Relative Reactivities of Various Sulfides, Selenides and Halides Towards $S_{\rm H}2$ Attack by Tributyltin Radicals

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Abstract

The order of reactivity towards $S_{\rm H}2$ attack by tributyltin radicals on various groups X in four different molecular environments (RCO₂CH₂X, RCH₂OCH₂X, XCH₂CO₂Et and RCH₂X) has been found by competition experiments to be Br > PhSe > Cl > p-CNC₆H₄S > PhS > p-MeC₆H₄S > MeS. The mechanism of the reaction of chloromethyl phenyl sulfide with alkoxides is discussed.

Introduction

During the course of our investigations into the mechanism and synthetic utility of free-radical cyclizations we required precursors to the but-3-en-1-oxymethyl (1) and 2,2-dimethylbutenoyloxymethyl (2) radicals.¹ Our immediate objective was to



develop mild and efficient syntheses of compounds of the general types RCO_2CH_2X and $\text{RCH}_2\text{OCH}_2X$ where R contains the alkyl moiety and X is readily subject to $S_{\rm H}^2$ attack by $\text{Bu}_3\text{Sn}^{\bullet}$ or some related radical. We were especially interested in suitably substituted esters as such compounds are potentially useful for the regio- and stereo-specific introduction of ring substituents in complex molecules by radical ring closure (Scheme 1).²



¹ Beckwith, A. L. J., and Pigou, P. E., unpublished data.
 ² Beckwith, A. L. J., and Pigou, P. E., J. Chem. Soc., Chem. Commun., in press.

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Since previous work in this laboratory³ had shown that the α -phenylthio group in esters such as PhSCH₂CO₂Et is readily attacked by tributyltin radicals we assumed that compounds (4) and (8) would be efficient radical precursors, and our preliminary experiments were conducted, therefore, with these substrates.

	RCO_2CH_2X		BuC	CH ₂ X	X	CH ₂ CO ₂ Et	RCH ₂ X		
	R	X		Х		x		R	Х
(3)	Bu	SMe	(8)	SPh	(11)	SC ₆ H ₄ Me-p	(15)	C ₉ H ₁₉	Cl
(4)	Pr	SPh	(9)	Cl	(12)	Cl	(16)	$C_{7}H_{15}$	Br
(5)	Bu	SC ₆ H ₄ CN-p	(10)	SePh	(13)	SePh	(17)	Ph	Cl
(6)	Pr	Cl			(14)	SPh	(18)	furan-3-yl	SePh
(7)	Bu	SePh							

Method and Results

Initial attempts to reduce phenylthiomethyl butanoate (4) to methyl butanoate by heating with tributylstannane $(0 \cdot 1 - 0 \cdot 4 \text{ M})$ at 80–120°C gave poor yields under normal conditions; regular addition of small amounts of radical initiator was required for complete reduction. The reaction of butyl phenylthiomethyl ether (8) with tributylstannane was only marginally more efficient.

One possible explanation for the low reactivity of the phenylthio compounds (4) and (8) by comparison with ethyl (phenylthio)acetate (14) is that attack of tributyltin radicals on sulfur is subject to polar effects, and is aided by electron-withdrawing substituents. In accord with this view the methylthio compound (3) was found to be inert whereas the 4-cyanophenylthio compound (5) was more reactive than the parent (4), although still not sufficiently easily reduced to be synthetically useful.

In the light of these qualitative results we decided to conduct a quantitative study of the relative reactivity of various substrates towards reduction by tributylstannane. The competitive method used was based on the mechanism illustrated in Scheme 2.

> initiation \longrightarrow Bu₃Sn[•] Bu₃Sn[•] + R¹X $\xrightarrow{k_X}$ R^1 + Bu₃SnX Bu₃Sn[•] + R²Y $\xrightarrow{k_Y}$ R^2 + Bu₃SnY R^1 + Bu₃SnH \longrightarrow R¹H + Bu₃Sn[•] R^2 + Bu₃SnH \longrightarrow R²H + Bu₃Sn[•]

Scheme 2

This shows that the relative rates of consumption of the two starting materials, R^1X and R^2Y , upon heating of a mixture of them with tributylstannane, depend upon the competition between them for reaction with tributyltin radicals, the limiting reagent in the mixture, i.e.

$$d[\mathbf{R}^{1}\mathbf{X}]/d[\mathbf{R}^{2}\mathbf{Y}] = k_{\mathbf{X}}[\mathbf{R}^{1}\mathbf{X}]/k_{\mathbf{Y}}[\mathbf{R}^{2}\mathbf{Y}]$$

