[4] or amine displacement of a 3-bromochromone 2 (path b)[5] suffer from either unacceptably low yields or difficult chromatographic separations of complex mixtures. The more practical Bantick procedure, starting from a 2′-hydroxyacetophenone, proceeds through amine displacement of an intermediate 2-thiochromone 3 (path c).[6] Recently, Gammill has developed an elegant one-step synthesis of 2-aminochromones via the reaction of salicylic esters with ynamines (path d).[1]

As a complement to known procedures, we chose to investigate a simple, one-step preparation of 2-aminochromones starting from 2′-hydroxyacetophenone (4). Many substituted 2′-hydroxyacetophenones are commercially available and moreover are easily prepared from the corresponding phenols via Friedel–Crafts acylation. Formally, this transformation to 1 requires the use of a stable, reactive carbamic acid equivalent, such as a dichloromethyleniminium chloride (phosgeniminium salt) (eq 1).[7]

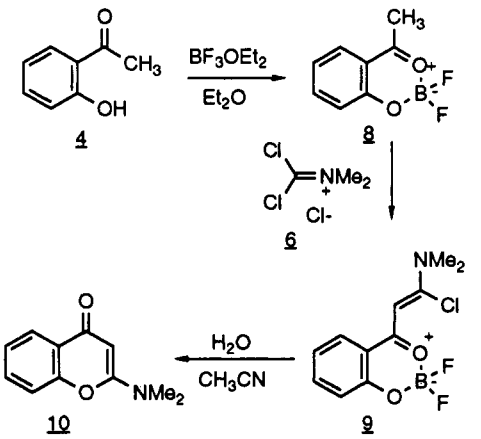


(1)

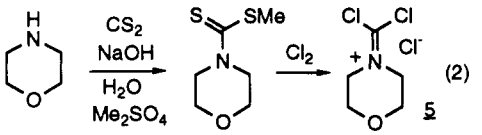
Scheme II



Scheme III



Vilsmeier reagents or equivalent formylating agents such as DMF–dimethyl acetal have been used previously for the synthesis of chromones unsubstituted in the 2-position.[8] Furthermore, the reaction of acetophenone with the commercially available dimethylphosgeniminium chloride (6) was known to afford *N,N*-dimethyl-β-chlorocinnamide upon hydrolysis of the initial adduct.[7] Phosgeniminium salts are readily prepared in two steps from the corresponding amine via the dithiocarbamate as shown in eq 2.[7] In this manner, iminium salt 5 is prepared in 95% overall yield.



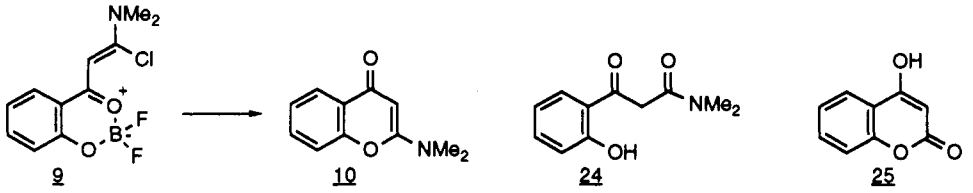
(2)

Our first attempt at the synthesis of 2-aminochromones via phosgeniminium salts is shown in Scheme II. Reaction of 2′-hydroxyacetophenone (4) with 6 (reflux, $Cl(CH_2)_2Cl$, 4 h) produced vinyl chloride carbamate 7 as the major product to the exclusion of the desired 2-aminochromone 10. Clearly, the initial reaction of 6 takes place at the phenol followed by chloride-assisted intramolecular attack of the ketone oxygen which leads to 7 upon breakdown of the resultant intermediate.[7c] It was clear that protection of the phenol was necessary in order to direct reaction of the phosgeniminium salt to the methyl ketone carbon. Ideally, such a scheme should avoid a lengthy protection–deprotection sequence which would dampen the efficiency of the overall process.

As a potential solution to this problem we proposed the initial formation of the 2′-hydroxyacetophenone–BF_2 complex 8, accomplished in 60% yield by the reaction of 4 with BF_3·OEt_2.[9,10] This "in situ" protection of the phenol

(1) Gammill, R. B.; Judge, T. M.; Morris, J. WO 90/06921.
(2) (a) Mazzei, M.; Balbi, A.; Roma, G.; Di Braccio, M.; Leoncini, G.; Buzzi, E.; Maresca, M. *Eur. J. Med Chem.* **1988**, *23*, 237. (b) Mazzei, M.; Sottofattori, E.; Di Braccio, M.; Balbi, A.; Leoncini, G.; Buzzi, E.; Maresca, M. *Eur. J. Med. Chem.* **1990**, *25*, 617. (c) Leoncini, G.; Maresca, M.; Colao, C.; Buzzi, E.; Mazzei, M. *Cell Biochem. Function* **1991**, *9*, 79.
(3) (a) Stein, B.; Fuster, V.; Israel, D. H.; Cohen, M.; Badimon, L.; Badimon, J. J.; Chesebrok, J. H. *J. Am. Coll. Cardiol.* **1989**, *14*, 813. (b) Shebuski, R. J. *Annu. Rep. Med. Chem.* **1991**, *26*, 93–101.
(4) (a) Ermili, A.; Mazzei, M.; Roma, G.; Cacciatore, C. *Farm. Ed. Sci.* **1977**, *32*, 375. (b) Ermili, A.; Balbi, A.; Di Braccio, M.; Roma, G. *Farm. Ed. Sci.* **1977**, *32*, 713. (c) Ermili, A.; Roma, G.; Mazzei, M.; Balbi, A.; Di Braccio, M.; Schianterelli, P.; Cadel, S. *Farm. Ed. Sci.* **1974**, *29*, 225.
(5) Nash, S. A.; Gammill, R. B. *Tetrahedron Lett.* **1983**, 3435.
(6) Bantick, J. R.; Suschitzky, J. L. *J. Heterocycl. Chem.* **1981**, *18*, 679.
(7) (a) Viehe, H. G.; Janousek, Z. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 573. (b) Janousek, Z.; Viehe, H. G. *Iminium Salts in Organic Chemistry*; Bohme, H., Viehe, H. G., Eds.; Advances in Organic Chemistry, 9; Part 1, pp 343–419. (c) Phosgeniminium salts have been used previously for the preparation of 2-amino-1,3-benzoxazines form the corresponding *o*-hydroxybenzonitrile, see: Kokel, B.; Menichi, G.; Hubert-Habart, M. *Tetrahedron Lett.* **1984**, 3837.
(8) (a) Fohlisch, B. *Chem. Ber.* **1971**, *104*, 348. (b) Bass, R. J. *J. Chem. Soc., Chem. Commun.* **1976**, 78.

