Dehydrobromination of Some Substituted Phenyl 3-Bromopropionates and Phenyl 3-Bromothiolopropionates. Transmission of Activation Effects through Acyl Bonds

Arthur B. Gilbert, III,[1] Frances B. Peters, and H. W. Johnson, Jr.*

Department of Chemistry, University of California, Riverside, California 92521

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Thirteen aryl 3-bromopropionates and nine aryl 3-bromothiolopropionates were prepared and subjected to dehydrohalogenation with sodium 3,4-dinitrophenoxide in dry tetrahydrofuran at 34.25 °C. The second-order rate constants for the sulfur esters were approximately 10 times those for the corresponding oxygen esters. Good Hammett plots with ρ's of +0.81 ± 0.04 and 0.98 ± 0.04 for the oxygen and sulfur series, respectively, were obtained by using σ^n. Activation parameters were measured for two oxygen and two sulfur esters; in both bases, low (12–13 kcal/mol) activation enthalpies and moderately large negative (19–21 eu) activation entropies were found. At 34.25 °C, 3′-nitrophenyl 3-bromopropionate dehydrohalogenated 14 times more rapidly than 3′-nitrophenyl 3-chloropropionate; phenyl 3-bromothiolopropionate dehydrohalogenated 11 times more rapidly than the phenyl 3-chlorothiolopropionate. The rate constant ratio for 4′-bromophenyl 3-bromopropionate vs. 4′-bromophenyl 3-bromopropionate-2-*d* was 1.84; the monodeuterated compound yielded olefinic product with 65% D. H was abstracted preferentially from 4′-chlorophenyl 3-bromothiolopropionate partially deuterated in the 2-position, but no kinetic results were obtained. No evidence of reversibility was found with 2,4-dinitrophenol-*d*, and the addition of 2,4-dinitrophenol to kinetic mixtures had essentially no effect on the rate constants. The results are interpreted to indicate an E2 process near the EL/E1cB borderline with the thiolo ester deviating somewhat more toward an E1cB-I process.

The transmission of activation effects through various chains has been studied since the publication of the Hammett equation.

Interest in both the experimental determination and the theoretical explanations continues to the present day.[2] We became interested in this area originally because there was no information in the literature concerning the transmission of electronic effects through amide bonds from a group on nitrogen to a group attached to the carbonyl carbon atom. A study indicated surprisingly efficient transfer of electronic effects in the elimination of hydrogen bromide as the R group was varied from methyl to phenyl to 4-nitrophenyl in compounds of the type $BrCH_2CH_2CONHC(O)NHR$.[3] A series of studies by us and others has shown that transmission of electronic effects through amide bonds is efficient if charge is developed in the transition state,[4] though some exceptions have been noted.[5]

We thought that comparison of nitrogen and phosphorus as components in the transmission chain might give insight into the transmission mechanism. Upon being advised that phosphorus might present experimental difficulties, we decided to study esters vs. thiolo esters as structural analogues. Since both esters and thiolo esters are important functionalities in biochemical systems, the choice was even more attractive. We settled upon elimination reactions when it became apparent that the acrylate thiol esters were very difficult to preserve for kinetic determinations of Michael additions, apparently undergoing polymerization much more rapidly than the oxygen esters. In addition, there seemed to be no studies of elimination reactions in the literature that utilized 3-halopropionic acid esters, a surprising finding given the importance of the ester functionality as an activating group in carbanion chemistry. In this work we report the rates of dehydrohalogenation of several substituted phenyl esters and thiolo esters of 3-bromopropionic acid with sodium 3,4-dinitrophenoxide in dry tetrahydrofuran, eq 1.

$$ArXCOCH_2CH_2Br + (O_2N)_2C_6H_3O^- \rightarrow ArXCOCH{=}CH_2 + (O_2N)_2C_6H_3OH + Br^- \quad (1)$$

$$X = O, S$$

The oxygen esters were prepared by reaction of the neat phenol with 3-bromopropionyl chloride[6] or by reaction of the substituted thallium phenoxide with the acid chloride.[7] The substituted phenyl 3-bromothiolopropionates were prepared by reaction of the lead salt of the thiophenol with the acid chloride in anhydrous ether.[8] Both series of compounds lose hydrogen bromide very easily, and purification was a problem. Samples of both series of compounds having satisfactory elemental analyses, infrared spectra, and proton NMR spectra were secured.

