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FACILE INTERMOLECULAR SUBSTITUTION AT α-SULFONYL CARBON

K. Hovius and Jan B.F.N. Engberts*
Department of Organic Chemistry, The University,
Zernikelaan, Groningen, The Netherlands.

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Intermolecular nucleophilic substitution at an α-sulfonyl carbon atom is strongly retarded due to the steric and field effects of the sulfonyl moiety.[1-3] For instance, nucleophilic displacement of halide in α-halosulfones has only been achieved[4] using strong nucleophiles such as mercaptide anions. However, in these cases the concomitant formation of reduction products in protic solvents has been taken as evidence that the substitution product may be formed via attack of the nucleophile on the halide atom.[4]

In recent work from this laboratory it was shown that covalent sulfonylmethylsulfonates[5a], -nitrates[5b], and even -perchlorates[5c] do not undergo nucleophilic displacement but react with sufficiently basic nucleophiles in a base-catalysed process. Only in the case of sulfonylmethyldiazonium ions, containing the exceptionally good leaving group $-N_2^{\oplus}$, could unequivocal evidence for nucleophilic substitution at α-sulfonyl carbon be obtained.[6]

We now wish to report the preparation of a simple, uncharged α-substituted sulfone which undergoes S_N-2 type displacement under mild conditions. Thus, treatment of 1 eq. of p-tolylsulfonyldiazomethane[5] with 1.5 eq. of CF_3SO_3H gives p-tolylsulfonylmethyl trifluoromethanesulfonate (I; m.p. 88.5-90.0°; NMR ($CDCl_3$): δ_{CH_2} at 5.18 ppm; IR (KBr): 1128, 1150, 1303, 1319, 1339 cm^{-1}; Anal.: Calc. C, 33.96; H, 2.86; F, 17.90; S, 20.15. Found: C, 34.0; H, 2.9; F, 17.8; S, 20.4) in a yield of 56%.

$$p\text{-}CH_3C_6H_4SO_2CHN_2 \quad + \quad CF_3SO_3H \quad \xrightarrow[0^{\circ}]{CH_3CO_2C_2H_5} \quad p\text{-}CH_3C_6H_4SO_2CH_2OSO_2CF_3 \quad + \quad N_2$$

Reaction of I with a number of monovalent anionic nucleophiles of low basicity in either DMF or ethanol at 40° led to a smooth displacement of the triflate moiety.

$$\underset{(0.06\ M)}{I} + \underset{(0.12\ M)}{Y^{\ominus}} \longrightarrow \underline{p}\text{-}CH_3C_6H_4SO_2CH_2Y + CF_3SO_3^{\ominus}$$

Representative results are given in the Table. No significant side reactions were observed.

Table. Reaction of I with nucleophiles at 40 ± 0.2°.

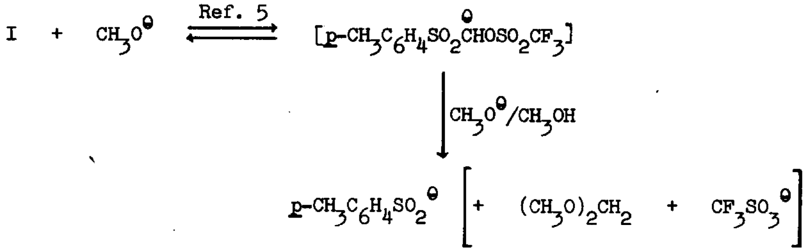
Nucleophile[a] ($Y^{\ominus}$)	Solvent	Reaction time (hrs)	Yield[b] of $\underline{p}\text{-}CH_3C_6H_4SO_2CH_2Y$ (%)
$Cl^{\ominus}$	DMF	2	30[c]
$Cl^{\ominus}$	DMF	48	96
$Br^{\ominus}$	DMF	2	92
$I^{\ominus}$	DMF	3	82
$I^{\ominus}$	C_2H_5OH	18	50[d]
$N_3^{\ominus}$	DMF	2	79
$C_6H_5S^{\ominus}$	DMF	2	75
$C_6H_5S^{\ominus}$	C_2H_5OH	20	83
$N{\equiv}CS^{\ominus}$	DMF	1	76

[a] $Na^{\oplus}$ gegenion. [b] Analytically pure compounds identified by comparison with authentic specimens. [c] 70% recovery of I. [d] 50% recovery of I.

It is difficult to account for the results given in the Table by other than a S_N-2 type process. The rate differences observed on variation of $Y^{\ominus}$ indicate that the nucleophile is involved in the rate determining step.[7] The observed reaction products, especially in ethanol as the solvent, cannot be reconciled with either a carbanion or a carbene as an intermediate.[8]

The above results demonstrate that intermolecular nucleophilic substitution at the normally highly unreactive α-sulfonyl carbon can be readily achieved using the excellent leaving ability[9,10] of the triflate group. This is powerfully demonstrated by the rapid reaction of I with NaI in DMF whereas p-tolylsulfonylmethyl p-nitrophenylsulfonate under the same conditions after 18 hrs. is recovered unchanged.

Some reactions with more strongly basic nucleophiles indicate that the preferred pathway for decomposition of I is determined by the nucleophilic vs. basic properties of $Y^{\ominus}$. For instance, when I is allowed to react with 2 eq. of CH_3ONa in DMF for 2 hrs. at 40°, sodium p-toluenesulfinate is the major product (yield 64%; isolated as p-toluenesulfinic acid)[11]; 4% of I was recovered.



$$\begin{tikzcd} \mathrm{I} + CH_3O^{\ominus} \arrow[r, shift left, "\text{Ref. 5}"] \arrow[r, leftarrow, shift right] & {[p\text{-}CH_3C_6H_4SO_2\overset{\ominus}{C}HOSO_2CF_3]} \arrow[d, "CH_3O^{\ominus}/CH_3OH"] \\ & p\text{-}CH_3C_6H_4SO_2^{\ominus} \left[+ (CH_3O)_2CH_2 + CF_3SO_3^{\ominus} \right] \end{tikzcd}$$

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7. It has been shown that the presence of the triflate leaving group does not result in a significant loss of the nucleophilic contribution to the transition state when compared with corresponding tosylates (cf. ref. 9).
8. The reaction carried out with I and NaI in C_2H_5OD at 40° for 18 hrs. indicated 75±5% H/D exchange in the methylene group of the reaction product. When I is kept in C_2H_5OD for

18 hrs. at 40°, 70 ± 5% exchange occurred while p-$CH_3C_6H_4SO_2CH_2I$ showed 50 ± 5% exchange under the same conditions.

9. A. Streitwieser, Jr., C.L. Wilkins and E. Kiehlmann, J. Amer. Chem. Soc. **90**, 1598 (1968) and references cited therein.

10. T.M. Su, W.F. Sliwinsky and P. von R. Schleyer, ibid. **91**, 5386 (1969).

11. The difficult work-up and purification resulted in loss of sulfinic acid.