+ k_2[CH$_3$OH] and suggest that A undergoes a unimolecular decay to form B in the absence of methanol, but when methanol is present, A is intercepted competitively to produce a species with no absorption in the region 450–750 nm.

The optical spectrum of *m*-NQM in cryogenic matrices shows a long-wavelength transition that is associated with the carrier of the characteristic EPR spectrum of the triplet biradical.[3] The position of this band is insensitive to the medium: λ_{max} = 500 (EtOH), 504 nm (5:1 isopentane/Et$_2$O). These features match those of the present transient B and support its assignment as triplet *m*-NQM.

Although the spectroscopic data alone do not exclude an excited state of ketone **1**, this alternative seems unlikely because the chemistry of the *m*-NQM[2a] and *m*-QM[2a,4] intermediates is independent of whether they are thermally or photochemically generated.[6] The most probable assignment of the A signal thus is to singlet *m*-NQM, and the unimolecular decay A → B measures the intersystem crossing (isc). Increases in isc rate with decreased solvent polarity, similar to those observed here, have been noted in other systems.[7,8]

The present observations constitute the first direct evidence for a cascade of states in the generation of *m*-naphthoquinomethane and identify singlet *m*-NQM as the reactive intermediate in the photomethanolysis of ketone **1**.

(6) Fluorescence during the lifetime of the A signal was not observed, which would be difficult to rationalize if the A signal were assigned to excited singlet **1**. Moreover, A is unlikely to be the n,π* triplet **1**, since that species would be expected to react with alcohols (by hydrogen abstraction) with rate constants[9] near 10^6 s^{-1}, about 100-fold slower than the k_2 observed here.

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A Molecular Beam of Tryptophan

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We report here the production of a supersonic molecular beam of the amino acid tryptophan. The significance of this report is that it demonstrates that a cold molecular beam of neutral molecules can be produced from a thermally labile nonvolatile solid. If the technique described in this communication proves to be generally applicable, it will allow the study of individual molecules of materials that ordinarily exist only as solids or in solution and will make it possible to distinguish intrinsic properties of single molecules from their properties in condensed phases.

In the past we have made extensive use of supersonic molecular beams to prepare gas-phase samples for study by electronic spectroscopy.[1] The supersonic expansion cools the vibrational and rotational degrees of freedom of the molecule without causing condensation out of the gas phase, and the electronic spectra of internally cold, isolated, gas-phase molecules have proven to be quite informative in many cases. To be suitable for supersonic

beam spectroscopy, a molecule of interest must have a sufficiently high vapor pressure. In cases where the room temperature vapor pressure is too low, the necessary volatility has been produced by heating the sample prior to cooling it in the supersonic expansion;[2] however, many solids thermally decompose at temperatures where the vapor pressure is still far below that necessary for molecular beam spectroscopy. The present work was motivated by the desire to prepare molecular beams of such substances.

Mass spectroscopists face a similar problem. In recent years they have developed a number of ingenious techniques to volatilize large organic molecules,[3] particularly appealing methods being electrospray[4] and the thermospray technique developed by Vestal and co-workers.[5] We have combined a thermospray jet and a seeded supersonic helium expansion to produce a molecular beam of tryptophan. Our method involves injecting a thermospray jet of a methanol solution of tryptophan into the throat of a pulsed nozzle producing a seeded supersonic free jet in a helium carrier gas. The free jet is skimmed, and the resulting molecular beam is directed into a time-of-flight mass spectrometer where the isolated, neutral tryptophan molecules are nonresonantly photoionized. The existence of a cold molecular beam of neutral tryptophan is inferred from analysis of the mass spectrum.

The thermospray jet is formed by continuously passing a 10^{-4} M solution of DL-tryptophan in methanol through a 0.004-in.-i.d. stainless steel capillary which terminates in a 35-μm nickel pinhole.[6] The last few centimeters of the capillary pass through a brass block that is heated by electric resistance heaters. The temperature of the block is chosen so that the interface between the liquid and vaporized solvent occurs just behind the pinhole, and this temperature is dependent on the pressure that is used to drive the solution through the capillary and pinhole. We typically use a pressure of ~10 atm, producing a solution flow rate of ~0.2 mL/min at a block temperature of ~200 °C.

