α to sulfur, rather than β to sulfur (where it would be closer to the halogen atom).

The trends in chemical shifts noted for 14 and 15 are continued in the spectrum of the dibromo derivative 16. The CHBr$_2$ singlet is at 1.37 p.p.m. and the quartet for the single ring hydrogen atom is at about 3.7 p.p.m. Peak B is shifted to 5.33, whereas peaks C and D remain essentially fixed [doublet centered at 5.88 ($J = 7.0$ c.p.s.)]. Peaks E and F are now resolved, as in the parent sultone 13, but are shifted downfield to 5.88 and 5.99 p.p.m. They are separated by a chemical shift ($\delta = 0.11$ p.p.m.) comparable in magnitude to that observed in 13 ($\delta = 0.07$ p.p.m.).

Sultone 17 was prepared by the sulfonation of 1-t-butylcyclohexene.[3] The structure assigned on the basis of the expected course of reaction[3,4] is that shown. This assignment is supported by the p.m.r. spectrum,

which can be compared with that of 13. Structurally, 17 differs from 13 by the fact that the cyclohexane ring has replaced one methyl group on each of the carbon atoms α and β to oxygen. The structural features held in common (gem-dimethyl group α to oxygen, methyl group β to oxygen, and single hydrogen atom γ to oxygen) give rise to closely similar p.m.r. signals (Table I). The chemical shifts observed in changing from 17 to 18 should be, and are, comparable to those in changing from 13 to 15.

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The Effect of the Carbonyl and Related Groups on the Reactivity of Halides in Sn2 Reactions

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The rates of reaction of potassium iodide in acetone solution with several series of compounds of the type Y(CH$_2$)$_n$Cl ($n = 1$ to 5) have been measured. The strong deactivating effects of F$_3$C and C$_6$H$_5$SO$_2$ groups when attached to the α-carbon atom are attributed to steric and field effects, their inductive effects being assumed to be mildly rate enhancing. The C$_6$H$_5$SO group was found to have a mild retarding effect. Neither these groups nor related groups, such as C$_6$H$_5$S, C$_6$H$_5$CO, or CN, exhibit much effect of any kind from β or more remote positions. The mild activating effect of the β-C$_6$H$_5$CO group is the one exception. The methanolysis rates for C$_6$H$_5$S(CH$_2$)$_n$Cl ($n = 1$ to 5) have been measured.

Conant, Kirner, and Hussey first called attention to the profound influence of Y groups on the reactivity of YCH$_2$Cl type halides toward potassium iodide in acetone.[1] The powerful activating effect of the carbonyl, cyano, and related groups in this and other Sn2 reactions has since been the subject of much study and speculation.[2] Our interest in this effect was first aroused several years ago by the observation that the activating effect of the carbonyl group, not only is not shared, but is actually *reversed*, by the sulfonyl group. This is surprising since the carbonyl and sulfonyl groups exert the same type of inductive and resonance effects as judged by their σ-constants.[3] It was suggested that the retarding effect of sulfonyl group was of steric origin.[2e,4] We decided to extend the study to the sulfinyl and trifluoromethyl groups, since these groups exhibit closely similar inductive and resonance

effects, and these are of the same general type as those of the carbonyl and sulfonyl groups, as judged by σ-constants.[5,6] On the other hand, C$_6$H$_5$SO and F$_3$C groups were expected to offer additional variation with regard to steric effects and field effects.

A further point that appeared to be worthy of additional investigation was the fact that the activating effect of the carbonyl group is apparently still operative when the group is attached to the β-carbon atom or the γ-carbon atom (C$_6$H$_5$COCH$_2$CH$_2$Cl and C$_6$H$_5$-COCH$_2$CH$_2$CH$_2$Cl were reported to be 80 and 230 times as reactive, respectively, as BuCl[1]). The effect of the C$_6$H$_5$SO, F$_3$C, and C$_6$H$_5$SO$_2$ groups was therefore determined, not only at the α-carbon atom, but also at the β-, γ-, δ-, and, in some instances, the ϵ-carbon atom.

Although use of the reaction of potassium iodide in acetone as a measure of Sn2 reactivity has been subjected to some criticism,[7] it offers the advantages of wide applicability, relative freedom from side reactions, and simplicity in measurement of rates. The difficulties in the use of the Andrew's titration method for the determination of iodide[8] were obviated by using amperometric and potentiometric titration methods. All

(1) J. B. Conant, W. R. Kirner, and R. E. Hussey, *J. Am. Chem. Soc.*, **47**, 488 (1925).

(2) (a) J. W. Baker, *J. Chem. Soc.*, 1148 (1932); (b) E. D. Hughes, *Trans. Faraday Soc.*, **37**, 603 (1941); (c) J. W. Baker, *ibid.*, **37**, 643 (1941); (d) M. J. S. Dewar, "The Electronic Theory of Organic Chemistry," Oxford University Press, London, 1949, p. 73; (e) F. G. Bordwell and G. D. Cooper, *J. Am. Chem. Soc.*, **73**, 5184 (1951); (f) R. G. Pearson, S. H. Langer, F. V. Williams, and W. J. McGuire, *ibid.*, **74**, 5130 (1952); (g) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw–Hill Book Co., Inc., New York, N. Y., 1962, p. 28; (h) P. D. Bartlett and E. N. Trachtenberg, *J. Am. Chem. Soc.*, **80**, 5808 (1958); (i) W. Reeve, E. L. McCaffery, and T. E. Kaiser, *ibid.*, **76**, 2280 (1954).

(3) F. G. Bordwell and G. D. Cooper, *ibid.*, **74**, 1058 (1952).

