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A CAUTIONARY COMMENT ON A RECENT COMMUNICATION ENTITLED "A MEASURE OF CHARGE TRANSFER (ρ) VERSUS A MEASURE OF BOND TIGHTNESS (ρ_{ij}) IN THE TRANSITION STATE"

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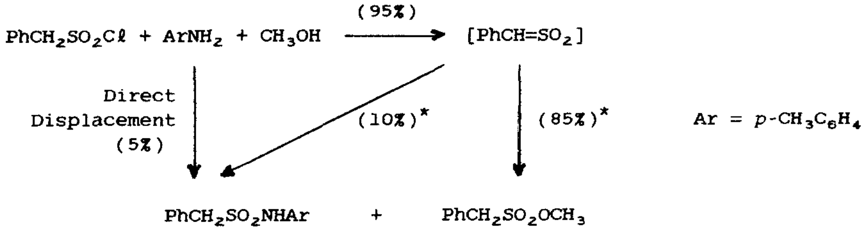
Summary: We present evidence that the reaction of anilines with $ArCH_2SO_2Cl$ and $ArCH_2SO_2F$ goes mainly via *the sulfene ($ArCH{=}SO_2$) and is not a simple nucleophilic displacement at sulfur, as was assumed in the above paper by I. Lee and H.K. Kang* (Tetrahedron Lett. *28, 1183 (1987)), and hence that their conclusions about the interpretation of ρ and ρ_{XY} values are unfounded.*

In a recent paper[1] Lee and Kang have used kinetic studies of reactions between substituted anilines and substituted phenylmethanesulfonyl chlorides and fluorides to explore the rôles of conventional and cross interaction ρ constants.[2] They state that they present "an example...in which ρ is only a measure of charge transfer whereas ρ_{ij} serves as a measure of bond tightness in the transition state", and conclude, "It is therefore *dangerous* to assess the degree of bond making at the TS by the magnitude of ρ_X and/or ρ_Y values alone".[1] This topic is an aspect of the broader field of the application of structure-reactivity coefficients to the elucidation of reaction mechanisms, and as such has considerable current interest.[3] Lee and Kang's arguments are based on the assumption that "in this reaction nucleophilic displacement takes place at sulfur with the halides, F^- and Cl^-, as the leaving group".[1] We wish to inject a note of caution by pointing out that the assumed mechanism of reaction of arylmethanesulfonyl halides is incorrect.

It was reported some years ago[4] that the reaction of phenylmethanesulfonyl chloride with amines and other basic reagents proceeds under a variety of reaction conditions by way of the sulfene, $PhCH{=}SO_2$; $PhCD_2SO_2Cl$ with aniline in refluxing benzene, for example, gave[4a] largely the monodeuterated product, $PhCHDSO_2NHPh$. It therefore seemed likely to us that under the conditions of Lee and Kang's experiments,[2] the reactions of arylmethanesulfonyl chlorides were also taking place by way of the arylsulfene, $ArCH{=}SO_2$. To examine the point we have carried out the reaction of $PhCH_2SO_2Cl$ with *p*-toluidine (respectively, 0.10 and 0.57 M) in methanol at 45°C, for 1 min and found the products to be methyl phenylmethanesulfonate (79%) and phenylmethanesulfon-*p*-toluidide (15%). The ester is gradually converted ($t_{\frac{1}{2}}$ 110 min, at 25°C) on standing in the mixture to the phenylmethanesulfonate anion, and later workup gives only the sulfonamide. In CH_3OD (91 atom% xs D) $PhCH_2SO_2Cl$ and *p*-toluidine-d_2 (94 atom% xs D) after 10 h at room temperature gave (after workup) the sulfonamide (31% yield) consisting of 72% $PhCHDNHSO_2$-*p*-Tol and 28% $PhCH_2SO_2NH$-*p*-Tol. In CD_3OD both the ester and the amide products of the reaction were mostly monodeuterated (97 and 93 ± 3%, respectively). These observations are consistent with the pathways shown in Scheme 1 and incompatible with any process incorporating any more than a minor (~5%) portion of the direct displacement reaction.

SCHEME 1



* These percentages, which vary with $ArNH_2$ concentration, refer to $[ArNH_2]$ ~0.5 M

Phenylmethanesulfonyl fluoride and *p*-toluidine (respectively, 0.26 and 1.28 M) also gave mainly $PhCH_2SO_3^-$ (~65%) and $PhCH_2SO_2NH$-*p*-Tol (16%), along with unreacted $PhCH_2SO_2F$ (16%), after 85 h at 45°C. In CD_3OD $PhCH_2SO_2F$ undergoes H–D exchange to $PhCHDSO_2F$ and $PhCD_2SO_2F$. The sulfonyl fluoride was warmed relatively briefly with CH_3OD and *p*-toluidine-d_2 (91 and 94 atom % xs D); the ratios of the CH_2:CHD:CD_2 materials of 75:24:1 for the recovered sulfonyl fluoride, and 15:80:5 for the sulfon-*p*-toluidide are consistent with a mechanism involving the sulfene route as the major process (>95%) and not with any significant direct displacement reaction.

