3-Cuprio-2-pyrone: An Extraordinary Organocopper Reagent

Gary H. Posner,* Wayne Harrison, and David G. Wettlaufer

Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218

Received June 18, 1985

3-Cuprio-2-pyrone (1) was prepared via Scheme I and was treated with a very wide variety of typically S_N2- and S_N1-reactive substrates as well as with typical acyl electrophiles. The only substrates that reacted via pyrone transfer were some α-halo ethers, allylic bromides and mesylates, and a thiosulfonate ester. Reactions of isomeric allylic mesylates 8 and 11 and of geranyl bromide with cupriopyrone 1 provided important mechanistic information. These results are discussed in terms of cupriopyrone 1 coordinating with and activating the substrate toward S_N2' and/or S_N2 substitution. Cupriopyrone 1 is the least nucleophilic organocopper reagent known.

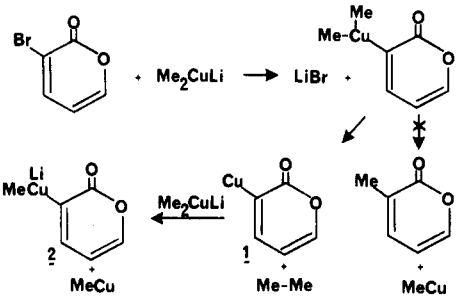
Typically, organocopper reagents are nucleophiles.[1] They have become very important and widely used, especially in nucleophilic substitution of diverse electrophiles[2] and in nucleophilic conjugate addition to multiple carbon–carbon bonds.[3] Several years ago, Marino reported the unusual reactivity of a 2-cuprioacrylate species failed to react with benzyl bromide but did react with allyl bromide,[5] and it also failed to undergo conjugate addition but did undergo carbonyl addition to 2-cyclohexenone. We have found a second example of this type of atypical pattern of reactivity for an organocopper reagent. We have explored in detail its behavior toward representative S_N2- and S_N1-reactive substrates in order to gain some understanding of its mechanism of action and its behavior on the nucleophilic–electrophilic reactivity scale. Our preliminary report on preparation of 3-cuprio-2-pyrone has just appeared in print.[6]

Results and Discussion

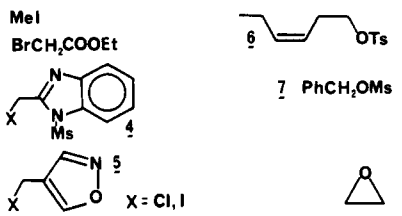
3-Bromo-2-pyrone reacted with 2 equiv of (dimethylcopper)lithium in an oxidative addition fashion presumably to give a copper(III) intermediate which could undergo reductive elimination in one or both of two modes (Scheme I). Because virtually no (i.e., <5%) 3-methyl-2-pyrone was detected, reductive elimination appeared to proceed only in the sense shown in Scheme I to form 3-cuprio-2-pyrone (1). In the presence of excess (dimethylcopper)lithium, cupriopyrone 1 could be transformed into mixed cuprate 2 and methylcopper (the typical yellow color of methylcopper was evident). Although the following discussion will refer to 3-cuprio-2-pyrone (1), we are not able at this time to distinguish unambiguously between organocopper species 1 and 2.[7]

3-Cuprio-2-pyrone (1) reacted within 4 h at 25 °C in diethyl ether with bromomethyl methyl ether and with chloromethyl benzyl ether to give the corresponding 3-

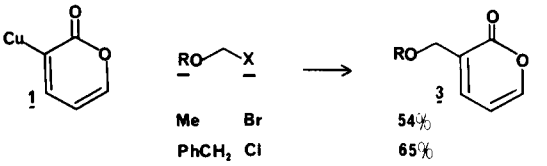
Scheme I



Scheme II

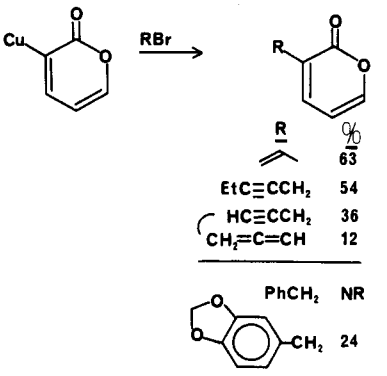


(alkoxymethyl)-2-pyrones 3 in 54% and 65% yields, respectively, after purification by preparative TLC (eq 1).