(4) The statement made . . . "one would expect only a small steric effect for the sulfonyl group, unless it is assumed that the partial negative charge on the oxygen atoms would greatly extend their effective radius in blocking an incoming nucleophilic reagent" . . . was meant to include a field effect with the steric effect. Recently, C. Y. Meyers, *Tetrahedron Letters*, **No. 24**, 1125 (1962), has suggested that the field effect is the dominating factor.

(5) F. G. Bordwell and P. J. Boutan, *J. Am. Chem. Soc.*, **79**, 717 (1957); H. H. Szmant and G. Suld, *ibid.*, **78**, 3400 (1956); J. D. Roberts, R. I. Webb, and E. A. McElhill, *ibid.*, **72**, 411 (1950).

(6) See R. W. Taft, Jr., "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 595, and R. W. Taft, Jr., and I. C. Lewis, *J. Am. Chem. Soc.*, **81**, 5343 (1959), for discussions of the relative magnitudes of inductive and resonance contributions for these groups.

(7) See ref. 2g, pp. 17 and 18.

(8) K. I. Senior, R. R. Hetrick, and J. G. Miller, *J. Am. Chem. Soc.*, **66**, 1987 (1944).

runs were made at nearly the same potassium iodide concentration (near 0.04 M) in order to minimize effects caused by differing reactivities of ion-pair aggregates.

As a prelude to the studies of the S_N2 reactions, the relative rates of methanolysis of the chloro sulfides, $C_6H_5S(CH_2)_nCl$, were determined ($n = 1$ to 5). Although measurements of the rates for one or more members in this series have been made in several different solvents,[9] the complete series does not seem to have been run previously in a single medium. The relative rates for methanolysis were found to be: $C_6H_5SCH_2Cl$, 3.3×10^4; $C_6H_5S(CH_2)_2Cl$, 1.5×10^2; $C_6H_5S(CH_2)_3Cl$, 1.0; $C_6H_5S(CH_2)_4Cl$, 1.3×10^2; $C_6H_5S(CH_2)_5Cl$, 4.3. Since $C_6H_5S(CH_2)_3Cl$ has been found to solvolyze in aqueous dioxane at a rate roughly comparable to that of n-hexyl chloride,[9b] the present results indicate that the π-bond conjugative effect of the α-C_6H_5S group causes an approximate 33,000-fold increase in methanolysis rate, and that participation of the sulfur atom leading to σ-bond formation causes about a 100-fold increase in rate when a three- or five-membered ring is formed (β- or δ-C_6H_5S group). The effect of the ϵ-C_6H_5S group is more modest, but is still significant. It was anticipated that these values for participation might be useful for comparison with the effects of C_6H_5S, C_6H_5SO, $C_6H_5SO_2$, and F_3C groups on S_N2 reactivity in $Y(CH_2)_nCl$ type series, since the reported activating effects of C_6H_5CO groups attached to β- and γ-carbon atoms also seemed likely to have their basis in participation. At least, the β- and γ-C_6H_5SO groups were expected to show activating effects. Actually, as it turned out, no appreciable effect on S_N2 reactivity was observed for any of these groups beyond the α-position. The C_6H_5S, $C_6H_5SO_2$, and F_3C groups were mildly deactivating from β-positions; the C_6H_5SO group was mildly activating (Table I). All of the groups, except F_3C, were mildly activating from more remote positions. It seemed advisable, in view of these results, to check the original reported carbonyl activation. Repetition of the earlier work failed to show any appreciable activating effect for the γ-C_6H_5CO group. The supposed activating effect also fails to materialize for γ-CH_3CO, γ-CN, or γ-EtO_2C groups. β-C_6H_5CO and β-CH_3CO groups were found to have activating effects, although not as large as expected. The relative rate data are summarized in Table I.

Since attachment of an alkyl substituent at either an α-carbon atom or a β-carbon atom is known to retard S_N2 reactions, the assumption has been made that an electron-releasing inductive effect is rate retarding, and that inductive electron withdrawal is rate accelerating.[2b] On the other hand, in view of the mild deactivating effect produced by attaching a halogen, RO, or RS grouping at a β-carbon atom, inductive electron withdrawal has been assumed to be rate retarding.[2h,10] The latter conclusion is weakened by the fact that C_6H_5CO, CH_3CO, C_6H_5SO, EtO_2C, and CN groups are mildly rate enhancing when attached to a β-carbon atom (Table I), despite their considerably larger electron-attracting inductive effects, as compared to X, RO, or RS groups.[6] Furthermore,

(9) (a) G. M. Bennett and A. L. Hock, *J. Chem. Soc.*, 477 (1927); (b) H. Böhme and K. Sell, *Ber.*, **81**, 123 (1948); (c) F. G. Bordwell, G. D. Cooper, and H. Morita, *J. Am. Chem. Soc.*, **79**, 376 (1957).

(10) See the discussion on p. 15 of ref. 2g.

TABLE I
RELATIVE RATES OF REACTION WITH POTASSIUM IODIDE IN ACETONE AT 75°

Series	Values for n				
	1	2	3	4	5
$CH_3CH_2CH_2CH_2Cl$[a]	1.0	1.0	1.0	1.0	1.0
$C_6H_5S(CH_2)_nCl$	540	0.79	3.1	1.8	1.4
$C_6H_5SO(CH_2)_nCl$	0.25	2.7	2.6	3.3	2.6
$C_6H_5SO_2(CH_2)_nCl$	< .02	0.38	3.6	3.8	2.7
$F_3C(CH_2)_nOTs$[b]	.00007	.22	0.79	...	...
$F_3C(CH_2)_nBr$[c]	.00016	.20	...	...	...
$CH_3CO(CH_2)_nCl$	~35,000[d]	7.0	1.4	...	...
$C_6H_5CO(CH_2)_nCl$	32,000	44.0	2.1	1.7	...
$N{\equiv}C(CH_2)_nCl$	3,000[d]	2.8	3.7	2.8	...
$EtO_2C(CH_2)_nCl$	1,700[d]	1.6[e]	1.6[e]	1.4[e]	...