Our present observations and those of Lee and Kang[1] may be readily fitted into a consistent mechanistic pattern with the aid of previous work on $ArCH_2SO_2Cl$ and related compounds of the general structure $ArCH_2SO_2OAr'$ summarized in Table 1.

TABLE 1. Summary of Previous Work on Arylsulfene Formation: $ArCH_2SO_2X \rightarrow ArCH=SO_2$

X	ρ^- [a] Pyridine	ρ^- [a] Et_3N	H–D exchange in starting material?	Base catalysis	Proposed mechanism	Ref.
Cl	2.35[b]	-	no	(general)	$(E1cB)_I$ or E1cB-like *E*2	4(b), 7(b)
2,4-dinitrophenoxy	2.38[c]	2.7[c]	no	general	$(E1cB)_I$ or E1cB-like *E*2	6, 7
p-nitrophenoxy	-	0.54[c]	yes	specific	$(E1cB)_R$	6, 7

[a] Correlation with σ^- was clearly better than with σ in the cases in which rates for the key substituents (*p*-NO_2 and *p*-CN) were available (i.e. all except the Et_3N - 2,4-dinitro-compound reaction).

[b] In 1,2-dimethoxyethane (0.4 M in water) at 20.0°C.[4b,c]

[c] In 1,2-dimethoxyethane–water (80–20) at 20°C.[7]

The ρ value of 2.16 (or 2.02)[1] and the lack of H-D exchange in the starting material in the reaction of $ArCH_2SO_2Cl$ with $PhNH_2$ in MeOH are similar to the observations on $ArCH_2SO_2Cl$ and 2,4-dinitrophenyl arylmethanesulfonates (Table 1), and hence a similar mechanism, *i.e.* an $(E1cB)_I$ or an *E*1cB-like *E*2 process, may be proposed for the $ArCH_2SO_2Cl$ – $ArNH_2$ reactions in MeOH.

On the other hand the H-D exchange and the relatively low ρ value (0.93 or 1.12)[1] shown by the reactions of $ArCH_2SO_2F$ with $PhNH_2$ in MeOH are features found in the $(E1cB)_R$ reaction of *p*-nitrophenyl arylmethanesulfonates (see Table 1) and hence the sulfonyl fluoride reaction may also be reasonably assigned this mechanism, as shown in eq. [1].[5]

$$[1]\quad ArCH_2SO_2F + Ar'NH_2 \xrightleftharpoons{MeOH} Ar\overset{-}{C}HSO_2F\ \overset{+}{N}H_3Ar' \longrightarrow ArCH{=}SO_2 \longrightarrow \text{Products (as in Scheme 1)}$$

It should be noted that the *p*-nitro esters show *specific* base catalysis in the aqueous medium used[6,7] and hence that interpretation of Lee and Kang's ρ_X value for the reaction of $PhCH_2SO_2F$ and aromatic amines should be avoided until the rôle of the amines in this system is determined.[5]

The reactions reported by Lee and Kang[1] evidently proceed largely *via* the arylsulfenes, with the rate-determining step of the chloride reactions being proton abstraction and that of the fluorides being fluoride ion expulsion. The reaction mechanisms in the chloride and fluoride series are therefore not only different from that assumed by Lee and Kang[1] but are also different from each other.

Lee and Kang's conclusions[1] concerning the interpretation of standard ρ values and cross interaction constants (ρ_{XY}) must, at this stage, be dismissed as lacking experimental basis.

Experimental:

$PhCH_2SO_2Cl$ reactions: (a) *p*-Toluidine (900 mg, 8.4 mmol) in CH_3OH (1.64 mL) was added dropwise over 1 min to a stirred solution of $PhCH_2SO_2Cl$ (291 mg, 1.53 mmol) in CH_3OH (13.0 mL) at 45°C. Immediate workup (by adding CH_2Cl_2, washing with dil. H_2SO_4, drying with $MgSO_4$, and evaporating the solvent under reduced pressure) gave a solid (285 mg) shown (by comparison of its ^{1}Hmr spectrum with those of authentic specimens) to be a 16:84 mixture of $PhCH_2SO_2NH$-*p*-Tol and $PhCH_2SO_2OMe$ (respective yields, 15% and 79%). (b) $PhCH_2SO_2Cl$ (235 mg, 1.23 mmol), *p*-toluidine-d_2 (500 mg, 4.6 mmol) and CH_3OD (4.44 mL) (respectively 94 and 91 atom % xs D) gave, on workup after 10 h at 45°C, 81 mg of the sulfonamide shown by concurring ^{1}Hmr, ^{13}Cmr and ms (molecular ion) analyses to consist of 28% $PhCH_2SO_2NH$-*p*-Tol and 78% (± 1%) $PhCHDSO_2NH$-*p*-Tol. (c) A series of ten ^{1}Hmr spectra were run at intervals from 1 to 1470 min of a mixture of $PhCH_2SO_2Cl$ (9 mg, 0.047 mmol) and *p*-toluidine-d_2 (30 mg, 0.275 mmol) in CD_3OD (0.639 mL). The first three spectra (1, 3, and 6 min) showed product peaks only for the methyl ester and the sulfon-*p*-toluidide (integration ratio about 7:3); the ester signal shrank while a peak at δ 4.04 due to the phenylmethanesulfonate ion grew ($t_{1/2}$ 110 ± 5 min, 25°C). The ester signal was a 1:1:1 triplet (δ 4.47) due to the CHD group with no clear sign of any CH_2 singlet; the sulfonamide signal consisted of a very small singlet (δ 4.31, CH_2) superimposed on the partly resolved CHD peak at δ 4.30.

