Tetrahedron Letters No.49, pp. 3703-3710, 1964. Pergamon Press Ltd.
Printed in Great Britain.

# NUCLEOPHILIC AROMATIC SUBSTITUTIONS: NEW RELATIONS BETWEEN REACTION CONSTANTS AND PHYSICAL PROPERTIES OF LEAVING GROUPS.

P.E. Todesco and P. Vivarelli
Istituto di Chimica Organica e Industriale dell'Università
Bologna, Italy

A. Ricci
Istituto Chimica Organica, Università, Modena

(Received 19 October 1964)

In the course of a study of nucleophilic substitutions on 2-halo-benzothiazoles (1) which dealt with the transmission of substituent effects in the benzothiazolic system (2), some interesting observations were made:

i) The reactivity towards 2-halo-benzothiazoles (methanol, 25°) of methoxide is generally of the same order of magnitude or larger than that of thiophenoxide ion, as the data in Table 1 indicate. In fact the ratio $k_{MeO^-}/k_{PhS^-}$ varies from 0,45 to 25 (3).

---

1. P.E. Tpdesco, P. Vivarelli, *Boll.sci.fac.chim.ind.* Bologna **20**, 129 (1962); **22**, 1, 16 (1964); Ib.id., *Gazz.chim.ital.* **94**, 372, 435 (1964).
2. P.E. Todesco, P. Vivarelli, *Gazz.chim.ital.* **92**, 1221 (1962); Ib.id., *Boll.sci. fac.chim.ind.* Bologna **20**, 143 (1962); A. Ricci, P.E. Todesco, P. Vivarelli, *Gazz.chim.ital.*, in the press.
3. The generally greater nucleophilic reactivity of thiophenoxide is well known: only recently have been reported cases where the reactivity of this group is comparable or even smaller than that of the methoxide anion. Cfr. J.F. Bunnett, "*Annual Review of Physical Chemistry*" **14**, 271 (1963); C.W. Bewan, J. Hirst, *J. Chem.Soc.* 254 (1956); G. Illuminati, G. Marino, this Journal **16**, 1055 (1963).

## TABLE 1

Reactions of 2-halo-6-X-benzothiazoles with nucleophilic reagents in methanol.

| Derivative | Rate coefficients at 25° $sec^{-1}$ $mol^{-1}$ l. $10^3k_{MeO^-}$ | $10^3k_{PhS^-}$ | $\frac{k_{MeO^-}}{k_{PhS^-}}$ |
|---|---|---|---|
| X=H Halg= F | 550 (a) | 22.0 | 25 |
| Cl | 0.55 (b) | 0.20 (a) | 2.75 |
| Br | 0.41 (a) | 0.44 (a) | 0.91 |
| J | 0.063 | 0.14 | 0.45 |
| $X=NO_2$ Halg=F | 60000±9000 | 60000±9000 | 1 |
| Cl | 278 (b) | 1660 (a) | 0.17 |
| Br | 152 (a) | 2550 (a) | 0.06 |
| J | 29.2 | 973 | 0.03 |

a) P.E. Todesco, P. Vivarelli, Boll.sci.fac.chim.ind.,Bologna **20**, 143 (1962).
b) P.E. Todesco, P. Vivarelli, Gazz.chim.ital. **92**, 1221 (1962)

ii) The logarithm of reaction constants for methoxy-dehalogenation in the two series of compounds investigated (2-halo-benzothiazoles and 2-halo-6-nitro-benzothiazoles) can be linearly correlated (fig. 1).

This correlation is likely to be a particular case of a more general relationship existing between reaction constants of series of aromatic halo-derivatives, since it may be extended also to 2-4-dinitro-halo-benzenes and to p-nitro-halo-benzenes.

