

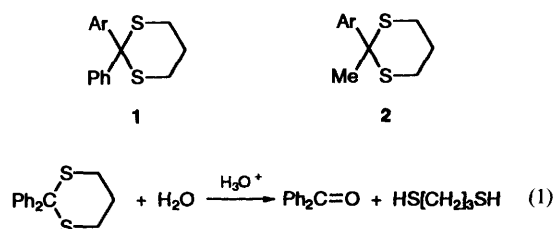
## Kinetics and Mechanism of Hydrolysis of Open-chain Thioacetals derived from Benzophenone and the reactivity of $\alpha$ -Thiophenyl Carbocations

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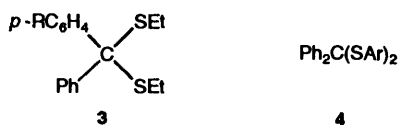
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In a 40% (v/v) dioxane–water solvent, in the presence of 0.3–4.0 mol dm<sup>-3</sup> perchloric acid, the rates of hydrolysis of diethyl and diphenyl thioacetals derived from substituted benzophenones exhibit substituent effects, acidity dependencies, activation parameters and solvent isotope effects which all suggest that the hydrolyses follow the A1 mechanism. The diethyl acetals are *ca.* 10<sup>4</sup>-fold less reactive than their *O,O*-analogues and *ca.* 10<sup>4</sup>-fold more reactive than the corresponding dithanes, for both of which classes of acetal the AS<sub>E</sub>2 mechanism of hydrolysis has been suggested. In concentrated aqueous perchloric acid the diaryl thioacetals are, like the diethyl compounds, rapidly and quantitatively converted into the corresponding  $\alpha$ -thio carbocations, which then undergo slow hydrolysis to the benzophenone. Kinetic measurements show that the  $\alpha$ -thiophenyl carbocation Ph<sub>2</sub>C<sup>+</sup>–SPh is *ca.* 20-fold more reactive towards hydrolysis than is Ph<sub>2</sub>C<sup>+</sup>–SEt, but that substituents in the thiophenyl group have little effect on reactivity ( $\rho \approx 0.6$ ). The detailed kinetic results are compatible with our previous suggestions about the mechanism of hydrolysis of  $\alpha$ -thio carbocations.

We recently provided evidence<sup>1,2</sup> which suggests that thioacetals 1 and 2 may hydrolyse [*e.g.* eqn.(1)] in moderately

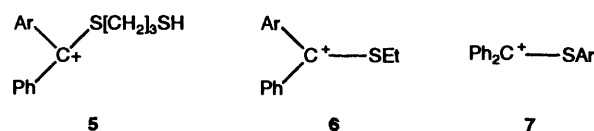


concentrated aqueous acid *via* the AS<sub>E</sub>2 mechanism. This mechanism, which has been found for various types of *O,O*-acetal, has proved to be unexpectedly rare for *O,S*- and *S,S*-acetals.<sup>3</sup> Since both cyclic and open-chain *O,O*-acetals derived from benzophenone are reported<sup>4,5</sup> to hydrolyse *via* the AS<sub>E</sub>2 route, we considered that acetals 3 and 4 might provide the



first clear examples of this mechanism among open-chain *S,S*-acetals. We report now on the hydrolyses of six acetals of this type and describe the effects on reaction rates of changes in acidity, in temperature and in the isotopic content of the solvent.

We have also shown recently<sup>1</sup> that, in very concentrated aqueous acid, *S,S*-acetals derived from alkyl thiols [*e.g.* 1, 2 and 3) are rapidly and quantitatively converted into the  $\alpha$ -thioalkyl carbocation intermediates (*e.g.* 5 and 6) that doubtless occur in low concentrations in the hydrolyses in moderately concentrated acid, but which, in very concentrated acid, react relatively slowly with the small amount of water available, so altering the slow step of the overall hydrolysis.<sup>1</sup> These  $\alpha$ -thioalkyl cations are surprisingly less reactive towards water than are their *O*-analogues<sup>1,6</sup> and we have now examined, over a range of acidities, the reactivity of five  $\alpha$ -thioaryl carbocations 7, derived from 4, since little kinetic information exists at present about

