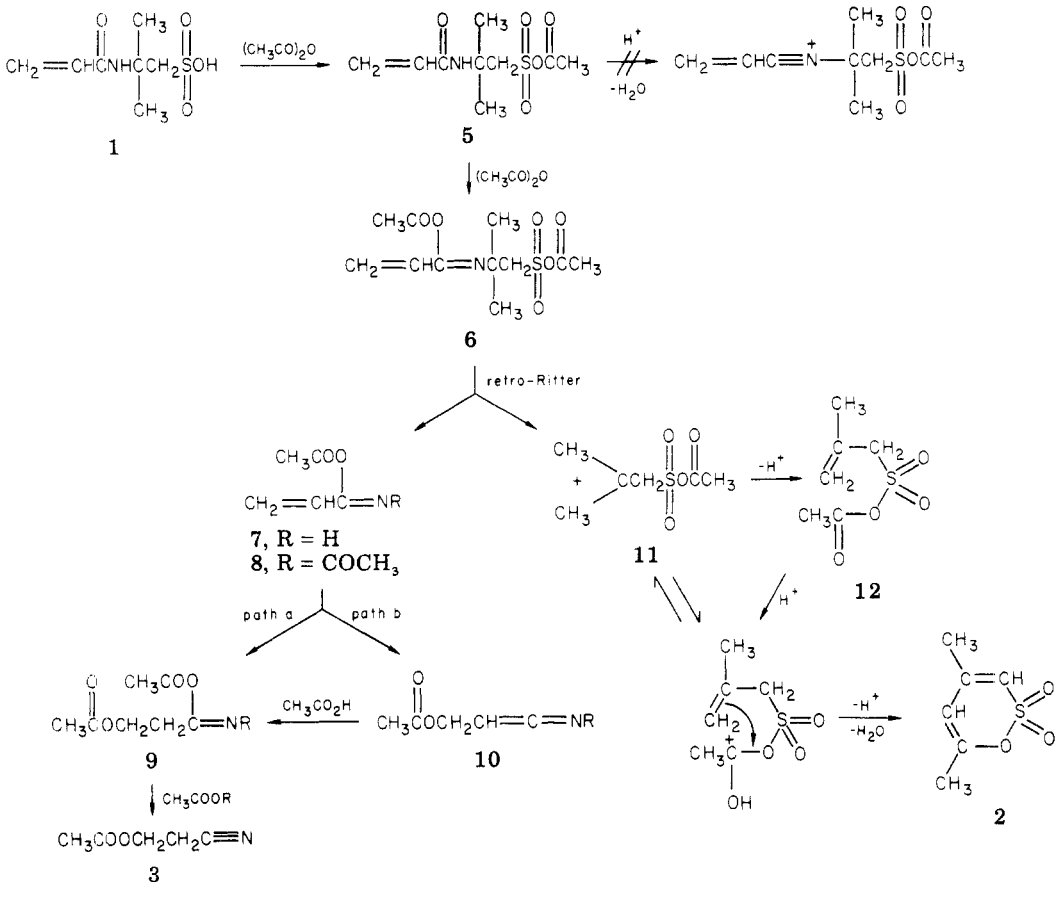
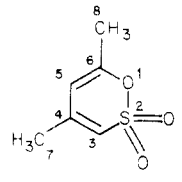
Scheme I



isolated from the fractional distillation forecut which was enriched in the two components by preparative GLPC, using the same conditions as previously described and a $^1/_4$-in.-diameter column containing the same packing. Component 1 was identified as 3-acetoxypropionitrile (**3**) by comparison with an authentic sample. Component 2 was identified as 2,4-dimethylbenzonitrile (**4**) by comparison with published spectra.[3]

The undecoupled ^{13}C spectrum of **2** has not been previously reported and the assignments are as follows: δ 19.9 (qd, ^1J = 130.1, ^3J = 2.7 Hz, C-8), 21.4 (qdd, ^1J = 129.1, ^3J = 5.3, ^3J = 3.7 Hz, C-7), 105.7 (dd heptet, ^1J = 167.7, ^3J = 6.8, ^3J = 4.6 Hz, C-5), 113.1 (d quintet, ^1J = 184.8, ^3J = 7 Hz, C-3), 146.1 (q, ^2J = 6 Hz, C-4), 156.6 (dq, ^2J = 7, ^2J = 6 Hz, C-6).



