Allowed and Forbidden Sigmatropic Pathways in the Stevens Rearrangement of a Phenacylammonium Ylide

Stanley H. Pine* and John Cheney

Department of Chemistry, California State University, Los Angeles, California 90032

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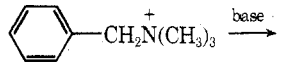
The possibility that the Stevens rearrangement of benzyldimethylphenacylammonium ylide (3) could proceed by a two-step allowed [1,4] and forbidden [1,3] sigmatropic pathway rather than the one-step [1,2] forbidden process has been investigated. The proposed enamine enol ether intermediate (5) was synthesized and shown *not* to rearrange to the Stevens product under typical Stevens rearrangement conditions. The conversion can be accomplished at elevated temperatures. No evidence for the involvement of the enamine enol ether intermediate in this example of the Stevens rearrangement was found. Comparison of this phenacylammonium ylide with related allylic and phenacylsulfonium ylides is considered.

The molecular rearrangements of ylides derived from ammonium and sulfonium salts have received considerable interest in regard to orbital symmetry consideration. Such considerations have provided theoretical support for the suggestion that the Stevens rearrangement—formally a [1,2] sigmatropic process—involves a stepwise rather than a concerted mechanism.[2] In the case of benzylammonium 1[3] (and related sulfonium)[4] salts the base-promoted reactions can proceed by two different pathways. The theoretically less favorable [1,2] Stevens rearrangement (paths a and c) and the more favorable [2,3] Sommelet–Hauser rearrangement (path b) are generally both observed. It has



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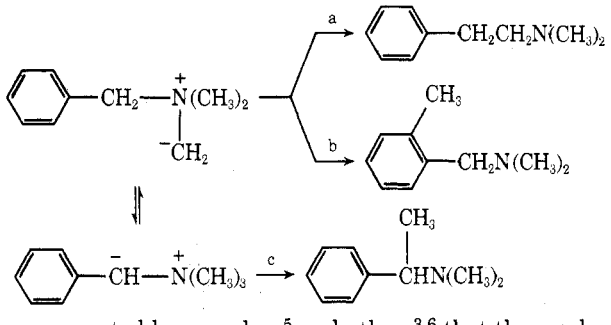
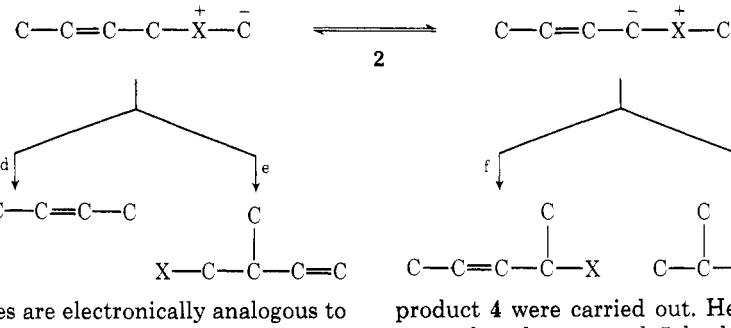


been suggested by ourselves[5] and others[3,6] that the marked dependence of these competing reactions on experimental parameters is explicable in terms of orbital symmetry considerations.

Related to the above are the competitive pathways available to allylic onium ylides 2. Again either [1,2] (path d) and [2,3] (path e) or [1,2] (path f) or [1,4] (path g) are observed depending on the precursor ylide.[7] Ollis has suggested that the nature of the onium atom plays a part in directing the rearrangement.[7c]



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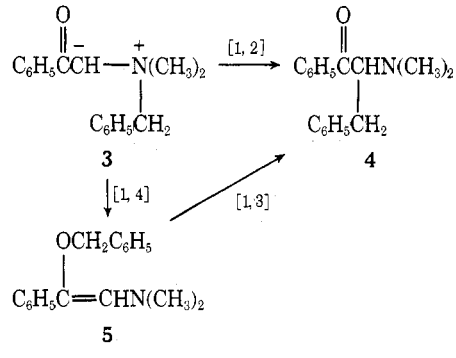
Phenacyl-stabilized ylides are electronically analogous to allylic ylides. Thus similar rearrangement pathways are feasible and products from these pathways have been observed. In regard to the Stevens rearrangement of phenacylammonium ylides the "allylic" [1,4] pathway could provide the first step as an alternative to the [1,2] process as outlined below for the benzyldimethylphenacylammonium ylide (3). Our question was, is the two-step 3 to 5 (allowed)



and 5 to 4 (forbidden) pathway more favorable energetically than the one-step 3 to 4 (forbidden) sequence? In the following we report our results in the study of this alternate rearrangement pathway.

