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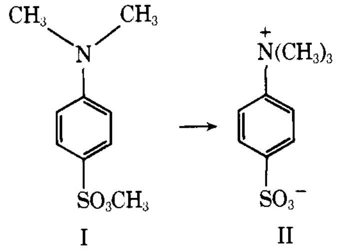
Enhancement of a Chemical Reaction Rate by Proper Orientation of Reacting Molecules in the Solid State

Sir:

Efforts to understand catalytic enhancement of chemical reaction rates have often been aided by attributing orienting and proximity-inducing properties to the catalysts.[1] Given the knowledge that proper orientation and proximity facilitate chemical reaction, chemists have looked to the crystalline state for situations in which particularly reaction-favorable molecular relationships might be found.[2] However, although many reports exist of topochemical control of product formation selectivity,[3] we have been unable to find an example in the literature (outside the polymerization area) of a solid-state accelerated thermal reaction. We now wish to report the identification of such a process, along with an X-ray diffraction study of the compound involved which shows that the molecules are nearly ideally oriented for reaction in the solid state.

We have reinvestigated the rearrangement of methyl *p*-dimethylaminobenzenesulfonate (I) to the *p*-trimethylammoniumbenzenesulfonate zwitterion (II).[4,5] At room temperature, compound I appears to be indefinitely stable in soluton, but (as reported by Kuhn and Ruelius[4]) it arranges with a half-life of about 7 days in the solid state. Isolation and NMR analysis of water-soluble II show it to be a demonstrably different chemical substance (and not simply a different crystalline modification of I[6]); consistent with this observation is the fact that we have been unable to reproduce the claimed reversion[6] of II to I in aqueous ethanol, but instead recover II unchanged after subjection to the reported[6] conditions.



I II

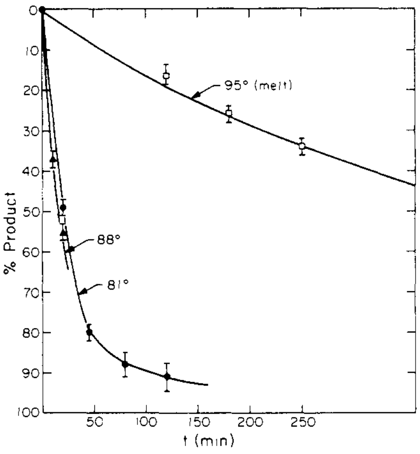


Figure 1. Time dependence of the per cent of product observed in the thermal conversion of methyl *p*-dimethylaminobenzenesulfonate (I) to *p*-trimethylammoniumbenzenesulfonate (II) at three different temperatures: ●, 81°, crystal; ▲, 88°, crystal; □, 95°, melt.

The rate of I → II rearrangement increases with temperature but, contrary to earlier statements,[4,5] *this is only true at temperatures below the melting point.* Higher temperatures, melting the material, introduce a sharp *decrease* in the rate of conversion. A simple plot of product concentration vs. time is shown in Figure 1;[7] based on these data it appears that the solid rearranges at least 25 times faster than the melt. Reaction of a roughly 50:50 mixture of I-d_0 and methyl-labeled I-d_9, and analysis of the product by field desorption mass spectrometry,[8] reveals extensive methyl scrambling in the product II, indicating that the reaction is inter- rather than intramolecular.

Both the intermolecularity and the rapid rate of this reaction are beautifully consistent with the single-crystal X-ray structure of I. Recrystallization of I from methanol gave monoclinic crystals. The data set used consisted of three subsets individually corrected for decay due to the solid state rearrangement, but collectively scaled together yielding 750 reflections whose intensities were greater than $3\sigma(I)$ ($3\sigma R = 0.098$). Lattice constants in the monoclinic space group $P2_1/c$ are $a = 8.942$ (2) Å, $b = 10.507$ (3) Å, $c = 11.232$ (2) Å and $\beta = 90.88$ (2)°; with four formula units per cell the calculated density is 1.43 g cm^{-3}. See paragraph at end of paper for supplementary material.

