Tetrahedron Letters,Vol.23,No.43,pp 4465-4468,1982 0040-4039/82/434465-04$03.00/0
Printed in Great Britain

THE MECHANISM OF BIMOLECULAR METHYL TRANSFER IN A METHYL AMINOALKANESULFONATE. APPLICATION OF ^{18}O ISOTOPE SHIFTS IN ^{13}CMR SPECTRA OF SULFONIC ESTERS.

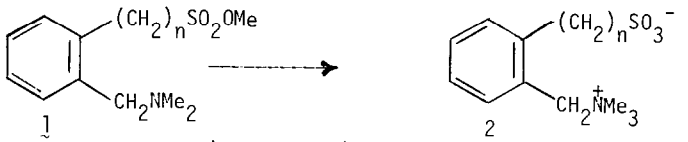
M.J. McGarrity, J.F. King, and J.B. Stothers

Department of Chemistry, University of Western Ontario,

London, Ontario, Canada, N6A 5B7

^{13}Cmr spectra show complete absence of scrambling of an ^{18}O label in 1a recovered after partial conversion to 2a thereby precluding an O-methylation mechanism for the bimolecular formation of 2a from 1a.

We have recently shown[1] by cross-labelling experiments that conversion of 1 to 2 is entirely bimolecular with 1a (n = 1) and largely so with 1b (n = 2), the endocyclic (unimolecular) process being observed as a minor pathway only at concentrations below 10^{-2} M.



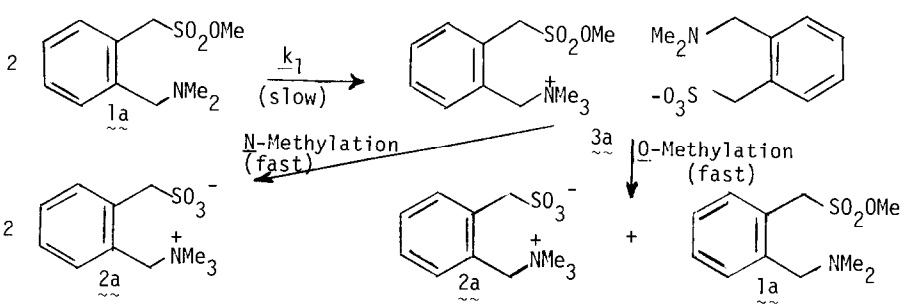
1 2

a) n = 1 b) n = 2

We now report experiments which not only provide insight into the nature of the bimolecular methyl transfer, but also (a) show the relative nucleophilicities of a tertiary amine and a sulfo anion toward a methyl group in a non-polar solvent, and (b) demonstrate the application of ^{18}O isotope shifts in ^{13}Cmr spectra to the study of reactions of sulfonic esters.

Scheme 1 shows two simple mechanisms, respectively the "N-methylation" and "O-methylation" processes, consistent with the observed bimolecular kinetics.[1,2]

SCHEME 1



N-Methylation of amines by sulfonic esters is well-known to be a facile reaction, and in aqueous media, at least, amines are much more nucleophilic than sulfo anions.[3] We have recently found,[4] however, that substrate-reagent ion-pair (SRIP) reactions of betylate sulfonates (4) readily give sulfonic esters (5) under essentially the same conditions as those used for the conversion of 1 to 2.

$$ROSO_2CH_2CH_2\overset{+}{N}Me_3 \quad R'SO_3^- \xrightarrow[\text{reflux}]{\text{PhH or PhMe}} ROSO_2R' + Me_3\overset{+}{N}CH_2CH_2SO_3^-$$

4 5

R = butyl, hexadecyl, 1-methylheptyl, etc.

R' = methyl, p=tolyl, ethenyl, etc.

In addition, methyl transfer to a sulfo anion (O-methylation) is a Hughes-Ingold "type 1" S_N reaction[5] and hence would be expected to be subject to a "small" rate increase with decrease in solvent polarity, while N-methylation is a "type 2" displacement in which there is an increase in charge separation on formation of the transition state and which should therefore show a "large" decrease in rate with lowering of solvent polarity.[5] The net result is that in the absence of more quantitative information the relative reactivities of the sulfo anion and the amino group in benzene cannot be safety predicted from their behavior in water.