Consequently, the ratio of rate constants is given by equation $(1)^4$ where $[\mathbf{R}^1 \mathbf{X}]_0$ and $[\mathbf{R}^2 \mathbf{Y}]_0$ are the initial concentrations of the two reactants and $[\mathbf{R}^1 \mathbf{X}]$ and $[\mathbf{R}^2 \mathbf{Y}]$ are

- ³ Beckwith, A. L. J., and Schiesser, C. H., unpublished data.
- ⁴ Walling, C., and Jacknow, B. B., J. Am. Chem. Soc., 1960, 82, 6108.

the final concentrations:

$$k_{\rm X}/k_{\rm Y} = (\log[{\rm R}^{1}{\rm X}] - \log[{\rm R}^{1}{\rm X}]_{\rm o})/(\log[{\rm R}^{2}{\rm Y}] - \log[{\rm R}^{2}{\rm Y}]_{\rm o})$$
(1)

In practice, initial and final values of reactant concentrations were determined against an internal reference by gas chromatography. In some cases the final concentrations of the products \mathbb{R}^1 H and \mathbb{R}^2 H were measured since, according to Scheme 2, these reflect changes in substrate concentrations. The compounds studied included esters of substituted alcohols (3)–(7) and of substituted acids (11)–(14), ethers (8)–(10), the alkyl phenyl selenide (18), 1-chlorodecane (15), benzyl chloride (17) and 1-bromooctane (16).

Com- pound	100°C	Relative rate 80°C	e 25°C ^A	$k \text{ at } 25^{\circ}\text{C}$ (mol ⁻¹ l. s ⁻¹) ^B
(3)	-	<1	· · · · · · · · · · · · · · · · · · ·	
(4)	1	- 1	(1)	4×10^{2}
(5)	2.6	2.5	(2.9)	1×10^{3}
(8)	2.6	2.7	(3.2)	1×10^{3}
(15)	10.6	14	18	7×10^{3}
(6)	36.5	52	116	4×10^{4}
(9)	44	118	290	1×10^{5}
(11)		215	(500)	2×10^{5}
(14)		224	(525)	2×10^{5}
(18)		660	(1800)	7×10^{5}
(12)		1060	(3140)	1×10^{6}
(17)		1500	(4700)	2×10^{6}
(7)		2140	7300	3×10^{6}
(10)		4350	(15800)	6×10 ⁶
(16)		16800	70400	3×10^{7}
(13)		53700	(337000)	1×10^{8}

 Table 1. Relative rates and rate constants for reactions of halogen-, sulfur-, and selenium-containing compounds with tributyltin radicals

^A The values in parentheses were estimated by extrapolation.

^B The absolute rates were computed from the value for (16) given by Ingold,

K. U., Lusztyk, J., and Scaiano, J. C., J. Am. Chem. Soc., 1984, 106, 343.

Table 1 gives the results obtained when suitable pairs of these compounds were treated at 80°C with tributylstannane, and the ratios of rate constants so obtained were related to an arbitrary relative rate constant of 1.0 for the phenylthio compound (4). The Table also contains some experimental data for reactions at 100°C and at 25°C, together with values (in parentheses) for 25°C estimated by extrapolation.

The first noteworthy feature of these data is the very large spread of reactivity, which at 80°C is considerably greater than four orders of magnitude between the least and most reactive compounds. Indeed, the methylthio ester (3) reacts so slowly with tributyltin radicals that we were unable to obtain accurate relative rates.

Suitable dissection of the data in Table 1 reveals a number of significant trends. For example, it indicates that the degree of stabilization of the product radical, R^{\bullet} , is one of the factors affecting the reactivity of RX with tributyltin radicals. Thus (see Table 2) the order of reactivity of any series of compounds where X remains constant is $XCH_2CO_2Et > RCH_2OCH_2X > RCO_2CH_2X > RCH_2X$. For the last three this order parallels the extent of delocalization of the unpaired electron in the corresponding radicals as reflected by e.s.r. hyperfine splitting constants:⁵ $RCH_2OCH_2^{\bullet} > RCO_2CH_2^{\bullet} > RCH_2^{\bullet}$. A similar effect has been reported⁶ for the reaction of alkyl bromides with tributyltin radicals, for which the order of reactivity is benzyl > tertiary alkyl > primary alkyl. Likewise, we observed that benzyl chloride (17) is very much more reactive than the primary chloride (15).

Series	$X = SPh^A$	$X = Cl^A$	$X = SePh^A$
RCH ₂ X		1 (15)	1 (18)
RCO_2CH_2X	1 (4)	3.7, 1 (6)	$3 \cdot 2, 1 \cdot 0$ (7)
RCH_2OCH_2X	2.7 (8)	8.4, 2.3 (9)	$6 \cdot 6, 2 \cdot 0 (10)$
EtOCOCH ₂ X	224 (14)	76, 20 (12)	81, 25 (13)
PhCH ₂ X		107, 29 (17)	

Table 2. Effect of leaving group structure on the relative rates of $S_{\rm H}2$ reactions of tributyltin radicals at 80°C

^A Formula numbers are given in parentheses.