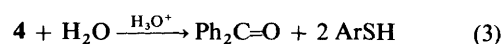
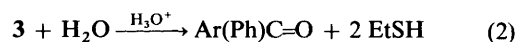


the effects of different  $\alpha$ -*S* (or *-O*) substituents on carbocation reactivity.<sup>1,6,7</sup>

### Experimental

**Materials.**—The thioacetals were prepared from the relevant benzophenone and thiophenol (or ethane thiol) by the method used previously for the corresponding thioacetals of benzaldehyde and acetophenone.<sup>8</sup> All the products had appropriate NMR spectra and hydrolysed in aqueous acid to give an effectively quantitative yield of the parent benzophenone. The other materials were those described in our previous work.<sup>1,2,8</sup>

**Kinetics.**—All the hydrolyses were conducted and monitored as before,<sup>1,8</sup> using a low (10<sup>-4</sup>–10<sup>-5</sup> mol dm<sup>-3</sup>) concentration of thioacetal in an excess of aqueous perchloric acid. In dilute or moderately concentrated acid (up to *ca.* 4 mol dm<sup>-3</sup>) acetals 3 and 4 are not as soluble in 1% dioxane–water as the thioacetals we studied earlier and for this acidity range we used 40% (v/v) dioxane–water as the solvent (for which acidity function measurements are available<sup>9</sup>). In concentrated acid (>9 mol dm<sup>-3</sup>) where acetals 4 are rapidly and quantitatively converted into carbocations, we were able to use a 1% dioxane–water solvent, as in most of our previous work. In dilute acid the appearance of the benzophenone product [eqns. (2) and (3)] was observed in the region 260–290 nm; in concentrated acid



this product is partially or fully protonated and its appearance was monitored at 300–340 nm. The carbocations absorb at 380–400 nm. In all cases excellent isosbestic points were

**Table 1** Derived parameters for the hydrolysis of acetals **3** and **4** in 40% (v/v) dioxane–water containing perchloric acid, the effects of temperature and of isotopic solvent

Acetal <sup>a</sup>	$k_H^b$ 10 <sup>-5</sup> dm <sup>3</sup> mol <sup>-1</sup> s <sup>-1</sup>	$m^*m^\ddagger$	$m^\ddagger$	Effects of temperature			Solvent isotope effect			
				[HClO <sub>4</sub> ] mol dm <sup>-3</sup>	$T$ °C	$k_{obs}$ 10 <sup>-4</sup> s <sup>-1</sup>	$\Delta H^\ddagger$ kJ mol <sup>-1</sup>	$\Delta S^\ddagger$ J K <sup>-1</sup> mol <sup>-1</sup>	$k_{obs}^H$ 10 <sup>-4</sup> s <sup>-1</sup>	$k_{obs}^D$ 10 <sup>-4</sup> s <sup>-1</sup>
<b>3</b> ( <i>p</i> -R)										
OMe	5.9	2.70	2.08	0.48	$\left\{ \begin{array}{l} 25.0 \ 1.81 \\ 32.0 \ 4.48 \\ 37.5 \ 9.06 \\ 44.0 \ 19.6 \end{array} \right\}$	96 ± 6	-4.0 ± 0.6	1.07	1.40	1.31 <sup>c</sup>
Me	2.4	2.52	1.94							
H	1.6	2.13	1.64							
				1.20	$\left\{ \begin{array}{l} 25.1 \ 3.55 \\ 35.0 \ 15.9 \\ 44.8 \ 55.6 \end{array} \right\}$	99 ± 7	-5.0 ± 0.7			
Cl	0.52	1.96	1.51	1.60	$\left\{ \begin{array}{l} 24.9 \ 0.66 \\ 34.8 \ 2.18 \\ 39.0 \ 4.33 \\ 44.6 \ 10.5 \end{array} \right\}$	103 ± 10	-8.0 ± 1.2	0.14	0.18	1.29 <sup>d</sup>
NO <sub>2</sub>	0.19	1.69	1.30							
<b>4</b> (Ar)										
3,5-										
Me <sub>2</sub> C <sub>6</sub> H <sub>3</sub> -	0.42	2.40	1.85							