Information on the point may be obtained, however, by a simple experiment starting with 1a labelled exclusively at the ether oxygen, as in E. It is evident from Scheme 1 that 2n molecules of 1a reacting by the N-methylation mechanism simply give 2n molecules of 2a. By the O-methylation route, however, 2n molecules of 1a give n molecules of 2a and n molecules of 1a; starting with 1a-E (1a labelled as in E - see Fig. 1) the 1a produced from 2n molecules would have the ^{18}O scrambled, i.e. would consist of n/3 molecules of 1a-E and 2n/3 molecules of 1a-S (neglecting isotope effects). The extent to which O-methylation contributes to formation of 2a may therefore be readily found by determining the amount of ^{18}O scrambling in unreacted starting material as the reaction of 1a-E proceeds.

The recent observations of useful ^{18}O-isotope effects in ^{13}Cmr chemical shifts in species such as carboxylic esters[6] prompted us to see if comparable effects would appear with sulfonic esters and hence provide a simple way of finding the extent of scrambling with labelled 1a. Accordingly, samples of ^{18}O-labelled norbetylate[7] 6 were prepared[8] and their ^{13}Cmr spectra examined.[9] From Fig. 1 (a)-(c) it is evident that the $^{18}OCH_3$ signal in a methoxysulfonyl grouping is about 1.7 Hz (at 50.3 MHz) upfield from that of the corresponding $^{16}OCH_3$ resonance (in either $-^{16}SO_2-^{16}OCH_3$ or $-S^{18}O^{16}O-^{16}OCH_3$ species) and, hence, that any formation of scrambled 1a would be easily detected. We have carried out partial reaction of ^{18}O-labelled 1a prepared from Sample A. Unreacted 1a after 33% and 66% conversion to 2a, was isolated as the norbetylate (6). The ^{13}Cmr spectra of these samples are shown in Fig. 1 (d) and (e), and it is evident that there is no sign of any scrambling whatsoever. This observation clearly precludes significant (>10%) incursion of the O-methylation process and is fully consistent with the N-methylation mechanism for the bimolecular reaction of 1a. In addition, this shows the tertiary amino group to be more nucleophilic than a sulfo anion toward a methoxysulfonyl function in benzene solution, and hence,

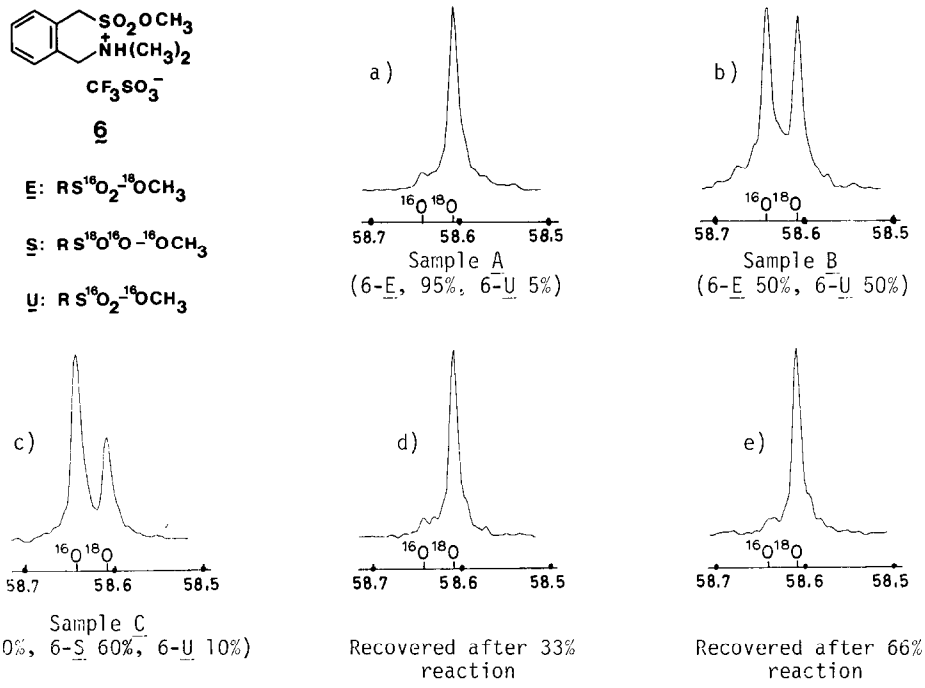


FIGURE 1. ^{13}Cmr signals of the methoxyl carbons of ^{18}O-labelled samples of 6. Numbers give chemical shifts in p.p.m. from TMS.

presumably, in other non-polar media as well.