 Table 3. Relative reactivity of halides, sulfides and selenides towards attack of tributyltin radicals at 80°C

X	RCH ₂ X ^A	$RCO_2CH_2X^A$	$RCH_2OCH_2X^A$	EtOCOCH ₂ X ^A		
SPh		1 (4)	1 (8)	1 (14)		
Cl	1 (15)	52, 1 (6)	44, 1 (9)	4.7, 1 (12)		
SePh	47 (18)	2140, 41 (7)	1610, 37 (10)	240, 51 (13)		
Br	1200 (16)			, , , ,		

^A Formula numbers are given in parentheses.

The behaviour of the substituted acetates, XCH_2CO_2Et , does not, however, conform to this pattern. The e.s.r. data⁵ for ${}^{\circ}CH_2CO_2Et$ indicate that the unpaired electron is less delocalized than it is in $RCO_2CH_2{}^{\circ}$ or $RCH_2OCH_2{}^{\circ}$ (i.e. the last two radicals are more stabilized than is ${}^{\circ}CH_2CO_2Et$). We conclude that the energies of the transition structures reflect polar effects as well as product stability.

Within any series of compounds, RX, in which R remains constant the order of reactivity of various groups X towards $S_{\rm H}^2$ attack by tributyltin radicals is Br > PhSe > Cl > ArS > MeS (see Tables 1 and 3). Other work⁶ has shown that iodides are more reactive than bromides. Clearly there is a general trend towards increasing reactivity down and to the right of the periodic table. However, the precise factors responsible for this trend are by no means apparent. The magnitude of the enthalpy change is commonly used as an index of reactivity in $S_{\rm H}^2$ reactions but seems inappropriate in this case, as available data⁷⁻⁹ (Table 4), although incomplete,

⁵ Fischer, H., in 'Magnetic Properties of Free Radicals' (Eds H. Fischer and K.-H. Hellwege) Landolt-Bornstein New Series 9b, 1977, p. 5.

⁶ Ingold, K. U., Lusztyk, J., and Scaiano, J. C., J. Am. Chem. Soc., 1984, 106, 343.

⁷ Jackson, R. A., in 'Essays on Free-Radical Chemistry' Chem. Soc. Spec. Publ. No. 24, 1970, 295, and references cited therein.

⁸ Kerr, J. A., Chem. Rev., 1966, 66, 465.

⁹ Distefano, G., Ricci, A., Danieli, R., Foffani, A., Innorta, G., and Torroni, S., J. Organomet. Chem., 1974, 65, 205.

suggest that reactions of bromides and chlorides are approximately equally exothermic whereas reactions of sulfides are approximately thermoneutral.

Another possibility is that $S_{\rm H}^2$ reactions of tributyltin radicals proceed through interaction of the SOMO of the attacking radical with a vacant d orbital in the group X. The present data are certainly qualitatively consistent with the notion that reactivity reflects the energy of available vacant d orbitals. In accord with this view is the observation that attack on sulfur is facilitated by electron-withdrawing substituents, e.g. $MeSR \le p-MeC_6H_4SR \le PhSR \le p-CNC_6H_4SR \le EtOCOCH_2SPh$. Also in accord with this view are suggestions¹⁰ that $S_{\rm H}2$ reactions on sulfides proceed via trivalent intermediates.

	Table 4.	Bond dissociation e	energies $D(\mathbf{R}-\mathbf{X})$	() ^A
R	X =	H $X = Br$	X = Cl	X = SPh
Me	435	288	343	251 ^B
Me ₃ Sn	293	347	393	251 ^C

^A All values are in kJ mol⁻¹ and are taken from ref. 7 unless stated otherwise. ^B Ref. 8. ^C Ref. 9.

E.s.r. experiments afforded further relevant evidence. When tributyltin radicals were generated in the presence of the phenylthio ether (8), we observed the spectrum expected for the radical BuOCH₂ $[a(\alpha H) 16.7; a(\gamma H) = 2.1 G]$. However, the signal intensity *increased* as the temperature of the cavity was raised from -70° C to 10°C. This behaviour is opposite to that for signals due to radicals generated by reaction of tributyltin radicals with bromides, which conform to the general pattern that e.s.r. signal intensity weakens with increase in temperature because of levelling of the Boltzmann distribution of spin states. A possible explanation for this unusual behaviour is that the mechanism incorporates a relatively slow temperature-dependent step giving rise to a trivalent sulfur intermediate which is not detectable by e.s.r.

