

THE ORTHO-ALKYLATION OF ANILIDES VIA THE [2,3]-SIGMATROPIC REARRANGEMENT
OF YLIDS DERIVED FROM N-ACYL-N-ARYLAZASULFONIUM SALTS

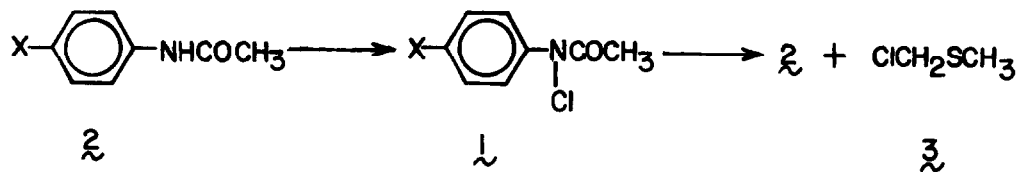
Paul G. Gassman* and Robert J. Balchunis

Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455

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Over the last five years we have demonstrated the vast potential of ylids derived from N-arylazasulfonium salts in the synthesis of ortho-alkylated aromatic amines,¹ indoles,² and oxindoles.³ In principle, the [2,3]-sigmatropic rearrangement⁴ of ylids derived from N-acyl-N-arylazasulfonium salts should have certain advantages over previously available procedures for the preparation of ortho-alkylated anilides. In order to generate such ylids, it was necessary to generate the previously unknown N-acyl-N-arylazasulfonium salts represented by general formula 4. While it might be anticipated that such salts could be prepared through the reaction of N-chloroacetanilides, 1, with dialkyl sulfides, the propensity for N-chloroacetanilides to undergo the Orton rearrangement⁵ and the unknown reactivity of sulfides with N-haloacetanilides⁶ made this approach appear tenuous. We now wish to report that we have succeeded in preparing N-acyl-N-arylazasulfonium salts by this approach, and that these salts, when treated with base, yield ylids which undergo spontaneous [2,3]-sigmatropic rearrangement to produce ortho-substituted anilides.

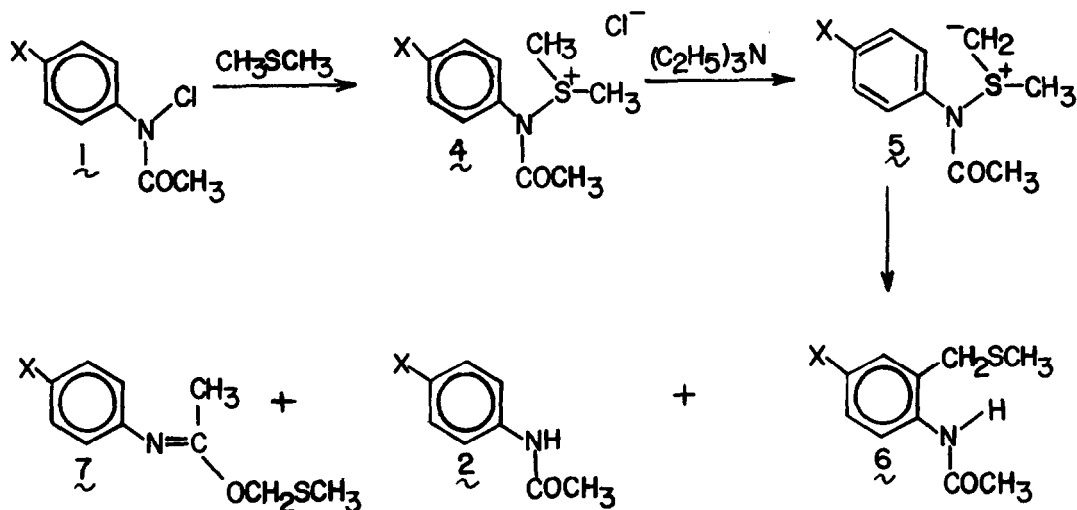
A series of N-chloroacetanilides were readily prepared through the reaction of the appropriate acetanilide with calcium hypochlorite. These compounds were readily purified and ex-



hibited excellent shelf life. At room temperature in chloroform, 1 reacted with dimethyl sulfide to regenerate the acetanilide 2 and to produce chloromethyl methyl sulfide (3). These results were similar to those of Vilsmaier's group, which found that N-chlorosuccinimide reacted with dimethyl sulfide to produce 3 at ambient temperature.⁷

Fortunately, when 1 was allowed to react with dimethyl sulfide at -15° in methylene chlor-

ide, the desired N-acyl-N-arylazasulfonium salt **4** was readily prepared. Treatment of **4** *in situ* with 1.2 equiv. of triethylamine gave the ylid, **5**, which readily rearranged to give a mixture of the desired ortho-methylthiomethylation product, **6**, the iminoether, **7**, and the starting material, **2**. As shown in table 1, the major product in all of the cases studied was **6**. It is



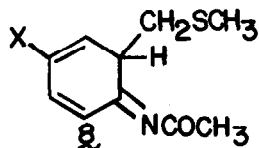
presumed that **5** was subject to a spontaneous [2,3]-sigmatropic rearrangement to give the diene imine, **8**, which should have undergone immediate hydrogen transfer and accompanying re-

Table 1. Yields obtained in the rearrangement of ylids derived from N-acyl-N-arylazasulfonium Salts **4**.