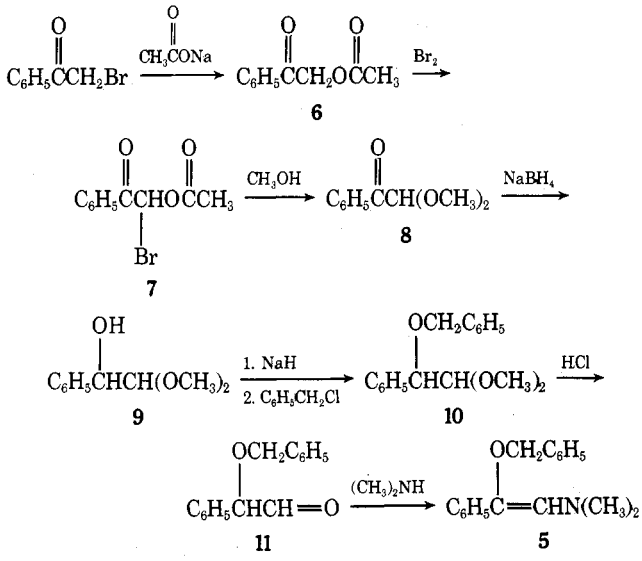
Results and Discussion

The formation of ylide 3 either in situ or as its stable hydrate and subsequent rearrangement to 4 has been investigated by ourselves and others.[8] To test for the involvement of the alternate rearrangement pathway we have synthesized the enamine enol ether 5 and studied its conversion to the Stevens rearrangement product 3.

Initial attempts to prepare 5 through benzylation of the enolate anion of dimethylphenacylamine provided only 4. From this result it was not clear whether the proposed intermediate 5 formed and rapidly rearranged to 4, or if 4 was directly formed by C-benzylation. The desired compound 5 was ultimately obtained as outlined in Scheme I.

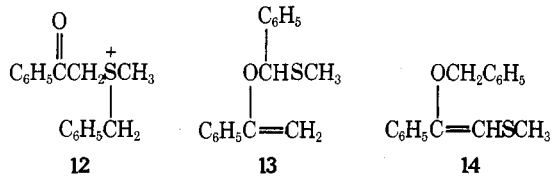
Various attempts to convert 5 to the rearrangement product 4 were carried out. Heating in water, chloroform, or methanol converted 5 back to the aldehyde 11, while heating in hot benzene or toluene yielded only a small

Scheme I



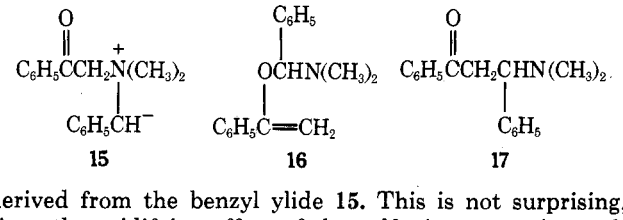
amount of rearrangement product **4**. Use of methanol–sodium methoxide to duplicate our typical Stevens rearrangement conditions resulted in little change at room temperature, while almost complete conversion of **5** to **4** occurred in 2–3 hr at 70°. In marked contrast to this result the rearrangement of **3** to **4** is complete in 1–2 min at 70°. It seems clear that the enamine enol ether **5** is not involved in the Stevens rearrangement of **3** to **4**.

It is of interest to compare our results on the ammonium ylide **3** with those observed in related sulfonium ylides. Ruiz[9] as well as Ratts and Yao[10] observed that phenacyl-stabilized sulfur ylides could undergo "allylic" type rearrangements involving the carbonyl oxygen atom as well as the normal Stevens rearrangement.[11] Thus sulfonium salt **12** could be converted to the enol ether **13** with base. Note that this transformation must involve the benzyl rather than the more favorable phenacyl ylide anion. More recently Baldwin[12] has reported a small yield of the sulfur analog **14** of our enol ether (**5**) from **12**. Schöllkopf has further



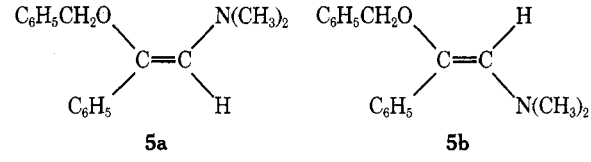
considered this system and finds that the phenacyl anion ylide derived from **12** rearranges to the normal Stevens rearrangement product in aprotic solvents while **13** is produced in the protic solvent methanol.[13] This solvent effect was attributed to the ability of methanol to aid in the formation of the requisite benzyl ylide precursor to **13**.