Chart I. Hydrolysis of Boron Difluoride Complex 9



	10	24	25
A. CH_3CN / H_2O (5:1) 50°C, 1h	90%	--	10%
B. CH_3CN / sat $NaHCO_3$ 50°C, 1h	54%*	27%*	8%
C. CH_3CN / 2N NaOH 50°C, 30 min	20%*	72%*	8%
D. MeOH, 50°C, 1h	96%	--	--

*^{1}H NMR yields

had the added benefits of activating the methyl ketone carbon toward electrophilic attack while simultaneously deactivating the aromatic ring. Moreover, we were influenced by the pioneering work of Reynolds and VanAllen which paved the road to unsubstituted chromones utilizing BF_2 complexes.[10] Reaction of the preformed complex **8** with **6** (80 °C, $Cl(CH_2)_2Cl$, 2 h) afforded the β-chlorovinylogous amide–BF_2 complex **9** as a stable, nonhygroscopic solid in 88% yield (Scheme III).[11] Treatment of **9** with 20% H_2O/CH_3CN (50 °C, 1 h) produced the 2-aminochromone **10** in 90% yield. A 10% recovery of 4-hydroxycoumarin (**25**) was also isolated from this reaction. Control experiments indicated that **25** was not produced from chromone **10** under the reaction conditions.

This reaction sequence has been used to prepare a variety of 2-aminochromones as shown in Table I. Several observations concerning the generality of the reaction are worthy of mention. In almost all cases the 2-aminochromone is isolated by simple recrystallization after hydrolysis (10% H_2O/CH_3CN, rt, 24 h or 50 °C, 1 h) of the initial adduct.[12] The reaction is successfully run by either preforming the BF_2 complex (method B) or by generating the complex in situ by the addition of $BF_3{\cdot}OEt_2$ to an $Cl(CH_2)_2Cl$ solution of the 2′-hydroxyacetophenone prior to the introduction of the iminium salt (method A). The method has been used to generate both the 2-(dimethylamino)- and 2-morpholinylchromones in comparable yields. The reaction is insensitive to the presence of a free phenol requiring only that an additional equivalent of reagent is used to account for the reactive functionality (**11–14**). The use of an acetate group as protection for additional phenol functionality results in significantly higher yields of the BF_2 complexes and allows one to perform the reaction utilizing a single equivalent of the phosgeniminium salt (**15–19**). The major limitation to this process occurs with compounds containing groups unstable to the highly acidic reaction conditions. Although a 4-OCH_3 group proved sufficiently robust (**21**), utilization of the corresponding 4-OCH_2Ph group produced products resulting from the loss of the benzyl group under the standard reaction conditions (70–80 °C). Lowering the reaction temperature to 60 °C allowed the reaction to proceed smoothly affording a 52% yield of **20**. However the corresponding reaction with iminium salt **5** was unsuccessful, presumably due to the relatively low solubility of **5** in $Cl(CH_2)_2Cl$ at 60 °C.

The reaction sequence was also successful using the corresponding BF_2 complex derived from a 2′-hydroxypropiophenone in contrast to literature reports that propiophenone itself is unreactive with phosgeniminium salts (**22, 23**).[7b] In these cases, it was necessary to perform the aqueous hydrolysis of the initial β-chlorovinylogous amide–BF_2 adducts at 60 °C (CH_3CN, 5 min) to avoid significant conversion of the 2-aminochromone products to their corresponding 4-hydroxycoumarins. The increased acid lability associated with this series may be explained by the unfavorable steric interaction between the 3-methyl and 2-amino substituents in the protonated chromone.

In the course of developing this 2-aminochromone synthesis, we observed that the product composition varied dramatically when alternative conditions were employed for the hydrolysis of the β-chlorovinylogous amide–BF_2 complex **9** (Chart I). For example, hydrolysis of **9** with 1:1 saturated $NaHCO_3/CH_3CN$ (50 °C, 1 h) yielded a 2:1 ratio (82%) of **10** and β-keto amide **24**, along with 8% of **25**. Increasing the basicity of the reaction with 2 N NaOH created further erosion of 2-aminochromone formation with **24** produced as the major product. When reaction times were increased under these conditions, 4-hydroxycoumarin (**25**) was formed at the expense of β-keto amide **24**. Control experiments indicated that **10** was stable to these basic hydrolysis conditions while **24** decomposed to **25** under both acidic and basic conditions (faster under acidic conditions). These results have led us to propose the mechanism outlined in Scheme IV for the hydrolysis of **9**. Under acidic conditions, the BF_2 complex of **9** appears to be hydrolyzed prior to displacement of the chlorine and the resulting intermediate **26** immediately cyclizes to the product chromone. In contrast, under increasingly more basic conditions, displacement of chlorine becomes more competitive affording the corresponding β-hydroxyvinylogous amide–BF_2 complex **27**[13] which, upon cleavage of the BF_2 complex, affords β-keto amide **24**.

In summary, we have developed a novel method for the

(9) (a) Cram, D. J. *J. Am. Chem. Soc.* **1949**, *71*, 3953. (b) Schiemenz, G. P.; Schmidt, U. *Justus Liebigs Ann. Chem.* **1982**, 1509. (c) Daniel, D. S.; Heseltine, D. W. U.S. Patent 3,567,439, 1971.