[a] The rates determined by amperometric titration were 0.244 ± 0.018 l. M^{-1} hr.$^{-1}$ at 60° and 0.783 ± 0.029 l. M^{-1} hr.$^{-1}$ at 75°. These rates are about 2.5-fold faster than that reported by Conant, *et al.*[1] [b] Relative to the rate of PrOTs at 40°. [c] Relative to the rate of PrBr at 35°; data of E. T. McBee, R. D. Battershell, and H. P. Braendlin, *J. Am. Chem. Soc.*, **84**, 3157 (1962). [d] Data of J. B. Conant, W. R. Kirner, and R. E. Hussey, ref. 1. [e] Data of J. B. Conant and W. R. Kirner, *ibid.*, **46**, 232 (1924).

electron-withdrawing substituents in $ArCOCH_2Cl$ and $ArSOCH_2Cl$ are rate enhancing (Tables III and V).[11] Finally, the reactivity of $YCH{=}CHCH_2Cl$ compounds toward potassium iodide in acetone has been observed to be mildly enhanced (10- to 100-fold) when Y is CN,[2e] $C_6H_5SO_2$,[2e] or F_3C.[12] These data suggest that the π-inductive effect[13] (and by inference the σ-inductive effect) of these groups is rate enhancing. The fact that the $C_6H_5SO_2$ and F_3C groups exhibit an effect comparable to that of CN when operating through the σ-bonds and π-bonds of a $Y{-}CH{=}CH{-}CH_2Cl$ system, but show an opposite effect in a $Y{-}CH_2Cl$ system, suggests that proximity effects other than inductive effects are causing the *large* rate retardations and rate enhancements observed in the latter system. Our view is that the inductive effect for electron-withdrawing groups is probably mildly rate enhancing, but that it is completely overshadowed in almost every $Y{-}CH_2Cl$ system by the presence of large steric effects, field effects, and/or conjugative effects.

Ingold[14] has classified the structural kinetic effects operating in simple S_N2 substitution reactions into three groups: (1) polar effects, depending on charge; (2) steric effects, depending on bulk; and (3) ponderal effects, depending on mass. When the atom attached to the α-carbon atom is unsaturated, or otherwise capable of entering into conjugation, we must add a fourth effect—(4) a conjugative effect, depending on effective orbital overlap. Of these factors, steric and polar effects appear to be most likely to be responsible for the large retarding effects of F_3C and $C_6H_5SO_2$ groups. Since we have assumed that the inductive effect plays a relatively minor role, which is probably rate enhancing, this suggests that a sizable rate-retarding field effect is combining with a steric

(11) An activating effect of electron-withdrawing substituents has also been observed in the reaction of $ArCOCH_2Br$ with pyridine in acetone solution [J. W. Baker, *J. Chem. Soc.*, 445 (1948)], for the reaction of Ar-$COCH_2Br$ with 2,6-dimethyl-4-thiopyrone in benzene solution [F. J. Ozog, V. Comte, and L. C. King, *J. Am. Chem. Soc.*, **74**, 6225 (1952)], and for the reactions of $ArCH_2CH_2Cl$, $ArSCH_2CH_2Cl$, and $ArSO_2CH_2CH_2Cl$ with potassium iodide in acetone (ref. 2g, p. 17).

(12) J. A. Pegolotti and W. G. Young, *J. Am. Chem. Soc.*, **83**, 3258 (1961).

(13) M. J. S. Dewar and P. J. Grisdale, *ibid.*, **84**, 3549 (1962).

(14) C. K. Ingold, *Quart. Rev.* (London), **11**, 1 (1957).

effect to give the F_3C and $C_6H_5SO_2$ groups their powerful deactivating effects. It is no doubt significant that the most probable path for the incoming nucleophile to the F_3CCH_2OTs and $C_6H_5SO_2CH_2Cl$ molecules is encumbered by an atom of high electron density, in sharp contrast to the situation with the $C_6H_5COCH_2Cl$ molecule (compare A or B with C).
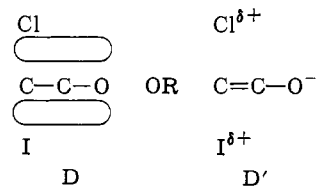
$$A \qquad B \qquad C$$
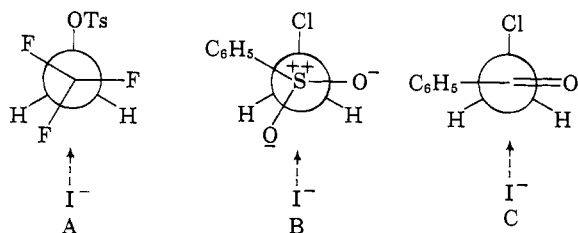
Furthermore, if we consider possible transition states for the reactions (A′, B′, and C′) we see that the repulsions between the entering and leaving groups with the highly electronegative atoms on the F_3C and C_6H_5-SO_2 groups are probably large, certainly much larger than for the C_6H_5CO group. (These repulsions are, of course, balanced to some extent by the positive charge on the β-atom.)