Preparation of 3-Acetoxypropionitrile. Acetic anhydride (51 g, 0.50 mol) and hydracrylonitrile (Aldrich) (35.5 g, 0.50 mol) were heated on a steam bath for 6.5 h. When cool, the reaction mixture was treated with solid Na_2CO_3 to remove acetic acid. The mixture was filtered, and the filtrate was fractionally distilled. The water-white fraction distilling at 99–102 °C (20 torr) [lit.[8] bp 110–111 °C (25 torr)] weighed 44 g (68% yield). Data for **3**: IR (neat) 2290, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ (Me_4Si) 2.10 (s, 3 H), 2.65 (t, J = 6 Hz, 2 H), 3.35 (t, J = 6 Hz, 2 H).

(7) R. H. Eastman and D. Gallup, *J. Am. Chem. Soc.*, **70**, 864 (1948).
(8) G. C. Tesoro and S. B. Sello, U.S. Patent 3 338 883 (1967).

Acknowledgment. The authors thank their colleague Dr. Frederick J. Palensky for valuable discussions during the course of this work.

Registry No. 1, 15214-89-8; 2, 4941-84-8; 3, 927-56-0; 4, 21789-36-6; acetic anhydride, 108-24-7.

Reaction of 3-Bromo-4*H*-1-benzopyran-4-one with β-Diketones and β-Keto Esters To Give Functionalized Furans

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4*H*-1-Benzopyran-4-ones (chromones) bearing a reactive functional group at carbon three have been receiving increased attention of late owing to the variety of heterocyclic compounds available from such substrates.[1] We

(1) U. Peterson and H. Heitzer, *Justus Liebigs Ann. Chem.*, 1663 (1976); S. Klutchko, J. Shavel, Jr., M. von Strandtmann, *J. Org. Chem.*, **39**, 2436 (1974); S. Klutchko, M. von Strandtmann, *Synthesis*, 61 (1977); C. K. Ghosh *Synth. Commun.* **8**(7), 487 (1978); C. K. Ghosh and K. K. Mukhopadhyay, *Synthesis*, 779 (1978).

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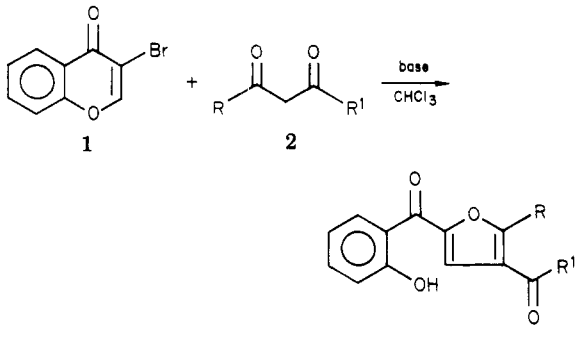
wish to report that treatment of a chloroform solution of 3-bromo-4*H*-1-benzopyran-4-one[2] (1) with a β-diketone or β-keto ester[3] 2 in the presence of 1,5-diazabicyclo-[4.3.0]non-5-ene (DBN) or 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) results in the facile formation of highly functionalized trisubstituted furans (i.e., 3) in good to excellent yield. As shown, depending on the substitution

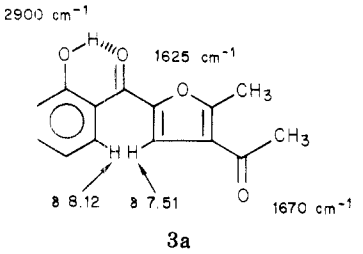


1 2

3a, R = R^1 = CH_3 (81%)
b, R = CH_3; R^1 = OEt (91%)
c, R = Ph; R^1 = OEt (89%)
d, R = CH_2-S Ph; R^1 = OEt (70%)
e, R = CH_2CO_2Et; R^1 = OEt (38%)
f, R,R^1 = $CH_2C(CH_3)_2CH_2$ (67%)

of the β-diketone or β-keto ester, a variety of substituted furans can be synthesized. In all cases, except for dimedone (i.e., **3f**), the reactions were complete after stirring at room temperature for 30–60 min. The reaction with dimedone took 4 h at room temperature. Replacement of DBU or DBN by triethylamine under identical reaction conditions, as well as extended reaction time periods, resulted in recovery of starting materials. Two equivalents of base was found to be necessary for complete conversion of starting material to product. Where only 1 equiv of base was used the reaction appeared to proceed to approximately 50% conversion. Addition of a second equivalent of base at this point then led to complete conversion to product.

