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Concerted Mechanisms of the Reactions of Ethyl *S*-Aryl Thiocarbonates with Substituted Phenoxide Ions

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The reactions of 4-nitrophenyl, 2,4-dinitrophenyl, and 2,4,6-trinitrophenyl *O*-ethyl thiolcarbonates with substituted phenoxide ions are subjected to a kinetic study in water, 25.0 °C, ionic strength 0.2 M (KCl). By following the reactions spectrophotometrically, pseudo-first-order rate coefficients (k_{obsd}) are found under excess of the nucleophile. Plots of k_{obsd} vs phenoxide anion concentration at constant pH are linear, with the slope (k_N) independent of pH. The Brönsted-type plots (log k_N vs pK_a of the phenols) are linear with slopes $\beta = 0.92$, 0.77, and 0.61 for the reactions of the 4-nitrophenyl, 2,4-dinitrophenyl, and 2,4,6-trinitrophenyl derivatives, respectively. For these reactions, a concerted mechanism is proposed since the slope values are similar to those found in the concerted phenolysis of aryl acetates; the slope magnitudes are not consistent with a stepwise mechanism where the formation of a tetrahedral intermediate is rate limiting. Our results are in line with the finding that the reactions of the 2,4-dinitrophenyl and 2,4,6-trinitrophenyl derivatives with secondary alicyclic amines in water are concerted. In contrast, the reactions of the same substrates with pyridines are stepwise, which means that substitution of a pyridine moiety in a tetrahedral intermediate with a benzenethio group by a phenoxy group destabilizes the intermediate.

Introduction

Although much attention has been drawn to the kinetics and mechanism of the aminolysis and pyridinolysis of carbonyl[1−4] and thiocarbonyl[5−9] compounds, the reactions of phenoxide anions with the latter substrates have been less studied.[10]

In the present work, we describe a kinetic and mechanistic study of the reactions of phenoxide anions with ethyl *S*-(4-nitrophenyl), ethyl *S*-(2,4-dinitrophenyl), and ethyl *S*-(2,4,6-trinitrophenyl) thiocarbonates (NPTC, DNPTC, and TNPTC, respectively) with the aim to shed more light on the reaction mechanisms of thiol compounds; we also compare these mechanisms with those for the aminolysis and pyridinolysis of the same substrates[8] and with those found in the phenolysis of other carbonyl and thiocarbonyl compounds.[10−13]

Experimental Section

Materials. The phenols (Aldrich) were purified either by distillation or recrystallization. NPTC, DNPTC, and TNPTC were obtained as previously.[8a−c] Ethyl phenyl carbonate (EtOCOOPh) was prepared by the same procedure used for methyl phenyl carbonate.[3d]

Determination of p*K*a. The pK_a values of the phenols were determined spectrophotometrically in water, at 25.0 ± 0.1 °C, ionic strength 0.2 M (KCl).

Kinetic Measurements. These were carried out by means of a Hewlett-Packard 8453 diode array spectrophotometer under the following conditions: aqueous solution, at 25.0 ± 0.1 °C, ionic strength 0.2 M (KCl), and in some cases, borate buffer 0.005 M. The reactions were followed at 400 nm (appearance of the substituted benzenethiolate anions).

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[1] Satterthwait, A. C.; Jencks, W. P. *J. Am. Chem. Soc.* **1974**, *96*, 7018.

[2] Gresser, M. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 6963, 6970.

[3] (a) Fife, T. H.; Hutchins, J. E. C. *J. Am. Chem. Soc.* **1981**, *103*, 4194. (b) Brunelle, D. J. *Tetrahedron Lett.* **1982**, *23*, 1739. (c) Castro, E. A.; Gil, F. J. *J. Am. Chem. Soc.* **1977**, *99*, 7611. (d) Castro, E. A.; Freudenberg, M. *J. Org. Chem.* **1980**, *45*, 906. (e) Castro, E. A.; Ibañez, F.; Lagos, S.; Schick, M.; Santos, J. G. *J. Org. Chem.* **1992**, *57*, 2691. (f) Hibbert, F.; Malana, M. A. *J. Chem. Soc., Perkin Trans. 2* **1990**, 711.

