NUCLEOPHILIC AROMATIC SUBSTITUTION. REACTIVITY OF THIOMETHOXIDE ION WITH SOME HALOGENO-AROMATIC COMPOUNDS.

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In previous papers (1) we proposed on an empirical basis equation 1

1] $\log k_p/k_o = A + B.\log[R_{C-Halg}]_D$

correlating the rates of nucleophilic halogeno-aromatic substitutions: i.e. we observed that the logarithm of the ratio between the reaction rates of a pair of nucleophiles (k_p rate coefficient of a polarisable nucleophile; k_o of a poorly polarisable nucleophile, like alkoxide ion) is linearly related with the polarisability of the leaving group (expressed by the refractivity constants of the C-halogen bond at the sodium D line).

The validity of equation 1 has been tested with a large number of reactions and it was found that the slope of the correlation line (B) increases with the differences of polarisability of the nucleophiles.

It follows that the reactivity ratio between fluoro- and iodo-derivatives should decrease with the increase of the polarisability of the nucleophile.

Recently Miller reported (2) that the reactivity of thiomethoxide ion with p.halogeno-nitro- and 1-halogeno-2,4-dinitro-benzenes in methanol showed high

values of the ratio F/I similar to that usually found for a nucleophile of low
polarisability like methoxide ion.

To verify the anomalous behaviour of thiomethoxide ion we undertook an
investigation and the results are reported in the present letter.

The rates of reaction of p.halogeno-nitro-benzenes-I and of 2-halogeno-
benzothiazoles-II with mercaptide ion have been measured in methanol and, in
the case of compounds-II also in propan-2-ol.
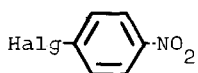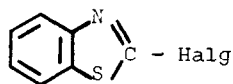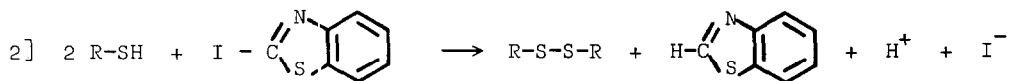

I   II

The rates of reaction of II with alkoxide ion in propan-2-ol have been
also measured (see table).

The study in propan-2-ol was carried out because the nucleophilic substi-
tution of 2-iodo-benzothiazole-II with thiomethoxide ion in methanol is compli-
cated by the concurrent reduction of II (equation 2)

by the free methyl-mercaptan present in the solution because of the equilibrium

3] $R-S^- + R-OH \rightleftharpoons R-SH + R-O^-$
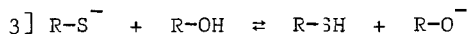
The reduction of II, which was already observed with thiophenol (3), is
strongly depressed in propan-2-ol because of its lower acidity.

The kinetics of the reactions have been followed by conventional methods
as previously reported (1).

Particular care was taken to check, specifically in some critical ca-
ses, that the expected substitution products were formed in every instance in
the theoretical amount both at completion of the reaction and at various de-
grees of conversion.

The rate coefficients measured together with those reported in the literatu-
re for the correspondent reactions with the methoxide ion are collected in
the table. (rate constants in $1.sec.^{-1}mole^{-1}$).

T A B L E

Experimental rate constants ($10^3.k$) for reactions of p.nitro-halogeno-benze-
nes (at 25°) and 2-halogeno-benzothiazoles (at 25°) with nucleophiles

| halogen in p.nitro--halogeno-benzenes	thiomethoxide in methanol	in propan-2-ol	methoxide in methanol	isopropoxide in propan-2-ol
F	19.	—	2.64 (a)	—
Cl	1.8	—	0.0085 (a)	—
Br	3.6	—	0.0072 (a)	—
I	3.3	—	0.0030 (a)	—
halogen in 2-halo-geno-benzothiazoles				
F	960.	6400.	550. (b)	310.
Cl	8.1	39.	0.55 (b)	0.092
Br	13.	63.	0.41 (b)	0.069
I	(c)	35.	0.063 (b)	0.020

a) data from P.Briner, J.Miller, M.Liveris and P.G.Lutz, J.Chem.Soc.,1265(1954)
b) data from P.E.Todesco and P.Vivarelli, Tetrahedron Letters 3703 (1964)
c) see text

The reactivity sequence in propan-2-ol is the same as in methanol and
the reaction rates are linearly correlated (fig. 1).