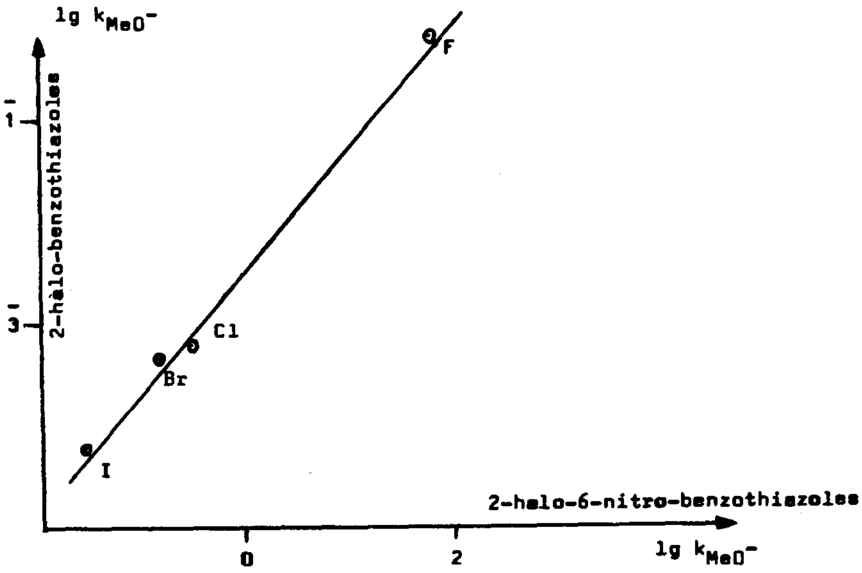

FIG. 1 - Rates of methoxy-dehalogenation for 2-halo-benzothiazoles versus corresponding values for 2-halo-6-nitro-benzothiazoles.

Moreover from preliminary results it seems that such a relation holds also for sets of compounds where the leaving groups are of different nature (for instance $-NO_2$, $-O-Ph-NO_2$, $-SO_2-Ph$, a.s.o.).

The correlation factor for the halogen-derivatives appears to be linear with the $\sigma$-para relative to the leaving halogen, as shown in fig. 2. Preliminary results indicate that when the leaving group is not a halogen the linear correlation with the corresponding $\sigma$-para is not observed.

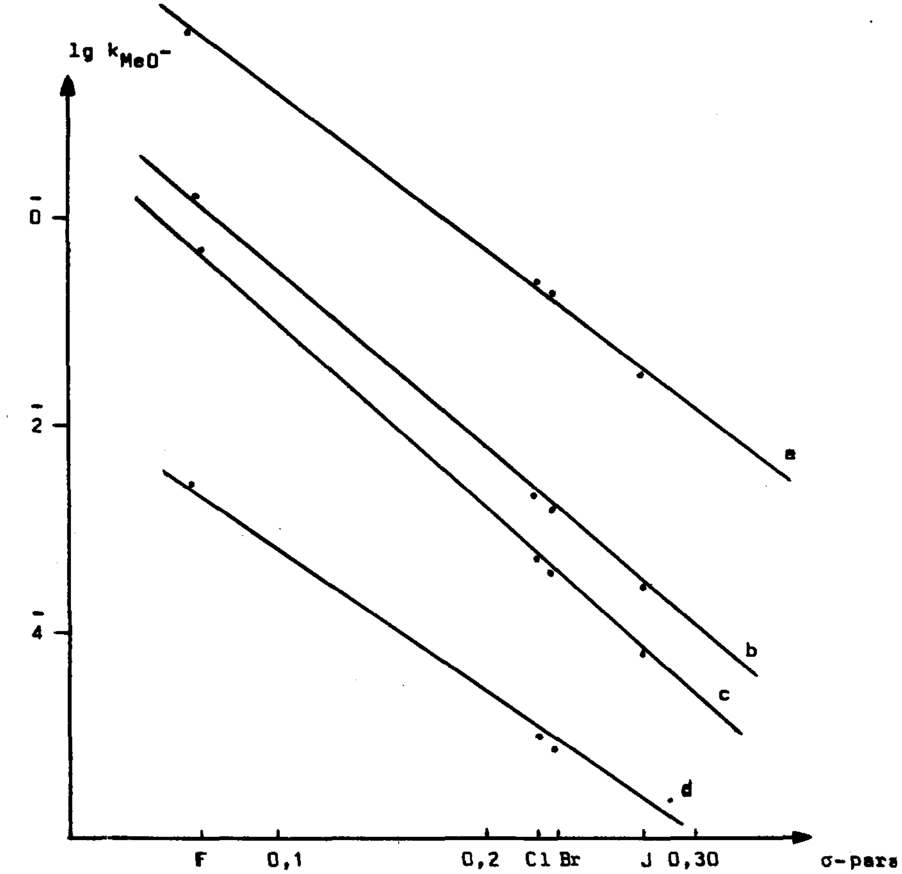

FIG. 2 - Plot of rates of methoxy-dehalogenation versus $\sigma_{para}$ of leaving halogen. Substrate: a) 2-halo-6-nitro-benzothiazoles (at 25°); b) 2-4-dinitro-halo-benzenes (at 0.0°) (4b,c); c) 2-halo-benzothiazoles (at 25°); d) p-nitro-halo-benzenes (at 50°) (4d,f).

iii) In both series of halo-benzothiazoles here investigated, a correlation exists between the corresponding log $k_{PhS^-}/k_{MeO^-}$ (fig. 3).