[4] Kovach, I. M.; Belz, M.; Larson, M.; Rousy, S.; Schowen, R. L. *J. Am. Chem. Soc.* **1985**, *107*, 7360. Neuvonen, H. *J. Chem. Soc., Perkin Trans. 2* **1987**, 159. Yoh, S.-D.; Kang, J.-K.; Kim, S.-H. *Tetrahedron* **1988**, *44*, 2167. Knowlton, R. C.; Byers, L. D. *J. Org. Chem.* **1988**, *53*, 3862. Koh, H. J.; Lee, H. C.; Lee, H. W.; Lee, I. *Bull. Korean Chem. Soc.* **1995**, *16*, 839.

[5] Campbell, P.; Lapinskas, B. A. *J. Am. Chem. Soc.* **1977**, *99*, 5378. Um, I.-H.; Kwon, H.-J.; Kwon, D.-S.; Park, J.-Y. *J. Chem. Res., Synop.* **1995**, 301. Um, I. H.; Choi, K. E.; Kwon, D. S. *Bull. Korean Chem. Soc.* **1990**, *11*, 362. Lee, I.; Shim, C. S.; Lee, H. W. *J. Chem. Res., Synop.* **1992**, 90. Oh, H. K.; Shin, C. H.; Lee, I. *Bull. Korean Chem. Soc.* **1995**, *16*, 657. Oh, H. K.; Shin, C. H.; Lee, I. *J. Chem. Soc., Perkin Trans. 2* **1995**, 1169.

[6] (a) Castro, E. A.; Ureta, C. *J. Chem. Soc., Perkin Trans. 2* **1991**, 63. (b) Castro, E. A.; Ibáñez, F.; Santos, J. G.; Ureta, C. *J. Org. Chem.* **1992**, *57*, 7024.

[7] (a) Castro, E. A.; Cubillos, M.; Ibáñez, F.; Moraga, I.; Santos, J. G. *J. Org. Chem.* **1993**, *58*, 5400. (b) Castro, E. A.; Araneda, C. A.; Santos, J. G. *J. Org. Chem.* **1997**, *62*, 126.

[8] (a) Castro, E. A.; Ibáñez, F.; Salas, M.; Santos, J. G. *J. Org. Chem.* **1991**, *56*, 4819. (b) Castro, E. A.; Salas, M.; Santos, J. G. *J. Org. Chem.* **1994**, *59*, 30. (c) Castro, E. A.; Cubillos, M.; Santos, J. G. *J. Org. Chem.* **1994**, *59*, 3572. (d) Castro, E. A.; Pizarro, M. I.; Santos, J. G. *J. Org. Chem.* **1996**, *61*, 5982.

[9] (a) Castro, E. A.; Cubillos, M.; Santos, J. G. *J. Org. Chem.* **1996**, *61*, 3501. (b) Castro, E. A.; Cubillos, M.; Santos, J. G.; Téllez, J. *J. Org. Chem.* **1997**, *62*, 2512. (c) Castro, E. A.; Santos, J. G.; Téllez, J.; Umaña, M. I. *J. Org. Chem.* **1997**, *62*, 6568.

[10] (a) Hupe, D. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 451. (b) Pohl, E. R.; Wu, D.; Hupe, D. J. *J. Am. Chem. Soc.* **1980**, *102*, 2759. (c) Pohl, E. R.; Hupe, D. J. *J. Am. Chem. Soc.* **1980**, *102*, 2763. (d) Um, I.-H.; Chun, S.-E.; Kwon, D.-S. *Bull. Korean Chem. Soc.* **1991**, *12*, 510.

[11] (a) Ba-Saif, S.; Luthra, A. K.; Williams, A. *J. Am. Chem. Soc.* **1987**, *109*, 6362. (b) Ba-Saif, S.; Luthra, A. K.; Williams, A. *J. Am. Chem. Soc.* **1989**,*111*, 2647. (c) Ba-Saif, S. A.; Colthurst, M.; Waring, M. A.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1991**, 1901. (d) Colthurst, M. J.; Nanni, M.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1996**, 2285. (e) Colthurst, M. J.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1493.