$$A' \qquad B' \qquad C'$$
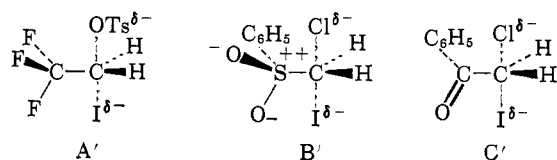
The favorable effect that the carbonyl and related (CN, CO_2R, etc.) groups have on SN2 reactivity probably stems in part from the absence of rate-retarding steric and field effects, coupled with a mildly rate-enhancing inductive effect. The very strong accelerating effect of these groups (compared to BuCl) must, however, include some sort of an additional conjugative factor, as first suggested by Dewar.[2d] This view is strongly supported by the observation of Bartlett and Trachtenberg[2h] that in a system incapable of achieving transition state C′ the enhancing effect of the carbonyl group is lost.[15]
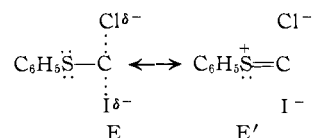
The nature and precise description of the conjugative effect is still open to question. One possibility is to utilize the electrons in the partially formed I–C and partially broken C–Cl bonds in a π-bond overlap with the p-orbital of the carbon atom of the carbonyl group acting as an electron pair *acceptor* (D or D′). This requires that bond formation leads over bond breaking

$$\text{D} \qquad \text{D}'$$

in the transition state. Besides the unattractiveness of structures such as D′, there are two arguments against this representation. First, there is good reason to believe that the activating effect of C=C, C≡C, RO,

and ArS groups in SN2 reactions (note, for example, the 540-fold acceleration listed in Table I for the α-C_6H_5S group) is caused by a conjugative effect of essentially the opposite type, where these groups act as electron-pair *donors* in a π-bond overlap (E and E′).[16]

$$E \qquad E'$$

This view is strengthened by the observation in the present work that electron-withdrawing groups have mild retarding effects on the rate for $ArSCH_2Cl$ (Table VI).[17] While it is conceivable that the transition state might have carbanion character in one type of SN2 reaction and carbonium ion character in another, it would be preferable to avoid this assumption.

A second argument against representations such as D and D′ is that one would expect on this basis that $C_6H_5SO_2$, C_6H_5SO, and F_3C groups would also activate, since they too are capable of acting as electron acceptors in conjugative type interactions.[5,6] Their activating effects would not be expected to be as large in magnitude, but should at least be in the same direction. This is clearly not the case (Table I).

It is possible to get around these difficulties by adopting the suggestion of Streitwieser[16b] that the conjugation responsible for carbonyl activation is caused by an overlap of the p-orbital of the carbon atom of the carbonyl group with orbitals on the entering and leaving groups (as in F′ and F″), rather than a π-bond type overlap.

$$F \qquad F' \qquad F''$$
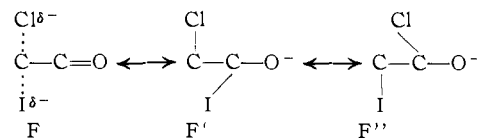
By adopting this view, the reasonable assumption can be made that the transition states for reactions of all types of YCH_2Cl compounds with iodide ion in acetone are similar in nature. Activation by α-C=C, -RO, -ArS, and like groups can be attributed primarily to their ability to provide electrons for a π-bond overlap. Activation by α-carbonyl and like groups can be attributed primarily to their ability to provide an electron-deficient p-orbital with which electrons on the entering and leaving groups can interact. Deactivation by α-$C_6H_5SO_2$, -F_3C, and like groups can be attributed to steric and field repulsions between the highly electronegative atoms on these groups and the entering and leaving groups.

The energy and entropy activation parameters for the SN2 reactions discussed above are summarized in Table II.

Most of the rate measurements are accurate to within ±5%, as judged by probable error. This means that the E_a values are good to roughly ±1 kcal./mole and the S^* values to roughly ±3 e.u. Deviations as high as ±2 kcal./mole or 6 e.u. are possible, however.

(15) Approach of the reagent as in C leading to transition state C′ not only offers the best opportunity for conjugation, but also appears to be best from an electrostatic view.[2f] It would appear, then, that electrostatic effects and conjugative effects act in consort to enhance SN2 reactivity, and that there is no reason to separate the two.

(16) (a) P. Ballinger, P. B. D. de la Mare, G. Kohnstam, and B. M. J. Presst, J. Chem. Soc., 3641 (1955); (b) ref. 2g, pp. 26–28.

(17) Note, however, that the p-NO₂ group has only a 2-fold deactivating effect as compared to about a 100-fold deactivating effect in the methanolysis of $ArSCH_2Cl$ (Table VII). This indicates that carbonium ion character in the SN2 reaction is probably not very highly developed.

Table II

ACTIVATION PARAMETERS FOR SN2 REACTIONS WITH
POTASSIUM IODIDE IN ACETONE

Compound	E_a, kcal./mole	S^*, e.u.
$CH_3CH_2CH_2CH_2Cl$	18	−26
$C_6H_5COCH_2Cl$	17	− 8
$C_6H_5CO(CH_2)_2Cl$	20[a]	−14
$C_6H_5CO(CH_2)_3Cl$	18	−20
$C_6H_5CO(CH_2)_4Cl$	18	−21
$C_6H_5SOCH_2Cl$	19	−24
$C_6H_5SO(CH_2)_2Cl$	17	−28
$C_6H_5SO(CH_2)_3Cl$	16	−29
$C_6H_5SO(CH_2)_4Cl$	18	−22
$C_6H_5SO(CH_2)_5Cl$	20	−19
$C_6H_5SO_2(CH_2)_2Cl$	19	−24
$C_6H_5SO_2(CH_2)_3Cl$	16	−30
$C_6H_5SO_2(CH_2)_4Cl$	20	−16
$C_6H_5SO_2(CH_2)_5Cl$	16	−29
$C_6H_5SO_2CH=CH(CH_2)_2Cl$[b]	18	−22
$C_6H_5SCH_2Cl$	18	−12
$C_6H_5S(CH_2)_2Cl$	17	−29
$C_6H_5S(CH_2)_3Cl$	18	−24
$C_6H_5S(CH_2)_4Cl$	18	−26
$C_6H_5S(CH_2)_5Cl$	15	−33
$CH_3CH_2CH_2OTs$	21[a]	− 6
F_3CCH_2OTs	22	−25
$F_3C(CH_2)_2OTs$	19[a]	−15
$F_3C(CH_2)_3OTs$	20[a]	− 8
$CH_3CH_2CH_2Br$[c]	18	−12
F_3CCH_2Br[c]	22	−17
$F_3C(CH_2)_2Br$[c]	20	− 8