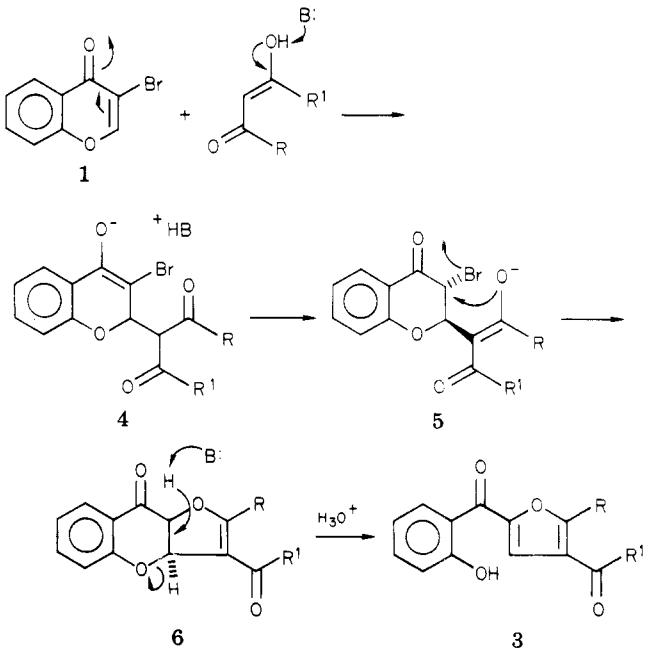
The structure of these furans was readily apparent from spectral data. For example, **3a** exhibited a broad OH absorption in the infrared at 2900 cm^{-1} (mull), revealing the expected hydrogen bonding between the OH and adjacent carbonyl as shown. Also present in this infrared



3a

spectrum were carbonyl absorptions at 1625 (hydrogen bonded) and 1670 cm^{-1}. The ^1H NMR contained a doublet of doublets (J = 8 Hz and J = 2 Hz) at δ 8.12 (1 H),

Scheme I



1 4 5 6 3

multiplets at δ 7.31–7.62 (1 H) and δ 6.80–7.10 (2 H), and a singlet at δ 7.51, the latter corresponding to the furan proton. Also in the ^1H NMR were signals at δ 2.70 and 2.45, corresponding to the furan methyl and methyl ketone, respectively. The UV (EtOH) exhibited a λ_{max} at 212 nm (ε 18 850) and 304 (13 600). In addition, a correct mass[4] and combustion analysis was obtained.

As illustrated in Scheme I, the above reaction appears to be initiated by base-catalyzed Michael addition of the β-diketone or β-keto ester to the unsaturated portion of the chromone, giving rise to bromoenolate **4**. This enolate then undergoes a proton transfer to give still another enolate **5** which is now capable of an intramolecular O-alkylation to give the dihydrofuran intermediate **6**. Intermediate **6** then collapses by base-induced phenoxide elimination to give, after protonation by acid, the observed trisubstituted furans. This mechanism is in agreement with the earlier observation that 2 equiv of base is necessary for complete conversion of starting materials to product.

3-Bromochromones bearing a methyl group at carbon two fail to undergo the above reaction even with heating for extended reaction periods. Furthermore, simple ketones, α-bromo ketones, esters, amides, imides, and 2-substituted β-keto esters either fail to react with 1 or give extremely complex mixtures.

Experimental Section

All analytical data, except for NMR spectra and several infrared spectra, were obtained by the Physical and Analytical Chemistry Department of The Upjohn Company. NMR spectra were obtained at 60 MHz in chloroform-*d* solutions containing tetramethylsilane as an internal standard. Infrared spectra were obtained on a Perkin-Elmer 197 spectrophotometer in chloroform solutions. Thin-layer chromatography (TLC) was conducted by using Merck glass plates precoated with silica gel 60 F-254. The

(2) A new method of synthesis of 3-halogenated 4*H*-1-benzopyran-4-ones has been accepted for publication in *Synthesis*.