(1)

Under very much milder conditions, 3-cuprio-2-pyrone (1) reacted within 1 h at −78 °C in ether with allyl bromide (63% yield), with 1-bromo-2-pentyne (54%), and with propargyl bromide (48%) to give the corresponding coupling products (eq 2). The reaction with propargyl



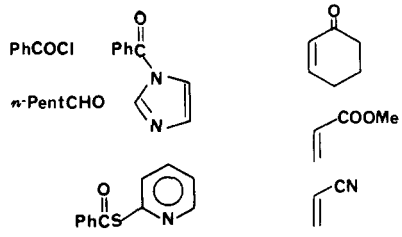
(2)

bromide was particularly revealing: $^1/_3$ of the substitution product was 3-*allenyl*-2-pyrone, which could not have been formed via a simple S_N2 type of reaction. Indeed, in general, organocopper reagents react with propargylic electrophiles to give allenic products, and propargylic–

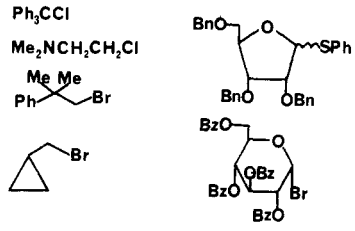
(1) Posner, G. H. "An Introduction to Synthesis Using Organocopper Reagents"; Wiley: New York, 1980.
(2) Posner, G. H. *Org. React. (N. Y.)* **1975**, *22*, 253.
(3) Posner, G. H. *Org. React. (N. Y.)* **1972**, *19*, 1.
(4) (a) Marino, J. P.; Floyd, D. M. *J. Am. Chem. Soc.* **1974**, *96*, 7138. (b) Marino, J. P.; Floyd, D. M. *Tetrahedron Lett.* **1975**, 3897. (c) Marino, J. P.; Linderman, R. J. *J. Org. Chem.* **1983**, *48*, 4621.
(5) For a similar reactivity pattern of cyanomethylcopper, see: Corey, E. J.; Kuwajima, I. *Tetrahedron Lett.* **1972**, 487.
(6) Posner, G. H.; Harrison, W. *J. Organomet. Chem.* **1985**, *285*, C27. See also Sokolovskaya, S. V.; Moldoranova, L. K. *Chem. Heterocycl. Compd. (Engl. Transl.)* **1979**, *15*, 142.
(7) Adding 3-bromo-2-pyrone to only 1 equiv of (dimethylcopper)-lithium at −78 °C in Et_2O caused appearance of a yellow color and essentially complete disappearance of the bromide by TLC analysis. Then adding 1 equiv of benzyl chloromethyl ether led to a 1:1 mixture of 3-[(benzyloxy)methyl]-2-pyrone (i.e., pyrone transfer) and benzyl ethyl ether (i.e., methyl transfer); only a minor amount of 3-methyl-2-pyrone was detected. Surprisingly, these results seem to support the major reactive intermediate being a dimethyl(3-pyronyl)copper(III) species.

0022-3263/85/1950-5041$01.50/0 © 1985 American Chemical Society

Scheme III



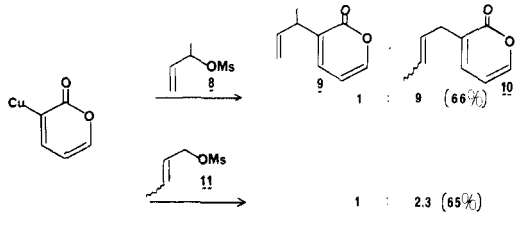
Scheme IV



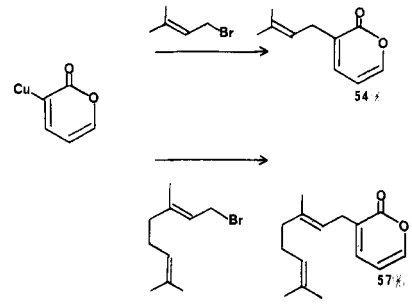
allenic copper species have been invoked as intermediates.[8] One additionally revealing pair of substrates shown in eq 2 are benzyl bromide and piperonyl bromide: as a truly extraordinary result, benzyl bromide failed to undergo pyrone transfer from 3-cuprio-2-pyrone (1) even at 25 °C for a prolonged time (12 h), but piperonyl bromide did react at 25 °C to produce a substitution product. This result would seem to support an S_N1 pattern of reactivity.

In exploring the S_N2–S_N1 scale of substrate reactivity toward organocopper reagent 1, we have found that S_N2-reactive substrates (Scheme II) such as methyl iodide, ethyl bromoacetate, and heteroallylic chlorides or even iodides 4 and 5 completely failed to undergo substitution by a pyrone group. Likewise, primary homoallylic tosylate 6, benzyl mesylate (7), and ethylene oxide in excess also did not undergo pyrone transfer from 3-cuprio-2-pyrone (1) even under forcing conditions. Normally potent acyl electrophiles (Scheme III) also failed to incorporate the pyrone group from organocopper species 1;[9] even excess benzoyl chloride, which is converted easily and cleanly into ketones by many different organocopper reagents,[10] was not transformed into 3-benzoyl-2-pyrone. To our great surprise, all of the typically S_N1-reactive electrophiles in Scheme IV also did not react with cupriopyrone 1. *The failure of the substrates in Schemes II–IV to undergo pyrone transfer from cupriopyrone 1 is a dramatic and unambiguous indication of the extraordinary nature of this organocopper species!*

To explore in more detail the mechanism(s) by which allylic electrophiles react with 3-cuprio-2-pyrone (1), we have carried out the reactions shown in eq 3 and 4.