[a] The activation energy was calculated by multiplying the slope of the line from the log k vs. $1/T$ plot by 4.58. [b] Rate relative to BuCl at 75° is 3.8. [c] E. T. McBee, R. C. Battershell, and H. P. Braendlin, *J. Am. Chem. Soc.*, **84**, 3157 (1962).

No significance can be attached to small differences in E_a and S^*, therefore. It is significant, however, that the large rate enhancement caused by the α-C_6H_5CO group is accompanied by a very sharp *increase* in activation entropy (see also Table III) when compared to n-butyl chloride, $C_6H_5SOCH_2Cl$, or chlorides where C_6H_5CO, C_6H_5SO, or $C_6H_5SO_2$ are in more remote positions (Table II). On the other hand, the large rate retardation caused by the α-F_3C group is accompanied by an equally sharp *decrease* in activation entropy in the tosylate series, and a lesser, but still significant, decrease in the bromide series (Table II). Although it is difficult to predict the manner in which activation parameters will change with changing structure in an SN2 reaction,[2g] it is possible to accommodate an increase in activation entropy in terms of lowered steric requirements and a decrease in activation entropy in terms of increased steric restriction in the transition state.[2g,14]

It is of interest that substitution of an electron-withdrawing group at a position more remote than α generally has but little effect on either the SN2 rate (Table I) or the activation parameters (Table II). The effects appear to be too small to warrant much speculation, except perhaps for the mild activating effect of the β-C_6H_5CO group. It is tempting to postulate some kind of conjugative effect here too. It would appear to be different in type from that of the α-C_6H_5CO group, however, since electron-withdrawing groups cause rate retardation rather than rate acceleration (compare Tables III and IV).

Table III

KINETIC DATA FOR THE REACTION OF ARYL CHLOROMETHYL
KETONES WITH POTASSIUM IODIDE IN ACETONE AT 0°

Substituent	Rel. rates	E_a, kcal./mole	S^*, e.u.
p-NO_2	10.8	15	−12
p-Br	2.64	17	− 6
p-Cl	2.44	16	− 9
p-CH_3O	1.21	15	−14
p-H	1.0	17	− 8

Table IV

KINETIC DATA FOR THE REACTION OF β-CHLOROETHYL
ARYL KETONES WITH POTASSIUM IODIDE IN ACETONE
SOLUTION AT 60°

Substituent	Rel. rates	E_a, kcal./mole	S^*, e.u.
p-H	1.0	19[a]	−14
p-Br	0.89	17[a]	−21
p-CH_3SO_2	.19	22	−10
p-Cl	.10	20[a]	−18
p-CH_3O	.065	18[a]	−23
p-CH_3S	.042	19	−23

[a] Activation energies were calculated by multiplying the slopes of the lines from log k vs. $1/T$ plots by 4.58.

Table V

KINETIC DATA FOR THE REACTION OF ARYL CHLOROMETHYL
SULFOXIDES WITH POTASSIUM IODIDE IN ACETONE AT 75°

Substituent	Rel. rates	E_a, kcal./mole	S^*, e.u.
p-H	1.0	19	−24
p-Br	1.9	22	−17
p-NO_2	3.2	20	−20

Table VI

KINETIC DATA FOR THE REACTION OF CHLOROMETHYL
ARYL SULFIDES WITH POTASSIUM IODIDE IN ACETONE

Compound	T, °C.	k_2, l. M^{-1} hr.$^{-1}$	E_a, kcal./mole	S^*, e.u.
$C_6H_5SCH_2Cl$	25	4.93 ± 0.27		
	35	13.5 ± .9	18	−12
p-$BrC_6H_4SCH_2Cl$	25	4.67 ± .35		
	35	12.1 ± .8	17	−16
p-$NO_2C_6H_4SCH_2Cl$	25	2.18 ± .06		
	35	5.30 ± .27	16	−21

Table VII

KINETIC DATA FOR THE METHANOLYSIS OF CHLOROALKYL
ARYL SULFIDES

Compound	T, °C.	k, l. M^{-1} hr.$^{-1}$	E_a, kcal./mole	S^*, e.u.
$C_6H_5SCH_2Cl$	25	8.64×10^{-3}		
	35	2.55×10^{-2}	20	−12
p-$BrC_6H_5SCH_2Cl$	25	1.57×10^{-3}		
	35	4.53×10^{-3}	19	−17
p-$NO_2C_6H_4SCH_2Cl$	25	8.72×10^{-5}		
	35	2.85×10^{-4}	22	−15
$C_6H_5SCH_2CH_2Cl$	40	2.51×10^{-4}		
	50	6.12×10^{-4}	18	−30

Experimental[18]

Kinetic Procedure.—Reagent grade potassium iodate and silver nitrate were dried and used as such. Commercial acetone was dried for several days over a large quantity of calcium chloride or Drierite; the mixture was then filtered and distilled. Tubes containing suitable quantities of the organic halide were thermostated at temperatures from −16 to 40° for 15 min., and to these were then added similarly thermostated acetone solutions of standard potassium iodide. The time of mixing was taken as zero time. At temperatures above 40° the halide and iodide solutions were mixed at room temperature in tubes and cooled to Dry Ice temperature. The tubes were removed for

sealing and placed immediately in the constant temperature bath. Initial time readings were recorded after 10 to 20 min. in the 50 to 100° range; blanks showed that less than 3% reaction had occurred during the time of mixing.