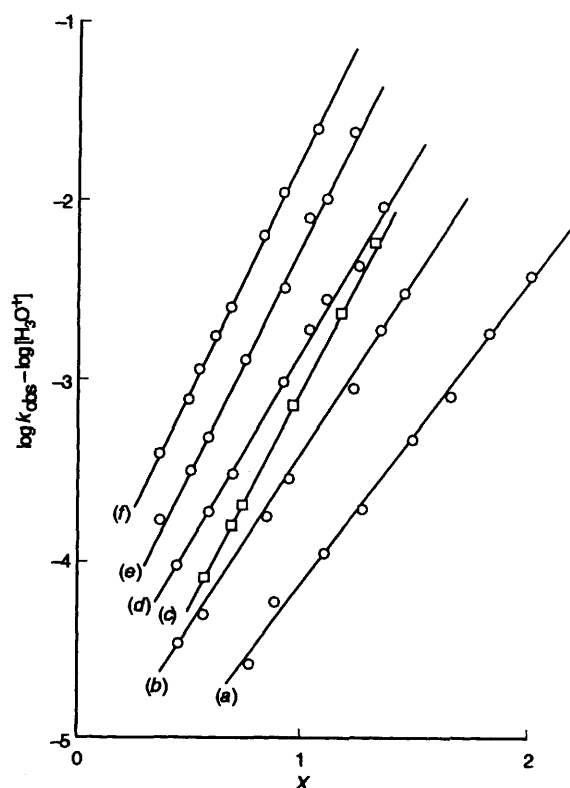
<sup>a</sup> [Acetal]<sub>initial</sub> ≈ 5 × 10<sup>-5</sup> mol dm<sup>-3</sup>. <sup>b</sup> See Discussion section. <sup>c</sup> [L<sub>3</sub>O<sup>+</sup>] = 0.84 mol dm<sup>-3</sup>, %D = 94. <sup>d</sup> [L<sub>3</sub>O<sup>+</sup>] = 1.30 mol dm<sup>-3</sup>, %D = 89.  $T = 25.0$  °C unless stated otherwise.

observed for conversion of the carbocation into benzophenone and the final spectra from kinetic runs corresponded closely to those of synthetic product mixtures at the appropriate acid concentration. The appearance of the ketone product was always an accurately first-order process over at least three half-lives, and the observed first-order rate constant,  $k_{obs}$ , was normally reproducible to within ±8%. Each acetal was observed over a range of acid concentrations and some experiments also examined the effect on  $k_{obs}$  of changes in temperature and in the isotopic content of the solvent. Typical results are in the Tables and Figures. In the absence of acid all the thioacetals hydrolyse negligibly slowly.

## Results and Discussion

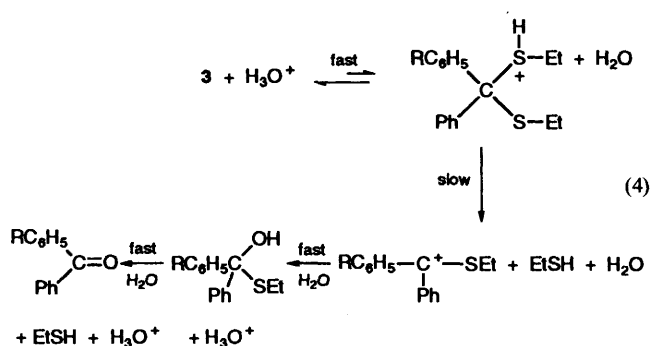
**Hydrolysis of 3.**—Acetals **3** with R = MeO, Me, H, Cl and NO<sub>2</sub> were studied in the range 0.3–4.0 mol dm<sup>-3</sup> perchloric acid. As before, the effect of acid concentration on  $k_{obs}$  was interpreted using the excess acidity ( $X$ ) approach.<sup>10,11</sup> Values of  $X$  referring to 40% dioxane–water can be obtained from the available  $H_0$  data by the method given in reference 1. (We took the difference in p*K*<sub>a</sub> of an aniline indicator in water and in the 40% dioxane–water,  $\Delta pK_a = 1.03$ .) Fig. 1 shows that plots of  $\log k_{obs} - \log [H_3O^+]$  against  $X$  are rectilinear with slopes<sup>11</sup> ( $m^*m^\ddagger$ ) varying from ca. 1.7 for **3** (R = NO<sub>2</sub>), the least reactive acetal, to ca. 2.7 for **3** (R = MeO), the most reactive (Table 1). This trend is similar to that found for a series of *para*-substituted benzaldehyde diethyl thioacetals *p*-RC<sub>6</sub>H<sub>4</sub>CH(SEt)<sub>2</sub>, **8**, studied earlier.<sup>8</sup> Taking  $m^* \approx 1.3$  for *S*-bases<sup>10</sup> as before, gives  $m^\ddagger \approx 1.3$ –2.1. Values of  $m^\ddagger$  of this magnitude are typical for reactions following A1 mechanisms.<sup>11</sup> For *S,S*-acetals this mechanism is shown in eqn. (4). In an A<sub>S</sub>E<sub>2</sub> (slow proton transfer) mechanism the first two steps of reaction (4) are amalgamated and in the transition state the proton is less strongly bound to S and there is less cleavage of the C–S bond.<sup>3,4</sup> The trend in the  $m^\ddagger$  values suggests for the present hydrolyses, as for those of acetals **8**, that their A1 character may become more pronounced (transition state closer to a free carbocation) as electron-release by R increases.<sup>8</sup>

