with vanillin/sulfuric acid. A Chromatotron (Harrison Research Laboratories) Model 7924 was used for preparative TLC with the plates prepared according to the instruction manual supplied by the manufacturer in thicknesses of 1, 2, or 4 mm using E. Merck 60 F254 silica gel on circular glass disks. DON and NIV were purchased from Research Foods Limited, Downsview, Ontario, Canada.

4,15-Hemiketal Form of 15-Hydroxytrichothec-9-ene-4,8-dione (2a). A mixture of 100 mg (0.36 mmol) of 8β-hydroxyverrucarol[13] and 800 mg of activated manganese dioxide[13] in 10 mL of acetone was stirred at reflux for 1 h. The reaction mixture was allowed to cool and filtered, and after the residue was washed with several small portions of acetone, the combined filtrates were concentrated. The residue was purified by preparative TLC (Chromatotron: silica, 2% methanol in dichloromethane) followed by crystallization from acetone to yield 65 mg (65%) of white crystalline **2a**: mp 170–172 °C; IR ($CHCl_3$) 3560, 1735, 1670, 1350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.75 (3 H, s, H-14), 1.78 (3 H, dd, J = 2.5, 2.0 Hz, H-16), 2.20 (1 H, dd, J = 16 and 4 Hz, H-3β), 2.59 and 2.39 (1 H each, AB, J = 16 Hz, H-7), 2.52 and 2.90 (1 H each, AB, J = 4 Hz, H-13), 2.31 (1 H, d, J = 16 Hz, H-3α), 3.78 and 3.95 (1 H each, AB, J = 14 Hz, H-15), 3.92 (1 H, d, J = 4 Hz, H-2), 4.55 (1 H, dd, J = 2.5, 2.0 Hz, H-11), 6.60 (1 H, dq, J = 2.5, 2.5 Hz, H-10); high-resolution mass spectrum (EI, 70 eV) calcd for $C_{15}H_{18}O_5$ (M^+) 278.1199, found 278.1154.

15-Acetoxytrichothec-9-ene-4,8-dione (2b). A 1:1 mixture of acetic anhydride and pyridine (0.1 mL each) was added to 10 mg of a 2:1 mixture of **2a** and **2**, and the resulting solution was left at room temperature overnight. Solvents were evaporated under a stream of nitrogen to yield **2b** as a glass, which was purified by preparative TLC (20% EtOAc/hexane): IR (CH_2Cl_2) 1745, 1685, 1370, 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80 (3 H, s, H-14), 1.82 (3 H, dd, J = 1.3, 1.0 Hz, H-16), 1.95 (3 H, s, acetate CH_3), 2.05 and 2.93 (1 H each, AB, J = 14 Hz, H-7), 2.45 (1 H, dd, J = 16, 2 Hz, H-3β), 2.90 (1 H, d, J = 16 Hz, H-3α), 2.70 and 3.25 (1 H each, AB, J = 4 Hz, H-13), 3.88 and 4.12 (1 H each, AB, J = 11.6 Hz, H-15), 4.18 (2 H, m, H-2 and H-11), 6.45 (1 H, dd, J = 4, 1.3 Hz, H-10); ^{13}C NMR ($CDCl_3$) 75.8 (C-2), 37.1 (C-3), 211.8 (C-4), 54.1 (C-5), 47.8 (C-6), 41.5 (C-7), 195.8 (C-8), 139.2 (C-9), 136.3 (C-10), 67.6 (C-11), 64.7 (C-12), 49.5 (C-13), 5.4 (C-14), 63.6 (C-15), 15.5 (C-16), 20.4 (CH_3COO), and 169.9 (CH_3COO).