Runs were made using a fivefold, or greater, ratio of halide to iodide.[1] Rate constants were calculated using the equation

$$k = \frac{2.303}{tb(w-1)} \log \frac{w-z}{w(1-z)}$$

where $w = a/b = [RCl]/[KI]$, $z = x/[KI]$, and x = amount of I^- reacting in time t.

The reactions gave good second-order constants in the range of concentrations 0.05 to 0.25 M in halide.

The amount of unreacted iodide ion was determined using either (or both) an amperometric or a potentiometric titration.

The amperometric titrations were performed, using a rotating platinum electrode and a coiled silver wire as the nonpolarized electrode, at a constant potential of 0.2 v., in a 0.01 M ammonium hydroxide solution.[19]

The potentiometric titrations were made using a Photovolt pH meter as the potentiometer, a coiled platinum wire as the indicating electrode, and a saturated calomel electrode as the reference electrode. The solution was placed in a beaker (held at 0°) containing 25 ml. of water, 25 ml. of concentrated hydrochloric acid, and 25 g. of crushed ice and titrated with standard 0.005 M potassium iodate.

$$KIO_3 + 2KI + 6HCl \longrightarrow 3ICl + 3H_2O^8 + 3KCl$$
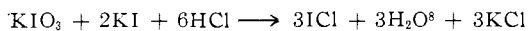
The amperometric titration was preferred since it can be carried out more rapidly (3 to 5 vs. 10 to 15 min.). It is unsuitable, however, for reactive halides. The α- and β-chloro ketones, α-chloro nitriles, and the β-phenylsulfonylethyl chloride were, therefore, titrated potentiometrically. Both titrations were used for β-trifluoromethylethyl tosylate, β-phenylsulfinylethyl chloride, γ-phenylsulfonylpropyl chloride, and γ-phenylsulfinylpropyl chloride. The agreement was good (within 5%).

The relative rates and activation parameters are summarized in Tables I–V.

Since halomethyl phenyl sulfides hydrolyze rapidly, the acetone solutions for these were poured directly into a separatory funnel containing 50 ml. of water and 100 ml. of chloroform. The chloroform layer was removed and subjected to one rapid wash (<2 min.). The combined aqueous layers were then treated with 6 ml. of concentrated ammonia and titrated amperometrically. The rate data (uncorrected for solvolysis) are summarized in Table VI (see also Table I). Blank runs indicate that these rates should be increased by about 30% to correct for solvolysis.

The solvolysis rates for the chloroalkyl aryl sulfides were carried out as described previously[9c] using methanol as a solvent. The kinetic data are summarized in Table VII.

Activation energies for reactions run at only two temperatures were calculated from the equation

$$E_a = 2.303RT_1T_2/(T_2 - T_1) \times \log(k_2/k_1)$$

Activation entropies were calculated using the equation

$$-S^* = 4.606[9.681 + \log T - \log k - (E_a - RT)/2.303RT]$$

Chloroalkyl phenyl sulfones were prepared by methods reported in the literature.[20] **Phenyl 5-chloropentyl sulfone** was purified by chromatography on silica gel, eluting with 5% ether-hexane; $n^{20}D$ 1.5360.

Anal. Calcd. for $C_{11}H_{15}ClO_2S$: C, 53.53; H, 6.14. Found: C, 53.70; H, 6.45.

Chloroalkyl Phenyl Sulfoxides.—The chloro sulfoxides were prepared by passing a stream of ozone through a solution containing 0.05 mole of chloro sulfide in 175 ml. of dry methylene chloride at −78°. When a blue color developed in the solution the ozonation was stopped and the solution was allowed to warm to room temperature. The solvent was removed under reduced pressure, and the residual oil chromatographed on a 2 × 50 cm. silica gel column. Elution with 10% ether-hexane gave starting

chloro sulfide in the first liter and traces of chloro sulfone in the next 1.5 l. On increasing the ether content (up to a maximum of 20%) small amounts of unidentified oils appeared in the first 3 l. of eluent, followed by the sulfoxide (strong infrared maximum near 1050 cm.$^{-1}$ and no sulfone bands). The yields and properties of the chloro sulfoxides are summarized in Table VIII.

TABLE VIII
PROPERTIES AND ANALYSES OF ω-CHLOROALKYL PHENYL SULFOXIDES

Compound	Yield, %	Physical properties	Calcd., % Carbon	Calcd., % Hydrogen	Found, % Carbon	Found, % Hydrogen
$C_6H_5SOCH_2Cl$	74	M.p. 28–29°	48.13	4.04	47.97	3.95
$C_6H_5SO(CH_2)_2Cl$	67	M.p. 31–32°	50.91	4.81	51.33	4.68
$C_6H_5SO(CH_2)_3Cl$	71	$n^{20}D$ 1.5710	53.31	5.48	52.79	5.26
$C_6H_5SO(CH_2)_4Cl$	55	$n^{20}D$ 1.5600	55.41	6.06	55.88	5.98
$C_6H_5SO(CH_2)_5Cl$	58	$n^{20}D$ 1.5378	57.24	6.56	56.49	7.10

α,α,α-Trifluoroethyl p-Toluenesulfonate.—To a solution of 5 g. (0.05 mole) of trifluoroethanol in 70 ml. of dry benzene was added 1.2 g. (0.05 g.-atom) of freshly cut sodium metal. After the initial reaction had subsided, the resulting mixture was refluxed until all the sodium had disappeared. The solution was cooled and 9.5 g. (0.05 mole) of p-toluenesulfonyl chloride was added and the mixture refluxed for 12 hr. The reaction mixture was then filtered free of sodium chloride, the solvent was removed, and the residue was recrystallized several times from hexane to yield 7.2 g. (56%) of a white crystalline solid melting at 39–41° (lit.[21] m.p. 41°).