The kinetic studies were carried out by monitoring the phenoxide peak at 432 nm continuously by using 1-mm cells in the thermostated cell block of a Beckman DB spectrophotometer; concentrations were approximately 10^{-3} M in tetrahydrofuran. Stronger bases than 3,4-dinitrophenoxide gave inconveniently short reaction times. Solvents such as ethanol or 2-methoxyethanol gave evidence of ester interchange and Michael addition. At reaction times beyond those needed for this work, 3,4-di-

(1) Taken in part from the Ph.D. Dissertation of A.B.G., III, U.C. Riverside, 1973. Present address: Whitestone Chemical, P.O. Box 2108, Spartanburg, SC 29304.

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Table I. Dehydrobromination Rates of Substituted Phenyl 3-Bromopropionates and 3-Bromothiolopropionates with Sodium 3,4-Dinitrophenoxide in THF at 34.25 °C

	rate constant, L mol^{-1} s^{-1}			
substituent	oxygen compound	sulfur compound	k_S/k_O	σ^n
4′-NO_2	0.429	6.08	14.2	0.78
3′-NO_2	0.340			0.71
4′-$COCH_3$	0.218	2.43	11.1	0.50
3′-$COCH_3$	0.185	1.83	9.9	0.38
4′-CO_2CH_3	0.197			0.38
4′-Br	0.169			0.26
3′-Br	0.212			0.39
4′-Cl	0.166	1.57	9.5	0.24
3′-OCH_3	0.102			0.12
4′-OCH_3	0.0740	0.746	10.0	−0.11
H	0.0916	0.954	10.4	0
3′-CH_3	0.0772			−0.09
4′-CH_3	0.0699	0.721	10.3	−0.14
4′-F		1.11		0.06
4′-$C(CH_3)_3$		0.645		−0.17
	ρ = 0.814	ρ = 0.980	av 10.8	

nitrophenol also seemed to add to the phenylacrylate product. Reproducible "infinity" absorbances were established for the present kinetic studies. The experimental data was analyzed by using a least-squares computer program to fit the integrated second-order rate constant expression for unequal concentrations.[9] The average deviation of points from the best straight line was less than 1% within a single run; deviations between duplicate runs were less than 3%. Normally, three runs were made; though in a few cases only two independent runs with new solutions were made.

The products of the reaction were the substituted phenyl acrylate and 3,4-dinitrophenol from the oxygen esters, and the phenyl thioloacrylate together with 3,4-dinitrophenol from the sulfur esters. Evaporation of a larger volume of the reactants at equal concentrations at room temperature gave a residue whose proton NMR spectrum in acetone-d_6 or Me_2SO-d_6 showed only the absorption maxima to be expected from the acrylate and 2,4-dinitrophenol. For the oxygen esters, both GLC and TLC were used to establish that only the expected compounds were present. The thioloacrylates polymerized very easily, and only TLC could be used to establish the number of compounds present, although proton NMR spectra showed acrylate to be present. In kinetic runs the maximum at 310 nm was used to determine the dinitrophenol concentration at the end of the reaction.

The rate constants for 13 substituted aryl 3-bromopropionates and 9 aryl 3-bromothiolopropionates at 34.25 °C are shown in Table I. Also included are the σ^n substituent constants[10] used in the Hammett-type correlation to be discussed later. The sulfur esters reacted substantially faster than the oxygen esters under the conditions of this study; for seven substituents common to both series, the average k_S/k_O was 10.8. The faster elimination rate for the sulfur compounds is consistent with the greater acidity of hydrogens α to the thiolo ester carbonyl compared with that of the oxygen esters.[11]

Table II. Temperature Dependence of Dehydrohalobromination Rates for Phenyl 3-Bromopropionates and 3-Bromothiolopropionates with 3,4-Dinitrophenoxide in THF

ester	substituent on Ph	temp, °C	k_2, M s^{-1}
O	3′-NO_2	10.75	0.0691
		22.20	0.1422
		34.25	0.340
		43.35	0.625
O	4′-H	22.20	0.03845
		34.25	0.0905
		43.35	0.1675
S	4′-H	22.20	0.4086
		34.25	0.9538
		43.35	1.773
S	4′-$COCH_3$	10.75	0.480
		22.20	1.00
		34.25	2.45
S	4′-NO_2	10.75	1.21
		22.20	2.40