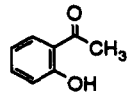
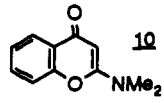
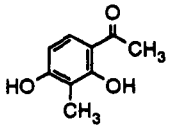
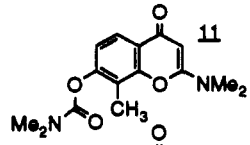
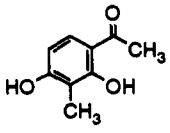
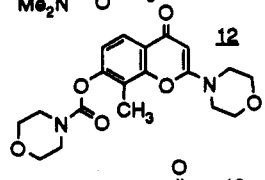
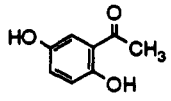
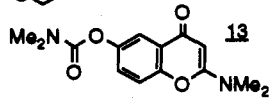
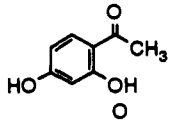
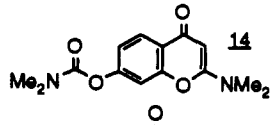
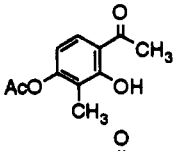
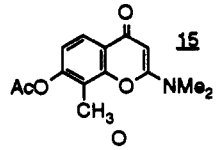
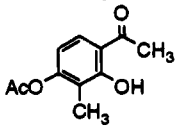
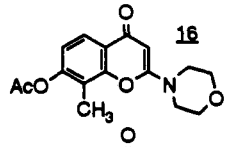
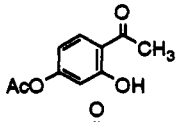
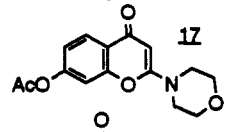
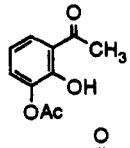
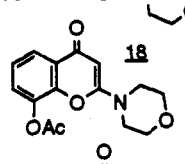
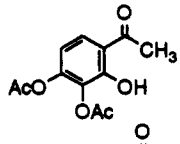
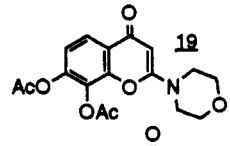
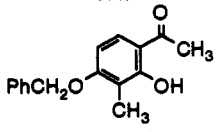
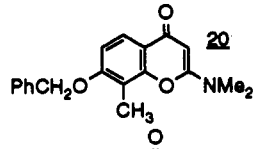
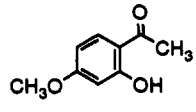
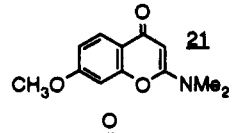
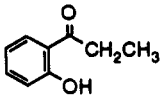
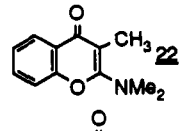
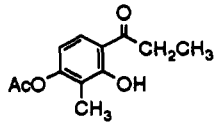
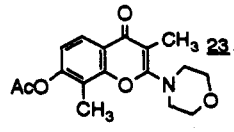
(10) (a) VanAllan, J. A.; Reynolds, G. A. *J. Heterocycl. Chem.* **1969**, *6*, 29. (b) Reynolds, G. A.; VanAllan, J. A. *J. Heterocycl. Chem.* **1969**, *6*, 375. (c) Reynolds, G. A.; VanAllan, J. A.; Seidel, A. K. *J. Heterocycl. Chem.* **1979**, *16*, 369.

(11) The ^{1}H NMR spectrum of **9** indicated a 16:1 ratio of geometric isomers. The stereochemistry of the major isomer was not determined.

(12) Hydrolysis of the β-chlorovinylogous amide–BF_2 complex **9** can also be carried out using methanol (rt, 24 h or 50 °C, 1 h) to afford 2-aminochromone **10** in 96% yield; see Chart I and the Experimental Section.

(13) An independent synthesis of the β-hydroxyvinylogous amide–BF_2 complex **27** indicates that the amide portion of this molecule exists in the enol form (Morris, J.; Fang, Y.; Wishka, D. G., manuscript in preparation).

Table I. Synthesis of 2-Aminochromones

2′-hydroxyacetophenone	iminium salt	method[a]	% yield BF_2 complex	reaction conditions	% yield chromone	product
	6	A	-	80°C, 2 h	56%	 10
		B	60%	reflux, 3.5 h	78%	
	6	A	-	reflux, 3.5 h	49%	 11
		B	53%	80°C, 2.5 h	79%	
	5	A	-	70°C, 3 h	44%	 12
		B	53%	70°C, 3 h	74%	
	6	A	-	reflux, 3.5 h	53%	 13
	6	A	-	reflux, 3.5 h	76%	 14
	6	B	86%	65°C, 4 h	61%	 15
	5	B	86%	70°C, 3 h	50%	 16
	5	B	93%	70°C, 4 h	50%	 17
	5	B	80%	70°C, 4 h	50%	 18
	5	B	90%	70°C, 24 h	45% + 19% bis-phenol	 19
	6	B	97%	60°C, 24 h	52%	 20
	6	B	93%	reflux, 3 h	64%	 21
	6	B	58%	reflux, 3 h	40%	 22
	5	B	90%	60°C, 3 h	51%	 23

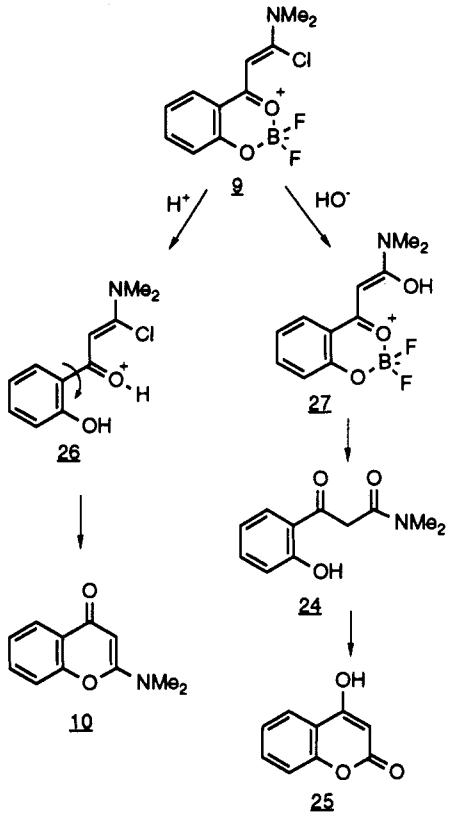
[a] Method A: in situ addition of BF_3-OEt_2. Method B: preformed BF_2 complex.

synthesis of antiplatelet 2-aminochromones making use of the reaction of 2′-hydroxyacetophenone–BF_2 complexes with phosgeniminium chlorides. This procedure efficiently produces the 2-aminochromone in good yield, without the need for chromatographic purification.

Experimental Section

IR spectra were taken as a Nujol mull (unless otherwise in-

Scheme IV



dicated). ^1H and ^{13}C NMR spectra were obtained in $CDCl_3$ (unless otherwise indicated) at 300 MHz. Melting points are corrected. Thin-layer chromatography was performed on Merck precoated glass TLC plates with silica gel 60-F254 and stained with a solution of 75 g of ammonium molybdate, 2.5 g of ceric sulfate, and 500 mL of 10% H_2SO_4 (V/V). Column chromatography was performed with Merck silica gel 60 (230–400 mesh).

