

THE IMPORTANCE OF STERIC BULK AND ACIDITY IN SOLVOLYSIS. THE MECHANISM  
OF SOLVOLYSIS OF 1-ADAMANTYL BROMIDE

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Summary Product selectivities from solvolysis of 1-adamantyl bromide in several binary protic solvents are revealing about the relative importance of solvent acidity and bulk

A careful search over the past fifteen years has revealed nucleophilic solvent assistance to be a significant factor in solvolysis of primary and secondary alkyl substrates.<sup>1-3</sup> There is even strong evidence that *t*-butyl chloride, which for so long served as the model for the classical S<sub>N</sub>1 mechanism of an unassisted ionization, undergoes solvolysis with measurable backside solvent assistance.<sup>3,4</sup> There is debate on the latter point, however, since other evidence accounts for abnormalities of substrate behavior in fluorinated solvents in terms of enhanced electrophilic solvent assistance.<sup>5,6</sup> The unfolding story seems to say that for too long physical organic chemists have attempted to exactly correlate solvolytic displacement reactions in terms of general effects when in fact variable specific effects were also important. For example, correlations with solvent ionizing power (Y)<sup>7</sup> have been extremely useful in developing our understanding of substrate reactivity, however, recent studies clearly show that the original Grunwald-Winstein Y values do not apply to leaving groups other than chloride.<sup>4,8,9</sup> The most probable reason for the variability of Y is the variable amount of specific solvation of different leaving groups by solvent molecules.

We have recently begun to study some aspects of electrophilic solvent assistance by concentrating on an interesting class of reactions whose products seem to be most affected by electrophilic assistance. The group of reactions of interest each give substitution with net retention of configuration<sup>1,2,10-13</sup> In such cases an unusual nucleophilic order is also observed. For example, water (W), ethanol (E), trifluoroethanol (T), and the azide ion (N) all react at similar rates ( $K_{\text{N}} \approx K_{\text{T}} \approx K_{\text{W}} \approx K_{\text{E}}$ ), whereas, in reactions where inversion of configuration or racemization is involved a greatly different trend is observed ( $K_{\text{N}} \gg K_{\text{E}} \approx K_{\text{W}} \gg K_{\text{T}}$ ).<sup>13-17</sup> Using 1-adamantyl bromide, which can only give retention of configuration upon solvolysis, it has been determined that solvent steric bulk and electrophilic properties are important in determining both the reaction rate and product composition.<sup>15,16</sup> An assessment of the relative importance of these factors has not been previously established. In this letter

we wish to report our results which bear on this point and help clarify the mechanism of solvolysis of substrates in protic solvents.

We have examined the products of solvolysis of 1-adamantyl bromide in several binary solvents using 2,6-lutidine as an acid scavenger. The selectivity values (S), calculated in the normal way,<sup>14a</sup> eq. 1, are shown in Table I. The aqueous alcohol series is seen to follow a frontside nucleophilicity

$$S = \frac{k_{\text{ROH}}}{k_{\text{R'OH}}} = \frac{[1\text{-AdOR}]}{[1\text{-AdOR}']} \times \frac{[\text{R'OH}]}{[\text{ROH}]} \quad (1)$$

order<sup>18</sup> which is the inverse of that expected based on oxygen basicity,<sup>17b</sup> but the observed order parallels the solution acidities<sup>19</sup> and order of increasing bulk. Our values in ethanol-trifluoroethanol are similar to those previously reported.<sup>15,16</sup> It was previously argued<sup>15</sup> that those selectivity values reflect the importance of both electrophilicity and bulkiness in the formation of the 1-adamantyl solvent-separated ion pairs which are involved in product determination. Hexafluoroisopropanol (HFIP) is even more acidic than trifluoroethanol and is between isopropyl and *t*-butyl alcohols in steric bulk. Nevertheless, HFIP is observed to be a poor frontside nucleophile although solvolysis in HFIP solutions of 1-adamantyl and 2-adamantyl substrates occurs more rapidly than in aqueous solutions of other alcohols including trifluoroethanol.<sup>8,20</sup> These results strongly support our earlier view<sup>21</sup> that at least two solvent molecules are involved in formation of solvent-separated ion pairs with substrates which have little or no backside nucleophilic solvation. It would appear that the more acidic solvent molecules will preferentially give specific solvation to the leaving group. If that solvent molecule is also relatively low in bulk it may fit well into the cavity between the cation and anion. In the case of water and trifluoroethanol, this appears to be the case as they are incorporated into product competitively with more "nucleophilic" solvent molecules. HFIP, however, is apparently too bulky to fit nicely into the cavity of the 1-adamantyl bromide solvent-separated ion pair and it is not as often incorporated yet it strongly assists formation of the solvent-separated ion pair. It is perhaps time that we modified our general view of solvent-separated ion pairs. Based on our current knowledge they are best represented much like Simonetta found them using computer models.<sup>22</sup> Grunwald<sup>23</sup> has experimental support for a similar view. We thus suggest that view for these reactions, Scheme 1, and for solvolytic reactions with backside assistance, Scheme 2.