Table III. Activation Parameters for Aryl 3-Bromopropionates and Aryl 3-Bromothiolopropionates

substituent	E_a, kcal/mol	$\Delta G^{\ddagger}$,[a] kcal/mol	$\Delta H^{\ddagger}$,[a] kcal/mol	$\Delta S^{\ddagger}$, eu
O-3′-NO_2	12.09	18.51	12.51	−21.3
O-4′-H	12.815	19.49	12.88	−21.0
S-4′-NO_2	11.87	16.72	11.90	−19.2
S-4′-$COCH_3$	11.98	17.25	12.03	−19.1
S-4′-H	12.72	18.02	12.84	−20.19

The temperature dependence of two aryl bromopropionates and three aryl bromothiolopropionate dehydrohalogenation rates was determined. The individual values are shown in Table II, and the derived activation parameters are listed in Table III. Both the sulfur and the oxygen esters show relatively low enthalpies of activation, 12.9 and 12.8 kcal/mol, respectively. The entropies of activation, −21.1 and −21.0 eu for the phenyl compounds, are moderately large negative numbers and may be related to the low dielectric constant of the solvent rather than to some intrinsic property of the elimination reaction itself. The reactions of the sulfur and oxygen esters are very similar in activation properties and presumably in the structure of the respective transition states.[12] DePuy and Bishop[13] determined activation parameters for the elimination reactions of β-phenylethyl chlorides in ethanol with ethoxide at 60 and 80 °C. The values of the activation enthalpy were found to be 22–23 kcal/mol, and the activation entropy varied from −1 to −6 eu. Their series of elimination reactions thus showed significantly higher activation enthalpies and less negative activation entropies than the esters reported in the present work.

In an attempt to define the nature of the elimination reaction more precisely, the rates of dehydrohalogenation of 3′-nitrophenyl 3-chloropropionate and phenyl 3-chlorothiolopropionate were subjected to the elimination reaction under conditions identical with the bromo compounds. At 34.25 °C, the ratio of the bromo/chloro oxygen ester rate constants was 14.1; the ratio of the Br/Cl thiolo ester rate constants was 10.8. There is a substantial element effect[14] in which bromide is eliminated faster than

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chlorine, which supports breaking of the C–Br and C–Cl bond in the elimination transition state.

The elimination reaction of 4′-nitrophenyl 3-bromopropionate with 3,4-dinitrophenoxide in THF at 34.25 °C was measured in the presence of a 100% excess of 3,4-dinitrophenol; the rate constant decreased by 3.4%, a value within or barely outside experimental error. Use of 3,4-dinitrophenol-*d* gave no evidence from proton NMR spectra, for incorporation of D into either the elimination product or unreacted starting material at 50% reaction. A study with phenyl 3-bromothiolopropionate gave similar results. Thus, neither oxygen nor sulfur esters appears to form a carbanion capturable by 3,4-dinitrophenol under the conditions used in this work.

Addition of dry DBr to 4′-bromophenyl acrylate in cyclohexane gave 4′-bromophenyl 3-bromopropionate-2-*d* as shown by the proton NMR spectra and mass spectra. This compound was subjected to elimination of HBr with 3,4-dinitrophenoxide in THF at 35.20 °C. The ratio of rate constants of the 2-H_2/2-HD compounds was 1.84. Mass spectra and NMR spectra indicated that the aryl acrylate product had 66% D in the olefin 2-position, indicating an internal k_H/k_D of 2.0. Translation of these numbers to a more normal rate constant ratio of $ArOCOCH_2CH_2Br$ vs. $ArOCOCD_2CH_2Br$ involves assumptions. One simple method is to ascribe $^1/_3$ of the rate constant of 1.07 to removal of D from the HD compound, giving 0.36 L mol^{-1} s^{-1}. Comparison of 2 × 0.36 with 1.97 from the 2-H_2 ester gives k_{H_2}/k_{D_2} = 2.7. However, this latter calculation may be done, there is a substantial H/D isotope effect, one that seems large enough to be consistent with an E2 mechanism rather than the alternative E1cB, though near the borderline.[15]

The ready polymerization of phenyl thioloacrylates in our hands prevented synthesis of sulfur esters comparable to the deuterated oxygen ester described above in pure form or in reasonable yield. In one partly successful attempt, 4′-chlorophenyl 3-bromothiolopropionate deuterated to the extent of 37% of one D in the 2-position was prepared by the addition of DBr to the mixture of acrylate and polyacrylate. After the elimination reaction was carried out to 50% completion with 3,4-dinitrophenoxide in THF, NMR and mass spectra indicated that the starting material recovered had 42% D in the 2-position. No kinetics were measured. This result shows that H is being removed selectively, but a numerical isotope effect cannot be assigned.