(3)



(4)

Secondary allylic mesylate 8 reacted within 20 min at −78 °C predominantly in an S_N2' sense to give a small amount of butenylpyrone 9 and mainly butenylpyrone 10. Similarly fast-reacting primary mesylate 11 gave, in contrast, a 1.0:2.3 mixture of butenylpyrones 9 and 10 (eq 3). γ,γ-Dimethylallyl *bromide* reacted to give exclusively 3-(γ,γ-dimethylallyl)-2-pyrone (eq 4), whereas γ,γ-dimethylallyl *acetate* was inert to 3-cuprio-2-pyrone (1).

These results can be interpreted reasonably in terms of 3-cuprio-2-pyrone (1) coordinating with and thereby activating the allylic electrophiles, leading preferentially to a concerted substitution with allylic rearrangement (i.e., S_N2').[11] When such a concerted S_N2' pathway is disfavored by one or more methyl substituents (e.g., primary allylic mesylate 11 and γ,γ-dimethylallyl bromide), then direct S_N2 substitution can compete partially or completely.

Although some coupling of organocopper reagents with allylic electrophiles (e.g., acetates) has been suggested to involve copper π-allyl cation intermediates,[11] our results in eq 3 strongly argue against the same allylic cation intermediate being formed from both allylic mesylates 8 and 11 (i.e., the coupling products 9 and 10 are formed in very different ratios).[11d] Reaction of geranyl bromide with 3-cuprio-2-pyrone (1) to give exclusively 3-geranyl-2-pyrone and no cyclohexyl coupling products (eq 4)[12] also supports the idea that no allylic cation intermediate is involved.

We conclude, therefore, that organocopper species 1 (and/or 2) acts like a Lewis acid coordinating with the leaving group of some substrates (e.g., α-halo ethers, piperonyl bromide) or possibly coordinating with the π-bond of some allylic and propargylic substrates[13,14] (e.g., allylic but not benzylic bromides and mesylates react). Because organocopper reagents have become so popular in organic synthesis, it is important to be aware that not all organocopper species have the same pattern of reactivity. Even though by far most organocopper reagents are strong nucleophiles,[1] the Lewis acidity of some organocopper reagents has been noticed previously in our laboratories[15] and by other investigators.[4,16] Whether organocopper reagents

(8) For 1985 articles with leading references, see: (a) Elsevier, C. J.; Vermeer, P.; Gedanken, A.; Runge, W. *J. Org. Chem.* **1985**, *50*, 364. (b) Okamura, W. H.; Peter, R.; Reischl, W. *J. Am. Chem. Soc.* **1985**, *107*, 1034. (c) Arseniyadis, S.; Sartoretti, J. *Tetrahedron Lett.* **1985**, *26*, 729.

(9) The complete unreactivity of chalcone under conditions in which Me_2CuLi would certainly produce a conjugate methyl adduct suggests strongly that no free Me_2CuLi is present and therefore that the reactive form of 3-cupriopyrone may be the mixed cuprate species 2 (Scheme I).

(10) (a) Posner, G. H.; Whitten, C. E.; McFarland, P. E. *J. Am. Chem. Soc.* **1972**, *94*, 5106. (b) Posner, G. H.; Whitten, C. E. *Org. Synth.* **1976**, *55*, 122.

(11) For S_N2' regioselectivity in organocopper alkylation of allylic alcohols and carboxylates, see: (a) Goering, H. L.; Kantner, S. S. *J. Org. Chem.* **1981**, *46*, 2144; *Ibid.* **1984**, *49*, 422. (b) Goering, H. L.; Tseng, C. C. *Ibid.* **1985**, *50*, 1597. (c) Cf.: Marshall, J. A.; Audia, V. H. *Ibid.* **1985**, *50*, 1607. (d) For another study of this butenyl system with Cu(I) species involving completely ionic intermediates, see: Lane, J. F.; Fentress, J.; Sherwood, L. T., Jr. *J. Am. Chem. Soc.* **1944**, *66*, 545.

(12) Cf.: Kitagawa, Y.; Hashimoto, S.; Iemura, S.; Yamanoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1976**, *98*, 5030.