X-ray crystallographic analysis of 1a: $C_{15}H_{12}O_5H_2O$, FW = 330.3, 0.18 × 0.24 × 0.32 mm colorless crystal, Nicolet R3m diffractometer, λ(Cu Kα) = 1.541 84 Å (incident beam graphite monochromator), orthorhombic space group $P2_12_12_1$, a = 6.730 (1) Å, b = 14.143 (3) Å, c = 15.482 (2) Å, V = 1473.7 (4) $Å^3$, Z = 4, ρ = 1.49 g cm^{-3}, μ = 9.8 cm^{-1}, $F(000)$ = 704, T = 295 K. Lattice parameters from 25 reflections in the range of $27 \le 2\theta \le 76°$, data collection range of $-7 \le h \le 2$, $0 \le k \le 16$, $0 \le l \le 18$, max sin θ/λ = 0.59 $Å^{-1}$, 2θ–θ scan with variable speed of θ = 8–30 deg min^{-1}, 2θ scan range = $[2\theta(K_{\alpha 1}) - 1.0]$ to $[2\theta(K_{\alpha 2}) + 1.0]$, 3 standard intensities monitored every 60 data, maximum change in standard intensities of 2.6%, 1495 unique reflections, 1399 with $F_o \ge 3\sigma(F_o)$, R_{sym} for equivalent reactions = 0.01. All calculations done with the SHELXTL[15] package on a CRAY-X/MP computer, structure solved with direct methods, refinement by full-matrix least-squares, $\sum w(|F_o| - |F_c|)^2$ minimized with $w[2(F_o) + 0.00025F_o^2]$, carbon and oxygen parameters refined with anisotropic parameters, hydrogen atoms with isotropic terms, secondary isotropic extinction parameter = 0.0035 (5), final R, wtd R and error-of-fit values of 0.033, 0.038, 1.43, minimum and maximum in final difference map of −0.17 and 0.18 e $Å^{-3}$.

X-ray crystallographic analysis of 2a: $C_{15}H_{12}O_5$, FW = 272.3, 0.2 × 0.3 × 0.34 mm colorless crystal, Enraf-Nonius CAD4 diffractometer, λ(Mo Kα) = 0.710 69 Å (incident beam graphite monochromator), monoclinic space group $P2_1$, a = 7.545 (1) Å, b = 8.210 (2) Å, c = 10.820 (2) Å, β = 108.74 (1)°, V = 6304.7 (4) $Å^3$, z = 2, ρ = 1.42 g cm^{-3}, μ = 0.71 cm^{-1}, $F(000)$ = 284, T = 293 K. Latice parameters from 25 reflections in the range of $12 \le \theta \le 26°$, data collection range of $0 \le h < 8$, $0 < k < -9$, $-11, < l < 12$, $2 < \theta \le 50°$, 2θ–θ scan with variable speed of θ = 8.14–1.81 deg min^{-1}, θ scan range = 1.5(0.96 + 0.34 tan θ)°, background values obtained from the lower and the upper sixths of scan range, 5 standard intensities monitored every 1 h of crystal X-ray exposure, maximum and average change in standard intensities of 3.6 and 1.4%, 1330 total reflections, 1295 without standards, 1112 with $I_o \gg 3\sigma(I_o)$, R_{sym} for equivalent reflections = 0.004. All calculations done with the TEXRAY[16] package on a DEC Microvax II computer, structure solved with the direct methods link MITHRIL,[17] refinement by full-matrix least-squares, $\sum w(|F_o| - |F_c|)^2$ minimized with $w = [2(F_o) + 0.009F_o^2]$, carbon and oxygen parameters refined with anisotropic parameters = 0.00002 (4), final R, wtd and error-of-fit values of 0.030, 0.036, 1.82 minimum and maximum in final difference map of −0.13 and 0.16 e $Å^{-3}$.

Acknowledgment. We thank the National Science Foundation for Grant No. CHE-85-02155 which provided a portion of the funds for purchase of the diffractometer/MicroVax system, and the National Institute of Health for Shared Instrumentation Award No. RR-03354 for purchase of a graphics workstation at the University of Maryland. B.B.J. acknowledges support from NIH Grant CA-25967.

Registry No. **1**, 23282-20-4; **1a**, 126640-47-9; **2**, 126503-40-0; **2a**, 126541-26-2; **2b**, 126541-27-3; **3**, 51481-10-8; **3a**, 126503-41-1; **4**, 63783-99-3.

Supplementary Material Available: ^1H and ^{13}C NMR spectra of **2b** and atomic coordinates, equivalent isotropic displacement parameters, bond lengths, and bond angles from the X-ray crystallographic analyses of **1a** and **2a** (9 pages). Ordering information is given on any current masthead page.