The results from the chlorine/bromine substitution, the nonreversibility of the proton removal, the lack of effect of addition of 3,4-dinitrophenol on the reaction rate, and the isotope effect (particularly for oxygen) suggest that these two reactions are both largely E2 in character, though skewing of the transition state toward early C–H bond breaking is probable. The somewhat smaller Br/Cl rate ratio for the thiolo compounds could indicate less C–X bond breaking in the transition state relative to the oxygen esters, a statement consistent with the slightly larger ρ for the thiolo esters.[14] This conclusion is at variance with the work of Fedor and Cavestri[16] who studied reactions of *tert*-butyl 3-(aryloxy)propionates and *tert*-butyl 3-(aryloxy)thiolopropionates to conclude (reasonably enough) that their compounds utilized the E1cB mechanism; the basis for the conclusion was the lack of a significant effect of substituents in the leaving aryloxy group. The compounds in the present work have better leaving groups that would favor the E2 mechanism over the E1cB.[17]

The Hammett-type ρ value using σ^n for the oxygen esters was 0.814 (r = 0.986, n = 11); the corresponding value for the thiolo esters was 0.980 (r = 0.993, n = 9). One of several other similar scales[9] could have been used for the correlations, both of which obey the Hammett equation reasonably well. The Taft correlation using $\sigma_I + \sigma_R$ was somewhat less successful.[10] Clearly, activation effects are being transmitted through the ester and thiolo ester links to the reactive site. The efficiency of transmission depends upon the standard chosen. Several reference reactions were found in the literature. The elimination reactions of β-phenethyl halides, sulfonium salts, and ammonium salts in ethanol with ethoxide gave ρ values that varied from 2.07 for the iodide to 3.77 for the trimethylammonium salt. The bromides gave ρ of 2.14.[15] The elimination reactions of phenylethyl fluorides with *tert*-butoxide in *tert*-butyl alcohol gave ρ of 3.24 compared with 3.12 in ethanol/ethoxide. Alunni and Baciocchi[18] studied the elimination reactions of phenylethyl bromides with sodium phenoxide and *p*-nitrophenoxide in ethanol; ρ decreased from 2.64 with phenoxide to 1.84 with *p*-nitrophenoxide, thus indicating a substantial decrease in ρ with the decrease in base strength. A change of solvent from ethanol to THF should affect the ρ of the elimination reaction as well. Presumably the most direct comparison is with the work of Alunni and Baciocchi. Without factoring in the corrections for the lower base strength of 3,4-dinitrophenoxide vs. *p*-nitrophenoxide or the solvent effect, 0.98/1.84 gives a ρ ratio of 0.53 for the sulfur esters vs. phenethyl bromide and 0.81/1.84 gives a ρ ratio of 0.44 for the oxygen esters vs. phenethyl bromide. We would expect that a ratio involving correction for base strength and solvent would yield a ratio more nearly equal to 1 but have no experimental evidence to prove the statement.

One final set of comparisons is worthwhile: Yano and Oae[19] studied the dehydrohalogenation of aryl 2-chloroethyl ethers and thioethers as well as the corresponding aryl 3-bromopropyl series with sodium ethoxide in ethanol at 60 °C. The chloroethyl ethers had a ρ of 1.50 and the chloroethyl thioethers showed a ρ of 2.14. The bromopropyl ethers had a ρ of 0, and the bromopropyl thioethers a ρ of 0.37. DePuy and Bishop[13] studied β-phenethyl chloride with sodium ethoxide in ethanol at 60 °C and found ρ to be 2.58. The sulfur series all show a somewhat higher ρ value than the corresponding oxygen series, a finding extended in the present work to the esters vs. thiolo esters.

The reason for the greater acidity of thiolo esters relative to oxygen esters has been the subject of substantial discussion. The most common explanation involves the importance of cannonical forms involving a positive charge on the ether oxygen of the oxygen esters (removing positive character from the carbonyl carbon atom) relative to the sulfur thiolo esters (where 3p-S/2p-C is presumed to be less efficient than in the 2p-O/2p-C case); the greater positive charge on the thiolo ester carbonyl carbon is responsible for the enhanced acidity of the α hydrogens.[11] Other workers have suggested that sulfur d orbitals have the effect of stabilizing a negative charge on sulfur while similar forms are not available to oxygen.[20] Our results,

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specifically the larger ρ value for the sulfur series and the lower Br/Cl ratio in the sulfur series, seem to support greater negative charge development on the 2-carbon in the sulfur esters. We see these as providing additional support to the active role of sulfur in supporting the negative charge rather than a lack of overlap between carbon and sulfur 2p–3p orbitals.