4-Morpholinecarbodithioic Acid, Methyl Ester. A mixture containing 250 mL of H_2O, morpholine (50.1 mL, 0.57 mol), and CS_2 (34.5 mL, 0.57 mol) was mechanically stirred and treated dropwise with a solution of NaOH (24.0 g, 0.60 mol) in 200 mL of H_2O. The reaction mixture was stirred at 23 °C until homogeneous (3 h), cooled to 0 °C, and treated with dimethyl sulfate (54.3 mL, 0.57 mol) dropwise. The thick white slurry was stirred for 30 min at 0 °C, diluted with 500 mL of H_2O, and filtered. The product was washed thoroughly with fresh H_2O and dried in vacuo at 35 °C for 40 h to provide 96.2 g (95%) of the dithiocarbamate as a white solid: mp 80–81 °C; ^1H NMR δ 2.68 (s, 3), 3.77 (m, 4), 4.20 (bs, 4); ^{13}C NMR δ 19.7, 50.3, 66.1, 198.4; R_f 0.54, 50% EtOAc/hexanes; IR 1448, 1424, 1265, 1116, 1042 cm^{-1}. Anal. Calcd for $C_6H_{11}NOS_2$: C, 40.65; H, 6.25; N, 7.90; Found: C, 40.92; H, 6.10; N, 8.09.

4-(Dichloromethylene)morpholinium Chloride (5). A predried solution ($MgSO_4$) of methyl 4-morpholinecarbodithioate (69.5 g, 0.392 mol) in 1 L of CH_2Cl_2 was treated with a steady stream of Cl_2 gas for 110 min. **CAUTION:** A mild exotherm was observed after 1 h. The reaction mixture was stirred for 1 h at ambient temperature, and the precipitated iminium salt was collected on a 350-mL pressure/drying filter under a steady stream of argon. The salt was washed with 1 L of CH_2Cl_2 and dried under a stream of argon to provide 80.18 g of 5 (100%): mp 165–167 °C; ^1H NMR δ 3.64–3.37 (m, 4); ^{13}C NMR δ 46.6, 48.8, 66.2, 66.5, 148.1.

Reaction of 2′-Hydroxyacetophenone (4) with *N,N*-Dimethyldichloromethyleniminium Chloride (6). A mixture of 1.36 g (10.0 mmol) of 4 and 3.25 g (20.0 mmol) of 6 in 30 mL of $Cl(CH_2)_2Cl$ was refluxed for 4 h. The cooled reaction mixture was treated with H_2O (30 mL), and the organics were washed with saturated $NaHCO_3$, dried over anhyd $MgSO_4$, and evaporated. The crude material (2.58 g) was chromatographed on silica gel (15% EtOAC/hexanes) to afford 2.29 g of a 2.4:1 mixture of 2-(1-chloroethenyl)phenyl *N,N*-dimethylcarbamate (7) and 2-(1,1-dichloroethyl)phenyl *N,N*-dimethylcarbamate, respectively. A partial separation of these compounds was achieved by trituration with hexane. Vinyl chloride 7: ^1H NMR δ 7.46 (m, 1), 7.36 (m, 1), 7.21 (m, 2), 5.63 (d, J = 1.3 Hz, 1), 5.51 (d, J = 1.3 Hz, 1), 3.12 (s, 3), 3.02 (s, 3); ^{13}C NMR δ 154.3, 148.3, 135.7, 131.7, 130.0, 129.9, 125.3, 123.5, 117.3, 36.8, 36.5; IR 1727, 1388, 1202, 1165 cm^{-1}; HRMS calcd for $C_{11}H_{12}NO_2Cl - H_1$ 224.0478, found 224.0478. Dichloro compound: mp 120–121 °C (EtOAc); ^1H NMR δ 7.62 (m, 1), 7.42 (m, 1), 7.22 (m, 2), 3.23 (s, 3), 3.05 (s, 3), 2.62 (s, 3); ^{13}C NMR δ 154.1, 149.1, 134.8, 130.6, 125.6, 125.1, 124.6, 84.1, 38.0, 37.0, 36.7; IR 1722, 1391, 1162 cm^{-1}. Anal. Calcd for $C_{11}H_{13}NO_2Cl_2$: C, 50.40; H, 5.00; N, 5.34. Found: C, 50.45; H, 4.77; N, 5.37.

1-(2-Hydroxyphenyl)ethanone, Boron Difluoride Complex (8). A solution of 2′-hydroxyacetophenone (4) (2.72 g, 20.0 mmol) in 20 mL of Et_2O was treated with 2.62 mL (20.0 mmol) of $BF_3{\cdot}OEt_2$ and stirred at rt for 1 h. The mixture was filtered and washed well with ether to give 2.15 g (58%) of 8 as a yellow solid: mp 143–144.5 °C (lit.[9c] mp 146–147 °C); ^1H NMR δ 7.80 (m, 2), 7.09 (m, 2), 2.89 (s, 3); ^{13}C NMR δ 203.7, 164.0, 143.9, 131.0, 121.3, 121.0, 117.2, 23.4; IR 1621, 1537, 1285, 1068, 768 cm^{-1}. Anal. Calcd for $C_8H_7BF_2O_2$: C, 52.24; H, 3.84; F, 20.66. Found: C, 51.88; H, 3.78; F, 20.78.

3-Chloro-3-(*N,N*-dimethylamino)-1-(2-hydroxyphenyl)-propenone, Boron Difluoride Complex (9). A suspension of 8 (22.5 g, 122 mmol) and *N,N*-dimethyldichloromethyleniminium chloride (6, 19.8 g, 122 mmol) in 400 mL of $Cl(CH_2)_2Cl$ was heated at 80 °C for 2 h. The mixture was cooled to 0 °C, and the solid was filtered and washed with cold $Cl(CH_2)_2Cl$ and Et_2O to afford 29.4 g (88%) of 9 as a yellow solid: mp 180–182 °C; ^1H NMR (CD_3CN) δ 7.76 (m, 1), 7.45 (m, 1), 6.68 (m, 2), 6.05 (s, 1), 3.40 (s, 6); R_f 0.66, 10% MeOH/CH_2Cl_2; IR 1611, 1566, 1540, 1494, 1311, 1259 cm^{-1}. Anal. Calcd for $C_{11}H_{11}BClF_2NO_2$: C, 48.31; H, 4.06; N, 5.12; Cl, 12.96; F, 13.90. Found: C, 48.05; H, 4.09; N, 5.10; Cl, 13.11; F, 13.86.

General Procedure for the Synthesis of 2-Aminochromones. Method A. A 0.25 M solution of the 2′-hydroxyacetophenone in $Cl(CH_2)_2Cl$ was treated with 2–3 equiv of $BF_3{\cdot}OEt_2$ at rt for 30 min. The mixture was treated with 2 equiv of the phosgeniminium salt and heated at 70–80 °C for 3.5 h. The cooled reaction mixture was diluted with Et_2O and filtered. The yellow solid was washed well with Et_2O, suspended in CH_3CN (4–5 mL/g), and cooled to 0 °C, and H_2O (0.4–0.5 mL/g) was added. The mixture was stirred at rt for 24 h, evaporated to dryness, carefully taken up in saturated $NaHCO_3$, and extracted three times with EtOAc or CH_2Cl_2. The combined organics were washed once with saturated NaCl, dried over $MgSO_4$, and evaporated to afford the crude product. Recrystallization from EtOAc or CH_2Cl_2/MeOH afforded the purified chromone.