Within each of the series listed in Tables 2 and 3 the spread of reactivity generally depends upon the overall reactivity of the system. For example, the spread of reactivity for phenyl selenides is less than it is for phenyl sulfides, and the spread of reactivity with change of X in ethers, RCH_2OCH_2X , is less than it is for esters, RCO₂CH₂X. This behaviour conforms to the general pattern that structural changes have less effect on the behaviour of highly reactive substrates than they do on that of relatively unreactive substrates. It reflects, presumably, the fact that the reactions of highly reactive substrates have early, reactant-like, transition structures.

Closer scrutiny of the data in Table 2 reveals that the relative reactivity of the phenylseleno ester (13) is somewhat greater than would have been expected on the basis of this simple generalization [compare the relative reactivities of compounds (12) and (13)]. This is probably a reflection of the greater polarizability of the selenium centre.

In addition to the results presented in Table 1 some data were obtained at 45°C for comparison with previous work. Thus, the relative reactivities at 45°C of benzyl chloride (17) and the primary bromide (16) was found to be 1:24 in fair agreement

¹⁰ Kampmeier, J. A., Jordan, R. B., Liu, M. S., Yamanaka, H., and Bishop, D. J., in 'Organic Free Radicals' Am. Chem. Soc. Symp. Ser. No. 69, 1978, p. 16.

with values reported by Ingold (1 : 30) and by Kuivila (1 : 21).¹¹ However, our value of 1 : 167 for the relative reactivity of a primary chloride (15) and benzyl chloride (17) is much less than that (1 : 540) previously reported.¹¹ Since our value is reproducible and lies on the straight line obtained when log(relative reactivity) is plotted against I/T we consider it to be reliable. A similar plot of the logarithm of the relative reactivity of benzyl chloride (17) and the chloro ester (6) also gave a good straight line (r > 0.987).

The relative rate data in Table 1 are not of themselves capable of affording absolute rate constants. However, the value at 25°C of the rate constant for the reaction of a primary bromide with tributyltin radicals has been determined by Ingold.⁶ When it is used as a standard for the reaction of the bromide (16) the other values shown in Table 1 are obtained. Although these are clearly subject to very considerable experimental error, they provide useful guidelines for synthetic work. For example, those groups, Br and ArSe, which show high rate constants (>10⁶ mol⁻¹ l. s⁻¹) in any molecular environment, will give efficient chain propagation with tributylstannane. Compounds containing these groups (or iodine, which is probably even more reactive towards attack by tributyltin radicals)⁶ are the substrates of choice for synthetic work.

Chloro compounds are of more limited application. Those which contain electronaccepting groups or which afford stabilized radicals will react readily, but simple alkyl chlorides may require forcing conditions.



The kinetic data indicate that aryl sulfides are at the borderline; unsatisfactory for reactions involving alkyl radicals or even moderately stabilized species, but showing acceptable behaviour when the radical is highly stabilized or when the substrate contains electron-accepting groups. It is pertinent that phenyl pyrrolidenyl sulfides [e.g. (19)]¹² react satisfactorily with tributylstannane, whereas corresponding β -lactams [e.g. (20)]¹³ require forcing conditions presumably because the four-membered radicals [e.g. (21)] are less stable than their higher homologues.

Finally we note that alkyl sulfides are unlikely to be satisfactory substrates for reactions involving tributyltin radicals.

Syntheses

Carboxylic acids were converted into the corresponding phenylthiomethyl esters in high yield by treatment with ethyldi(isopropyl)amine, sodium iodide and chloromethyl phenyl sulfide in 1,2-dimethoxyethane (dme) [equation (2)]:

$$RCO_{2}H + PhSCH_{2}Cl \xrightarrow{Pr_{2}^{i}NEt/Nal}_{dme} RCO_{2}CH_{2}SPh \qquad (2)$$

¹¹ Carlsson, D. J., and Ingold, K. U., J. Am. Chem. Soc., 1968, **90**, 7047; Menapace, L. W., and Kuiliva, H. G., J. Am. Chem. Soc., 1964, **86**, 3047.

¹² Hart, D. J., and Tsai, Y.-M., J. Am. Chem. Soc., 1982, 104, 1430.

¹³ Beckwith, A. L. J., and Boate, D. R., *Tetrahedron Lett.*, 1985, 26, 1761.