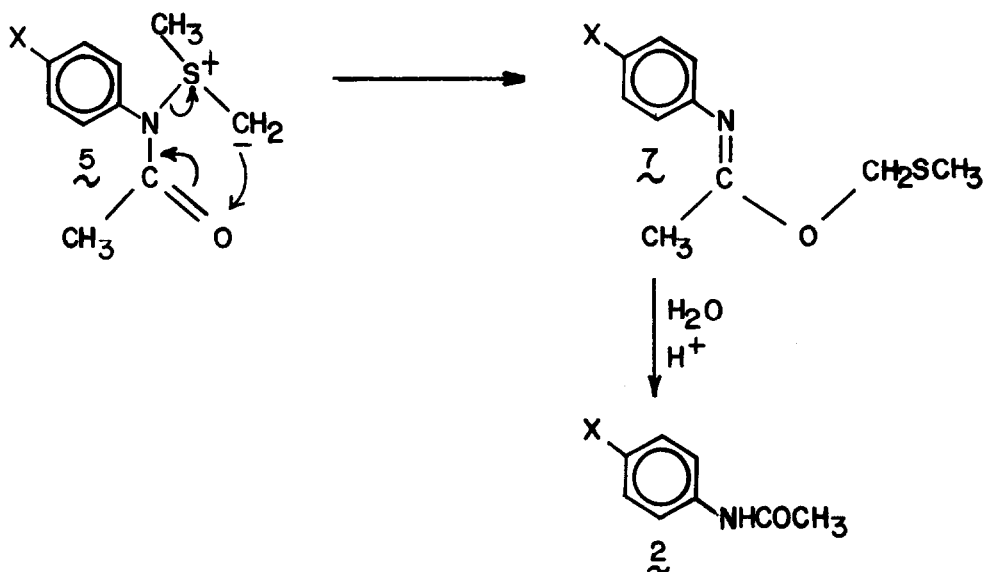
\underline{X}	% yields		
	$\underline{6}^a$	$\underline{2}^b$	$\underline{7}^b$
H	66	9	9
Cl	48	12	12
CH_3	42	10	5
$\text{CO}_2\text{C}_2\text{H}_5$	45	20	4

(a) Yields of recrystallized product. (b) Minimum yields based on the determination of the amount of **2** and **7** relative to **6** by NMR spectroscopy.

aromatization. Competitive with rearrangement to **8**, was an alternate [2,3]-sigmatropic process



in which the ylid ζ rearranged to produce the iminoether η .^{7,8} The fact that this process would appear to involve attack of an anionic species on a carbonyl oxygen would not constitute a ma-



ajor problem if the rearrangement were truly concerted. Ample precedent for this type of rearrangement exists in the studies of Vilsmaier's group on the rearrangement of N-acyl-N-alkyl-azasulfonium salt derived ylids.^{6,7} The iminoethers were extremely unstable and as a result could not be rigorously purified. Their structure was established on the basis of their NMR spectra, which for the parent acetanilide derived iminoether showed absorption at δ 7.50-6.70 (5H, m), 5.30 (2H, s), 2.30 (3H, s), and 1.86 (3H, s); exact mass M/e calcd for C₁₀H₁₃NOS: 195.0717, observed: 195.0725; and IR absorption at 1672 cm⁻¹. In addition, η was readily hydrolyzed to produce ξ on treatment with dilute hydrochloric acid at room temperature.

In summary, we have provided what we believe to be the first example of the ortho-methylthiomethylation of acetanilides.⁹

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References and Footnotes

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6. N-Halo-N-alkylamides have previously been converted into N-alkyl-N-acylazasulfonium salts [E. Vilsmaier and R. Bayer, *Synthesis*, 46 (1976)]. However, to our knowledge, acetanilides have not been converted to N-aryl-N-acylazasulfonium salts previously. For an alternate route to such salts see P.K. Claus, H.A. Schwarz, W. Rieder, and W. Vycudilik, *Phosphorous and Sulfur*, **1**, 11 (1976). We have recently developed an alternate synthesis of such salts from sulfilimines (P.G. Gassman and R.L. Parton, *Tetrahedron Lett.*, in press).
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8. An alternate mechanism for the formation of **7** from **5** could involve initial ionization of **5** to yield the acetanilide anion and $\text{CH}_3\overset{+}{\text{S}}=\text{CH}_2$. Recombination via attack of the ambient amide anion on this reactive sulfonium ion could then produce **7** as previously proposed⁷ in a Pummerer type rearrangement. We feel that this is unlikely on the following grounds. The excess of chloride ion should have, at least in part, converted the reactive sulfonium ion into chloromethyl methyl sulfide. We have independently shown that chloromethyl methyl sulfide reacts with acetanilide anion to give only N-alkylation. No N-alkylated products could be detected in the product mixture. In addition, it would be difficult to rationalize why the reactive sulfonium ion should give only O-alkylation, while chloromethyl methyl sulfide gave only N-alkylation.
9. Satisfactory elemental analyses and spectral data were obtained on all new ortho-methylthiomethylated acetanilides.