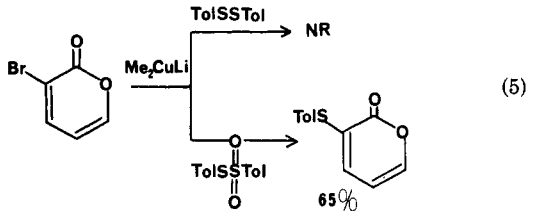
(13) That such copper–olefin π-complexation influences the regiochemistry of allylic substitution by organocopper reagents has precedent in the work of Goering and Marshall (ref 11). For other evidence supporting copper–enone π-complexation, see: Kraus, S. R.; Smith, S. G. *J. Am. Chem. Soc.* **1981**, *103*, 141. Hallnemo, G.; Olsson, T.; Ullenius, C. *J. Organomet. Chem.* **1985**, *282*, 133.

(14) Cf.: Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1984**, *25*, 3059, 3063.

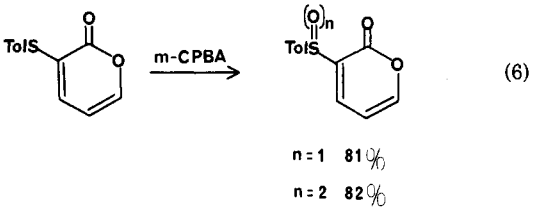
(15) (a) Posner, G. H.; Ting, J.-S.; Lentz, C. M. *Tetrahedron Lett.* **1976**, *32*, 2281. (b) Posner, G. H.; Ting, J.-S. *Ibid.* **1974**, 683.

behave in a nucleophilic or an electrophilic fashion clearly is influenced strongly by the nature of the organocopper species itself. 3-Cuprio-2-pyrone (1) is truly an extraordinary organocopper reagent in that *it has dramatically less nucleophilic character than any other organocopper species described thus far*!

Finally, conversion of 3-bromo into 3-cuprio-2-pyrone represents an important and useful umpolung[17] or reversal of reactivity at C-3 from an electrophilic to a nucleophilic center. Attempts to achieve bromine → lithium exchange (i.e., to prepare 3-lithio-2-pyrone) using *n*-butyllithium at −78 °C failed, giving only what appeared to be *n*-butyl addition products.[18] We have now used 3-cuprio-2-pyrone to prepare 3-sulfur-substituted 2-pyrones as shown in eq 5 and 6. The very rich chemistry of such 3-sulfinyl- and 3-sulfonyl-2-pyrones as dienes in asymmetric[19] inverse electron demand[20] Diels–Alder reactions will soon be the subject of publications from our laboratories.[21]



(5)



(6)

Experimental Section

Melting points were determined with a Mel-Temp or a Sybron/Thermolyne Model MP-12615 melting point apparatus; melting points and boiling points are uncorrected. IR spectra were recorded on a Perkin-Elmer 599B spectrometer and were calibrated with the 1601-cm^{-1} polystyrene absorption as reference. ^1H NMR spectra were obtained with a Varian CFT-20 or a Varian XL-400 spectrometer operating at 80 or 400 MHz, respectively. Chemical shifts are reported in ppm downfield from a tetramethylsilane (Me_4Si) internal standard, and the resonances are noted as being a singlet (s), a doublet (d), a triplet (t), or a multiplet (m). ^{13}C NMR spectra were recorded using a Varian XL-400 spectrometer operating at 100 MHz; all spectra reported are proton-noise decoupled and the chemical shifts (δ) are reported in ppm relative to chloroform (76.9 ppm). Mass spectra were performed by the University of Minnesota Mass Spectrometry Service Laboratory. Microanalytical combustion analyses were performed by Galbraith Laboratories, Knoxville, TN.

The tetrahydrofuran and diethyl ether were distilled from sodium/benzophenone. The methylene chloride was distilled from phosphorus pentoxide. The *m*-chloroperbenzoic acid was stirred with phosphate buffer (pH 7.5) prior to use. Alkyllithiums were titrated with diphenylacetic acid/tetrahydrofuran (methyllithium)[22] or 2,5-dimethoxybenzyl alcohol/benzene (*n*-butyllithium, *tert*-butyllithium).[23]

The following reagents were used as received: 5,6-dihydro-2-pyrone, cuprous iodide (Fisher), propargyl bromide, bromomethyl methyl ether, and chloromethyl benzyl ether.