However, when dimethylformamide (dmf) was employed as the solvent large amounts of bis(phenylthio)methane (22) were produced at the expense of the ester. A similar problem was encountered with the ether syntheses [equation (3)] from which relatively high yields of (22) were obtained:

$$PhSCH_{2}Cl \xrightarrow{(i) \text{ NaI/dme}} RCH_{2}OCH_{2}SPh + (PhS)_{2}CH_{2} \qquad (3)$$

$$(22)$$

Table 5.	Effect of reaction	conditions on	1 the	preparation of	of 1	-(pheny	lthiomethox	y)butane	(8)
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En- try	Molar BuONa	equivalents PhSCH ₂ Cl	NaI	Sol- vent	Temp. (°C)	Time (h)	R_p (8)	rod ^A (22)	PhSCH ₂ Cl(I) remaining (%)
1	1	1	1	dme	25	2	56	44	5
2	1	2	2	dme	25	16	16	84	49
3	1	1	1	dme/BuOH ^B	25	2	84	16	0
4	1	1	1	dme/Bu ^t OH ^B	25	16	43	57	10
_5	1 ^C	1	1	dme	80	22	44	56	15

A Product ratio estimated from ¹H n.m.r.

^B 1 : 1 mixtures by volume.

^C The base used was PrⁱNEt, not NaH.

The data of Table 5 show that the use of excess chloromethyl phenyl sulfide failed to enhance the yield of the ether, whereas use of the alcohol as both substrate and co-solvent substantially curtailed the formation of (22), with a complementary increase in the desired reaction pathway. Clearly this approach is not viable if the alcohol is of limited availability. In an attempt to overcome this shortcoming, t-butyl alcohol was used as a non-nucleophilic co-solvent with dme, but it proved to have little effect on the outcome. Similarly there was little change observed when the weaker base ethyldi(isopropyl)amine was used in place of sodium hydride.

 $2ArSCH_2CI \longrightarrow ArSCH_2CI \xrightarrow{RO} ArSCH_2CI \longrightarrow ArSCH_2SAr + CHCI$ $CH_2Ar CH_2SAr Scheme 3$

It has been suggested that sulfides such as chloromethyl phenyl sulfide undergo ylide-type reactions^{14,15} (Scheme 3). This would explain the base-sensitive appearance of (22) and the suppression of its formation by the addition of excess alcohol, which shifts the equilibrium indicated to the left. The fate of the carbene is unknown. Another reaction which might be expected to proceed under basic conditions is the abstraction of a proton from the chloromethyl sulfide, followed by nucleophilic attack of the resultant anion on more of the sulfide to give the adduct (23) which could rapidly eliminate HCl (Scheme 4a) to give 1,2-di(phenylthio)ethene (24). In agreement with this hypothesis when little or no sodium iodide was used approximately 10% of the total

¹⁴ Julia, S., Huynh, C., and Michelot, D., Tetrahedron Lett., 1972, 3587.

¹⁵ Campbell, M. M., Jigajinni, V. B., MacLean, K. A., and Wightman, R. H., *Tetrahedron Lett.*, 1980, **21**, 3305.

product mixture comprised a 3:7 mixture of (Z)- and (E)-1,2-di(phenylthio)ethene respectively. Once again the equilibrium is displaced by use of excess alcohol. The other pathway open to the carbanion is fragmentation to an anion and a carbene. The arylsulfur anion arising from path b would clearly give rise to a product analogous to (22) but the nature of the products derived from path c is unclear. Conversion of chloromethyl phenyl sulfide into the iodide *in situ*, prior to treatment with the alcohol and base, eliminated the formation of (24), due probably to the lowered acidity of the methylene protons.



The selenium compounds (7) and (10) were prepared in a similar manner to the sulfur analogues and the ether synthesis presented the problems described above even more acutely. For example, the equivalent experiments to entries 1 and 3 of Table 5, but with chloromethyl phenyl selenide as the substrate, gave 17:83 and 65:35 mixtures of (10) and bis(phenylseleno)methane respectively. Use of the tributylstannane alkoxide¹⁶ in place of the more basic sodium salt improved the yield of the ether to 35:65 but the reaction was very sluggish in refluxing benzene. Counter-ions of intermediate nature such as zinc or magnesium may prove useful in providing greater nucleophilicity than the tin salt while preserving, to a large degree, the reduced basicity of the alkoxide.

Experimental

Infrared spectra were recorded on a Perkin-Elmer 683 grating spectrometer, and mass spectra were obtained on a VG-Micromass 7070F instrument (70 eV). ¹H n.m.r. spectra were recorded on a Jeol Minimar spectrometer (100 MHz), and carbon n.m.r. spectra on a Jeol FX-200 instrument. All n.m.r. spectra were run in $CDCl_3$ with $SiMe_4$ as internal standard unless otherwise stated. Chemical shifts are given in ppm downfield from $SiMe_4$. G.l.c. was carried out on a Varian 6000 chromatograph with a flame ionization detector and a Hewlett-Packard 3390A integrating recorder. Generally a 2-m 3% OV-17 on Chromosorb W glass column was used. E.s.r. spectra were recorded on a Bruker ER-200D instrument. Melting points were determined on a Reichert hot-stage apparatus and are uncorrected, as are boiling points. Microanalyses were performed by the A.N.U. Analytical Service.