The usefulness of ^{18}O-labelling in studying reactions of sulfonic esters has been shown by the extensive pioneering work of Goering and co-workers.[10] The present results show that ^{18}O isotope shifts in ^{13}Cmr spectra of these compounds provide a particularly easy method for making use of this valuable technique.

Finally, making the reasonable assumption that the bimolecular reaction of 1b is similar to that of 1a we may now improve our assignment of the effective concentration, C_{eff}, of the endocyclic (i.e. unimolecular) methyl transfer reaction[1] of 1b.

Defining

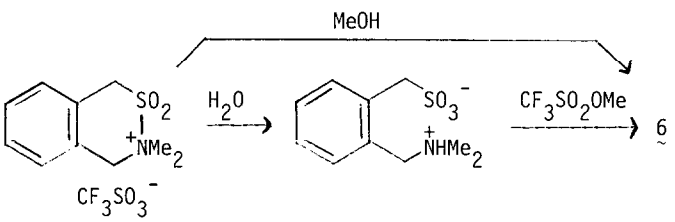
$$C_{eff} = \frac{k_{endocyclic}}{k_1}$$

and assigning $k_1 = k_{obs}/2$ on the basis of the N-methylation mechanism (rather than $k_1 = k_{obs}$ as would be required by the O-methylation route), we obtain a value of 2.1×10^{-3} M as our best estimate for C_{eff} for the endocyclic reaction of 1b.

We thank the Natural Sciences and Engineering Research Council of Canada for support of this work.

References and footnotes

1. J.F. King and M.J. McGarrity, J. Chem. Soc. Chem. Comm. 175 (1982).
2. The cross-labelling experiments were run in benzene solution at 110°C and the kinetic studies in benzene-d_6 at 37°, 92° and 110°C.
3. C.G. Swain and C.B. Scott, J. Am. Chem. Soc., 75, 141 (1953).
4. J.F. King and M. Aslam, Tetrahedron Lett. 3573 (1981).
5. E.D. Hughes and C.K. Ingold, J. Chem. Soc. 244 (1935), see also C.K. Ingold, Structure and Mechanism in Organic Chemistry, 2nd ed. Cornell University Press, Ithaca, N.Y., 1969, pp 457 ff.
6. J.M. Risley and R.L. Van Etten, J. Am. Chem. Soc., 101, 252 (1979) and 102, 4609 (1980); D.C. Darensbourg, J. Organomet. Chem. 174, C74 (1979); D.C. Darensbourg, and B.J. Baldwin, J. Am. Chem. Soc., 101, 6447 (1979); J.C. Vederas, J. Am. Chem. Soc., 102, 374 (1980); J. Diakur, T.T. Nakashima, and J.C. Vederas, Can. J. Chem. 58, 1311 (1980).
7. All weighing, purification, and spectroscopic examination of 1a are done using the norbetylate salt (6); 6 is made from 1a with 1 eq. of CF_3SO_3H and transformed back to 1a (in benzene solution) by shaking with excess aqueous Na_2CO_3:benzene.
8. Samples A and C were respectively prepared by the methanolysis and hydrolysis routes shown below, using $Me^{18}OH$ (prepared as described by C.B. Sawyer, J. Org. Chem., 37, 4225 (1972)), and $H_2{}^{18}O$ (supplied as 97.5% ^{18}O by Merck Sharp & Dohme Canada Limited).



Sample B was a mixture of equal amounts of A and unlabelled 6.

^{18}O contents were obtained from mass spectra and are rounded to the nearest 5%.

9. ^{13}Cmr spectra were obtained at 50.3 MHz with a Varian XL-200 spectrometer under conditions of complete proton-decoupling. The samples (0.5 M) in nitromethane-d_3 : acetonitrile-d_3 (1:1) were examined in 5 mm tubes. Operating conditions were: 2 KHz sweep width (sp^3 region), 5-8K transients, 30° pulse, 2 s repetition rate, and 32K transforms.
10. H.L. Goering and B.E. Jones, J. Am. Chem. Soc., 102, 1628 (1980) and references cited.

(Received in USA 29 June 1982)