The following compounds were prepared according to literature procedures: piperonyl bromide,[24] geranyl bromide,[25] 2-pyridyl thiobenzoate,[26] benzoylimidazole,[27] 2-chloromethyl-1-(methylsulfonyl)benzimidazole,[28] benzyl mesylate,[29] crotyl mesylate,[29] and 3-buten-2-yl mesylate.[29]

2-Pyrone. This compound was prepared from 5,6-dihydro-2-pyrone according to the literature experimental procedure[30a] or by decarboxylation of coumalic acid.[30b]

3-Bromo-2-pyrone. The bromination of 2-pyrone was accomplished by using a modification of the procedure described by Pirkle and Dines.[31] To 1.5 g (15.6 mmol) of 2-pyrone in 11 mL of carbon tetrachloride was added 2.18 g (13.6 mmol) of bromine, and the resulting mixture was heated at reflux for 40 h. Concentration of the reaction mixture and purification by column chromatography using ether–hexanes (2:1) as the eluent provided 1.56 g (8.9 mmol, 57%) of 3-bromo-2-pyrone (R_f 0.29), mp 64–66 °C (lit.[31] mp 64–65 °C). The ^1H NMR spectrum was identical with that reported in the literature.[32] The remaining fractions from the column which contained 5,6-dibromo-5,6-dihydro-2-pyrone (R_f 0.57) and 2-pyrone (R_f 0.19) could again be treated with bromine to produce more 3-bromo-2-pyrone.

3-Allyl-2-pyrone. To a 0 °C suspension of 45 mg (0.236 mol) of cuprous iodide in 4 mL of dry ether was added 0.270 mL of 1.70 m methyllithium (0.459 mmol). The resulting solution was stirred at 0 °C for 10 min and then cooled to −78 °C. A solution of 20 mg (0.114 mmol) of 3-bromo-2-pyrone in 1 mL of dry ether was added dropwise and the yellow, heterogeneous reaction mixture was stirred at −78 °C for 1.5 h. Then 55 mg (0.455 mmol) of allyl bromide was added, and stirring was continued at −78 °C for 1 h followed by the addition of ammonium chloride in aqueous tetrahydrofuran. The mixture was warmed to room temperature, diluted with ether and washed with 2 × 20 mL of saturated ammonium chloride. The aqueous layer was saturated with solid sodium chloride and reextracted with dichloromethane. The organic extracts were combined, dried ($MgSO_4$), and concentrated. Purification of the residue by preparative TLC using ether–hexanes (2:1) as the eluent provided 9.8 mg (0.072 mmol, 63%) of 3-allyl-2-pyrone (R_f 0.40): ^1H NMR ($CDCl_3$) δ 3.22 (d, 2 H, J = 6.6 Hz, CH_2), 4.98–5.27 (m, 2 H, H_2C=C), 5.62–6.03 (m, 1 H, C=CH), 6.17 (dd, 1 H, J = 6.6, 5.1 Hz, H-5), 7.02–7.18 (m, 1 H, H-4), 7.40 (dd, 1 H, J = 5.1, 2.0 Hz, H-6); IR (CCl_4) 1725 (C=O) cm^{-1}; exact mass calcd for $C_8H_8O_2$ m/e 136.0524, found m/e 136.0523.

The following compounds were prepared in a manner similar to that described for 3-allyl-2-pyrone.

3-(2-Pentynyl)-2-pyrone: yield 54%; isolated by preparative TLC using ether–hexanes (2:1), R_f 0.46; ^1H NMR ($CDCl_3$) δ 1.18 (t, 3 H, J = 7.0 Hz, CH_3), 2.05–2.45 (m, 2 H, CH_2), 3.27–3.46 (m, 2 H, C≡CCH_2), 6.23 (dd, 1 H, J = 6.6, 5.1 Hz, H-5), 7.32–7.46 (m, 1 H, H-4), 7.52 (dd, 1 H, J = 5.1, 2.0 Hz, H-6); IR (CCl_4) 1725 (C=O) cm^{-1}; exact mass calcd for $C_{10}H_{10}O_2$ m/e 162.0681, found m/e 162.0680.

3-(2-Propynyl)-2-pyrone and 3-(1,2-propadienyl)-2-pyrone: yield 48%; isolated by preparative TLC using ether–hexanes (2:1),