[12] (a) Kwon, D. S.; Lee, G. J.; Um I. H. *Bull. Korean Chem. Soc.* **1990**, *11*, 262. (b) Buncel, E.; Um, I. H.; Hoz, S. *J. Am. Chem. Soc.* **1989**, *111*, 971.

[13] Stefanidis, D.; Cho, S.; Dhe-Paganon, S.; Jencks, W. P. *J. Am. Chem. Soc.* **1993**, *115*, 1650.

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Table 1. Experimental Conditions and k_{obsd} Values for the Reactions of Phenoxide Anions with Ethyl *S*-(4-Nitrophenyl) Thiocarbonate[a]

phenoxide substituent	pH	$10^2[ArOH]_{tot}{}^b$/M	$10^4k_{obsd}/s^{-1}$	no. of runs
4-methoxy	9.44^c	0.5−4.0	4.7−17	4
	9.74^c	0.5−7.0	5.4−42	6
	10.4	1.0−9.0	16−137	6
none	9.44	0.5−7.0	2.3−12	6
	9.74	0.5−7.0	2.5−19	6
	10.4	1.0−7.0	6.0−34	5
4-chloro	8.96	1.0−5.0	2.1−7.3	4
	9.26	1.0−9.0	3.8−14	6
	9.56	0.5−5.0	2.5−15	5
4-cyano	7.50	1.0−9.0	0.04−0.3	6
	7.80	1.0−9.0	0.08−0.5	6
	8.10	1.0−9.0	0.1−0.6	6

[a] In water, at 25.0 °C. Ionic strength 0.2 M (KCl). [b] Total concentration of substituted phenol (acid plus conjugate base). [c] Buffer borate 0.005 M.

Table 2. Experimental Conditions and k_{obsd} Values for the Reactions of Phenoxide Anions with Ethyl *S*-(2,4-Dinitrophenyl) Thiocarbonate[a]

phenoxide substituent	pH	$10^2[ArOH]_{tot}{}^b$/M	$10^3k_{obsd}/s^{-1}$	no. of runs
4-methoxy	9.44^c	0.5−5.0	7.5−64	5
	9.74^c	0.3−4.0	8.3−94	5
	10.4	0.3−1.0	20−53	3
none	9.44	0.5−7.0	3.4−26	6
	9.74	0.5−7.0	3.0−37	6
	10.4	0.5−7.0	11−94	6
4-chloro	8.96	1.0−7.0	4.1−19	5
	9.26	0.1−5.0	1.4−29	6
	9.56	0.5−7.0	4.7−51	6
4-cyano	7.50	1.0−9.0	0.06−0.13	6
	7.80	1.0−9.0	0.10−0.18	6
	8.10	1.0−9.0	0.12−0.22	6
pentafluoro	8.00^c	2.5−9.0	0.4−1.2	5
	8.50^c	1.0−9.0	0.2−2.1	6
	9.00^c	1.0−9.0	0.3−2.6	6

[a] In water, at 25.0 °C. Ionic strength 0.2 M (KCl). [b] Total concentration of substituted phenol (acid plus conjugate base). [c] Buffer borate 0.005 M.

All reactions were studied under excess of the phenol over the substrate (10-fold at least). The initial substrate concentration was 2×10^{-5} M.

Pseudo-first-order rate coefficients (k_{obsd}) were found throughout, mostly by means of the "infinity" method; for the slowest reactions (NPTC with 4-cyanophenoxide) the initial rate method was used.[11a] The experimental conditions of the reactions and the k_{obsd} values are shown in Tables 1−3.

Product Studies. For the reactions of the substrates with the different phenoxide ions, one of the products was identified as the corresponding benzenethiolate; this was achieved by comparison of the UV−vis spectra after completion of the reactions with those of authentic samples under the same conditions. The other product of the reactions of phenoxide ion with the three substrates was identified as ethyl phenyl carbonate, as indicated by HPLC comparison of an authentic sample with those after completion of the reactions. HPLC conditions: column Eurospher C-18 (10 cm, 7 μm), eluant acetonitrile/water = 70/30, isocratic mode 0.7 mL/min. The yield of ethyl phenyl carbonate obtained in these reactions was in accordance with a nucleophilic attack of phenoxide ion on the substrates. A general base-catalyzed pathway cannot be rigorously excluded, but it would amount to no more than 5% (within the error of the analysis) of the total phenoxide reaction.