Experimental Section

Uncorrected melting points were determined in a Thomas-Hoover capillary melting point apparatus. Gas chromatograms were run with an F&M Model 700 temperature-programmed dual column chromatograph with 6 ft × $^1/_8$ in. columns packed with 10% SE-30 on 80–100-mesh acid-washed DMSS. Infrared spectra were recorded with Perkin-Elmer Model 137 and 621 spectrophotometers. A Varian Associates Model A 60D spectrometer was used for NMR spectra. Chemicals were purchased from commercial sources and were the highest grade available. THF was distilled from calcium hydride as needed. Analyses were performed by C. F. Geiger, Ontario, CA, and by Elek Labs., Torrence, CA.

Synthesis of Phenyl 3-Bromopropionates. The neat procedure of Kratzl[6] was used for seven compounds on a 10-g scale. IR and GLC were used to monitor the reaction. The crude mixtures were diluted with benzene and washed with 0.1% sodium hydroxide, 0.1% sodium bicarbonate, and water. After the solution was dried ($MgSO_4$) and the solvent removed on a rotary evaporator, the residue was distilled with a 6-in. Vigreux column in vacuo. Solids were crystallized from benzene/petroleum ether.

The following compounds were prepared (aromatic-ring substituent: mp or bp (torr); NMR spectrum (δ) in $CHCl_3$).

4′-Nitro: mp 32–33 °C; 3.21 (t), 3.68 (t), 7.82 (q).

3′-Nitro: mp 50–51 °C; 3.02 (t), 3.80 (t), 7.43 (m), 7.98 (m).

4′-Bromo: mp 29–30 °C; 3.12 (t), 3.65 (t), 7.23 (q).

4′-Chloro: mp 25.5–26.5 °C; bp 132 °C (0.9); 3.13 (t), 3.68 (t), 7.21 (q).

4′-Methoxy: bp 126 C (0.45); 3.74, 3.10 (t), 3.65 (t), 6.94 (q).

3′-Methoxy: bp 128 °C (0.4); 3.75 (s), 3.12 (t), 3.63 (t), 6.7 (m), 7.2 (m).

4′-Methyl: bp 118 °C (0.3); 3.15 (t), 3.55 (t), 7.37 (q).

The thallium phenoxide method of Taylor and McKillop[7] was used for the remaining phenyl 3-bromopropionates. The thallium phenoxide was prepared from equimolar quantities of thallium ethoxide and the phenol on a 10-g scale in absolute ethanol. The precipitated solid was crystallized from ethanol/water and dried over P_2O_5 in a drying pistol. Reaction of equimolar quantities of the thallium phenoxide with 3-bromopropionyl bromide in anhydrous ether yielded the ester. Solids were crystallized from benzene/petroleum ether; liquids were distilled under vacuum in a Vigreux column or by Kugelrohr distillation (for the latter, no boiling points are given since they all distilled at about 110 °C (1 torr)). Yields of purified product approximated 50% in the second step.

The following compounds were prepared in this way (substituent: mp or bp (torr); NMR (δ) maxima in $CDCl_3$).

4′-Carbomethoxy: 72–73 °C; 3.19 (t), 3.68 (t), 7.67 (q).

4′-Acetyl: 79.5–81 °C; 2.60 (s), 3.18 (t), 3.68 (t), 7.61 (q).

3′-Bromo: Kugelrohr; 3.15 (t), 3.67 (t), 7.4 (m).

3′-Methyl: Kugelrohr; 2.20 (s), 3.13 (t), 3.65 (t).

Characteristic IR bands were 1765 and 1265 cm^{-1}.