(3) For the reaction of active methylene compounds with 4*H*-1-benzopyran-4-one see: F. Eiden and H. Fenner, *Arch. Pharm. (Weinheim, Ger.)*, **302**, 229 (1969); A. I. Tohmachev, *J. Gen. Chem. USSR (Engl. Transl.)*, **32**, 3672 (1962); G. A. Caplin, W. D. Ollis, and I. O. Sutherland, *J. Chem. Soc. C*, 3202 (1968); G. Menichi, C. Pene, M. H. Habort, N. Platzes, A. Chentin, and R. Royer, *Bull. Chem. Thermodyn.* 422 (1970); 111 (1970); F. Eiden and W. Schikorr, *Arch. Pharm. (Weinheim, Ger.)*, **305**, 187 (1972); A. Nohara, T. Ishiguro and Y. Sanns, *Tetrahedron Lett.*, 1183 (1974); W. D. Jones and W. L. Albrecht, *J. Org. Chem.*, **41**, 706 (1976); H. Harmisch, *Justus Liebigs Ann. Chem.*, **765**, 8 (1972); A. Nohara, H. Kunki, T. Saijo, K. Ukawa, T. Murata, M. Kanno, and Y. Sono, *J. Med. Chem.*, **18**, 24 (1975).

(4) The major ions present in the mass spectrum of **3a** were as follows: *m/e* (rel intensity) 244 (54, parent), 121 (81), 120 (63), 109 (32), 93 (17), 92 (26), 65 (41), 43 (100), 39 (38). Smaller ions representing the loss of CH_3 (*m/e* 229) and $C(O)CH_3$ (*m/e* 201) were also present. All compounds (i.e., **3a–f**) had the characteristic fragments at *m/e* 121 and/or 120 representative of aromatic *o*-hydroxy carbonyl compounds; see E. M. Emery, *Anal. Chem.*, **32**, 1495 (1960), for examples. For a discussion on the fragmentation of 2-benzoylfuran see R. Grigg, M. V. Sargent, and D. H. Williams, *Tetrahedron*, **21**, 3441 (1965).

TLC plates were visualized by UV light or iodine. Column chromatography was conducted at medium pressure by utilizing silica gel 60 (E. Merck, 230–400 mesh). All solvents were reagent grade distilled from glass (Burdick and Jackson).

3-Acetyl-5-(2-hydroxybenzoyl)-2-methylfuran (3a). To a chloroform solution (100 mL) of 3-bromochromone (1; 4.50 g, 20 mmol) and acetylacetone (2.0 g, 20 mmol) was added a chloroform solution (10 mL) of DBN (4.96 g, 40 mmol) over a period of 2–3 min. The reaction immediately turned black. After being stirred at room temperature for 1 h, the reaction was quenched by the addition of 5% HCl (100 mL). The organic layer was separated and the aqueous layer extracted with chloroform (2 × 50 mL). The combined chloroform solutions were then dried ($MgSO_4$), and the solvent was removed in vacuo to give 4.1 g of a yellow solid. This material was chromatographed[5] over 200 g of silica gel packed in 10% EtOAc/$CHCl_3$. Fractions of 100 mL each were collected. Fractions 13–17 contained 3.94 g (81%) of **3a**: mp 98–100 °C; IR ($CHCl_3$) ν_{max} 3000 (OH), 1670, 1620 (C=O), 1580, 1560 (C=C), 1350, 1200, 1160 cm^{-1} (C–O/other); NMR ($CDCl_3$) δ 8.12 (dd, 1 H, aromatic, J = 8 and 2 Hz), 7.52 (s, 1 H, furan proton), 7.31–7.62 (m, 1 H, aromatic), 6.80–7.10 (m, 2 H, aromatic), 2.7 (s, 3 H, furan methyl), 2.45 (s, 3 H, methyl ketone); UV (EtOH) λ_{max} 212 (sh) nm (ϵ 18 850) and 304 (13 600). Anal. Calcd for $C_{14}H_{12}O_4$ (mol wt 243.6): C, 68.96; H, 4.96. Found: C, 68.74; H, 4.92.