Method B. A 0.1–0.5 M solution/suspension of the 2′-hydroxyacetophenone in Et_2O was treated with 1–2 equiv of $BF_3{\cdot}OEt_2$. After 1–18 h the solid was filtered and washed well with Et_2O to afford the BF_2 complex. A 0.25 M solution/suspension of the 2′-hydroxyacetophenone–BF_2 complex and 1–2 equiv of the phosgeniminium salt in $Cl(CH_2)_2Cl$ was heated at 60–80 °C for 2–18 h. The cooled reaction mixture was filtered to afford the β-chlorovinylogous amide–BF_2 complex. The solid was washed well with cold $Cl(CH_2)_2Cl$ and Et_2O and suspended in 10–15 mL/g of CH_3CN. The cooled (0 °C) mixture was treated with 1–1.5 mL/g of H_2O and stirred at ambient temperature overnight. Alternatively, the mixture could be heated at 40–50 °C for 20–30 min. Workup as reported for method A afforded the purified chromone.

2-(Dimethylamino)-4*H*-1-benzopyran-4-one (10): method A, yield 3.19 g (56%); method B, BF_2 complex yield 3.29 g (60%); ^1H NMR δ 7.79 (m, 2), 7.09 (m, 2), 2.89 (s, 3); ^{13}C NMR δ 203.7, 164.4, 143.8, 131.0, 121.0, 120.9, 117.2, 23.3. Chromone: yield 2.62 g (78%); mp 122–123.5 °C; ^1H NMR δ 8.13 (m, 1), 7.52 (m, 1), 7.29 (m, 2), 5.38 (s, 1), 3.08 (s, 6); ^{13}C NMR δ 176.3, 162.8, 153.5, 131.7, 125.3, 124.4, 122.7, 116.1, 85.9, 37.3; IR 1628, 1604, 1442, 1380 cm^{-1}. Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.71; H, 5.85; N, 7.39.

2-(Dimethylamino)-8-methyl-4-oxo-4*H*-1-benzopyran-7-yl dimethylcarbamate (11): method A, yield 1.94 g (49%); method B, boron complex yield 5.11 g (53%); ^1H NMR δ 7.54 (d, J = 9.0

Hz, 1), 6.54 (d, J = 9.0 Hz, 1), 2.73 (s, 3), 2.16 (s, 3). Chromone: yield 1.15 g (79%); mp 191–192 °C; ^{1}H NMR δ 8.01 (d, J = 8.7 Hz, 1), 7.07 (d, J = 8.7 Hz, 1), 5.40 (s, 1), 3.16 (s, 3), 3.12 (s, 6), 3.04 (s, 3), 2.28 (s, 3); ^{13}C NMR δ 176.5, 163.1, 154.0, 152.6, 152.5, 123.3, 120.2, 119.1, 118.5, 85.8, 37.6, 36.9, 36.5, 9.2; IR 1725, 1627, 1595, 1401, 1170 cm^{-1}. Anal. Calcd for $C_{15}H_{18}N_2O_4$: C, 62.06; H, 6.25; N, 9.65. Found: C, 61.91; H, 5.91; N, 9.74.

8-Methyl-2-(4-morpholinyl)-4-oxo-4*H*-1-benzopyran-7-yl 4-morpholinecarboxylate (12): method A, yield 0.98 g (44%); method B, boron complex same as for **11**. Chromone: yield 14.1 g (74%); mp 232–234 °C; ^{1}H NMR δ 2.27 (s, 3), 3.51 (m, 4), 5.59 (bs, 4), 3.78 (m, 4), 3.85 (m, 4), 5.55 (s, 1), 7.10 (d, 1), 8.00 (d, 1); ^{13}C NMR δ 9.28, 44.0, 44.6, 44.7, 65.8, 66.5, 86.9, 118.6, 119.2, 120.2, 123.3, 152.3, 152.6, 162.7, 176.7; IR 1706, 1630, 1569, 1457, 1112 cm^{-1}. Anal. Calcd for $C_{19}H_{22}N_2O_6$: C, 60.95; H, 5.92; N, 7.48. Found: C, 61.35; H, 6.03; N, 7.79.

2-(Dimethylamino)-4-oxo-4*H*-1-benzopyran-6-yl dimethylcarbamate (13): method A, yield 2.16 g (53%); mp 179.5–180 °C; ^{1}H NMR δ 7.82 (m, 1), 7.31 (m, 2), 5.35 (s, 1), 3.10 (s, 3), 3.06 (s, 6), 3.01 (s, 3); ^{13}C NMR δ 175.6, 163.0, 154.7, 150.6, 148.1, 126.0, 123.5, 117.6, 117.0, 85.7, 37.4, 36.7, 36.4; IR 1726, 1625, 1575, 1457, 1284, 1180 cm^{-1}. Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.53; H, 6.00; N, 9.94.

2-(Dimethylamino)-4-oxo-4*H*-1-benzopyran-7-yl dimethylcarbamate (14): method A, yield 6.30 g (76%); mp 158–159 °C; ^{1}H NMR δ 8.12 (d, J = 8.6 Hz, 1), 7.20 (d, J = 2.1 Hz, 1), 7.08 (dd, J = 2.1, 8.6 Hz, 1), 5.34 (s, 1), 3.11 (s, 3), 3.05 (s, 6), 3.03 (s, 3); ^{13}C NMR δ 175.8, 163.0, 154.0, 153.8, 126.2, 119.9, 118.3, 109.5, 85.7, 37.3, 36.6, 36.4; IR 1731, 1721, 1619, 1565, 1443, 1176 cm^{-1}. Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.75; H, 5.97; N, 9.98.

7-(Acetyloxy)-2-(dimethylamino)-8-methyl-4*H*-1-benzopyran-4-one (15): method B, boron complex yield 2.71 g (86%); ^{1}H NMR δ 2.14 (s, 3), 2.38 (s, 3), 2.85 (s, 3), 6.81 (d, 1), 7.66 (d, 1); ^{13}C NMR δ 8.7, 20.7, 23.3, 116.2, 122.5, 128.9, 160.8, 164.4, 167.5, 201.9. Chromone: yield 0.80 g (61%); mp 179–180.5 °C; ^{1}H NMR δ 2.24 (s, 3), 2.37 (s, 3), 3.11 (s, 6), 5.39 (s, 1), 7.03 (d, 1), 8.03 (d, 1); ^{13}C NMR δ 9.2, 20.6, 37.4, 85.5, 118.3, 118.4, 120.6, 123.3, 151.5, 152.2, 162.9, 168.6, 176.0; R_f 0.58, 10% MeOH/CH_2Cl_2; IR 1750, 1638, 1582, 1454, 1216 cm^{-1}. Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.76; N, 5.36. Found: C, 64.08; H, 5.94; N, 5.36.