The molecular beam is formed by using a solenoid actuated pulsed valve that discharges the helium carrier gas at a stagnation pressure of ~2 atm into a 1 mm diameter × 9 mm long cylindrical channel in the brass block. The valve pulse width is adjustable down to a few hundred microseconds. The thermospray jet is continuously injected into the middle of the helium channel with the flow axis of the thermospray perpendicular to that of the helium expansion. A 0.2 mL/min flow of a 10^{-4} M solution of tryptophan in methanol corresponds to a flow of 8 × 10^{-5} mol/s of methanol and 3 × 10^{-10} mol/s of tryptophan. The measured average flow rate of helium is 140 mtorr L/s, and the duty cycle was 2 × 10^{-3} (200-μs pulse width × 10 Hz) implying a flow rate of 70 torr L/s or 4 × 10^{-3} mol/s when the valve is open. If the helium pulse contains only methanol and tryptophan that are injected while the pulse passes the thermospray jet, then the molecular beam would be formed from helium containing 2 mol % methanol and 10^{-5} mol % tryptophan. However, it may well be that methanol and tryptophan thermosprayed prior to the opening of the helium valve manage to penetrate the shock structure of the expanding helium, producing a molecular beam richer in seed molecules than that calculated above.

The helium–methanol–tryptophan free jet is skimmed by a 1-mm conical skimmer, and the resulting molecular beam is passed through a time-of-flight mass spectrometer having a triple grid ion extraction region,[7] an einzel lens, a 1-m flight tube, and a microchannel plate electron multiplier.[8] Photoionization is

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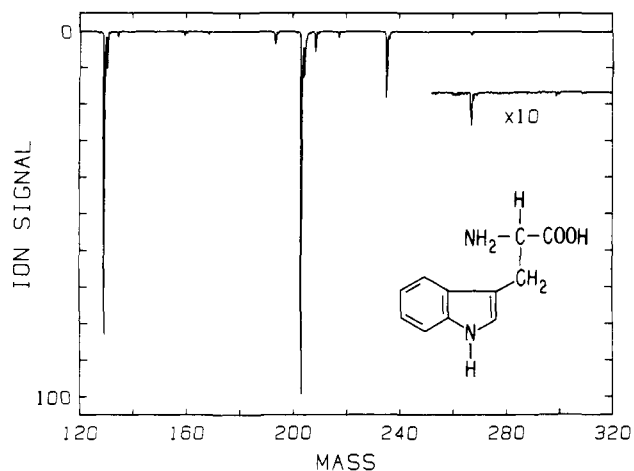
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Figure 1. Mass spectrum of tryptophan obtained from a thermospray jet of 10^{-4} M tryptophan in methanol expanded in a supersonic molecular beam of helium. The data are an average over 1200 laser shots. Prominent features are assigned to ions of CH_2–indole (mass 130), tryptophan (mass 204), Trp–CH_3OH (mass 236), and Trp–$(CH_3OH)_2$ (mass 268). The mass spectrum was produced by photoionization at 285 nm.

produced by the second harmonic of a Nd:YAG pumped pulsed dye laser operating at a 10-Hz repetition rate. Thus far, we have observed nonresonant two-photon ionization with the laser operating at various wavelengths in the region 265–295 nm. The entire mass spectrum was collected at each laser shot by a 10 ns/channel transient digitizer, and the results of many laser shots were averaged by a computer. Appropriate synchronization of the valve opening, the laser pulse, and the transient digitizer was produced by digital delay generators.