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Solvolysis of 2-Aryl-2-propyl Benzoates. Validity of the Assumption of Constant *p*-Nitrobenzoate/Benzoate Rate Ratios

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The Hammett correlation analysis, modified by using σ^+ constants,[1] $\log (k_X/k_H) = \sigma^+\rho$,[2] has long been a useful probe for elucidating the mechanism of solvolytic reactions.[3,4] In carrying out such an analysis sometimes an estimation of rate constants is necessary if the reactivity of a substrate is too high or too low to measure directly. An assumption of a constant rate ratio for substrates containing two different leaving groups is generally applied to the structurally related systems. Thus, a factor of 20.8[5] was used to multiply the rate constant for a benzoate ester to obtain that for the corresponding p-nitrobenzoate in 80% acetone.[6] A decade ago this assumption was chal-

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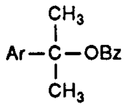
Table I. Kinetic Data for the Solvolysis of 2-Aryl-2-propyl Derivatives

substrate	k, s^{-1} (temp, °C)	k, s^{-1} at 25 °C	k_{OPNB}/k_{OBz}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
1a		$1.72 \times 10^{-5\,a}$	21.6^{a}		
1b		$5.69 \times 10^{-6\,b}$			
1c	3.71×10^{-4} (100)				
	3.30×10^{-5} (75)	$7.73 \times 10^{-8\,c}$	19.9^{d}	24.4	−9.3
1d	4.84×10^{-4} (125)				
	2.07×10^{-4} (115)				
	3.03×10^{-5} (95)	$5.31 \times 10^{-9\,c}$		26.3	−7.9
1e	2.63×10^{-4} (125)				
	2.77×10^{-5} (100)	$3.36 \times 10^{-9\,c}$	21.4^{d}	26.0	−10.1
1f	1.60×10^{-5} (125)				
	2.36×10^{-6} (105)				
	8.07×10^{-7} (95)	$7.51 \times 10^{-11\,c}$	24.8	28.3	−9.7
2f	1.93×10^{-4} (125)				
	3.10×10^{-5} (105)				
	1.17×10^{-5} (95)	$1.86 \times 10^{-9\,c}$		26.6	−9.1
1g	4.62×10^{-6} (125)^{e}				
	5.83×10^{-7} (105)^{e}	$9.19 \times 10^{-12\,c}$		30.4	−7.1

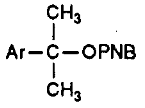
[a] Reference 10. [b] Literature value,[11] 5.76×10^{-6}. [c] Extrapolated from data obtained at other temperatures. [d] k_{OPNB} was taken from the literature.[8] [e] From k(70% acetone)/3.79.[10]

lenged on the grounds that the ρ values for the benzoate and the p-nitrobenzoate were unlikely to be equal.[7] However, this argument has not yet been tested. Therefore, we undertook to study the solvolytic reactivities of a number of 2-aryl-2-propyl benzoates (**1a–g**), and a ρ value of −4.77, very close to −4.72 for that of the p-nitrobenzoates,[8] was obtained.



$$\mathrm{Ar{-}C(CH_3)_2{-}OBz}$$

1a: Ar = 4'-$CH_3OC_6H_4$
b: Ar = 3',4'-$OCH_2OC_6H_3$
c: Ar = 4'-$CH_3C_6H_4$
d: Ar = 4'-FC_6H_4
e: Ar = C_6H_5
f: Ar = 3'-FC_6H_4
g: Ar = 3'-$CF_3C_6H_4$



$$\mathrm{Ar{-}C(CH_3)_2{-}OPNB}$$

2f: Ar = 3'-FC_6H_4

The benzoates **1** and the p-nitrobenzoate **2f** were prepared from acetone and the appropriate aryl halides via the one-pot procedure.[9] The rates of solvolysis were measured titrimetrically (for **1c–g** and **2f**) or conductimetrically (for **1b**) in 80% acetone, except that of **1g** which was measured in 70% acetone[10] because of its instability in 80% acetone at higher temperature. The deviation of the rate constants was less than 2% in at least two independent experiments. The results are listed in Table I.

An excellent linear plot with ρ of −4.77 (correlation coefficient = 0.999) was obtained from the Hammett–Brown treatment[2] of the rate constants for **1a,c–g** (Figure 1). Obviously, the reaction constant ρ is nearly the same for both 2-aryl-2-propyl p-nitrobenzoates and benzoates, contrary to that has been inferred.[7] Moreover, the measured rate ratios, k_{OPNB}/k_{OBZ} = 19.9–24.8, do not show a large deviation from the average value 21.9, which is fairly close to the conversion factor 20.8, proposed earlier. The σ^{+} values estimated previously from the rate constants of benzoates[11] can then be considered suitable. From the interpolation on the log k − σ^{+} plot, a value of −0.688 can be obtained as the substituent constant for 3',4'-methylenedioxy group (the open circle in Figure 1), which is almost identical to −0.676, suggested previously.[11] It also agrees with the value −0.667 calculated from the oxygen-17 chemical shift[12,13] for the carbonyl oxygen in 3',4'-(methylenedioxy)phenyl trifluoromethyl ketone.