7-(Acetyloxy)-8-methyl-2-morpholinyl-4*H*-1-benzopyran-4-one (16). Boron complex same as for **15**. Chromone: yield 0.77 g (50%); mp 201–201.5 °C; ^{1}H NMR δ 2.26 (s, 3), 2.38 (s, 3), 3.49 (m, 4), 3.84 (m, 4), 5.48 (s, 1), 7.04 (d, 1), 8.00 (d, 1); ^{13}C NMR δ 9.3, 20.6, 44.6, 65.8, 86.9, 118.4, 118.8, 120.6, 123.4, 151.8, 152.5, 162.6, 168.5, 176.7; IR 1757, 1650, 1584, 1225 cm^{-1}. Anal. Calcd for $C_{16}H_{17}NO_5$: C, 63.36; H, 5.65; N, 4.62. Found: C, 63.20; H, 5.84; N, 4.63.

7-(Acetyloxy)-2-morpholinyl-4*H*-1-benzopyran-4-one (17): method B, boron complex yield 7.41 g (93%); ^{1}H NMR δ 2.35 (s, 3), 2.85 (s, 3), 6.87 (m, 2), 7.80 (m, 1). Chromone: yield 2.9 g (50%) after silica gel chromatography (3% MeOH/CH_2Cl_2) of the mother liquor after recrystallization; mp 145.5–146.5 °C; ^{1}H NMR δ 2.34 (s, 3), 3.49 (m, 4), 3.82 (m, 4), 5.47 (s, 1), 7.07 (d, 1), 7.15 (d, 1), 8.15 (d, 1); ^{13}C NMR δ 21.0, 44.6, 65.8, 87.1, 109.6, 118.5, 120.7, 126.7, 153.3, 153.8, 162.7, 168.6, 176.3; R_f 0.54, 10% MeOH/CH_2Cl_2; IR 1761, 1640, 1572, 1456, 1223 cm^{-1}. Anal. Calcd for $C_{15}H_{15}NO_5$: C, 62.28; H, 5.23; N, 4.84. Found: C, 62.23; H, 5.26; N, 4.93.

8-(Acetyloxy)-2-morpholinyl-4*H*-1-benzopyran-4-one (18): method B, boron complex yield 1.33 g (80%, 90% pure); ^{1}H NMR δ 2.36 (s, 3), 2.90 (s, 3), 7.03 (m, 1), 7.56 (m, 1) 7.70 (m, 1); ^{13}C NMR δ 20.4, 23.8, 117.2, 120.1, 127.2, 128.3, 135.7, 140.9, 168.1, 204.4. Chromone: yield 0.76 g (50%); mp 210–212 °C; ^{1}H NMR δ 2.38 (s, 3), 3.45 (m, 4), 3.82 (m, 4), 5.50 (s, 1), 7.33 (m, 2), 8.02 (m, 1); ^{13}C NMR δ 20.5, 44.6, 65.7, 87.4, 122.9, 124.3, 125.4, 137.9, 145.6, 161.9, 167.9, 176.3; R_f 0.53, 10% MeOH/CH_2Cl_2; IR 1757, 1619, 1409, 1248 cm^{-1}. Anal. Calcd for $C_{15}H_{15}NO_5$ (0.09% H_2O found): C, 62.22; H, 5.23; N, 4.83. Found: C, 61.83; H, 5.13; N, 4.78.

7,8-Bis(acetyloxy)-2-(4-morpholinyl)-4*H*-1-benzopyran-4-one (19): method B, boron complex yield 17.0 g (90%, 80% pure); ^{1}H NMR δ 7.69 (d, J = 9.1 Hz, 1), 6.95 (d, J = 9.1 Hz, 1), 2.87 (s, 3), 2.36 (s, 3), 2.33 (s, 3). Chromone: yield 8.94 g (45%), yield of bisphenol after acidification of the aqueous layer 2.82 g (19%); mp 231.5–233 °C; ^{1}H NMR δ 8.03 (d, J = 8.7 Hz, 1), 7.17 (d, J = 8.7 Hz, 1), 5.56 (s, 1), 3.81 (m, 4), 3.45 (m, 4), 2.36 (s, 3), 2.33 (s, 3); ^{13}C NMR δ 175.6, 167.8, 166.8, 162.2, 146.8, 145.6, 130.6, 122.9, 121.8, 119.3, 87.3, 65.7, 44.7, 20.5, 20.1; IR 1776, 1638, 1622, 1265 cm^{-1}. Anal. Calcd for $C_{17}H_{17}NO_7$: C, 58.79; H, 4.93; N, 4.03. Found: C, 58.62; H, 4.99; N, 4.09. Phenol: mp >300 °C; ^{1}H NMR (DMSO-d_6) δ 7.23 (d, J = 8.5 Hz, 1), 6.80 (d, J = 8.5 Hz, 1), 5.33 (s, 1), 3.70 (m, 4), 3.49 (m, 4); ^{13}C NMR 177.4, 163.9, 151.1, 145.9, 134.1, 117.5, 116.3, 114.4, 87.0, 67.1, 46.1; IR 1631, 1615, 1576, 1426, 1246 cm^{-1}. Anal. Calcd for $C_{13}H_{13}NO_5$ (4.48% H_2O found): C, 56.65; H, 5.25; N, 5.08. Found: C, 56.25; H, 5.21; N, 4.98.

2-(Dimethylamino)-8-methyl-7-(phenylmethoxy)-4*H*-1-benzopyran-4-one (20): method B, boron complex yield 8.87 g (97%, 90% pure); ^{1}H NMR δ 7.62 (d, J = 9.3 Hz, 1), 7.39 (m, 5), 6.69 (d, J = 9.3 Hz, 1), 5.28 (s, 2), 2.73 (s, 3), 2.19 (s, 3). Chromone: yield 0.73 g (52%); mp 165–166 °C; ^{1}H NMR δ 7.98 (d, J = 8.7 Hz, 1), 7.38 (m, 5), 6.96 (d, J = 8.7 Hz, 1), 5.34 (s, 1), 5.17 (s, 2), 3.13 (s, 6), 2.33 (s, 3); ^{13}C NMR 176.8, 163.1, 159.4, 152.8, 136.6, 128.6, 128.1, 127.2, 123.7, 116.2, 113.3, 108.8, 85.2, 70.5, 37.5, 8.5; R_f 0.44, 10% MeOH/CH_2Cl_2; IR 1617, 1594, 1424, 1268, 1192 cm^{-1}. Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.37; H, 6.39; N, 4.49.