Other facts that support an essentially A1 mechanism for **3** are the relatively high values of  $\Delta H^\ddagger$ , the small negative values



**Fig. 1**  $X$ -Plots for acetals **3** and **4** (Ar = Me<sub>2</sub>C<sub>6</sub>H<sub>3</sub>). Solvent: 40% (v/v) dioxane–water;  $T = 25$  °C; (a), (b), (d), (e), (f): **3**, R = NO<sub>2</sub>, Cl, H, Me, MeO, respectively; (c): **4**, Ar = 3,5-Me<sub>2</sub>C<sub>6</sub>H<sub>3</sub>.

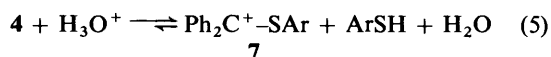
of  $\Delta S^\ddagger$  and the deuterium isotope effects of ca. 1.3 (Table 1). Solvent deuterium isotope effects for *S*-bases are still in short supply, but values of ca. 1.3–1.5 have been found for other reactions for which A1 schemes are postulated.<sup>8,12</sup> In contrast to the ( $\approx 10^4$ -fold faster) hydrolysis of the corresponding *O,O*-acetals,<sup>5</sup> there is little evidence for any pronounced A<sub>S</sub>E<sub>2</sub> character for the present hydrolyses. The parallelism with the A<sub>S</sub>E<sub>2</sub> behaviour of the *O,O*-analogues apparent<sup>1,2</sup> for the cyclic *S,S*-acetals **1**, is therefore not maintained with **3**. Moreover,



although increased electron withdrawal by the leaving group can<sup>3</sup> shift the transition state in acetal hydrolysis towards that typical of an  $\text{A}_{\text{S}}\text{E}2$  mechanism, the behaviour of **4** ( $\text{Ar} = 3,5\text{-Me}_2\text{C}_6\text{H}_3\text{-}$ ) for which such electron withdrawal will<sup>13</sup> be larger than when the leaving group is  $-\text{SEt}$ , is, if anything, more  $\text{A}1$ -like than that of **3** ( $\text{R} = \text{H}$ ):  $m^\ddagger$  is larger. ( $k_{\text{H}^+}$  is also smaller, as expected<sup>3,12</sup> for an  $\text{A}1$  scheme, Table 1.) All our current evidence strongly suggests that, in aqueous acid, the mechanisms of hydrolysis of analogous open-chain and cyclic  $\text{S},\text{S}$ -acetals are importantly different (see also preceding paper).\*

Extrapolation of the  $X$ -plots (Fig. 1) to  $X = 0$  leads<sup>11</sup> to values of  $k_{\text{H}^+}$ , the second-order catalytic rate constant, for the various acetals (Table 1). A Hammett plot of the  $\log k_{\text{H}^+}$  against  $\sigma^+$  is a good straight line with slope  $\rho^+ \approx -2.2$ . The plot against  $\sigma$  is less satisfactory. This type of substituent effect is also compatible with an  $\text{A}1$  mechanism of hydrolysis.<sup>4,8</sup> In 1% dioxane–water as solvent,  $k_{\text{H}^+}$  for **8** ( $\text{R} = \text{H}$ ) is<sup>8</sup> *ca.* 12-fold larger than that for **3** ( $\text{R} = \text{H}$ ) given in Table 1. The comparison suggests that, in the same solvent, acetals **8** would be slightly more reactive towards catalysed hydrolysis than their diphenyl analogues **3**. This is a reasonable result: the extra Ph group in **3** will discourage protonation, but stabilize the carbocation (and therefore facilitate its formation).