(16) (a) Bourgain, M.; Villieras, J.; Normant, J. F. *C. R. Seances Acad. Sci., Ser. C* **1973**, *276*, 1477. (b) House, H. O. *Acc. Chem. Res.* **1976**, *9*, 59.
(17) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239.
(18) For a study of Grignard reagents adding to 2-pyrones, see: Lhuste, P.; Moreau, M.; Dreux, J. *Tetrahedron* **1984**, *40*, 1551 and references therein.
(19) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 876 and references therein.
(20) Cf.: (a) Boger, D. L.; Mullican, M. D. *J. Org. Chem.* **1984**, *49*, 4033, 4045. (b) Boger, D. L.; Brotherton, C. E. *Ibid.* **1984**, *49*, 4050 and references therein.
(21) (a) Posner, G. H.; Harrison, W. *J. Chem. Soc., Chem. Commun.*, in press; (b) Posner, G. H.; Wettlaufer, D. G. *Tetrahedron Lett.*, submitted for publication.
(22) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879.
(23) Winkle, M. R.; Lansinger, J. T.; Ronald, R. C. *J. Chem. Soc., Chem. Commun.* **1980**, 87.
(24) Robinson, G. M.; Robinson, R. *J. Chem. Soc.* **1914**, *105*, 1456.
(25) Grieco, P. A.; Masaki, Y. *J. Org. Chem.* **1974**, *39*, 2135.
(26) Avaki, M.; Sakata, S.; Takei, H.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 1777.
(27) Iwasaki, S. *Helv. Chim. Acta* **1976**, *59*, 2738.
(28) Charlson, A. J. *Carbohydr. Res.* **1973**, *29*, 89.
(29) Crossland, R. K.; Servis, K. L. *J. Org. Chem.* **1970**, *35*, 3195.
(30) (a) Nakagawa, M., Tonozuka, M.; Obi, M.; Kinchi, M.; Hino, T.; Ban Y. *Synthesis* **1974**, 510. (b) Zimmerman, H. E.; Grunewald, G. L.; Pufler, R. M. *Org. Synth.* **1966**, *46*, 101.
(31) Pirkle, W. H.; Dines, M. *J. Org. Chem.* **1969**, *34*, 2239.
(32) Pirkle, W. H.; Dines, M. *J. Heterocycl. Chem.* **1969**, *6*, 1.

R_f 0.40; ^{1}H NMR ($CDCl_3$) δ 2.28 (t, 1 H, J = 2.7 Hz, C≡CH), 3.37–3.48 (m, 2 H, C≡CCH_2) 5.18 (d, 2 H, J = 7 Hz, H_2C=C of allene), 6.26 (dd, 1 H, J = 6.5, 5.0 Hz, H-5), 7.34–7.63 (m, 3 H, H-4, H-6, and =CH of allene); IR (CCl_4) 1730 (C=O) cm^{-1}; exact mass calcd for $C_8H_6O_2$ m/e 134.0368, found m/e 134.0366.

3-(Methoxymethyl)-2-pyrone. The reaction with bromomethyl methyl ether was performed for 3 h at room temperature: yield 54%; isolated by preparative TLC using double elution with ether–hexanes (2:1), R_f 0.37; ^{1}H NMR ($CDCl_3$) δ 3.46 (s, 3 H, OCH_3), 4.30 (br s, 2 H, CH_2), 6.25 (dd, 1 H, J = 6.6, 5.2 Hz, H-5), 7.33–7.49 (m, 2 H, H-4, H-6); IR (CCl_4) 1720 (C=O) cm^{-1}; exact mass calcd for $C_7H_8O_3$ m/e 140.0474, found m/e 140.0475.

3-[(Benzyloxy)methyl]-2-pyrone. The reaction with chloromethyl benzyl ether was performed for 3 h at room temperature: yield 65%; isolated by preparative TLC using double elution with ether–hexanes (2:1), R_f 0.43; ^{1}H NMR ($CDCl_3$) δ 4.41 (br s, 2 H, CH_2), 4.64 (s, 2 H, $ArCH_2O$), 6.25 (dd, 1 H, J = 6.7, 5.2 Hz, H-5), 7.31–7.51 (m, 7 H, C_6H_5, H-4, H-6); IR (CCl_4) 1720 (C=O) cm^{-1}; exact mass calcd for $C_6H_5O_3$ (M^+ – benzyl) m/e 125.0239, found m/e 125.0245.

3-Piperonyl-2-pyrone. The reaction with piperonyl bromide was performed for 6 h at room temperature: yield 24%; isolated by preparative TLC using double elution with hexanes–ethyl acetate–dichloroethane (4:1:1), R_f 0.33; ^{1}H NMR ($CDCl_3$) δ 3.69 (s, 2 H, CH_2), 5.94 (s, 2 H, OCH_2O), 6.12 (dd, 1 H, J = 6.6, 5.2 Hz, H-5), 6.72–7.08 (m, 4 H, C_6H_3, H-4), 7.38 (dd, 1 H, J = 5.2, 2.0 Hz, H-6); IR (CCl_4) 1720 (C=O) cm^{-1}; exact mass calcd for $C_{13}H_{10}O_4$ m/e 230.0579, found m/e 230.0577.

3-(3-Methyl-2-butenyl)-2-pyrone. The reaction with dimethylallyl bromide was performed for 1.5 h at room temperature: yield 54%; isolated by preparative TLC using ether–hexanes (2:1), R_f 0.45; ^{1}H NMR ($CDCl_3$) δ 1.65 (s, 3 H, CH_3), 1.77 (s, 3 H, CH_3), 3.15 (d, 2 H, J = 7.3 Hz, CH_2), 5.21–5.28 (m, 1 H, C=CH), 6.16 (dd, 1 H, J = 6.7 5.2 Hz, H-5), 7.07 (dd, 1 H, J = 6.7, 2.0 Hz, H-4), 7.37 (dd, 1 H, J = 5.2, 2.0 Hz, H-6); IR (CCl_4) 1720 (C=O) cm^{-1}; exact mass calcd for $C_{10}H_{12}O_2$ m/e 164.0837, found m/e 164.0839.