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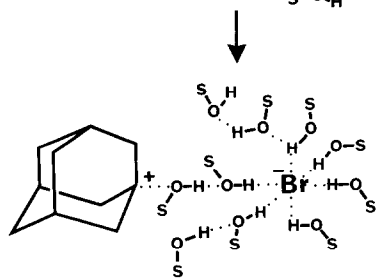
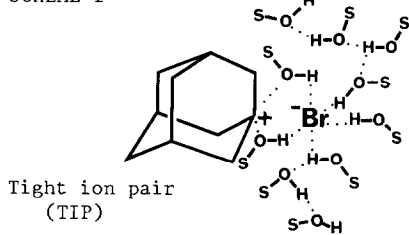
Table I. Product Ratios and Selectivities from Solvolysis of 1-Adamantyl Bromide in Binary Protic Solvents.

| Solvent Composition <sup>a</sup>      | Temperature | ROH              | R'OH           | [1-AdOR]/[1-AdOR'] <sup>b</sup> | S <sup>c</sup> |
|---------------------------------------|-------------|------------------|----------------|---------------------------------|----------------|
| 70:30 MeOH:H <sub>2</sub> O           | 100°C       | H <sub>2</sub> O | MeOH           | 0.871                           | 0.906          |
| 80:20 MeOH:H <sub>2</sub> O           | 100         | H <sub>2</sub> O | MeOH           | 0.603                           | 1.07           |
| 70:30 EtOH:H <sub>2</sub> O           | 100         | H <sub>2</sub> O | EtOH           | 1.64                            | 1.18           |
| 80:20 EtOH:H <sub>2</sub> O           | 100         | H <sub>2</sub> O | EtOH           | 1.09                            | 1.35           |
| 70:30 <i>i</i> -PrOH:H <sub>2</sub> O | 100         | H <sub>2</sub> O | <i>i</i> -PrOH | 8.62                            | 4.75           |
| 80:20 <i>i</i> -PrOH:H <sub>2</sub> O | 100         | H <sub>2</sub> O | <i>i</i> -PrOH | 5.27                            | 4.95           |
| 70:30 <i>t</i> -BuOH:H <sub>2</sub> O | 100         | H <sub>2</sub> O | <i>t</i> -BuOH | 19.2                            | 8.60           |
| 80:20 <i>t</i> -BuOH:H <sub>2</sub> O | 100         | H <sub>2</sub> O | <i>t</i> -BuOH | 11.3                            | 8.71           |
| 20:80 EtOH:TFE                        | 25          | TFE              | EtOH           | 5.71                            | 1.66           |
| 60:40 EtOH:TFE                        | 25          | TFE              | EtOH           | 0.767                           | 1.34           |
| 5:95 MeOH:HFIP                        | 100         | HFIP             | MeOH           | 0.760                           | 0.104          |
| 20:80 MeOH:HFIP                       | 25          | HFIP             | MeOH           | 0.297                           | 0.193          |
| 5:95 EtOH:HFIP                        | 100         | HFIP             | EtOH           | 1.39                            | 0.132          |
| 20:80 EtOH:HFIP                       | 25          | HFIP             | EtOH           | 0.523                           | 0.236          |
| 30:70 TFE:HFIP                        | 25          | HFIP             | TFE            | 0.148                           | 0.0980         |
| 70:30 TFE:HFIP                        | 25          | HFIP             | TFE            | 0.0358                          | 0.129          |

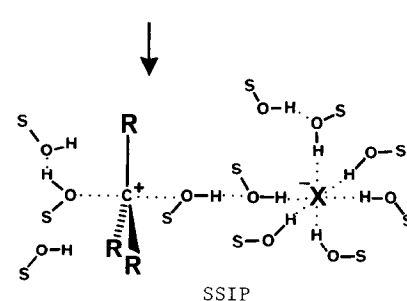
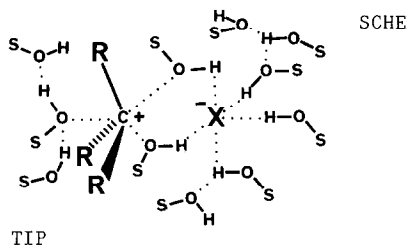
<sup>a</sup>MeOH = methanol; EtOH = ethanol; *i*-PrOH = 2-propanol; *t*-BuOH = 2-methyl-2-propanol; TFE = trifluoroethanol; HFIP = hexafluoroisopropanol. All solutions were vol. to vol. at 25° using pure solvents.

<sup>b</sup>All products were stable under reaction and analysis conditions. Analyses were performed gas chromatographically using a 50 m capillary column coated with Carbowax. Integrations were automatically performed by the Varian CDS 401 data station of the Vista system. Response factors were found to reflect carbon content (± 3%). Product compositions were determined by averaging the results of three to five samples. Standard deviations were better than ± 5%. <sup>c</sup>Calculated according to eq. 1.

SCHEME 1



SCHEME 2



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