The mass spectrum of the molecular beam generated by this apparatus, as shown in Figure 1, is dominated by a large peak at mass 204, the parent mass of tryptophan, with a second intense peak appearing at mass 130, the mass of the CH_2–indole fragment. Under the conditions used to produce Figure 1, no significant peaks are seen at masses higher than those shown. In particular, we were unable to observe a peak at mass 408, the mass of the tryptophan dimer. Satellite peaks appear at masses 205 and 131 with intensities consistent with naturally abundant ^{13}C substitution in ions containing 11 and 9 carbon atoms, respectively.[9] When we use a CH_3OH–D_2O solvent, the mass spectrum contains peaks at masses 130, 131, 206, 207, and 208 with relative intensities appropriate for deuterium substitution of the four exchangeable hydrogens of tryptophan[10] or the single exchangeable hydrogen of CH_2–indole. The mass spectrum produced under identical conditions but using a pure methanol–water solvent without tryptophan produces none of the above mass peaks.

Of particular interest are the mass peaks at 236 and 268. These are the parent ions of the clusters Trp–CH_3OH and Trp–$(CH_3OH)_2$, respectively. The existence of these small, weakly bound clusters suggests that the supersonic expansion has indeed produced the cooling necessary for the production of these clusters. The nature of these partially solvated molecules is a matter of some interest.

We believe that the mass 204 peak is produced by photoionization of single uncomplexed neutral tryptophan molecules that are present in the supersonic molecular beam. An alternative explanation would be that the molecular beam contains only large clusters or droplets of solvated tryptophan and that the mass 204 ion is produced by laser desorption ionization from the surface of these large clusters. We find that when we greatly increase the methanol flow rate, we do observe cluster ions containing up

to 20 methanol molecules and the fraction of mass 204 ion decreases substantially. This observation indicates that when larger clusters are produced in the jet, the clusters survive the ionization process and appear as high-mass ions. This being the case, it seems highly unlikely under the conditions used to obtain Figure 1 that larger neutral clusters would fragment during ionization to produce only mass 204 and lighter ions without also producing larger cluster ions.

It should be noted that the fringing field of the mass spectrometer grids will prevent ions from entering the mass spectrometer, and in fact we see no ions that are not synchronous with the firing of the laser. In the experiments of Vestal and co-workers,[5] the thermospray of ionic solutions produced gas-phase ions and allowed the observation of mass spectra with no auxiliary source of ionization. Our results indicate that, although under our conditions ions may be produced, there is a significant neutral component to the molecular beam.

1-Methyl-2-(2-hydroxyphenyl)imidazole: A Catalytic Phosphate Protecting Group in Deoxyoligonucleotide Synthesis[†]

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Protecting groups serve a key function in the chemical synthesis of deoxyoligonucletides.[1,2] DNA synthesis, via the phosphotriester method, typically utilizes an aryl protecting group at the phosphate diester to prevent unwanted reactions at that site (Figure 1).[3] The blocking moiety, commonly an *o*- or *p*-chlorophenyl ester (**1a,1b**, Figure 1), is positioned at the site of reaction when forming the internucleotide bond between the electrophilic 3′-phosphate (**1**, Figure 1) and the nucleophilic 5′-hydroxyl (**2**, Figure 1). We report the use of a phenyl protecting group bearing a 1-methylimidazole moiety in the proper position to significantly enhance the rate of internucleotide bond formation.

Rate enhancement of chemical reactions by neighboring-group participation is well-known[4] the ultimate example of such phenomenon being enzyme catalysis.[5] The mechanism for hydrolysis of phosphorylethanolamine triesters has also been well studied, and a large rate enhancement due to neighboring-group participation of the amino function was observed.[6] The condensation reaction of a nucleotide 3′-phosphate diester and a nucleotide 5′-hydroxyl using an aryl sulfonyl chloride (Figure 1) is catalyzed by addition of heterocyclic amines such as 1-methylimidazole, 4-(dimethylamino)pyridine, and 5*H*-tetrazole.[7] While the mechanism of such catalysis has not been rigorously elucidated, the heterocyclic amine presumably serves as a nucleophilic catalyst. We investigated whether the positioning of a 1-methylimidazolyl moiety ortho to the phosphate ester (**1c**, Figure 1) would lead to increased rate of condensation, possibly via an active cyclic intermediate.

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