β,β,β-Trifluoropropyl p-Toluenesulfonate.—A solution of 20 g. (0.089 mole) of 3,3,3-trifluoropropyl iodide[22] and 30 g. (0.11 mole) of silver p-toluenesulfonate in 150 ml. of dry acetonitrile was refluxed for 48 hr. The mixture was filtered and the filtrate poured into 300 ml. of water. Ether extraction and vacuum evaporation gave a residual oil which was vacuum distilled to give 15.1 g. (63%) of a colorless liquid, b.p. 120–122° (1 mm.), $n^{20}D$ 1.4730 (single peak on g.l.c. analysis).

Anal. Calcd. for $C_{10}H_{11}F_3O_3S$: C, 44.77; H, 4.14. Found: C, 45.53; H, 4.11.

γ,γ,γ-Trifluorobutyl p-Toluenesulfonate.—To a solution of 4 g. (0.03 mole) of 4,4,4-trifluorobutanol[23] in 75 ml. of dry benzene was added, in one portion, 1.4 g. (0.03 mole) of sodium hydride (50% in mineral oil) and, subsequently, 6 g. (0.031 mole) of p-toluenesulfonyl chloride. The solution was refluxed for 2.5 hr., filtered free of sodium chloride, and the solvent removed under reduced pressure. The residual oil was crystallized from ether-hexane, giving 5.1 g. (60%) of a white solid melting at 15–16°, $n^{20}D$ 1.4690.

Anal. Calcd. for $C_{11}H_{13}F_3O_3S$: C, 46.80; H, 4.65. Found: C, 46.38; H, 4.59.

β-Chloroethyl Methyl Ketone.—Using the procedure of Blaise and Maire,[24] but substituting cadmium chloride for zinc chloride, gave 46% of a colorless liquid, b.p. 57–60° (15 mm.) (<97% pure by g.l.c. analysis). The product decomposed upon standing over long periods of time.

γ-Chloropropyl Methyl Ketone.—Use of the modified procedure, as recorded above, gave 42% of product boiling at 70–73° (20 mm.) (lit.[25] b.p. 71–72° (20 mm.)).

Phenacyl Chloride Series.—Phenacyl chloride, purchased from Distillation Products, was recrystallized twice. The p-chloro, p-bromo, p-methoxy, m-nitro, and p-nitro analogs of phenacyl chloride were prepared according to methods given in the literature.[20] Table III lists the relative rates and activation parameters for the substituted phenacyl chloride reactions with potassium iodide in acetone at 0°.

β-Chloropropiophenone Series.—β-Chloropropiophenone as well as its p-chloro analog were prepared according to methods given in the literature.[20] The syntheses of the remaining compounds in this series are given below.

p-Bromophenyl β-Chloroethyl Ketone.—To a suspension of 31.4 g. (0.2 mole) of bromobenzene and 60 g. (0.46 mole) of anhydrous aluminum chloride in 200 ml. of dry carbon disulfide was added with stirring 25.4 g. (0.2 mole) of β-chloropropionyl

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(20) Details as to the methods used and the physical constants of the compounds prepared are contained in the Ph.D. Dissertation of W. T. Brannen, Jr., submitted to Northwestern University, August, 1962.

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TABLE IX

Starting chloride	Reflux time, hr.	Iodo compound	M.p., °C.	Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found
p-NO₂C₆H₅SOCH₂Cl	18	C₇H₆INO₃S	158–159	27.02	27.41	1.95	1.92
C₆H₅SOCH₂CH₂Cl	36	C₈H₉IOS	63–64	34.29	34.93	3.24	3.09
C₆H₅SO₂CH₂CH₂Cl	144	C₈H₉IO₂S	85–86	32.44	33.26	3.07	3.16
C₆H₅SO₂(CH₂)₄Cl	36	C₁₀H₁₃IO₂S	71–73	37.05	37.49	4.05	4.06

chloride. The mixture was refluxed 1 hr. and poured cautiously into 1 kg. of ice and 150 ml. of concentrated hydrochloric acid. This mixture was extracted with two 100-ml. portions of ether, dried over anhydrous sodium sulfate, and the ether removed under reduced pressure. The residual oil was crystallized from ether–hexane, giving 39.5 g. (80%) of a white solid melting at 59–61°.

Anal. Calcd. for C₉H₈ClBrO: C, 43.66; H, 3.26. Found: C, 43.93; H, 3.18.

β-Chloroethyl p-Methylthiophenyl Ketone.—To a suspension composed of 12.4 g. (0.1 mole) of methyl phenyl sulfide and 30 g. (0.23 mole) of anhydrous aluminum chloride in 100 ml. of *sym*-tetrachloroethane was added with stirring 12.7 g. (0.1 mole) of β-chloropropionyl chloride. Upon completion of the addition the mixture was heated on a steam bath for 1 hr. and poured cautiously onto 1 kg. of ice and 175 ml. of concentrated hydrochloric acid. The organic layer was separated and the aqueous layer extracted with three 100-ml. portions of ether. The organic layer and ethereal solutions were combined and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure (the pot temperature was kept below 40° to prevent decomposition of product). The residual oil solidified: several crystallizations from acetic acid gave 16.2 g. (75%) of a red crystalline solid, m.p. 111–113°.