Results and Discussion

The kinetic law obtained in the present reactions is given by eq 1, where k_{obsd} is the pseudo-first-order rate coefficient, k_o and k_N are the rate coefficients for hydrolysis and phenolysis, respectively, and ArO^- represents a phenoxide ion.

$$k_{obsd} = k_o + k_N[ArO^-] \tag{1}$$

The values of k_o and k_N were obtained as the intercept and slope, respectively, of linear plots of k_{obsd} vs $[ArO^-]$ at constant pH. For all the reactions the same straight line for three different pH values was found, except those of DNPTC with pentafluorophenoxide where three parallel lines were obtained for the different pH values. These results show that both the k_N and k_o values are independent of pH, except the k_o values for the latter reactions.

In the 7.5−8.1 pH range, the k_o values obtained are 4×10^{-6}, 1×10^{-4}, and 6×10^{-4} s^{-1} for the hydrolysis reactions of NPTC, DNPTC, and TNPTC, respectively, showing the dependence of k_o on the basicity of the leaving group. On the other hand, in the reaction of DNPTC with pentafluorophenoxide, the k_o values are 5×10^{-5}, 9×10^{-5}, and 1.1×10^{-4} s^{-1} at pH 8.0, 8.5, and 9.0, respectively.

The k_N values are shown in Table 4 together with the pK_a of the phenols. Figure 1 shows the Brönsted-type plots obtained with the data in Table 4. The Brönsted slopes of the plots in Figure 1 are $\beta = 0.92 \pm 0.09$, 0.77 ± 0.06, and 0.61 ± 0.09 for the reactions of NPTC, DNPTC, and TNPTC, respectively. The values of the slopes for the reactions of the two latter substrates are in agreement with those found in the concerted reactions of phenoxide ions with phenyl esters and similar compounds: 1-acetoxy-8-hydroxynaphthalene ($\beta = 0.48$),[3f] 4-chloro-2-nitrophenyl acetate ($\beta = 0.64 \pm 0.05$),[11b] acetic anhydride ($\beta = 0.58 \pm 0.05$),[11c] 2,4-dinitrophenyl acetate ($\beta = 0.57 \pm 0.03$),[11c] 3-nitrophenyl, 4-nitrophenyl, and 3,4-dinitrophenyl formates ($\beta = 0.64$, 0.51, and 0.43, respectively),[13] and the corresponding acetates ($\beta = 0.66$, 0.59, and 0.53, respectively).[13] All these reactions have been found to be governed by concerted mechanisms.

If the phenolyses of DNPTC and TNPTC were stepwise, the rate-determining step would be the formation of the intermediate in view of the greater nucleofugality from the putative tetrahedral intermediate of 2,4-dinitro- and 2,4,6-trinitrobenzenethiolate anions (pK_a 3.4 and 1.4,

Table 3. Experimental Conditions and k_{obsd} Values for the Reactions of Phenoxide Anions with Ethyl *S*-(2,4,6-Trinirophenyl) Thiocarbonate[a]

phenoxide substituent	pH	$10^2[ArOH]_{tot}{}^b$/M	$10^3k_{obsd}/s^{-1}$	no. of runs
4-methoxy	9.44^c	0.1−4.0	8.1−107	5
	9.74^c	0.1−2.5	8.4−73	4
	10.4	0.1−1.0	19−94	3
none	9.44	0.5−4.0	5.1−39	4
	9.74	0.5−7.0	6.6−92	6
	10.4	0.5−4.0	12−82	4
4-chloro	8.96	1.0−7.0	7.7−37	5
	9.26	0.1−4.0	4.0−32	5
	9.56	0.5−7.0	8.7−84	6
4-cyano	7.50	5.0−9.0	1.7−2.9	3
	7.80	1.0−9.0	0.8−4.2	5
	8.10	1.0−9.0	1.1−5.7	6
pentafluoro	8.00^c	1.0−9.0	0.21−1.0	6
	8.50^c	1.0−9.0	0.23−1.1	6
	9.00^c	1.0−9.0	0.26−1.0	6

[a] In water, at 25.0 °C. Ionic strength 0.2 M (KCl). [b] Total concentration of substituted phenol (acid plus conjugate base). [c] Buffer borate 0.005 M.