Tributylstannane, 1-bromooctane (16), 1-chlorodecane (15), ethyl chloroacetate (12) and benzyl chloride (17) were commercially available. 1-(Phenylselenomethoxy)butane (10) was donated by Dr S. A. Glover, and ethyl *p*-toluenethioacetate (11) by Mr C. H. Schiesser. The following were prepared by literature procedures: chloro(phenylthio)methane, 17 b.p.

¹⁶ Davies, A. G., Kleinschmidt, D. C., Palan, P. R., and Vasishtha, S. C., J. Chem. Soc. C, 1971, 3972.

¹⁷ Tuleen, D. L., and Stephens, T. B., J. Org. Chem., 1969, 34, 31.

72-74°/0.2 mm, chloro(methylthio)methane,¹⁸ b.p. 103-106°, chloromethyl butanoate (6),¹⁹ b.p. 62-64°/25 mm, ¹H n.m.r. (CCl₄): δ 5.44, s, 2H; 2.24, t, 2H, J 7 Hz; 1.6, sym m, 2H; 0.94, t, 3H, J 7 Hz, 1-(chloromethoxy)butane (9),^{20,21} b.p. 68-74°/100 mm, ¹H n.m.r.: δ 5.35, s, 2H; 3.64, t, 2H; 1.80-1.20, m, 4H; 0.99, t, 3H, and 3-(phenylselenomethyl)tetrahydrofuran (18).¹ Ethyl phenylthioacetate (14), b.p. 74°/0.1 mm, and ethyl phenylselenoacetate (13), b.p. 72-76°/0.15 mm, were prepared by treatment of ethyl chloroacetate (12) with sodium benzenethiolate and diphenyldiselenide/sodium borohydride respectively, and showed physical data consistent with the literature.²²

4-(Methylthio)benzonitrile

4-(Methylthio)benzaldehyde (5.0 g, 32.8 mmol) was added to a slurry of hydroxyammonium chloride (2.28 g, 32.8 mmol) in pyridine (2.62 g, 33.1 mmol). After the mixture had solidified, toluene (35 ml) was added and the contents heated under reflux until the theoretical amount of water had been collected in a Dean and Stark water separator (c. 6 h). The cooled solution was filtered and the solvent evaporated. Recrystallization of the residue from light petroleum/benzene furnished colourless plates (4.08 g, 83%) of the required nitrile, m.p. $60.5-63^{\circ}$ (lit.²³ 63-64°). ¹H n.m.r. (CCl₄): δ 7.42, sym m, 4H; 2.50, s, 3H.

4-(Chloromethylthio)benzonitrile

4-(Methylthio)benzonitrile (1.0 g, 6.71 mmol) was treated with N-chlorosuccinimide (0.94 g, 7.05 mmol) in dry carbon tetrachloride (6.5 ml) at room temperature overnight. The insoluble succinimide was filtered from the solution and the solvent evaporated. The residue was recrystallized from carbon tetrachloride/pentane to yield the *chlorinated product* (1.01 g, 82%), m.p. 61.5–62.0° (Found: C, 52.3; H, 3.2; Cl, 19.2; N, 7.7. C₈H₆ClNS requires C, 52.3; H, 3.3; Cl, 19.3; N, 7.6%). v_{max} (CCl₄): 2230, 1595, 1495, 1485, 1228, 1090, 1017 cm⁻¹. ¹H n.m.r. (CCl₄): δ 7.50, distorted s, 4H; 4.93, s, 2H. ¹³C n.m.r.: δ 140.59, C4; 132.59, C2,6; 128.42, C3,5; 118.34, CN; 110.43, C1; 47.83, CH₂. Mass spectrum *m*/*z* 185 (M, 17%), 183 (M, 47), 150 (10), 149 (47), 148 (100), 134 (18).

Chloro(phenylseleno)methane

Sodium borohydride $(1 \cdot 0 \text{ g}, 26 \text{ mmol})$ was introduced slowly into a solution of diphenyl diselenide $(3 \cdot 12 \text{ g}, 10 \text{ mmol})$ in absolute ethanol (50 ml). When the solution had lost its yellow colour it was added, over 5 min, to dry dichloromethane (200 ml) and then warmed to reflux for 1 h. The crude mixture was washed with dilute hydrochloric acid, water and brine, then it was dried and the solvent evaporated. Distillation of the residue provided chloro(phenylseleno)methane $(3 \cdot 07 \text{ g}, 75\%)$ as an almost colourless oil, b.p. (Kugelrohr): $58-62^{\circ}/0.5 \text{ mm}$ (lit.²⁴ 63-65°/0.1 mm). In our hands this procedure²⁵ proved vastly superior to the phase-transfer method of Comasseto *et al.*²⁶