$PhCH_2SO_2F$ reactions: (a) A solution of $PhCH_2SO_2F$ (312 mg, 1.8 mmol) and *p*-toluidine (960 mg, 9.0 mmol) in CH_3OH (7.0 mL) after 8.5 h at 45°C, gave, on workup (addition of PhH (20 mL), five washings with H_2O which were then evaporated, dilution with CH_2Cl_2, washing with dil. H_2SO_4, drying and evaporation of the solvent), (i) organic layer: 124 mg (solid) shown by ^{1}Hmr to be an equimolar mixture of $PhCH_2SO_2NH$-*p*-Tol and recovered $PhCH_2SO_2F$ (16% each), (ii) H_2O wash: 449 mg shown by ^{1}Hmr to be $PhCH_2SO_3^-$ (est. 65-70% yield) plus xs $MeC_6H_4NH_3^+$ (presumably also as the F^-

salt). (b) $PhCH_2SO_2F$ (43 mg, 0.247 mmol), *p*-toluidine-d_2 (20 mg, 0.083 mmol) and CH_3OD (2.22 mL) was heated at 45°C for 150 min and then worked up by washing with dil. H_2SO_4 water (3×), drying and evaporation of solvent; the mass spectrum (molecular ion peaks, under conditions showing no *M*-1 signals) gave the isotopic compositions presented in the text.

Acknowledgement:

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References and Notes:

1. I. Lee and H.K. Kang, *Tetrahedron Lett.* **28**, 1183 (1987).

2. Reported[1] reactions, definitions, and methods: $X\text{-}C_6H_4\text{-}NH_2 + Y\text{-}C_6H_4CH_2SO_2Z$ at 45°C, where X = *p*-OMe, *p*-Me, H, *p*-Cℓ, Y = *p*-OMe, *p*-Me, H, *p*-Cℓ, *p*-NO_2, Z = Cℓ, F; values of ρ_X, ρ_Y, and ρ_{XY} obtained by multiple regression analysis using 16 values of k_{XY} and the equation $\log(k_{XY}/k_{HH}) = \rho_X\sigma_X + \rho_Y\sigma_Y + \rho_{XY}\sigma_X\sigma_Y$; also reported parenthetically were ρ_X and ρ_Y values obtained conventionally from $\log(k_i/k_H) = \rho_i\sigma_i$ where i = X or Y.

3. See, for example, W.P. Jencks, *Chem. Rev.* **85**, 511 (1985), also J.E. Dubois, M.-F. Ruasse, and A. Argile, *J. Am. Chem. Soc.*, **106**, 4840 (1984), I. Lee and S.C. Sohn, *J. Chem. Soc. Chem. Comm.* 1055 (1986), R. Ta-Shma and W.P. Jencks, *J. Am. Chem. Soc.*, **108**, 8040 (1986).

4. (a) J.F. King and T. Durst, *J. Am. Chem. Soc.* **87**, 5684 (1965), (b) J.F. King and T.W.S. Lee, *J. Am. Chem Soc.* **91**, 6524 (1969), (c) T.W.S. Lee, Ph.D. Thesis, University of Western Ontario, 1969, (d) J.F. King, *Acc. Chem. Res.* **8**, 10 (1975).

5. The mechanism of the reaction of $PhCH_2SO_2F$ is evidently susceptible to change with change in reagent and medium; this is indicated by the difference between the results found for the reactions with *p*-toluidine in methanol (at 45°C) described here, and those of Williams and co-workers,[6] whose results from experiments with hydroxide in water (μ = 1.0 M with NaCℓ, 25°C) are appropriate to a reaction with rate determining proton transfer, *i.e.* either the irreversible *E*1cB or the *E*2 process.

6. A. Williams, K.T. Douglas, and J.S. Loran, *J. Chem. Soc., Chem. Comm.* 689 (1974); M.B. Davy, K.T. Douglas, J.S. Loran , A. Steltner, and A. Williams, *J. Am. Chem. Soc.* **99**, 1196 (1977).

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