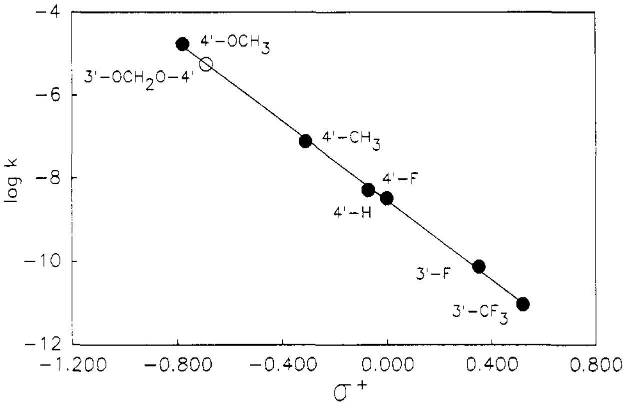


Figure 1. log k − σ^{+} plot for 2-aryl-2-propyl benzoates (1) in 80% acetone at 25 °C.

It has been demonstrated that for substrates containing leaving groups of significantly different reactivities, such as tosylates and bromides with $k_{OTs}/k_{Br} > 10^{4}$,[14] the ρ values are quite different from each other and the rate ratios are not constant. The present observation of similar reaction constants for benzoates and p-nitrobenzoates in 80% acetone suggests the validity of the assumption of a constant k_{OPNB}/k_{OBz} in the same solvent system. Accordingly, this type of relation is likely to hold in the cases that the leaving groups do not differ appreciably in nucleofugality. Constant rate ratio for dinitrobenzoate/p-nitrobenzoate,[10] or for bromide/chloride, are likely to be observed.

Experimental Section

Capillary melting points were uncorrected. Infrared spectra were recorded with a Perkin-Elmer Model 983G spectrometer and proton NMR spectra with a Varian Model EM390 instrument.

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(10) The rate constant k (80% acetone) was estimated by dividing k(70% acetone) by a factor of 3.79, which was obtained by comparing the literature rate data of 2-phenyl-2-propyl p-nitrobenzoate. (Reference 8 and Tanida, H.; Matsumura, H. *J. Am. Chem. Soc.* **1973**, *95*, 1586–1593.)

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Elemental analyses were performed in the Elemental Analysis Laboratory of this Department.

Preparations of 2-Aryl-2-propyl Benzoates 1b–g and *p*-Nitrobenzoate 2f. The substrates were prepared by using the one-pot procedure[9] from acetone, butyllithium, aryl halides, and benzoyl or *p*-nitrobenzoyl chloride on 30-mmol scale. The crude esters (50–60% yield) were recrystallized from hexanes to give pure compounds, mp: **1b**, oil;[11] **1c**, 80.5–81.5 °C; **1d**, oil; **1e**, 48–48.5 °C; **1f**, oil; **1g**, 67–67.5 °C; **2f**, 126–127 °C. Correct C and H analyses (<0.3%) were observed for all new compounds. Infrared and proton magnetic resonance spectra were in agreement with the assigned structures.

Kinetic Measurements. (a) Titrimetric method: A 0.005–0.01 M solution of the substrate in 80% acetone or in 70% acetone was prepared at about 25 °C, and aliquots of 2 mL were sealed under nitrogen. The ampules were removed from the thermostat at suitable time intervals and were titrated as described before.[15] All reactions were followed to about 2 half-lives with excellent first-order behavior (9–11 points, $r > 0.995$). (b) Conductimetric method: The sample was dissolved to make 10 mL of a 10^{-4} M solution, which was placed in a conductivity cell with platinum electrodes. The rates of solvolysis were monitored at 1-s intervals with an on-line conductivity amplifier[16] to 2 or more half-lives. Excellent linear correlation for a first-order plot was observed.

The rate constants and the calculated activation parameters are shown in Table I.

Acknowledgment. We are indebted to the National Science Council for financial support of this work.

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[16] The details about this instrument will be reported elsewhere.