General Procedure for the Preparation of RCO₂ CH₂X

A mixture of the carboxylic acid (10 mmol), ethyldi(isopropyl)amine (10 mmol), sodium iodide (10 mmol) and the alkylating agent ($ClCH_2X$) (10 mmol) in 1,2-dimethoxyethane (10 ml) was stirred at 80° for 6–18 h (monitored by t.l.c.). The cooled solution was then diluted with 2% hydrochloric acid and extracted with ether. The combined ether extracts were washed sequentially with dilute hydrochloric acid, water (2×), aqueous sodium hydrogen carbonate

¹⁸ Bordwell, F. G., and Pitt, B. M., J. Am. Chem. Soc., 1955, 77, 572.

¹⁹ Ulich, L. H., and Adams, R., J. Am. Chem. Soc., 1921, 43, 660.

²⁰ Connor, D. S., Klein, G. W., and Taylor, G. N., Org. Synth., 1972, 52, 16.

²¹ Hill, A. J., and Keach, D. T., J. Am. Chem. Soc., 1926, 48, 257.

²² Detty, M. R., and Wood, G. P., J. Org. Chem., 1980, 45, 80.

²³ Uneyama, K., Namba, H., and Oae, S., Bull. Chem. Soc. Jpn, 1968, 41, 1928.

²⁴ Schollkopf, U., and Kuppers, H., Tetrahedron Lett., 1963, 105.

²⁵ Sharpless, K. B., and Lauer, R. F., J. Am. Chem. Soc., 1973, 95, 2697.

²⁶ Comasseto, J. V., Ferreira, J. T. B., Brandt, C. A., and Petragnani, N., J. Chem. Res. (S), 1982, 212.

solution and brine. After drying of the extract, and evaporation of the solvent, the crude product was purified by flash chromatography (silica gel/40% dichloromethane in hexane) and then distilled to give analytically pure samples in yields of 75–90%. Compounds prepared by this method included:

Phenylthiomethyl butanoate (4), b.p. (Kugelrohr): $76^{\circ}/0.2$ mm, (Found: C, 62.8; H, 6.4. $C_{11}H_{14}O_2S$ requires C, 62.8; H, 6.7%). v_{max} (neat): 1743, 1586, 1485, 1441, 1156, 979, 743, 694 cm^{-1} . ¹H n.m.r. δ 7.3–6.9, m, 5H; 5.18, s, 2H; 2.20, t, 2H, J 7 Hz; 1.57, m, 2H; 0.88, t, 3H, J 7 Hz. ¹³C n.m.r.: 172.52, C1; 134.74, C_{ipso} ; 130.15, C_{ortho} ; 128.90, C_{meta} ; 127.09, C_{para} ; 67.58, OCH₂; 35.99, C2; 18.15, C3; 13.39, C4. Mass spectrum m/z 210 (M, 15%) (Found: M⁺, 210.0708. $C_{11}H_{14}O_2S$ requires 210.0715), 180 (14), 123 (13), 110 (52), 109 (18), 85 (58), 71 (100).

(Methylthio)ethyl pentanoate (3), b.p. (Kugelrohr): 86°/15 mm, (Found: C, 51.7; H, 8.5. $C_7H_{14}O_2S$ requires C, 51.8; H, 8.7%). v_{max} (neat): 1742, 1159 cm⁻¹. ¹H n.m.r. (CCl₄): δ 5.08, s, 2H; 2.54–2.00, m, 5H, includes at 2.18, s, 3H; 1.80–1.10, m, 4H; 0.94, t, 3H, J 6 Hz. Mass spectrum m/z 162 (M, 30%) (Found: M⁺, 162.0711. $C_7H_{14}O_2S$ requires 162.0715), 85 (100), 61 (40), 57 (44).

(4-Cyanophenylthio)methyl pentanoate (5), b.p. (Kugelrohr): $116-118^{\circ}/0.05 \text{ mm}$ (Found: C, 62.5; H, 5.9; N, 5.6. $C_{13}H_{15}NO_2S$ requires C, 62.6; H, 6.1; N, 5.6%). ν_{max} (neat): 2230, 1745, 1596, 1490, 1150, 1090, 828 cm⁻¹, ¹H n.m.r.: δ 7.46, s, 4H; 5.45, s, 2H; 2.33, t, 2H, J 6 Hz; 1.90-1.10, m, 4H; 1.10-0.67, m, 3H. Mass spectrum m/z 249 (M, 9%) (Found: M⁺, 249.0832. $C_{13}H_{15}NO_2S$ requires 249.0823), 183 (23), 149 (33), 148 (82), 134 (26), 104 (12), 90 (11), 85 (100).