The bond distances and angles are all within acceptable values. The stacking of the molecules within one chain in the crystal, viewed perpendicular to the [101] plane, is shown in Figure 2. The molecules stack in alternating directions with the aromatic rings inclined 76° to each other and with each nitrogen atom in nearly perfect alignment with the sulfonate ester methyl group of the adjacent molecule. The C(9)···N distance is 3.54 Å and the O(1)–C(9)···N angle is 147°. The system therefore requires only minimal structural change to transfer the methyl group from the oxygen atom of one molecule to the nitrogen atom of the adjacent molecule along the chain, and this is presumably how the reaction occurs.

An arrangement of the atoms within a chain of molecules of I in the solid state which would be "completely ideal" for the nucleophilic substitution would be identical with that of the transition state for reaction, and such a crystal is therefore by definition not isolable.[9] The structure of I is almost, but not quite, ideal, and converson to the transition state structure requires just enough energy to allow isolation of the material at room temperature. This, combined

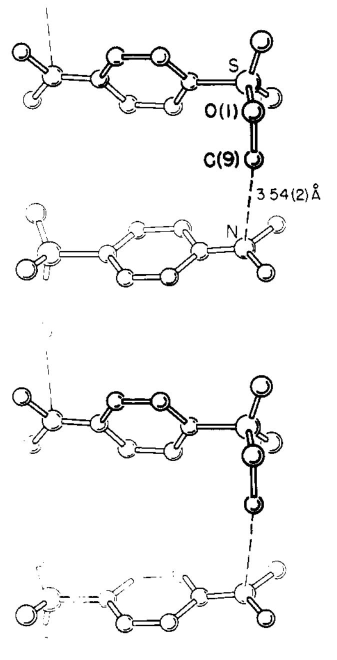


Figure 2. A view of the stacking along one chain of molecules in crystals of methyl *p*-dimethylaminobenzenesulfonate (I), as seen perpendicular to the [101] plane. Distance indicated is that between the carbon atom of the methyl group, which undergoes transfer in the solid state reaction, and the nitrogen atom to which it moves.

with the fact that the melting point of the material is in a temperature region where the reaction proceeds at a measurable rate, has allowed us to identify it as a rare example of a nonpolymerizing thermal reaction whose rate is actually accelerated by proper orientation in a crystal. It is now clear that such systems can exist; we look forward to the discovery of other solid state accelerated reactions in the future.[10]

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Supplementary Material Available. A summary of the physical properties of I and II, an ORTEP drawing of a molecule of I, and interatomic distances and angles, fractional coordinates, and intensity data will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Business Office, Books and Journals Division, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for $4.50 for photocopy or $2.50 for microfiche, referring to code number JACS-75-5290.

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(8) Because II is extremely nonvolatile, it proved impossible to obtain conventional mass spectra of the material. Using FDMS, however, good spectra having appreciable parent peaks were obtained, and this allowed us to carry out the isotopic analysis conveniently. FDMS analysis of a standard synthetic mixture of II-d_0 and II-d_9 showed that significant, but not complete, label scrambling occurs during the FDMS experiment. To determine the extent of intermolecularity in the I → II reaction, therefore, the peak intensities measured on the product formed from the I-d_0/I-d_9 mixture were corrected for FDMS scrambling as measured using the synthetic mixture. The data indicate that the I → II solid state reaction is ≥75% intermolecular. To our knowledge, this constitutes the first evaluation of FDMS as a quantitative technique. Reproducibility was fairly good (relative error ca. 10% on 5–15 scans), suggesting that the technique may find application in biomedical quantitation studies.

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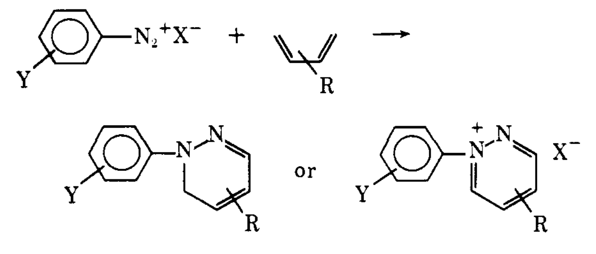
The Reaction of Diazonium Salts with Dienes. A Route to Pyridazines and Pyridazinium Salts

Sir:

Aromatic diazonium salts undergo cycloaddition to dienes to produce N-substituted 1,6-dihydropyridazines or pyridazinium salts depending on the nature of the substituents on the aromatic ring (eq 1).



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