A Comparison of the Oxidative Reactivities of Mustard (2,2′-Dichlorodiethyl Sulfide) and Bivalent Sulfides

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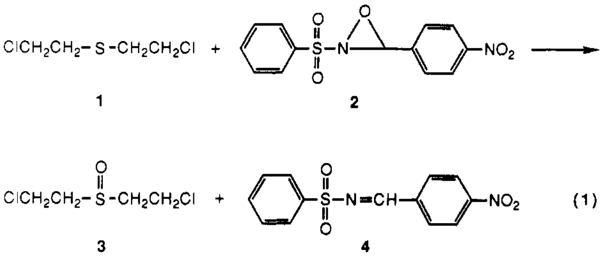
Mustard (**1**, 2,2′-dichlorodiethyl sulfide), a liquid vesicant, can be detoxified to the crystalline sulfoxide and sulfone by oxidation, although the sulfone has been reported to still exhibit some vesicant toxicity.[1,2] The sulfur in mustard is believed to be oxidatively less reactive than that in alkyl sulfides because of the presence of two large electron-withdrawing chlorine atoms. However, alkyl sulfides have often been used to simulate the oxidation of mustard.[3] Recently, *N*-sulfonyloxaziridine derivatives such as **2** were presented as a new class of neutral organic oxidants that selectively oxidize bivalent sulfides to sulfoxides in organic solvents.[4,5] In fact, the reaction rate was so fast that no rate coefficient could be measured at room temperature. In this study, the oxidation of mustard and a series of bivalent sulfides by **2** was examined, and the reaction rates were determined using NMR. Our purpose was to determine if mustard could be quickly detoxified by **2** via the same S_N2 mechanism previously reported for most sulfides (eq 1),[4,5] and to compare the oxidative reactivity of mustard with its monofunctional derivatives (i.e. simulants) as well as the alkyl and aryl sulfides (see list of compounds in Table I).

Table I. Competition Oxidation Rates of Bivalent Sulfides[a,b]

sulfides	competition oxidation rate	relative hydrolysis rate[c]
$(ClCH_2CH_2)_2S$ (**1**)	1.0	1.0[d]
$C_2H_5SCH_2CH_2Cl$ (**1a**)	4.8	5.9
$(C_2H_5)_2S$ (**1b**)	23	
$(n\text{-}C_4H_9)_2S$ (**1c**)	9.6	
$(C_6H_5)_2S$ (**1d**)	0.96	
$C_6H_5SCH_2CH_2Cl$ (**1e**)	0.92	0.095
$C_6H_5SCH_2CH_2Br$ (**1f**)	1.8	0.76
$C_6H_5SCH_2CH_2OH$ (**1g**)	4.0	
$CH_3SCH_2CH_2Cl$ (**1h**)	4.2	4.8
$CH_3SCH_2CH_2OH$ (**1i**)	10	
$i\text{-}C_3H_7SCH_2CH_2Cl$ (**1j**)	5.0	7.6
$i\text{-}C_4H_9SCH_2CH_2Cl$ (**1k**)	5.0	*e*
$n\text{-}C_4H_9SCH_2CH_2Cl$ (**1l**)	5.0	9.0
$i\text{-}C_5H_{11}SCH_2CH_2Cl$ (**1m**)	5.4	*e*

[a] The competition oxidation rate is the ratio of the sulfoxide products from the oxidation of two sulfides present in equal moles by a minimum amount of **2** in the reaction mixture. The accuracy of the reported competition oxidation rate is 5–10%. [b] The observed first-order rate of **1e** at 0.01 M excess **2** at 18 °C was measured to be 0.11 ± 0.01 min^{-1}. [c] Calculated from published first-order hydrolysis rate constants at 25 °C in the presence of 5–10 vol% ethanol, acetone, or acetonitrile (ref 7 and 8). [d] Based on the rate of displacement of the first chlorine in mustard, see ref 8. [e] The rate at 25 °C was too fast to be measured accurately.



To a solution of 0.053 M mustard in $CDCl_3$ at 20 °C was added 0.1 M of **2**. In less than 2 min, ^{13}C NMR showed that all of the mustard (**1**) was converted to one product, mustard sulfoxide (**3**, $OSCH_2$, 55.1 ppm and CH_2Cl, 36.7 ppm), with half of the initial oxidant left unreacted. A second sample containing approximately 0.2 M **1** and 0.1 M **2** was examined. Immediate ^{13}C NMR analysis showed that 45% of **1** had reacted to produce **3**, and all of the initial **2** was reduced to **4**. Therefore, mustard was effectively detoxified by **2** in chloroform, and the stoichiometry shown in eq 1 was confirmed. The presence of chlorines did not provide any additional oxidation sites for reacting with **2**.

Subsequently, the oxidation of a series of bivalent sulfides by **2** was examined using ^{13}C or ^1H NMR in $CDCl_3$ at 0.05 to 0.1 M sulfide concentrations. All of the compounds reacted with the identical stoichiometry as that of mustard in less than 2 min. Thus, competition oxidation

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