Ethyl 5-(2-Hydroxybenzoyl)-2-methyl-3-furancarboxylate (3b). To a chloroform solution (100 mL) of 3-bromochromone (1: 2.25 g, 10 mmol) and ethyl acetoacetate (1.30 g, 10 mmol) was added a chloroform solution (5 mL) of DBU (3.04 g, 20 mmol) over a period of 2–3 min. The reaction immediately began to turn bright orange. After being stirred at room temperature for 30 min, the reaction was quenched by the addition of 5% HCl (50 mL). The organic layer was separated and the aqueous layer extracted with chloroform (2 × 50 mL). The combined chloroform solutions were dried ($MgSO_4$), and the solvent was removed in vacuo to give 2.75 g of a yellow oil. This oil was chromatographed over 250 g of silica gel packed in 50% EtOAc/hexane. Fractions of 18 mL were collected. Fractions 35–50 were combined to give 2.48 g (91%) of **3b**: mp 40–42 °C; IR (mull) ν_{max} 2900 (OH), 1720 (ester), 1625 (C=O), 1605, 1585 (C=C), 1275, 1240, 1160, 1100 cm^{-1} (C–O/other); NMR ($CDCl_3$) δ 8.1 (d, 1 H, aromatic J = 8 Hz), 7.53 (s, 1 H, furan proton), 7.3–7.6 (m, 1 H, aromatic), 6.75–7.11 (m, 2 H, aromatic), 4.27 (q, 2 H, OCH_2CH_3, J = 7 Hz), 2.65 (s, 3 H, furan methyl), 1.35 (t, 3 H, OCH_2CH_3, J = 7 Hz). Anal. Calcd for $C_{15}H_{14}O_5$ (mol wt 273.5): C, 65.81; H, 5.11. Found: C, 65.86: H, 5.10.

Ethyl 5-(2-Hydroxybenzoyl)-2-phenyl-3-furancarboxylate (3c). By use of the same procedure as that for **3b**, 2.25 g of 1 afforded 3.5 g of a yellow solid which was chromatographed over 250 g of silica gel packed in 50% EtOAc/hexane. Fractions of 18 mL were collected. Fractions 29–48 were combined to give 2.98 g (89%) of **3c**: mp 103–105 °C; IR (mull) ν_{max} 2900 (OH), 1725 (ester), 1620 (C=O), 1590, 1570, 1520 cm^{-1} (C=C); NMR ($CDCl_3$) δ 8.14 (dd, 1 H, aromatic, J = 8 and 2 Hz), 7.75 (s, 1 H, furan proton), 7.25–7.65 (m, 6 H, aromatic), 6.85–7.10 (m, 2 H, aromatic), 4.33 (q, 2 H, OCH_2CH_3, J = 7 Hz), 1.35 (t, 3 H, OCH_2CH_3, J = 7 Hz). Anal. Calcd for $C_{20}H_{16}O_5$ (mol wt 335.5): C, 71.53; H, 4.76. Found: C, 71.42; H, 4.76.

Ethyl 5-(2-Hydroxybenzoyl)-2-[(phenylthio)methyl]-3-furancarboxylate (3d). By use of the same procedure as that for **3b**, 1.0 g of 1 afforded 1.65 g of a yellow oil which was chromatographed over three Merck B columns packed in 50% EtOAc/hexane. Fractions of 18 mL were collected. Fractions 19–22 were combined to give 1.18 (75%) of **3d**: mp 76–77 °C; IR (mull) ν_{max} 3000 (OH), 1720 (ester), 1625 (C=O), 1600, 1520 (C=C), 1285, 1240, 1160 cm^{-1} (C–O/other); NMR ($CDCl_3$) δ 7.95 (dd, 1 H, aromatic, J = 8 and 2 Hz), 7.50 (s, 1 H, furan proton), 6.7–7.4 (m, 8 H, aromatic), 4.47 (s, 2 H, CH_2–S), 4.2 (q, 2 H, OCH_2CH_3, J = 7 Hz), 1.28 (t, 3 H, OCH_2CH_3, J = 7 Hz). Anal. Calcd for $C_{21}H_{18}O_5S$ (mol wt 381.5): C, 66.05; H, 4.71; S, 8.38. Found: C, 65.69; H, 4.84; S, 8.53.