**Hydrolysis of Carbocations from 4.**—As<sup>1</sup> with compounds **1–3**, in sufficiently concentrated acid, thioacetals **4** are rapidly and effectively completely converted into the corresponding carbocations **7** [eqn. (5)] which, like those from **1**, **2** and **3**, absorb strongly at 380–400 nm. The cations subsequently react to give ketone (or protonated ketone) at rates dependent upon the water activity. The latter falls as the acidity rises, so that the



cations are most stable at the highest acidities. We found that cations are notably more reactive than those we studied previously<sup>1</sup> (*e.g.* **5** and **6**), but provide convenient rates of hydrolysis in 10–12 mol  $\text{dm}^{-3}$  perchloric acid.

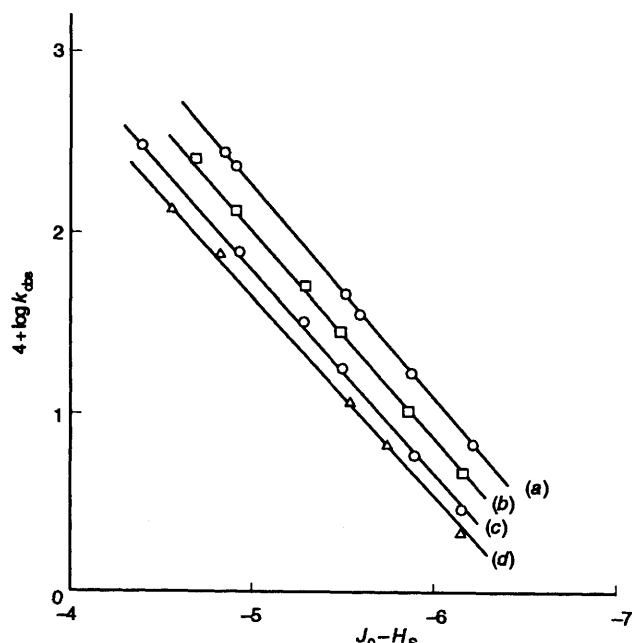
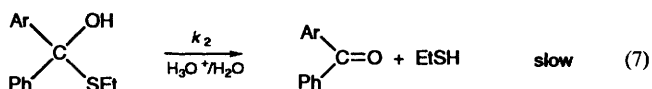
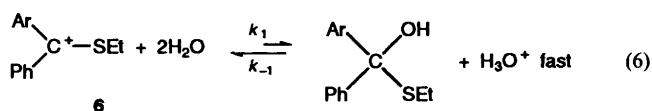


Fig. 2 Plots of eqn. (8) for carbocations **7**.  $T = 25^\circ\text{C}$ ; solvent: 1% dioxane–water containing perchloric acid; (a), (b), (c), (d):  $\text{Ar} = 4\text{-ClC}_6\text{H}_4$ ,  $4\text{-FC}_6\text{H}_4$ , Ph,  $4\text{-MeOC}_6\text{H}_4$ , respectively; similar results for  $\text{Ar} = 3,5\text{-Me}_2\text{C}_6\text{H}_3$ .

Arguments<sup>1</sup> based on studies of  $\alpha$ -oxoalkyl and of  $\alpha$ -thioalkyl carbocations derived from orthoesters and ketene acetals<sup>7,14</sup> led us to represent the hydrolyses of **5** and **6** as in eqns. (6) and (7). Assuming that the pre-equilibrium (6) obeys the  $J_0(H_{\text{R}})$  acidity function, and that the rate of reaction (7) is governed by the  $H_{\text{S}}$  acidity function (for  $\text{S}$ -bases), we showed that the corresponding rate equation is (8), in which  $k'_2$  represents  $k_1k_2/k_{-1}$  in dilute acid solution. Our previous results<sup>1</sup> were