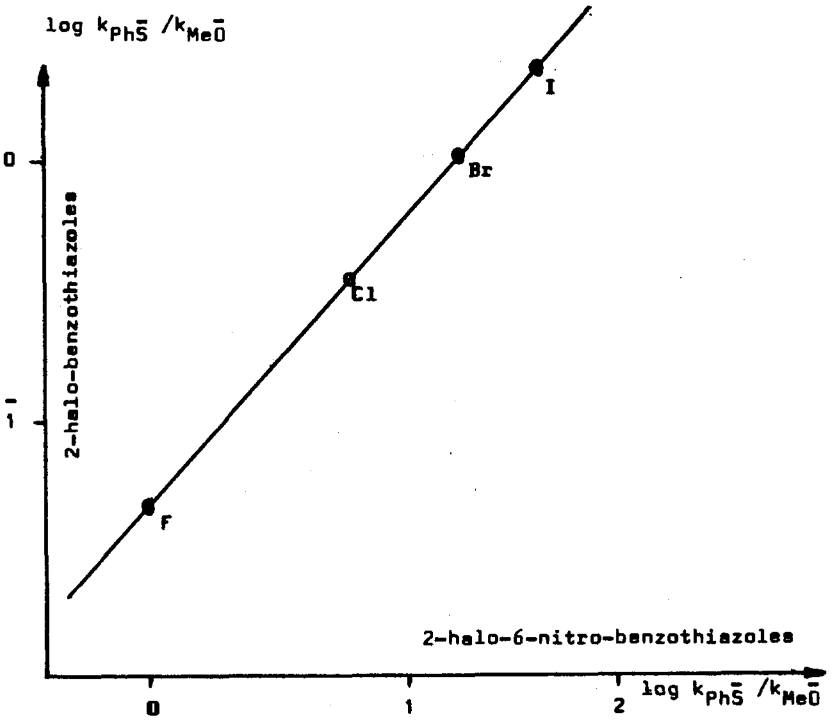

FIG. 3 - Plot of log $k_{PhS^-}$ / $k_{MeO^-}$ for 2-halo-benzothiazoles versus corresponding values for 2-halo-6-nitro-benzothiazoles

Here too this correlation seems to be a particular case of a more general relationship, since from data of the literature (4)

---

4. a) J.F. Bunnett, W.D. Merritt, J.Am.Chem.Soc. 79, 5967 (1957); b) A.L. Beckwitt, J. Miller, G.D. Leahy, J.Chem.Soc. 3552 (1952); c) C.W.L. Beven, G.C. Bye, J.Chem.Soc. 3091 (1954); d) C.W.L. Bevan, J. Hirst, J.Chem.Soc. 2340 (1951); e) ib.ib. 254 (1956); f) G.P. Briner, J. Miller, M. Liveris, P.G. Lutz, J.Chem.Soc. 1265 (1954); g) A.M. Adeniran, C.W.L. Bevan, J. Hirst, J.Chem. Soc. 5868 (1963); h) Darienko e Saporhnikov, Isvest. Vyssikh Ucheb Zavedenii, Kim.I.Kiim.Tecknol. 3, 461 (1960); i) Backer, Mels, Rec.trav.chim. 49, 457 (1930); l) J.F.Bunnett, E.W.Garbisch, K.M. Pruitt, J.Am.Chem.Soc. 79, 385 (1957); m) J.F. Bunnett, J.J. Randall, J.Am.Chem.Soc. 80, 6020 (1958); n) A. Ricci, P.E. Todesco, P. Vivarelli, in the press.

it can be extended also for other couples of nucleophilic reagents acting on different substrates. In this case the correlation factor is connected to the polarizability of the leaving group, as measured, in the case of halogens, by the logarithm of the refractivity constant $(R)_D$ of the C-halg. bond (5). These considerations are summarized in fig. 4 for the systems listed in tab. 2.