Table 4. Values of pK_a of Phenols and k_N for the Reactions of Phenoxides with Ethyl *S*-Aryl Thiocarbonates[a]

		$10^2 k_N$/s^{-1} M^{-1}		
nucleophile anion	pK_a of phenol	NPTC	DNPTC	TNPTC
4-methoxyphenoxide	10.3	27.2 ± 0.6	1060 ± 30	1820 ± 90
phenoxide	9.9	5.7 ± 0.1	135 ± 5	260 ± 8
4-chlorophenoxide	9.4	3.8 ± 0.2	121 ± 5	197 ± 5
4-cyanophenoxide	7.8	0.11 ± 0.04	4.8 ± 0.2	9.4 ± 0.5
pentafluorophenoxide	5.3		0.094 ± 0.004	1.1 ± 0.4

[a] Both pK_a and k_N values were determined in water, at 25.0 °C, ionic strength 0.2 M (KCl).

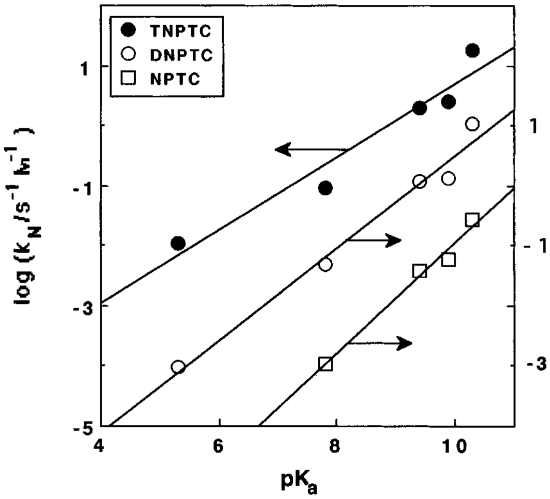
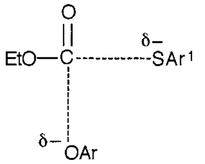


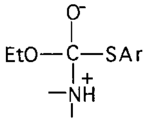
Figure 1. Brönsted-type plots obtained in the reactions of 4-nitrophenyl, 2,4-dinitrophenyl, and 2,4,6-trinitrophenyl *O*-ethyl thiolcarbonates (NPTC, DNPTC, and TNPTC, respectively) with a series of phenoxide anions in aqueous solution, 25.0 °C, ionic strength 0.2 M (KCl).

respectively)[6a] relative to the series of phenoxide nucleophiles. The Brönsted slopes usually found for the stepwise thiolysis of aryl acetates[10a] and aminolysis of aryl acetates,[1] diaryl carbonates,[2] and their thioanalogues[6,7] is $\beta_N = 0.1-0.3$, when the formation of the tetrahedral intermediate is rate determining. These β values are not in agreement with those found in this work for the phenolysis of DNPTC and TNPTC (Figure 1). Therefore, it is likely that these reactions are concerted, through transition state **1** (Ar^1 = 2,4-dinitrophenyl or 2,4,6-trinitrophenyl).



1

In the reactions of DNPTC and TNPTC with secondary alicyclic amines,[8a,b] under the same conditions as this study, the magnitudes of β together with the fact that the predicted hypothetical breaks for stepwise reactions were not observed led to the conclusion that these reaction mechanisms are concerted. This means that the tetrahedral intermediate **2** (Ar = 2,4-dinitrophenyl or 2,4,6-trinitrophenyl) is either too unstable to exist or it is very unstable and the reaction bypasses it, choosing a path of lower free energy barrier (the concerted process). Therefore, it is very likely that the putative intermediate formed in the phenolysis of the same substrates (this work, **3**) is more unstable than **2** because substitution of amine by phenoxy should result in a further destabilization of the intermediate, as explained below.