Synthesis of Phenyl 3-Bromothiolopropionates. The lead salt method of Braude was adopted.[8] On a 10-g scale, 2 molar equiv of thiophenol were mixed with 1 molar equiv of lead acetate in 50 mL of 1:1 water:ethanol with rapid stirring. The lead thiophenoxide precipitate was filtered and washed with water (2×), ethanol (3×), and anhydrous ether (5×); the salt was dried over P_2O_5 under vacuum for 24 h in the dark. Then 0.01 mol of lead thiophenoxide was added to 0.015 mol of 3-bromopropionyl bromide in anhydrous ether; stirring at room temperature was continued until the yellow color of the lead thiophenoxide was replaced by the very pale cream-yellow of lead bromide. The mixture was filtered, and the filtrate was washed repeatedly with 0.1% sodium bicarbonate and twice with water. The ether solution was dried ($MgSO_4$), and the solvent was removed at room temperature with a rotary evaporator. The solid compounds were crystallized from benzene/petroleum ether. The liquid compounds could not be distilled without decomposition. Continuous pumping at 10^{-3} torr for 48 h gave materials with correct analysis and no impurities in the NMR spectrum or IR spectrum. The compounds prepared were the following (phenyl substituent: mp; NMR maxima (δ) in $CDCl_3$).

4′-Butyl: liquid; 1.33 (s), 3.19 (t), 3.42 (t), 7.34 (q).

4′-Methyl: liquid; 2.83 (s), 3.15 (t), 3.55 (t), 7.21 (q).

4′-Methoxy: mp 43–44 °C; 3.79 (s), 3.15 (t), 3.58 (t), 7.0 (t).

4′-Fluoro: liquid; 3.18 (t), 3.61 (t), 7.23 (t).

4′-Bromo: mp 49–50 °C; 3.05 (t), 3.48 (t), 7.15 (q).

4′-Chloro: liquid; 3.00 (t), 3.41 (t), 7.18 (t).

4′-Acetyl: mp 43–44 °C; 2.52 (s), 3.20 (t), 3.60 (t), 7.60 (q).

4′-Nitro: 3.26 (t), 3.66 (t), 7.98 (t).

Unsubstituted: liquid; 3.15 (t), 3.60 (t), 7.40 (s).

All had IR absorptions at approximately 1690, 1040, 1015, and 960 cm^{-1}.

Synthesis of Sodium 3,4-Dinitrophenoxide. The procedure was that of Sidgwick[21] adapted from Holleman and Wilhelmy.[22] Upon nitration of 20 g of 3-nitrophenol, there was obtained 6.9 g of 3,4-dinitrophenol. After crystallizing five times from 95% ethanol, the phenol was dried over P_2O_5 at 76 °C (0.01 torr) to yield 4.7 g of material of mp 135.0–136.5 °C (lit. mp 135.1–135.5 °C). No attempt was made to recover the crude 2,3-dinitrophenol also formed in the nitration.

To 2.9 mL of 6 M NaOH was added 3.0 g of 3,4-dinitrophenol with stirring; 2 mL of water was added to effect solution of the sodium salt. After removal of water under vacuum, the orange solid was crystallized twice from acetone and dried over P_2O_5 at 76 °C (0.01 torr) for 36 h: NMR (THF) δ 7.5 (d), 6.3 (d); ϵ_{found} 15 720 (pH 12, water) [lit.[23] ϵ 13 700 (4000 nm)].

Kinetics Procedure. Reactions were carried out in a standard 1-mm path length UV cell with a Teflon brand stopper in the thermostated cell block of a Beckmann DB spectrophotometer with a Sargent recorder. A Precision Scientific Co. constant temperature bath was used to maintain the cell at $T \pm 0.02°$ as monitored by an iron constant in thermocouple calibrated against a Hewlett-Packard Quartz Thermometer Probe with digital readout. Stock solutions of anhydrous sodium dinitrophenoxide and the bromo esters were prepared by direct weighing in dried 10-mL volumetric flasks at room temperature (22.5 °C) with dry THF. Bromo ester solutions were used within 24 h of preparation; the extinction coefficient of the dinitrophenoxide solution was checked prior to each kinetic run. For each run, approximately 0.35 mL of sodium dinitrophenoxide solution was placed in the cell in the DB cell block and allowed to equilibrate for at least 15 min. To this was added 35 μL of stock ester solution from a 50-μL Hamilton syringe, and the cell was inverted five times and returned to the cell compartment. Ratio of base:halide was about 0.6; concentration of base, 1.0×10^{-3} M; concentration of ester, 1.7×10^{-3} M. The absorbance at 432 nm was recorded continuously. The initial absorbance was usually about 1.050, and the infinite time absorbance was approximately 0.035. Initial absorbance was calculated by extrapolation to the time of addition and by calculation of the initial absorbance from the known dilution ratio; agreement was within 1%. The data were fit by least squares to the integrated second-order rate expression $kt = (1/(B_0 - A_0)) \ln (A_0B/B_0A)$ at time intervals of about 2.5 min by using a computer program. Within any run, the correlation coefficient for at least 10 points was never less than $r = 0.999$ over at least two half-lines. Agreement between presumably duplicate runs was usually within 1% in k and almost always within 3%.