3-(2-Butenyl)-2-pyrone and 3-(3-Buten-2-yl)-2-pyrone. The reaction with 3-buten-2-yl mesylate was performed for 20 min at –78 °C to produce a 9:1 mixture of 3-(2-butenyl)-2-pyrone and 3-(3-buten-2-yl)-2-pyrone: yield 66%; isolated by preparative TLC using either–hexanes (2:1), R_f 0.42; IR (CCl_4) 1720 (C=O) cm^{-1}; exact mass calcd for $C_9H_{10}O_2$ m/e 150.0681, found m/e 150.0682. 3-(2-butenyl)-2-pyrone: ^{1}H NMR ($CDCl_3$) δ 1.62 (d, 3H, J = 7.1 Hz, CH_3), 3.14 (d, 2 H, J = 6.6 Hz, CH_2), 5.46–5.64 (m, 2 H, HC=CH), 6.16 (dd, 1 H, J = 6.7, 5.1 Hz, H-5), 7.07 (dd, 1 H, J = 6.7, 2.0 Hz, H-4), 7.36 (dd, 1 H, J = 5.1, 2.0 Hz, H-6). 3-(3-buten-2-yl)-2-pyrone: ^{1}H NMR ($CDCl_3$) δ 1.27 (d, 3 H, J = 7.2 Hz, CH_3), 3.56–3.66 (m, 1 H, CH), 5.11–5.18 (m, 2 H, H_2C=C), 5.92–6.01 (m, 1 H, C=CH), 6.16 (dd, 1 H, J = 6.7, 5.1 Hz, H-5), 7.07 (dd, 1 H, J = 6.7, 2.0 Hz, H-4), 7.36 (dd, 1 H, J = 5.1, 2.0 Hz, H-6).

The reaction was also performed with crotyl mesylate for 20 min at –78 °C to produce a 2.3:1 mixture of 3-(2-butenyl)-2-pyrone and 3-(3-buten-2-yl)-2-pyrone in a yield of 65%.

3-Geranyl-2-pyrone. The reaction with geranyl bromide was performed for 1.5 h at room temperature: yield 57%; isolated by preparative TLC using ether–hexanes (2:1), R_f 0.51; ^{1}H NMR ($CDCl_3$) δ 1.61 (s, 3 H, CH_3), 1.64 (s, 3 H, CH_3), 1.69 (s, 3 H, CH_3), 2.07–2.14 (m, 4 H, CH_2), 3.16 (d, 2 H, J = 7.3 Hz, CH_2), 5.06–5.27 (m, 2 H, C=CH), 6.16 (dd, 1 H, J = 6.7, 5.2 Hz, H-5), 7.06 (dd, 1 H, J = 6.7, 2.1 Hz, H-4), 7.38 (dd, 1 H, J = 5.2, 2.1 Hz, H-6); IR (CCl_4) 1720 (C=O) cm^{-1}; exact mass calcd for $C_{15}H_{20}O_2$ m/e 232.1463, found m/e 232.1462.

3-(*p*-Tolylthio)-2-pyrone. To a 0 °C suspension of 2.28 g (12.0 mmol) of cuprous iodide in 110 mL of dry ether was added 12.3 mL of 1.85 M methyllithium (22.8 mmol). The grey suspension became yellow, midway through the addition, becoming clear and near colorless several minutes after complete addition. Stirring was continued for an additional 15 min, after which time the cuprate solution was diluted with 55 mL of ether and cooled to –78 °C. A solution of 1.00 g (5.7 mmol) of 3-bromo-2-pyrone in 185 mL of dry ether was added rapidly at the same time via both cannula and syringe (3–5 min). The resulting yellow-brown solution was stirred at –78 °C until complete reaction was realized by TLC (66% ether/hexanes 2–2.5 h). The reaction mixture was quenched by addition, via cannula, of 6.43 g (22.8 mmol) of *S*-*p*-tolyl *p*-toluenethiosulfonate in 25 mL of dry tetrahydrofuran. The temperature of the cold bath was maintained at –78 °C for an additional hour, followed by slow warming to room temperature over 3 h. To this slurry was added 50 mL of dilute aqueous ammonium chloride and 75 mL of dichloromethane, and the layers were separated. The organic layer was washed with 4–5 × 100 mL of 5% aqueous ammonium hydroxide, until the blue copper color was no longer extracted. The combined aqueous layers were back-extracted with 1 × 100 mL of dichloromethane. The combined organic layers were washed with brine and dried ($MgSO_4$) followed by filtration and concentration to give the crude sulfide. Purification via short path column chromatography using 0–20% ethyl acetate–hexanes as the eluent provided 0.83 g (3.80 mmol, 67%) of the sulfide as a light brown solid: mp 70–72 °C; ^{1}H NMR ($CDCl_3$) δ 2.39 (s, 3 H, CH_3), 6.06 (dd, 1 H, J = 6.9, 5.0 Hz, H-5), 6.54 (dd, 1 H, J = 6.9, 1.9 Hz, H-4), 7.19–7.49 (m, 5 H, C_6H_4, H-6); IR ($CHCl_3$) 1730 (C=O) cm^{-1}. Anal. Calcd for $C_{12}H_{10}O_2S$: C, 66.03; H, 4.62; S, 14.69. Found: C, 65.93; H, 4.60; S, 14.79.