In our ammonium system **3** we have found no evidence for enol ether intermediate **16** or rearrangement product **17**



derived from the benzyl ylide **15**. This is not surprising, since the acidifying effect of the sulfonium atom is much greater than that of the ammonium atom. Thus it is expected that the formation of the benzylic anion from **12** in methanol–methoxide is considerably more favorable than with the ammonium salt. Ratts[14] has reported the pK_a of similar phenacylsulfonium salts to be approximately 7 while our observations suggest that the ammonium salts have a pK_a near 14.

One final consideration related to the possible involvement of **5** in the Stevens rearrangement is stereochemical. The enamine enol ether could exist as two geometrical isomers, **5a** or **5b**. If our synthesis had provided the "wrong"



isomer then our experimental results could be invalid. However, we believe that the desired isomer is **5a** and that this is what we have synthesized. Models suggest that nonbonded repulsions favor isomer **5a**. We see only one set of peaks in the NMR spectrum of **5** suggesting that only one isomer is present. The ultraviolet spectrum (λ_{max} 308 nm) suggests trans coplanarity between the phenyl and dimethylamino groups in this styrene system.[15] Calculation of the expected NMR chemical shift position for the olefinic hydrogen atom[16] is also more consistent with the **5a** structure. Finally, we believe that **5a** would have been the isomer formed during the reaction of **3** if this were the pathway for the migration of the benzyl group to the oxygen atom. The transition state would involve a five-membered ring for this concerted [1,4] process.

Thus we conclude that the direct conversion of **3** to **4** is energetically more favorable than the two-step pathway **3** to **5** to **4**. This conclusion is similar to that reached by Baldwin[12] in a related sulfur ylide. It is important to note, however, that this work does not answer the question of whether the conversion of **3** to **4** involves a symmetry-forbidden [1,2] sigmatropic rearrangement[17] or a dissociation–recombination ion-pair or radical-pair pathway.

Our results further demonstrate that a rapid reversible [1,4] sigmatropic conversion between ylide **3** and enol ether **5** does not take place. The question of why the carbonyl oxygen atom becomes involved in many carbonyl-stabilized sulfur ylide reactions but not in similar nitrogen ylide reactions must await further results and speculations.

Experimental Section

Phenacyl Acetate (6). A mixture of 10 g of phenacyl bromide, 10 g of sodium acetate, and 20 ml of methanol was refluxed for 1 hr, then poured into 300 ml of ice water and extracted with chloroform. Drying and evaporation of the solvent gave a yellow oil which was not purified further: NMR (CCl_4) δ 2.1 (s, 3), 5.1 (s, 2), 7.2–7.8 (m, 5).

α-Bromophenacyl Acetate (7). The crude acetate **6** was dissolved in carbon disulfide and bromine was added dropwise with stirring, under nitrogen, until the brown color persisted (ca. 3 ml). Evaporation of the solvent under vacuum (without heating) gave a brown oil: nmr (CCl_4) δ 2.1 (s, 3), 7.3 (s, 1), 7.2–8.1 (m, 5).

Phenylglyoxal Dimethyl Acetal (8). The crude bromoacetate **7** was dissolved in 30 ml of methanol and the solution was refluxed for 1 hr. Evaporation of the solvent under vacuum gave a viscous liquid which was not further purified: NMR (neat) δ 3.3 (s, 6), 5.3 (s, 1), 7.2–8.1 (m 5).

2-Hydroxy-2-phenylethanal Dimethyl Acetal (9). The crude acetal **8** was dissolved in 70 ml of absolute ethanol: then 3 g of sodium borohydride was carefully added. After stirring for 2 hr at room temperature the solvent was evaporated under vacuum. The hard, foamy residue was dissolved in water and extracted with ether. Drying with $MgSO_4$ and evaporation gave a pale yellow oil which was not further purified: NMR (CCl_4) δ 2.5 (s, 1), 3.1 (s, 3), 3.3 (s, 3), 4.0 (d, J = 6 Hz, 1), 4.4 (d, J = 6 Hz, 1), 7.1 (broad s).

2-Benzoxy-2-phenylethanal Dimethyl Acetal (10). The crude hydroxy acetal **9** was dissolved in dry THF; then 2 g of sodi-

um hydride was carefully added with stirring and cooling. Excess benzyl chloride (20 g) was added, and the solution was refluxed for 3 hr and then left at room temperature overnight. Excess hydride was destroyed by careful addition of methanol; then water was added and the product was recovered by ether extraction. The crude product (6 g) was purified by chromatography on grade II neutral alumina using petroleum ether (bp 60–70°) and then 10% ethyl ether in petroleum ether to give 3.5 g of pure liquid product: NMR (CCl_4) δ 3.15 (s, 3), 3.35 (s, 3), 4.24 (s, 2), 4.35 (AB, 2), 7.20 (s, 5), 7.25 (s, 5).