For activation parameters, rates were measured at three temperatures: 22.20, 34.25, and 43.35 °C. With the faster compounds it was necessary to use 10.75 °C. For 4′-acetylphenyl 3-bromothiolopropionate, only two temperatures were used. Least-squares methods were used to fit the experimental data to standard equations.[9]

Product Studies. A mixture of 2 mL of stock 3,4-dinitrophenoxide solution with 2 mL of the stock solution of 4′-meth-

(21) Sidgwick, N. V.; Aldous, W. M. *J. Chem. Soc.* **1921**, 1001.

(22) Holleman, M. A. F.; Wilhelmy, M. G. *Recl. Trav. Chim. Pay-Bas Belg.* **1902**, *21*, 432.

(23) Robinson, R. A.; Davies, M. M.; Paabo, M.; bower, V. E. *J. Res. Natl. Bur. Stand., Sect. A* **1960**, *64A*, 347.

oxyphenyl 3-bromopropionate from kinetic runs was allowed to stand until no change in color occurred (1 day). Gas chromatograms showed only peaks with retention times of the acrylate ester, the bromo ester, and 3,4-dinitrophenol. TLC on microscope slides using Silic AR 7FG adsorbent developed with 9:1 pentane:benzene (v/v) showed only the expected spots on fixing with iodine vapor. On evaporation to dryness and dissolution in Me_2SO-d_6, the NMR spectrum showed absorption maxima at δ 5.87 (q) and 6.19, identical with those from a sample prepared from acrolyl chloride and hydroquinone monomethyl ether. Similar NMR patterns were found for the 3′-nitro ester (δ 5.85 and 6.21), 4′-methyl ester (δ 5.7 and 6.18), and the 4′-bromo ester (δ 5.82 and 6.20). Reaction products from the 3-bromothiolopropionates were more difficult to identify. On evaporation of reaction mixtures, films of obviously polymeric nature were found. Attempted determination of TLC R_f values of phenyl 3-bromothiolopropionates using Silic AR 7GF with pentane/benzene as before gave spots identified as the thiophenol, 3-bromopropionic acid, and the unsaturated thiolo ester. Using the same TLC adsorbent with reaction mixtures showed no spots other than the dinitrophenol, thiophenol, 3-bromopropionic acid, and the unsaturated thiolo ester. The NMR spectrum showed bromothiolo ester, unsaturated thiolo ester, and 3,4-dinitrophenol. The phenyl thioloacrylates could not be prepared without substantial polymerization.

Preparation of 4′-Bromophenyl 3-Bromopropionate-*2*-*d*. A twofold excess of DBr was allowed to bubble through a solution of 2 g of 4′-bromophenyl acrylate (from 4′-bromophenyl 3-bromopropionate with 3,4-dinitrophenoxide) in cyclohexane at room temperature, and the reaction mixture was stirred for 1 h. The DBr was prepared from D_2O and PBr_3 and purified by passage in a N_2 stream through a U-tube containing PBr_3, a trap at −30 °C to capture PBr_3, and a trap at −78 °C to capture DBr. The DBr was subsequently allowed to flow into the flask containing the 4′-bromophenyl acrylate. The product of DBr addition was extracted into cyclohexane/benzene and washed with D_2O three times, and dried with $MgCO_3$, and the solvent was evaporated. Crystallization from benzene/petroleum ether gave the deuterated bromo ester, mp 30–31 °C. Assay for deuterium was carried out by using parent peaks at 307, 309, and 311 daltons (ratio 1.00:2.00:1.00) and by NMR peak-area integrations of δ 3.2 and 3.7 maxima (area 1:2).

Kinetics were carried out as previously described. Three runs were made at 35.20 °C. k_2 for perhydro compounds, 1.89, 1.82, 1.73, (av 1.81); k_2 for HD compound, 1.07, 1.02, 1.07 (av 1.05). The rate ratio for H_2/HD = 1.69. Mass spectra were used to determine H/D ratios in the product 4′-bromophenyl acrylate with 226 and 228 dalton peaks for the H_2 and 227 and 229 dalton peaks for the HD compound. The ratio of HD/H_2 was found to be 1:2.00.