2-(Dimethylamino)-7-methoxy-4*H*-1-benzopyran-4-one (21): method B, BF_2 complex yield 5.95 g (93%); ^{1}H NMR δ 7.64 (d, J = 9.2 Hz, 1), 6.58 (dd, J = 9.2, 2.1 Hz, 1), 6.45 (d, J = 2.1 Hz, 1), 3.93 (s, 3), 2.73 (s, 3); ^{13}C NMR δ 197.2, 172.4, 167.7, 132.7, 113.2, 111.1, 101.2, 56.5, 22.5. Chromone: yield 1.40 g (64%); mp 175–175.5 °C; ^{1}H NMR δ 8.06 (d, J = 8.8 Hz, 1), 6.89 (dd, J = 8.8, 2.3 Hz, 1), 6.74 (d, J = 2.3 Hz, 1), 5.35 (s, 1), 3.88 (s, 3), 3.09 (s, 6). ^{13}C NMR δ 176.4, 163.1, 162.8, 155.1, 126.8, 116.4, 112.5, 100.0, 85.5, 55.7, 37.5; R_f 0.40, 10% MeOH/CH_2Cl_2; IR 1625, 1599, 1564, 1433, 1261 cm^{-1}. Anal. Calcd for $C_{12}H_{13}NO_3$ (0.62% H_2O found): C, 65.33; H, 6.01; N, 6.35. Found: C, 64.99; H, 5.93; N, 6.23.

7-(Acetyloxy)-3,8-dimethyl-2-(4-morpholinyl)-4*H*-1-benzopyran-4-one (23): method B, BF_2 complex yield 6.8 g (90%); ^{1}H NMR δ 1.23 (t, J = 7 Hz, 3), 2.13 (s, 3), 2.37 (s, 3), 3.10 (q, J = 7 Hz, 2), 6.79 (d, J = 9 Hz, 1), 7.70 (d, J = 9 Hz, 1); ^{13}C NMR δ 9.4, 10.2, 20.8, 29.5, 113.4, 116.3, 122.5, 128.4, 160.4, 164.3, 167.7, 205.6. A suspension of the BF_2 complex (1.05 g, 5.13 mmol) and **5** (1.25 g, 4.63 mmol) in 12 mL of $Cl(CH_2)_2Cl$ was warmed to 60 °C for 3 h. The cooled mixture was evaporated and taken up in 12 mL of CH_3CN. Upon warming to 60 °C, the mixture was diluted with 10 mL of H_2O and stirred for 5 min. The mixture was immediately neutralized with 25 mL of saturated $NaHCO_3$, and the organics were removed in vacuo. The mixture was extracted four times with 25 mL of CH_2Cl_2, and the combined organics were dried ($MgSO_4$) and evaporated to afford 0.75 g (51%) of the chromone; mp 142.5–144.5 °C; ^{1}H NMR δ 2.03 (s, 3), 2.25 (s, 3), 3.43 (m, 4), 3.85 (m, 4), 7.03 (d, J = 8.7 Hz, 1), 8.05 (d, J = 8.7 Hz, 1); ^{13}C NMR δ 9.1, 10.8, 20.8, 48.5, 66.7, 102.6, 118.8, 118.9, 120.3, 123.9, 151.9, 152.6, 162.0, 168.7, 178.4; R_f 0.66, 10% MeOH/CH_2Cl_2; IR 1761, 1625, 1572, 1408, 1209 cm^{-1}. Anal. Calcd for $C_{17}H_{19}NO_5$: C, 64.34; H, 6.05; N, 4.41. Found: C, 64.20; H, 6.32; N, 4.36.

2-(Dimethylamino)-3-methyl-4*H*-1-benzopyran-4-one (22): method B, BF_2 complex yield 10.4 g (58%); ^{1}H NMR δ 7.80 (m, 2), 7.06 (m, 2), 3.27 (q, J = 7.3 Hz, 2), 1.42 (t, J = 7.3 Hz, 3); ^{13}C NMR δ 206.9, 163.9, 143.5, 130.3, 121.4, 120.9, 116.0, 29.5, 9.1. The reaction was carried out as for **23**. The chromone yield after silica gel chromatography (5% MeOH/CH_2Cl_2) was 0.82 g (40%); mp 102–102.5 °C; ^{1}H NMR δ 8.18 (m, 1), 7.53 (m, 1), 7.31 (m, 2), 3.09 (s, 6), 2.10 (s, 3); ^{13}C NMR δ 177.9, 162.9, 153.1, 131.6, 125.4, 124.0, 122.1, 116.2, 98.8, 40.1, 11.0, 10.9; R_f 0.50, 10% MeOH/CH_2Cl_2; IR 1610, 1550, 1394, 1167, 763 cm^{-1}. Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.59; H, 6.39; N, 6.77.

Hydrolysis of BF_2 Complex 9. Method A: A suspension of BF_2 complex **9** (273 mg, 1.0 mmol) in 5 mL of CH_3CN and 1 mL of H_2O was stirred at 50 °C for 1 h. The solvent was evaporated, and the solid was taken up in saturated $NaHCO_3$ and extracted three times with CH_2Cl_2. The combined organics were washed with brine, dried over anhyd Na_2SO_4, and evaporated to give 171 mg (90%) of **10**. The aqueous layer was acidified with 10% HCl and extracted three times with CH_2Cl_2. The combined organics were evaporated to afford 20.9 mg of **25**. **10**: Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.58; H, 5.72; N, 7.44. Method B: To a prewarmed (50 °C) mixture of 10 mL