$$\log k_{\text{obs}} = \log k'_2 + (J_0 - H_{\text{S}}) \quad (8)$$

fully in accord with this equation: plots of  $\log k_{\text{obs}}$  against  $(J_0 - H_{\text{S}})$  for different carbocations yielded a series of parallel straight lines with slopes of 0.98. The success of the plots was a little surprising in that  $J_0$  and  $H_{\text{S}}$  were both calculated from  $H_0$  values using the approximations<sup>15,16</sup>  $J_0 = 2H_0$  and  $H_{\text{S}} = 1.3H_0 + 0.3 \log [\text{H}_3\text{O}^+]$ . Values of  $k'_2$  can be obtained by extrapolating plots of eqn. (8) to  $(J_0 - H_{\text{S}}) = 0$ . The acidity range covered by the cations in this previous study was *ca.* 8–11 mol  $\text{dm}^{-3}$  perchloric acid. Using the same approach for the present  $\alpha$ -thioaryl carbocations (**7**) studied in the range 10–12 mol  $\text{dm}^{-3}$  perchloric acid leads to the plots in Fig. 2. All the cations provide good straight lines with slopes again close to unity, but now 1.05–1.10. We suggest that the new results support our previous treatment of these hydrolyses.†

Values of  $k'_2$  for **7** are compared in Table 2 with some of our previous values for the alkyl ions. Two conclusions follow: (i) the cation **7** ( $\text{Ar} = \text{Ph}$ ) is *ca.* 20-fold more reactive than is **6** ( $\text{R} = \text{H}$ ), so that substitution of Ph for Et on the  $\alpha$ -S atom considerably increases the cation reactivity and (ii) substituent changes in the Ar group of **7** have rather little further effect on reactivity. (A Hammett plot of  $\log k'_2$  against  $\sigma$  has a slope of  $\rho \approx 0.6$ ). Substituents in the phenyl groups directly attached to the cationic carbon atom have a much larger

\* T. F. Mohiuddin, D. P. N. Satchell and R. S. Satchell, *J. Chem. Soc., Perkin Trans. 2*, 1995, 163.

† In ref. 1 we used our own  $H_0$  values and those given by Rochester;<sup>15</sup> in the present work (involving higher acid concentrations) we used those quoted by Boyd: R. H. Boyd, in *Solute–Solvent Interactions*, ed. J. F. Coetzee and C. D. Richie, Marcel Dekker, New York, 1969, ch. 3.

**Table 2** Values of  $k'_2$  for the hydrolysis of  $\alpha$ -thiocarbocations in aqueous perchloric acid at 25.0 °C

Carbocation <sup>a</sup>	$k'_2$ <sup>b</sup> /10 <sup>3</sup> dm <sup>3</sup> mol <sup>-1</sup> s <sup>-1</sup>
From 4 (Ar)	
4-ClC <sub>6</sub> H <sub>4</sub>	8.3
4-FC <sub>6</sub> H <sub>4</sub>	5.8
Ph	4.5
3,5-Me <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	4.0
4-MeOC <sub>6</sub> H <sub>4</sub>	3.4
From 3 ( <i>p</i> -R) <sup>c</sup>	
H	0.22
MeO	0.0089

<sup>a</sup> [Carbocation]<sub>initial</sub>  $\approx 2 \times 10^{-5}$  mol dm<sup>-3</sup>. <sup>b</sup> For  $k'_2$  see Discussion section. <sup>c</sup> From ref. 1.

effect<sup>1</sup> ( $\rho^+ = 1.8$ ). These results can be understood as follows. Concerning point (i),  $\alpha$ -thiocarbocations are probably powerfully stabilised by a soft-soft interaction between the  $\equiv\text{C}^+$ -centre and the adjacent S atom. The substitution of Et by Ph on the S atom will lead to interaction of the S lone pair electrons with the  $\pi$ -electron system of the phenyl ring and render them less available for the interaction with  $\equiv\text{C}^+$ . This effect would be expected to lead to an increase in the ratio  $k_1/k_{-1}$ . The substitution of Ph for Et will also increase  $k_2$  if, as we suggest,<sup>1</sup> the mechanism of reaction (7) is similar to that favoured for other hemiacetal hydrolyses.<sup>17</sup> All the effects will therefore increase  $k'_2$ . Concerning conclusion (ii), further increases in (say) electron-withdrawal as a result of substituent changes in the phenyl group should lead to further increases in  $k'_2$  (as found) Table 2, but the magnitude of this substituent effect would be expected to be smaller than that for a phenyl group

directly attached to the cationic carbon atom (as found). In all, our new results are compatible with our previous conclusions about the behaviour of  $\alpha$ -thiocarbocations.

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