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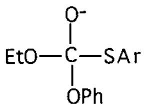

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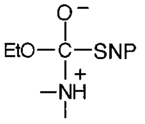
The reactions of substituted phenyl acetates,[11] benzoates,[11b,d] formates,[13] and chlorothionoformates,[14] as well as those of acetic anhydride[11c] with phenoxide ions are concerted, in contrast to those with amines that are known to proceed through a tetrahedral intermediate in a two-step reaction.[1,15] Therefore, in all these reactions substitution of an amine in the tetrahedral intermediate by a substituted phenoxy group results in destabilization of the intermediate.

Concerning the phenolysis of NPTC, the Brönsted slope ($\beta = 0.92$) of Figure 1 is in accord with those found in the concerted phenolysis of 4-nitrophenyl, 4-formylphenyl, and 3-nitrophenyl acetates, $\beta = 0.75$, 0.79, and 1.04, respectively.[11b] Had the phenolysis of NPTC been stepwise, the formation of the tetrahedral intermediate would have been rate limiting since 4-nitrobenzenethiolate is a much better nucleofuge from the intermediate than the four phenoxide nucleophiles studied (pK_a ca. 8−10 for the latter phenols compared to 4.6 for 4-nitrobenzenethiol[6a]). Although the 4-nitrobenzenethio group should stabilize the intermediate relative to the 2,4-dinitro- and 2,4,6-trinitrobenzenethio groups, we are more inclined toward the concerted mechanism for the phenolysis of NPTC since its β value is far too great for a stepwise mechanism where the formation of the intermediate is rate determining. Moreover, for the reactions studied in this work, a plot of β_N vs pK_a of the leaving group is linear (not shown) with slope 0.09 and correlation coefficient 0.994 (albeit three points), which suggests that these three reactions are governed by a common mechanism.

The mechanism of the aminolysis of NPTC is stepwise;[8c] therefore, the tetrahedral intermediate **4** (NP = 4-nitrophenyl) exists; a change of the amine by a phenoxy group leads to compound **5**, which according to what has been discussed previously should be more unstable than **4**.



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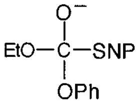

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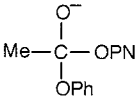
(14) Castro, E. A.; Cubillos, M.; Santos, J. G. *J. Org. Chem.* **1998**, *63*, 6820.

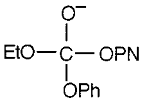
(15) Castro, E. A.; Valdivia, J. L. *J. Org. Chem.* **1986**, *51*, 1668. Yang, C. C.; Jencks, W. P. *J. Am. Chem. Soc.* **1988**, *110*, 2972. Castro, C.; Castro, E. A. *J. Org. Chem.* **1981**, *46*, 2939. Castro, E. A.; Cubillos, M.; Santos, J. G., *J. Org. Chem.* **1997**, *62*, 4395.

It is known that in the reactions of phenoxide ions with 4-nitrophenyl acetate the mechanism is concerted; therefore, the tetrahedral intermediate **6** either does not exist or it is very unstable.[11b] It is also known that the change of methyl by an ethoxy group destabilizes the tetrahedral intermediate;[8a,b] therefore, the intermediate **7** should be more unstable than **6**. On the other hand, since a stepwise mechanism was found for the thiolysis of aryl acetates,[10a] it means that tetrahedral compound **8** has a lifetime long enough to qualify as an intermediate.



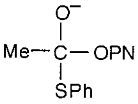
$\mathrm{Me{-}C(O^-)(OPh){-}OPN}$

6



$\mathrm{EtO{-}C(O^-)(OPh){-}OPN}$

7



$\mathrm{Me{-}C(O^-)(SPh){-}OPN}$

8

A comparison of intermediates **6** and **8** suggests that a change of phenoxy by a benzenethio group stabilizes the intermediate. Therefore the tetrahedral intermediate **5** should be more stable than **7**, in line with the stabilization of tetrahedral intermediates caused by substitution of O groups attached to the central carbon by S groups.[16]

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(16) Capon, B.; Ghosh, A. K.; Grieve, D. M. A. *Acc. Chem. Res.* **1981**, *14*, 306. Capon, B.; Dosunumu, M. I.; de Matus-Sanchez, M. N. *Adv. Phys. Org. Chem.* **1985**, *21*, 37 and references therein.