Ethyl 3-(Ethoxycarbonyl)-5-(2-hydroxybenzoyl)-2-furanacetate (3e). By use of the same procedure as that for **3b**, 2.25 g of 1 afforded 3.34 g of a light yellow oil which was distilled [230 °C (0.8 mm Hg)] and then chromatographed over three Merck B columns packed in chloroform. Fractions of 18 mL were collected. Fractions 26–39 contained 1.31 g (38%) of **3e**: mp 81–83 °C; IR ($CHCl_3$) ν_{max} 3000 (OH), 1735, 1715 (ester), 1620 (C=O), 1610, 1530, (C=C), 1300, 1290, 1245, 1085 cm^{-1} (C–O/other); NMR ($CDCl_3$) δ 8.15 (d, 1 H, atomatic, J = 8 Hz), 7.59 (s, 1 H, furan proton), 7.30–7.65 (m, 1 H, aromatic), 6.75–7.12 (m, 2 H, aromatic), 4.30 (q, 2 H, OCH_2CH_3, J = 7 Hz), 4.25 (q, 2H, OCH_2CH_3, J = 7 Hz), 4.18 (s, 2 H, CH_2CO_2Et), 1.32 (t, 3 H, OCH_2CH_3, J = 7 Hz), 1.25 (t, 3 H, OCH_2CH_3, J = 7 Hz). Anal. Calcd for $C_{18}H_{18}O_7$ (mol wt 345.3): C, 62.55; H, 5.21. Found: C, 62.50; H, 5.22.

6,7-Dihydro-2-(2-hydroxybenzoyl)-6,6-dimethyl-4(5*H*)-benzofuranone (3f). To a chloroform solution (50 mL) of 3-bromochromone (1; 2.25 g, 10 mmol) and 5,5-dimethylcyclohexane-1,3-dione (1.40 g, 10 mmol) was added a chloroform solution (5 mL) of DBN (2.48 g, 20 mmol) over a 2–3-min time period. After the reaction was stirred at room temperature for 4 h, the reaction was quenched by addition of 5% HCl (50 mL). The organic layer was separated and the aqueous layer extracted with chloroform (2 × 50 mL). The combined organic solutions were dried ($MgSO_4$), and the solvent was removed in vacuo to give a yellow solid which when chromatographed over 250 g of silica gel packed in 5% CH_3OH/CH_2Cl_2 afforded 1.90 g (67%) of **3f**: mp 100–102 °C; IR (mull) 2900 (OH), 1685 (C=O), 1620 (C=O, hdyrogen bonded), 1585, 1515 (C=C), 1305, 1240, 1165, 895 cm^{-1} (C–O/other); NMR ($CDCl_3$) δ 8.08 (d, 1 H, aromatic, J = 9 Hz), 7.55 (s, 1 H, furan proton), 7.3–7.6 (m, 1 H, aromatic), 6.8–7.15 (m, 2 H, aromatic), 2.90 (s, 2 H, CH_2), 2.45 (s, 2 H, CH_2), 1.20 (s, 6 H, *gem*-dimethyl). Anal. Calcd for $C_{17}H_{16}O_4$ (mol wt 283.6): C, 71.93; H, 5.64. Found: C, 71.67; H, 5.46.

Registry No. 1, 49619-82-1; **2a**, 123-54-6; **2b**, 141-97-9; **2c**, 94-02-0; **2d**, 25907-38-4; **2e**, 105-50-0; **2f**, 126-81-8; **3a**, 71426-02-3; **3b**, 71426-03-4; **3c**, 71426-04-5; **3d**, 71426-05-6; **3e**, 71463-32-6; **3f**, 71426-06-7.

(5) Purification via silica gel chromatography was necessary to remove small amounts of starting materials and more polar impurities formed during the reaction. Attempts to purify the crude reaction by recrystallization (5–20% EtOAc/hexane) either resulted in much lower yields or was completely unsuccessful.

Pummerer Reaction of Para-Substituted Benzylic Sulfoxides

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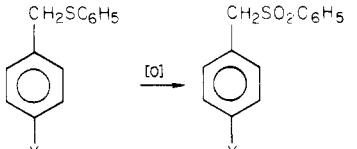
Received February 8, 1979

In the course of a study of the $S_{RN}1$ displacement reaction, a series of para-substituted benzyl phenyl sulfides, sulfoxides, and sulfones were required.[2] We observed that the sulfides **1a–e** can be oxidized to the corresponding



1a, X = CH_3O
b, X = H
c, X = Cl
d, X = CN
e, X = NO_2

sulfones in essentially quantitative yield by the use of 30% hydrogen peroxide in glacial acetic acid. However, oxidation with 30% hydrogen peroxide in a mixture of acetic acid (60%)–water (40%) acidified to 3 M with sulfuric acid, although successful for **1a–d**, led to the Pummerer reaction

(1) R. Pummerer, *Ber. Dtsch. Chem. Ges.*, **42**, 2282 (1909); *ibid.*, **43**, 1401 (1910).
(2) G. A. Russell and J. M. Pecoraro, *J. Am. Chem. Soc.*, **101**, 3331 (1979).

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