Fig. 1. — Solvent effect (methanol/propan-2-ol) in the nucleophilic substitu-

tions of 2-halogeno-benzothiazoles with thiomethoxide (a) and with

alkoxide ions (b) at 25°
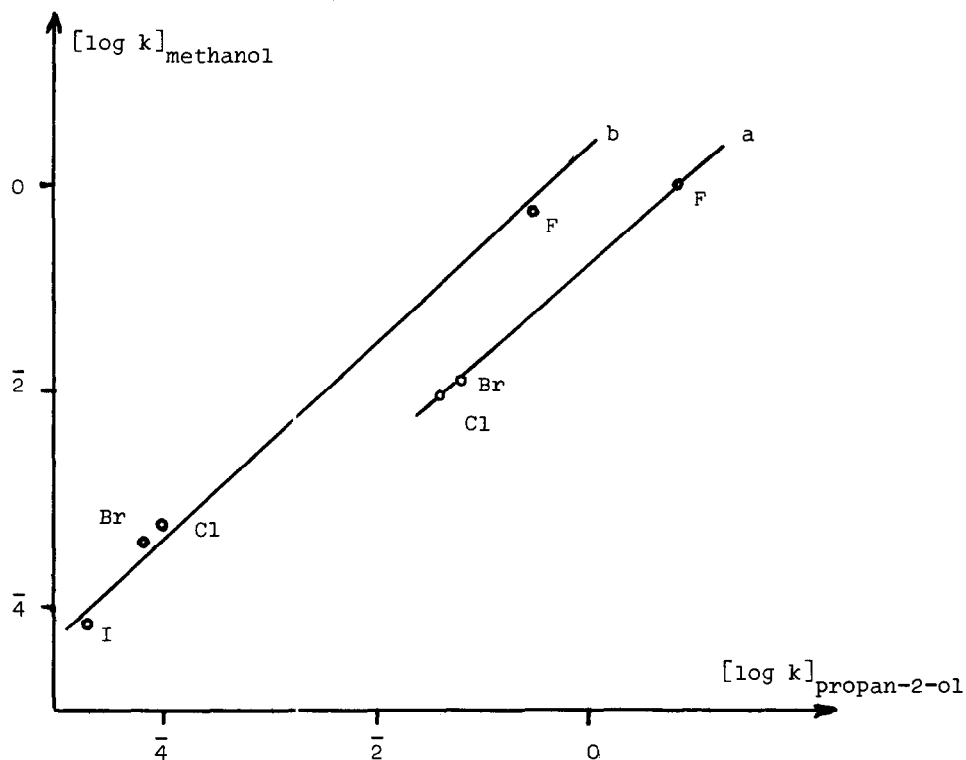
However, whereas the reactions of thiomethoxide ion are faster in propan-
-2-ol than in methanol, as required by the simple Hughes-Ingold's theory of ki-
netic solvent effect (4', the reactions of alkoxide ion in propan-2-ol are slo-
wer than those in methanol contrary to the findings of Murto   (5) in the case of
the similar reactions   -fluoro-2,4-dinitro-benzene and to the result expected from
the well known higher basicity of propan-2-ol in respect to methanol; on
this point further research is in progress.

In both solvents and with both substrates the equation 1 is well verified
as shown in fig. 2.

Fig. 2. - <u>Plot of log</u> $k_{CH_3S}^{-}/k_{Alk-O}^{-}$ <u>versus the polarisabilities of leaving</u>
<u>groups (logarithms of the refractivity constants of the C-Halogen</u>
<u>bond at the D_{line}</u>); a) 2-halogeno-benzothiazoles in propan-2-ol
at 25°; b) p.halogeno-nitro-benzenes in methanol at 50°; c) 2-halo-
geno-benzothiazoles in methanol at 25°.

log $k_{CH_3S}^{-}/k_{Alk.O}^{-}$
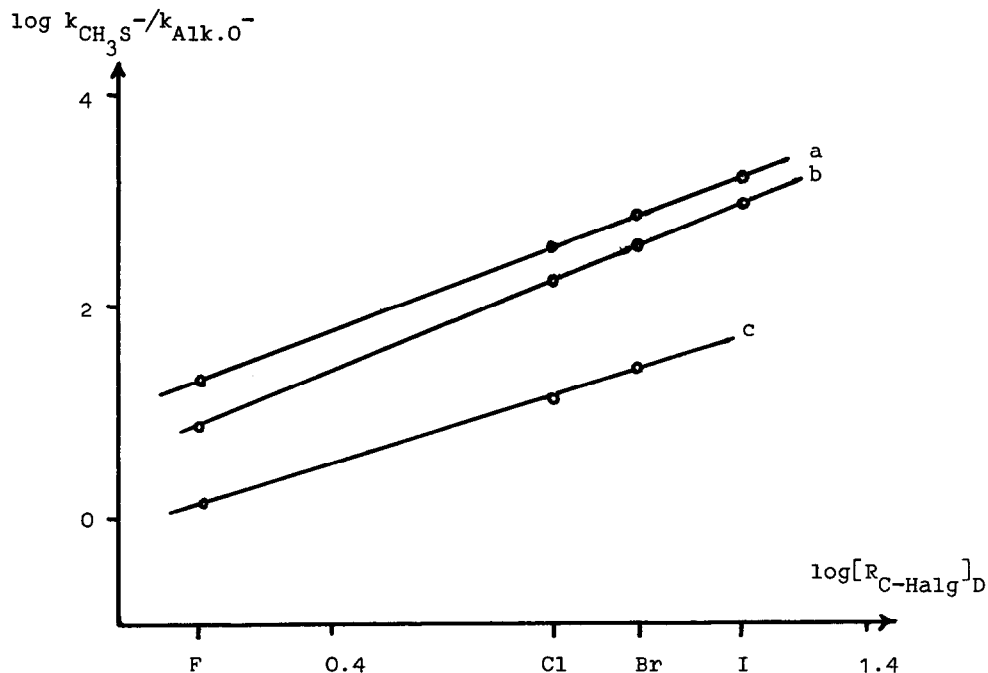
The validity of equation I also for   thiomethoxide and alkoxide ions
indicates that the thiomethoxide ion behaves as polarisable reagent as expec-
ted, and confirms the relevance of polarisability factors in determining the
nucleophilic aromatic reactivity, contrary to that stated by Miller   (2).

References

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