Anal. Calcd. for C₁₀H₁₁ClSO: C, 55.93; H, 5.17. Found: C, 55.64; H, 4.61.

β-Chloroethyl p-Methylsulfonylphenyl Ketone.—To 250 g. (1.3 moles) of 40% peracetic acid at 0° was added with rapid stirring 36 g. (0.17 mole) of β-chloroethyl p-methylthiophenyl ketone. The solution was stirred at 0° for 0.5 hr. and at room temperature for 1.5 hr. after which it was poured into 600 ml. of water and extracted with three 100-ml. portions of ether. The ethereal solutions were combined and dried over anhydrous sodium sulfate. The ether was removed under reduced pressure and the oil crystallized from ether–hexane, yielding 14.6 g. (35%) of a white crystalline solid melting at 85–87°.

Anal. Calcd. for C₁₀H₁₁ClO₃S: C, 48.67; H, 4.50. Found: C, 49.09; H, 4.47.

β-Chloroethyl p-Methoxyphenyl Ketone.—To a suspension made up of 54 g. (0.5 mole) of anisole and 150 g. (1.1 moles) of anhydrous aluminum chloride in 200 ml. of dry carbon disulfide was added with stirring 63.5 g. (0.5 mole) of β-chloropropionyl chloride. Upon completion of the addition the mixture was refluxed 1 hr. and poured very cautiously onto 1.5 kg. of ice and 300 ml. of concentrated hydrochloric acid. The resulting mixture was extracted with three 100-ml. portions of ether, the combined ether extracts were washed with 10% sodium hydroxide and water, and dried over anhydrous sodium sulfate, and the ether was removed under reduced pressure. The resulting oil was crystallized from ether–hexane, giving 47.6 g. (48%) of a white crystalline solid melting at 66–68°.

Anal. Calcd. for C₁₀H₁₁ClO₂: C, 60.45; H, 5.59. Found: C, 60.53; H, 5.39.

γ-Chlorobutyrophenone.—Since the compound prepared by the method described previously[26] did not give the reported rate constant, an alternative preparative route was used. γ-Chlorobutyryl chloride (14.2 g., 0.1 mole) was added with stirring to a suspension of 30 g. (0.23 mole) of anhydrous aluminum chloride in 7.8 g. (0.1 mole) of dry benzene and 100 ml. of dry carbon di-

sulfide. After 1 hr. of reflux the mixture was cooled and poured slowly onto 400 g. of ice–water mixture. The oil obtained by ether extraction was dissolved in methanol and the solution decolorized twice with activated charcoal. After removal of the methanol the oil was crystallized from ether–hexane to give 10.2 g. (56%) of solid, m.p. 19–20° (lit.[26] m.p. 19–20°). The two samples were identical.

δ-Chlorobutyl Phenyl Ketone.—To a Grignard prepared from 15.7 g. (0.1 mole) of bromobenzene and 2.6 g. (0.1 g.-atom) of magnesium in 100 ml. of dry ether was added with stirring 10.6 g. (0.09 mole) of δ-chlorovaleronitrile in 100 ml. of dry ether. The mixture was refluxed for 1 hr., hydrolyzed with 100 ml. of ice–water followed by 100 ml. of 12 N sulfuric acid, the ether layer separated, and the aqueous layer further extracted with two 100-ml. portions of ether. The ether extracts were combined, washed with 50-ml. portions of 10% sodium carbonate and water, dried over anhydrous sodium sulfate, and the ether removed under reduced pressure. The oil obtained was crystallized from ether–hexane giving 13.9 g. (79%) of a white solid melting at 48–50° (lit.[27] m.p. 51°).

Isolation of Products.—The iodo compounds were isolated in a number of instances by refluxing the chlorides with a three-fourfold excess of potassium iodide in acetone solution for an extended period of time. A 65% yield of phenacyl iodide, m.p. 23–24° (lit. 28°[28]) was obtained after 4 hr.; a 72% yield of iodopropiophenone, m.p. 61–62° (lit.[29] 61°) was obtained.

The other iodo compounds obtained do not appear to have been prepared previously. Analyses for carbon were generally high, indicating that they were not entirely free of the starting chloro compound. Their properties are summarized in Table IX.

1-Benzenesulfonyl-4-chloro-1-butene.—To a solution of 20 g. (0.1 mole) of δ-chlorobutyl phenyl sulfide in 300 ml. of dry hexane at 0° was added slowly with stirring 14.9 g. (0.11 mole) of freshly distilled sulfuryl chloride. The mixture was allowed to come slowly to room temperature and, upon disappearance of the chlorosulfonium salt, was refluxed for 1.5 hr. The solvent was removed under reduced pressure and the residual oil fractionated under a vacuum giving 15.1 g. (76%) of a colorless liquid boiling at 112–115° (0.35 mm.), n²⁰D 1.5840. An infrared spectrum indicated the presence of a double bond. A solution of 7 g. (0.035 mole) of the above material and 11.3 g. (0.1 mole) of 30% hydrogen peroxide in 100 ml. of acetic acid was refluxed for 18 hr. It was then poured into water, extracted with two 100-ml. portions of chloroform, and the chloroform removed under reduced pressure. The oil obtained was dissolved in 10 ml. of chloroform and the solution chromatographed on a 2 × 50 cm. silica gel column, eluting with 10% ether–hexane. After the elution of 2.5 l., which contained only small amounts of unidentifiable oils, a sharp band containing a colorless liquid resulted weighing 3.4 g. (41%), n²⁰D 1.5603. The n.m.r. spectrum and carbon and hydrogen analyses were consistent with the structure assigned.

Anal. Calcd. for C₁₀H₁₁ClO₂S: C, 52.05; H, 4.81. Found: C, 51.86; H, 4.77.

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