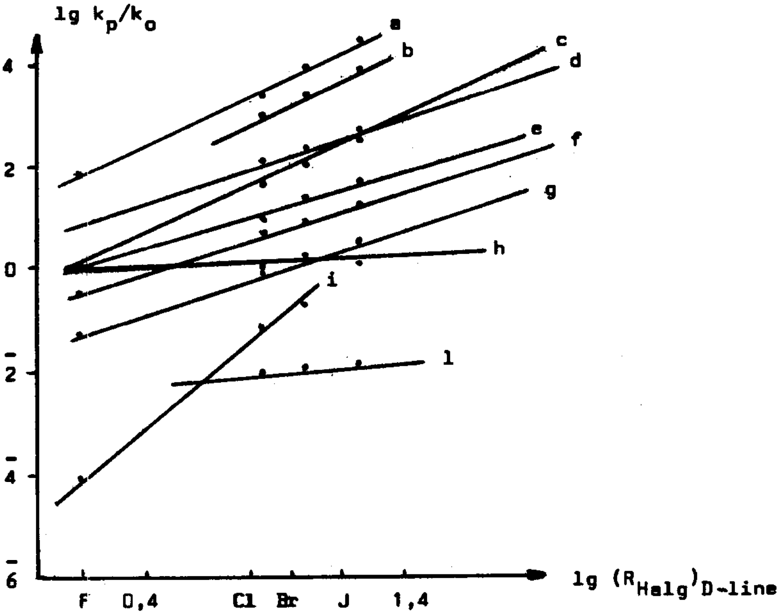

FIG. 4 - Plot of log $K_p/K_o$ for couples of nucleophilic reagents versus the polarizabilities of leaving halogens as measured by the logarithms of the refractivity constants $(R)_D$ of the C-halg bond. The substrates are listed in table 2.

The lines in fig. 4 indicates that generally the more polarizable nucleophilic reagent is more favoured than the less polarizable

---

5. J. Partington "An advanced treatise of Physical Chemistry" Longmans Green and Co., London, 1953, vol. IV, pag. 71.

## TABLE 2

| line in fig. 4 | $k_p$ more polarizable reagent | $k_o$ less polarizable reagent | Substrate | Solvent | t°C | References in loc. cit. 4 |
|---|---|---|---|---|---|---|
| a | $PhS^-$ | $MeO^-$ | 2-4-dinitro-halo-benzenes | MeOH | 0 | a,b,c, |
| b | " | " | 2-4-dinitro-halo-benzenes | " | 25 | a,b, |
| c | " | " | p-nitro-halo-benzenes | " | 50 | a,d,f, |
| d | $SO_3^{--}$ | $OH^-$ | halo-acetates | " | 25 | g,h,i, |
| e | $PhS^-$ | $MeO^-$ | 2-halo-6-nitro-benzothiazoles | " | 25 | this work |
| f | $SO_3^{--}$ | " | 2-4-dinitro-halo-benzenes | " | 0 | b,c,g, |
| g | $PhS^-$ | " | 2-halo-benzothiazoles | " | 25 | this work |
| h | Piperidine | " | 2-4-dinitro-halo-benzenes | " | 0 | b,c,l, |
| i | Ph-NH-Me | " | 2-4-dinitro-halo-benzenes | EtOH;MeOH | 70,0 | b,c,m, |
| l | $(Eth)_2NH$ | " | 2-halo-6-nitro-benzothiazoles | MeOH | 25 | this work,n |

one with increasing polarizability of the leaving group, in accord with the considerations put forward by Bunnett (6).

Supposing that to the reactivity of a nucleophilic reagent concur both the attitude to bind a positive group (roughly measured by the correspondent pK) and polarizability effects (7), it may be understood from the correlations presented here, that when the polarizability factor is the lesser [case of 2-halo-benzothiazoles; i)] the methoxide is a better nucleophile than the thiophenoxide anion, according to the relative basicities. However, when the polarizability factors are more important, as it is very often the case [examples of 2-halo-6-nitro-benzothiazoles; 2-4-dinitro-halobenzenes, p-nitro-halo-benzenes a.s.o.], the relative nucleophilic abilities of the two groups are reversed.

---

6. J.F. Bunnett, J.Am.Chem.Soc. **79**, 5969 (1957).
7. J.O. Edwards, J.Am.Chem.Soc. **76**, 1540 (1954); 78, 1819 (1956).