(Phenylseleno)methyl pentanoate (7) as a liquid (Found: $M^{+\bullet}$, 272.0284. $C_{12}H_{16}O_2Se$ requires $M^{+\bullet}$, 272.0315). v_{max} (neat): 1745, 1583, 1482, 1441, 1152, 1108, 740, 695 cm⁻¹. ¹H n.m.r.: δ 7.72-7.40, m, 2H; 7.40-7.00, m, 3H; 5.48, s, 2H; 2.29, t, 2H, J 7.5 Hz; 1.76-1.08, m, 4H; 0.87, t, 3H, J 7 Hz. Mass spectrum m/z (⁸⁰Se only) 272 (M, 100%), 242 (84), 171 (41), 157 (62).

1-(Phenylthiomethoxy)butane (8)

A mixture of chloro(phenylthio)methane (1.59 g, 10 mmol) and sodium iodide (1.5 g, 10 mmol) in 1,2-dimethoxyethane (10 ml) was stirred at room temperature for c. 1 h before 1 equiv. of sodium butoxide in butan-1-ol (6 ml) was introduced. After 2 h reaction was complete and the mixture was diluted with water and extracted with ether. The ether extracts were washed with water, dried and evaporated. The pale yellow residue was distilled to give a colourless *oil* (8) (1.67 g, 84%), b.p. (Kugelrohr): $60^{\circ}/0.1 \text{ mm}$ (Found: M⁺⁺, 196.0913. C₁₁H₁₆OS requires M⁺⁺, 196.0922). v_{max} (neat): 1587, 1484, 1442, 1108, 1085, 732, 695 cm⁻¹. ¹H n.m.r.: δ 7.36-6.88, m, 5H; 4.81, s, 2H; 3.46, t, 2H, J 7 Hz; 1.64-1.08, m, 4H; 0.85, t, 3H, J 7 Hz. Mass spectrum *m*/*z* 196 (M, 33%), 123 (13), 110 (53), 109 (14), 87 (38), 57 (100).

By-products isolated from the ether synthesis under certain conditions (see text) are:

Bis(phenylthio)methane (22), isolated by flash chromatography (silica gel/40% CH₂Cl₂ in hexane). ¹H n.m.r. (CCl₄): δ 7.50–7.00, m, 10H; 4.17, s, 2H, which is consistent with literature data.²⁷ ¹³C n.m.r.: δ 134.91, C_{ipso}; 130.36, C_{ortho}; 128.84, C_{meta}; 126.86, C_{para}; 40.19, CH₂. Mass spectrum *m*/*z*: 232 (m, 23%), 123 (100), 109 (5).

(E)-1,2-Di(phenylthio)ethene, isolated by flash chromatography (silica gel/10% CH₂Cl₂ in hexane, $R_{\rm F}$ 0.50), m.p. 59.5–62.5° (lit.²⁸ 64°). ¹H n.m.r.: δ 7.52–7.04, 5H, major peak at 7.28; 6.37, s, 2H. ¹³C n.m.r.: δ 134.90, C_{ipso} ; 129.44, 129.15, $C_{ortho,meta}$; 126.96, C_{para} ; 125.32, C_{alkene} . Mass spectrum m/z: 244 (M, 100%), 199 (7), 167 (6), 136 (7), 135 (62), 134 (40).

(Z)-1,2-Di(phenylthio)ethene, isolated as above alkene ($R_{\rm F}$ 0.37) as a semi-solid (lit.²⁸ m.p. 32°). ¹H n.m.r.: δ 7.50–7.00, m, 10H, major peak at 7.22; 6.40, s, 2H. ¹³C n.m.r.: δ 135.25, C_{ipso}; 129.53, 129.90, C_{ortho,meta}; 126.90, C_{para}; 125.03, C_{alkene}.

Typical Competition Reaction

A pyrex ampoule was charged with approximately equimolar amounts of the two substrates (c. 0.04 mmol), a few crystals of aibn (c. 0.5 mg), an internal standard (octane or decane) and

- ²⁷ Corey, E. J., and Seebach, D., J. Org. Chem., 1966, 31, 4097.
- ²⁸ Parham, W. E., and Heberling, J., J. Am. Chem. Soc., 1955, 77, 1175.

t-butylbenzene (0.20 ml). A gas chromatograph of this solution gives the $[RX]_0$ values for use in equation (1). The mixture was cooled and tributylstannane (c. 0.01 mmol) was introduced. The ampoule was then degassed by repeated freeze-thaw cycles in a vacuum, sealed, and heated in a constant-temperature bath for 5-18 h. The contents were then analysed by g.c. to find the [RX] values for the disappearance of the substrates and/or to measure the relative proportion of reaction products. Reactions carried out at 25° were initiated photochemically.

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