3-(*p*-Tolylsulfinyl)-2-pyrone. To a 0 °C solution of 300 mg (1.38 mmol) of 3-(*p*-tolylthio)-2-pyrone in 5 mL of dichloromethane was added 238 mg (1.38 mmol) of 99% *m*-chloroperbenzoic acid in 5 mL of dichloromethane. The solution was stirred at 0 °C for 1.5 h, diluted with dichloromethane, washed with saturated sodium bicarbonate, dried ($MgSO_4$), and concentrated. The concentrate was purified by preparative TLC using ether–hexanes (2:1) as the eluent to yield 260 mg (1.11 mmol, 81%) of the desired sulfoxide (R_f 0.10), which was recrystallized from dichloromethane–ether–petroleum ether: mp 112–113 °C; ^{1}H NMR ($CDCl_3$) δ 2.38 (s, 3 H, CH_3), 6.49 (dd, 1 H, J = 6.7, 5.1 Hz, H-5), 7.26 (d, 2 H, J = 8.0 Hz, Ar), 7.54 (dd, 1 H, J = 5.1, 2.1 Hz, H-6), 7.70 (d, 2 H, J = 8.0 Hz, Ar), 8.08 (dd, 1 H, J = 6.7, 2.1 Hz, H-4); ^{13}C NMR ($CDCl_3$) δ 21.36, 106.33, 125.46, 129.83, 134.33, 138.79, 138.89, 142.48, 152.97, 157.21; IR ($CHCl_3$) 1730 (C=O) cm^{-1}. Anal. Calcd for $C_{12}H_{10}O_3S$: C, 61.52; H, 4.30; S, 13.69. Found: C, 61.50; H, 4.35; S, 13.79.

3-(*p*-Tolylsulfonyl)-2-pyrone. To a 0 °C solution of 300 mg (1.37 mmol) of 3-(*p*-tolylthio)-2-pyrone in 50 mL of dichloromethane was added 590 mg (3.15 mmol) of 92% *m*-chloroperbenzoic acid. Stirring was continued as the flask was allowed to warm to room temperature overnight. The mixture was diluted with 25 mL of dichloromethane and washed with 2 × 50 mL of dilute aqueous sodium bisulfite, 3 × 50 mL of dilute aqueous sodium bicarbonate, and brine. Drying ($MgSO_4$) followed by filtration and concentration gave the crude sulfone. Purification via short path column chromatography using 20% dichloromethane–0–20% ethyl acetate–hexanes as the eluent, followed by washing of the solid with pentane, afforded 280 mg (1.12 mmol, 82%) of the sulfone as a white solid: mp 160–162 °C; ^{1}H NMR ($CDCl_3$) δ 2.42 (s, 3 H, CH_3), 6.46 (dd, 1 H, J = 7, 5 Hz, H-5), 7.32 (d, 2 H, J = 9 Hz, tolyl), 7.69 (dd, 1 H, J = 5, 2 Hz, H-6), 7.95 (d, 2 H, J = 9 Hz, tolyl), 8.37 (dd, 1 H, J = 7, 2 Hz, H-4); IR ($CHCl_3$) 1740 (C=O), 1328 (S=O) cm^{-1}. Anal. Calcd for $C_{12}H_{10}O_4S$: C, 57.58; H, 4.03; S, 12.80. Found: C, 57.43; H, 3.78; S, 12.97.

Acknowledgment. We thank the National Science Foundation for financial assistance in the form of a research grant (CHE-83-12161) and a grant (PCM83-03176) toward purchase of a departmental 400-MHz NMR spectrometer. We also thank the NIH for contributing toward purchase of the NMR spectrometer (Grant 1 S10 RR01934). We acknowledge Dr. Stephen Haines and Edward Asirvatham of these laboratories for preparation of the two sugars in Scheme IV and of 1-bromo-2-pentyne, respectively.