2-Benzoxy-2-phenyl-*N*,*N*-dimethylethenylamine (5). The acetal ether (0.1 g) was dissolved in 9 ml of acetonitrile and 3 ml of 4 *N* HCl, heated to 60–65° for 20 min, then added to 10 ml of cold water and rapidly extracted with chloroform. The colorless oil recovered was about 25% acetal ether **10** and 75% aldehyde ether **11**: NMR (CCl_4) δ 4.55 (s, 2), 4.63 (d, J = 2 Hz, 1), 7.20 (s, 5), 7.25 (s, 5), 9.45 (d, J = 2 Hz, 1). Attempts to more effectively hydrolyze the ketal gave undesirable side products. The crude aldehyde ether was dissolved in 20 ml of benzene and 5 ml of dimethylamine was added. After 15 min at room temperature, the solvent was evaporated under vacuum without heating to give a light yellow oil: NMR (CCl_4) δ 2.7 (s, 6), 4.6 (s, 2), 5.6 (s, 1), 6.9–7.4 (m, 10); methiodide mp 159–160° (chloroform).

Anal. Calcd for $C_{18}H_{22}NOI$: C, 54.69; H, 5.61; N, 3.54. Found: C, 54.87; H, 5.60; N, 3.33.

Conversion of Enol Ether 5 to Rearrangement Product 4. Freshly prepared enol ether (0.1 g, 4×10^{-4} mol) was dissolved in 0.5 ml of 1 *N* $NaOCH_3$–CH_3OH. The nmr spectrum taken at room temperature showed no change. The NMR probe temperature was raised to 70° and the change followed. After 2 hr essentially all of the enol ether was converted to rearrangement product. The product could be recovered as a light yellow solid: NMR (CCl_4) δ 2.38 (s, 6), 2.8–3.5 (m, 2), 4.2–4.5 (m, 1), 7.1–7.4 (m, 8), 7.8–8.0 (m, 2).

Registry No.—**4**, 30669-80-8; **5a**, 53907-31-6; **5a** methiodide, 53907-32-7; **6**, 2243-35-8; **7**, 53907-33-8; **8**, 6956-56-5; **9**, 21504-23-4; **10**, 53907-36-1; **11**, 38968-65-9.

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Electronic and Steric Effects in Nucleophilic Aromatic Substitution. Reaction by Phenoxides as Nucleophiles in Dimethyl Sulfoxide

G. Bartoli, F. Ciminale,* and P. E. Todesco

Istituto di Chimica Organica, Universita' di Bologna, Bologna, Italy

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Kinetics of reactions of X-substituted sodium phenolates with *p*-nitrohalogenobenzenes at 25° and 2,6-dimethyl-4-nitrohalogenobenzenes at 50° in DMSO are reported. The electronic effects in the nucleophile, as revealed by ρ values, are large and may depend on the leaving halogen. For these reasons the ratios k_F/k_{Cl} are not a direct measure of the dependence of steric effects on the leaving halogen. Ortho substitution in phenolate shows steric effects which depend on the size of the leaving halogen, the following order of steric effect being observed: F < Cl < Br < I.

Steric effects in nucleophilic aromatic substitutions appear to be an open question mainly as far as steric interaction between the entering and the leaving groups is concerned.

In reactions with 2,4-dinitrohalogenobenzenes, it was established long ago[1,2] that primary and secondary amines reveal differences in rate correlated with interference by alkyl groups branching from the nitrogen atom or adjacent carbons. This behavior is displayed also by anionic nucleophiles such as mercaptides,[3] alkoxides,[4] and phenolates.[5] In all cases the observed steric retardation is also dependent on the size of the leaving halogen.

Moreover, Pietra, studying substitutions on halogenonitrobenzenes by α-alkyl piperidines,[6,7] primary, secondary, or tertiary aliphatic amines in aprotic solvents,[8] and alkoxides,[9] attributed steric retardation to interactions between the nucleophile and the benzene ring carbons and hydrogens in the transition state, rejecting previous ideas[3,5] of steric interactions between entering and leaving groups.

These contrasting interpretations probably result because the data available do not provide good correlation of expected effects with rates of reaction. Also they do not take into account the electronic changes which are operative when the substituents of the nucleophile or the leaving group of the substrate must be changed.

We have investigated the reactions of substituted phenoxides with *p*-nitrohalogenobenzenes and with 2,6-dimethyl-4-nitrohalogenobenzenes in order to evaluate both steric and electronic effects in a more meaningful way.

Results

The reaction rates were measured in dimethyl sulfoxide.

In order to minimize association phenomena low concentrations of phenolates ($<10^{-2}$ *M*) were employed. Under