of CH_3CN and 10 mL of saturated $NaHCO_3$ was added **9** (273 mg, 1.00 mmol). The mixture was stirred at 50 °C for 1 h. Workup as in method A afforded 161 mg (82% mass) of a 2:1 mixture of **10:24** (determined by ^1H NMR). Acidification and extraction of the aqueous layer gave 13 mg (8%) of **25**. Method C: To a prewarmed (50 °C) mixture of 10 mL of CH_3CN and 10 mL of 2 N NaOH was added **9** (273 mg, 1.00 mmol). The mixture was stirred at 50 °C for 30 min, evaporated, and neutralized with 10% HCl. Workup as in method A produced 187 mg (92% mass) of a mixture of a 1:3.7 mixture of **10:24**. Acidification and extraction of the aqueous layer gave 13 mg (8%) of **25**. Method D: A solution of **9** (273 mg, 1.0 mmol) in 20 mL of methanol was stirred at 50 °C for 30 min. Workup as in method A afforded 182 mg (96%) of **10**. β-Keto amide **24** was cleanly isolated via 2 N NaOH extraction of a CH_2Cl_2 solution of a mixture of **10** and **24** followed by reacidification and extraction of the aqueous layer. **24**: mp 67.5–68.5 °C; ^1H NMR δ 11.96 (s, 1), 7.83 (m, 1), 7.49 (m, 1), 6.96 (m, 2), 4.13 (s, 2), 3.08 (s, 3), 3.02 (s, 3); ^{13}C NMR δ 199.8, 166.3, 162.5, 136.9, 130.7, 119.2, 118.4, 116.4, 45.5, 38.0, 35.5; R_f 0.53, 10% MeOH/CH_2Cl_2; IR 1630, 1452, 1257, 1147, 766 cm^{-1}. Anal. Calcd for $C_{11}H_{13}NO_3$: C, 63.76; H, 6.32; N, 6.76. Found: C, 63.42; H, 6.24; N, 6.83. **25**: mp 214–214.5 °C (lit.[14] mp 216 °C dec); ^1H NMR (acetone-d_6) δ 11.40 (s, 1), 8.08 (m, 1), 7.84 (m, 1), 7.52 (m, 2), 5.87 (s, 1); ^{13}C NMR (acetone-d_6) δ 165.7, 162.3, 154.8, 133.2, 124.4, 123.9, 117.0, 116.5, 92.3; IR 1704, 1611, 1313, 1277 cm^{-1}. Anal. Calcd for $C_9H_6O_3$ (0.45% H_2O found): C, 66.37; H, 3.76. Found: C, 66.10; H, 3.73.

(14) Aldrich Chemical Co.

Reactions of Ethyl Phosphites with β-Nitrostyrenes. The Role of Nitrosoalkenes as Intermediates

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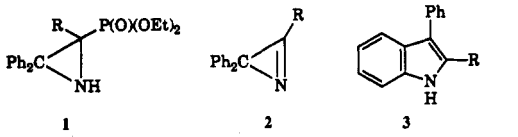
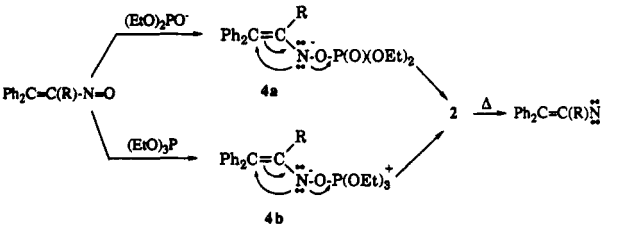
3-Phenyl-2-substituted-indoles are formed in high yields in the reaction of $Ph_2C{=}C(R)NO_2$ (R = H, Me, Ph) with $(EtO)_3P$ at 150 °C while reaction with $(EtO)_2PO^-/(EtO)_2P(O)H$ at room temperature forms the aziridines **1** with R = H, Me, Ph. 2,2-Diphenyl-3-substituted-2*H*-azirines formed by deoxygenation of the Michael-type adducts are postulated as intermediates. Reactions of $PhCH{=}C(R)NO_2$ (R = H, Me, Ph) with $(EtO)_3P$ at 150 °C or $(EtO)_2PO^-/(EtO)_2P(O)H$ at room temperature give products resulting from the addition of the phosphorus nucleophile at the benzylidene carbon atom. Evidence for the formartion of cyclic structures with pentacoordinated phosphorus atoms is presented for the reaction of $Ph_2C{=}C(Me)NO_2$ with $(EtO)_2PO^-/EtO)_2P(O)H$ and for $PhCH{=}C(R)NO_2$ (R = H, Me, Ph) with $(EtO)_3P$. The Michael-type adducts $PhCH[P(O)(OEt)_2]CH(R)NO_2$ (R = Me, Ph) undergo reaction upon treatment with aqueous base at 80–100 °C followed by acidification to yield the 3-(diethoxyphosphinyl)-2-R-*N*-hydroxyindoles. 4-(Diethoxyphosphinyl)-3-R-4*H*-1,2-benzoxazines (**13**, R = Me, Ph) are formed by reaction with 85% H_2SO_4 of the adducts of $PhCH{=}C(R)NO_2$ with $(EtO)_2PO^-$ (R = Me) or $(EtO)_3P$ (R = Ph).

We have previously reported that reactions of $(EtO)_2PO^-$ with $Ph_2C{=}CHNO_2$ or $Ph_2C[P(O)(OEt)_2]CH_2NO_2$ in Me_2SO or $(EtO)_2P(O)H$ solutions at room temperature yield the aziridine **1** (R = H), presumably formed via the 2*H*-azirine **2** (R = H).[1] Under similar conditions, $Ph_2C{=}C(SCMe_3)NO_2$ yielded **2** with R = *t*-BuS as the final product.[1] Heating $Ph_2C{=}C(R)NO_2$ at 150 °C in $(EtO)_3P$ formed the indoles **3** (R = H, *t*-BuS, PhS) in high yield, undoubtedly by a process involving the conversion of the azirine to the nitrene ($Ph_2C{=}C(R)\ddot{N}$:).[1] One possible deoxygenation process involves the intermediacy of nitrosoalkenes followed by reactions with $(EtO)_2PO^-$ or $(EtO)_3P$ to yield the reactive intermediates **4a** and **4b** (Scheme I) as precursors to the azirines. However, there is no direct evidence for the intermediacy of the nitrosoalkenes, and we will demonstrate that in several instances the key intermediates **4** are more reasonably formulated as arising from the deoxygenation of intermediate Michael-type adducts. Reactions of $PhCH{=}CHNO_2$ with $(EtO)_2PO^-$ (room temperature) or $(EtO)_3P$ (25–150 °C) fail to produce azirine or nitrene derived products and instead yield only products derived from other reactions of the initial Michael-type adducts.[1,2] To explore further the possibilities of azirine/nitrene formation and whether the addition of the phosphorus nucleophile precedes or follows deoxygenation of the nitro group, the reactions of **5** and **6** with R = Me and Ph have been examined.



Scheme I



$Ph_2C{=}C(R)NO_2$: **5**, a, R=H; b, R=Me; c, R=Ph; d, R=OPh

$PhCH{=}C(R)NO_2$: **6**, a, R=H; b, R=Me; c, R=Ph

Results and Discussion

1-Nitro-2,2-diphenylethylenes. Compounds **5b,c** gave reactions consistent with those previously observed for **5a**.[1] Heating the nitroalkenes in $(EtO)_3P$ solution at 150 °C formed the corresponding indoles (**3**, R = H, Me, Ph, OPh) in high yield although at room temperature there was no

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