Reaction of 1 g of 4′-chlorophenyl 3-bromothiolopropionate in 20 mL of ether with 10 mL of 0.2 M aqueous KOH gave the etherial solution of 4′-chlorophenyl thioloacrylate. Excess DBr from acetyl bromide and D_2O was passed through the ether solution with N_2. The ether as evaporated by using a rotary evaporator at room temperature. The residue was evacuated at 0.001 torr for 48 h. A mass spectrum using the m/e 262 and 264 peaks for H compound and m/e 263 and 265 peaks for the D compound at 20-eV ionizing potential gave 37% of one D. After 50% reaction in THF with 3,4-dinitrophenoxide, the mass spectrum showed the same peak ratios to yield 41.8% D. So much polymer and so little bromo thiolo ester were formed that it was judged not to be worth further experiments.

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Registry No. 4′-Nitrophenyl 3-bromopropionate, 78939-58-9; 3′-nitrophenyl 3-bromopropionate, 86259-93-0; 4′-acetylphenyl 3-bromopropionate, 86259-94-1; 3′-acetylphenyl 3-bromopropionate, 86259-95-2; 4′-bromophenyl 3-bromopropionate, 86259-96-3; 4′-acetoxyphenyl 3-bromopropionate, 86259-97-4; 3′-bromophenyl 3-bromopropionate, 86259-98-5; 4′-chlorophenyl 3-bromopropionate, 86259-99-6; 3′-methoxyphenyl 3-bromopropionate, 86260-00-6; 4′-methoxyphenyl 3-bromopropionate, 6329-88-0; phenyl 3-bromopropionate, 27850-43-7; 3′-methylphenyl 3-bromopropionate, 86260-01-7; 4′-methylphenyl 3-bromopropionate, 86260-02-8; 4′-fluorophenyl 3-bromopropionate, 86260-03-9; 4′-*tert*-butylphenyl 3-bromopropionate, 86260-04-0; 4′-nitrophenyl 3-bromothiolopropionate, 86260-05-1; 4′-acetylphenyl 3-bromothiolopropionate, 86260-06-2; 3′-acetylphenyl 3-bromothiolopropionate, 86260-07-3; 4′-chlorophenyl 3-bromothiolopropionate, 86260-08-4; 4′-methoxyphenyl 3-bromothiolopropionate, 86260-09-5; phenyl 3-bromothoilopropionate, 31677-04-0; 4′-methylphenyl 3-bromothioloprionate, 86260-10-8; 4′-bromophenyl 3-bromopropionate-2-*d*, 86260-11-9; 3,4-dinitrophenoxide sodium salt, 64993-95-9; deuterium, 7782-39-0.

Chemical Reactivity and Molecular Structure Relationship of Highly Strained Cage Oxetanes

Kazunobu Harano, Yasushi Okamoto, Masami Yasuda, Kaoru Ueyama, and Ken Kanematsu*

Institute of Synthetic Organic Chemistry, Faculty of Pharmaceutical Sciences, Kyushu University, 62, Fukuoka 812, Japan

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The strained cage oxetane 11,12-dimethyl-3,4-diphenyl-5,7-bis(methoxycarbonyl)-2-oxapentacyclo-[6.4.0.0^{1,4}.0^{3,7}.0^{5,9}]dodec-11-ene-6,10-dione (**1cl**) was shown by single-crystal X-ray analysis not to have an abnormal bond elongation caused by through-bond interaction. However, **1cl** underwent rapid decarbonylation at 120 °C to give the tricyclic diene 2-oxatricyclo[4.3.2.0^{1,5}]undeca-3,8,10-trien-7-one derivative (**4cl**), while **1al** isomerized to a 1-oxacyclopenta-3a,8b-dihydrobenzo[*b*]furan derivative (**7al**). The reactivity differences are discussed in terms of a frontier molecular orbital theory based on X-ray data, molecular mechanics calculations, and kinetic data.

During the course of a study of strained cage compounds, we have proposed that two factors influence their reactivity: (1) a through-bond interaction enhanced by inherent strain produces an elongated σ bond, which plays an important role in thermal reactions; (2) a frontier molecular orbital interaction enhances the rate of decarbonylation reactions.

Cage oxetane **1** (Chart I) is of interest in this study because it is a highly strained molecule that contains several functional groups: ether, enone, bridge carbonyl, and vicinal phenyl groups. We here report on studies of **1** that include bond lengths, the conformation of the two phenyl rings, and its reactions under thermal or acidic conditions.

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