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**Supplementary Material Available:** Comparative mass spectrometric data for the labeled and unlabeled samples of the diacetates corresponding to ***meso*-3** (1 page). Ordering information is given on any current masthead page.

## Laser Desorption Molecular Beam Spectroscopy: The Electronic Spectra of Tryptophan Peptides in the Gas Phase

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We report the observation of the high resolution gas phase electronic spectra of the peptides Trp-Gly, Gly-Trp, and Trp-Gly-Gly in a supersonic molecular beam. These peptides were seeded in the molecular beam by laser desorption from a sample film placed in the throat of a pulsed valve assembly. The laser desorbed peptides were entrained in a pulse of helium carrier gas, cooled in a supersonic expansion, and directed into a time-of-flight mass spectrometer where the resonantly enhanced two-photon ionization spectra were observed. The mass spectra are dominated by peaks at the parent peptide masses and show little or no cracking. The electronic spectra of the peptides suggest an extensive distribution of stable conformations and invite comparison with the spectrum of tryptophan which has also recently been studied in a supersonic expansion.[1]

Many techniques for volatilizing large, thermally labile molecules have been developed, primarily for application in mass spectrometry. These include particle-induced desorption techniques[2] and laser desorption,[3] as well as thermospray[4] and electrospray.[5] Laser desorption seems particularly well suited as a method for seeding a pulsed supersonic expansion as several groups have demonstrated.[6] Although such studies have focussed primarily on mass spectrometry, translational cooling of the seeded molecules has been inferred from mass spectral line widths.[7] In this paper, we demonstrate that these large molecules can also be prepared internally very cold, and, therefore, the selectivity of optical spectroscopy can be coupled with the sensitivity of mass spectrometry in the analysis and study of large molecules of biological interest.

The majority of the apparatus used in this work has been described in detail elsewhere,[8] and only the laser desorption source will be discussed here. Samples were desorbed from a film of peptide doped with a small amount of the dye Rhodamine 6G. The film was deposited on a 1-in. diameter brass disk by evaporating the dissolved peptide and dye from a methanol solution. A supersonic expansion was produced by a pulsed valve, having a 500 $\mu$s duration, discharging helium at a pressure of 14 atmospheres into a cylindrical gas channel 50-mm long by 2-mm diameter. This main gas channel was crossed by a second channel, 1-mm diameter, into which a 530-nm light pulse from an excimer pumped dye laser was focussed.[9] The sample disk was located at the opposite end of this second channel, approximately 1.5 mm behind the main gas channel. During the experiment, the disc was simultaneously rotated about its axis and translated perpendicular to its axis[10] so that a fresh surface was exposed to each shot of the desorption laser. The desorbed material entered the main channel and was entrained in the helium pulse which was then expanded to form a supersonic free jet. The supersonic jet was skimmed, and the resulting molecular beam was directed into a time-of-flight mass spectrometer where the neutral peptide was photoionized with the frequency doubled output of a Nd:YAG pumped dye laser. The firing of the ionization laser was delayed approximately 150 $\mu$s from the desorption laser to allow for the transit time of the seeded helium pulse. Optical spectra were taken by monitoring the intensity of the ion signal corresponding to the parent mass of the peptide as the frequency of the ionizing laser was tuned.

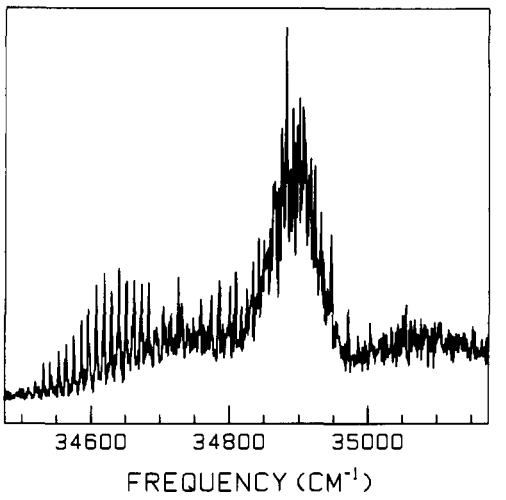


**Figure 1.** Resonantly enhanced two-photon ionization spectrum of Trp-Gly obtained by monitoring the ion signal corresponding to the parent dipeptide at mass 261. The carrier gas is helium at a backing pressure of 14 atm. No correction has been made for variation in the ionization laser power.

Figure 1 displays the resonant two-photon ionization spectrum of Trp-Gly obtained by monitoring the parent ion signal at mass 261. Centered at 34 900 $cm^{-1}$ is a broad, unresolved band which lies in the same region as the origin transitions in tryptophan.[1] The origin region of the tryptophan spectrum has several sharp features which were assigned to at least six different conformers. Addition of a glycine residue should lead to an even greater number of stable conformers. We believe that the broad peak seen with Trp-Gly reflects spectral congestion arising from an extensive conformer distribution. The jet cooled electronic spectrum of Gly-Trp has also been observed under identical experimental conditions and lends support to our argument. In this same spectral region a dense, but resolved, set of sharp features is found, again suggesting contributions from a large number of conformers. Whether individual conformer lines are resolved or not will depend on the magnitude of their spectral shifts as well as on the total number of conformers present.

Approximately 400 $cm^{-1}$ to the red of the broad band in Figure 1, we observe the beginning of a harmonic vibrational progression containing at least 15 members with a spacing of approximately 11 $cm^{-1}$. It is likely that this progression arises from a single conformer having a large equilibrium displacement in its excited state along the 11-$cm^{-1}$ vibrational mode. A low-frequency progression was also seen in the spectrum of one of the tryptophan

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conformers. When this conformer was excited and its fluorescence spectrum examined, a broad, red-shifted band was found, while excitation of other conformers resulted in sharp, structured fluorescence.[11] In tryptophan derivatives, the existence of a single conformer showing broad, red-shifted fluorescence and having an extended low-frequency progression in its excitation spectrum was found to correlate with the ability of the molecule to form a zwitterion by proton transfer from the carboxylic acid to the amine group. If such reasoning can be applied to the Trp-Gly dipeptide, one would predict that the conformer with the low-frequency vibrational progression should also show a red-shifted fluorescence spectrum. In Trp-Gly, however, zwitterion formation must involve proton transfer from the glycine to the tryptophan residue since the tryptophan carboxylic acid group is used to form the peptide bond.

Laser desorption has been used in mass spectroscopy to volatilize much larger molecules than the peptides reported here, and it may also provide a general technique for obtaining supersonic molecular beam spectra of such molecules. Although not dramatically larger than Trp-Gly, the tripeptide Trp-Gly-Gly has also been studied in a supersonic molecular beam. Its spectrum, obtained by monitoring the parent ion signal at mass 318, contains an intense, unresolved band that is much narrower than and red-shifted approximately 100 $cm^{-1}$ from the broad Trp-Gly band. A low-frequency progression in a 26-$cm^{-1}$ vibration is also seen approximately 260 $cm^{-1}$ to the red of the main band. As with the dipeptides, the interpretation of the Trp-Gly-Gly spectrum will certainly require the existence of multiple conformers.

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## Intramolecular Photocycloaddition. Cyclobutane Fragmentation: Total Synthesis of (±)-Laurenene

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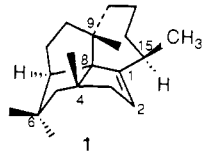
Laurenene (**1**), nature's only known existing fenestrane, was isolated by Corbett and co-workers in 1979 from *Dacrydium cupressinum*. Its unique structure was elucidated by a combi-

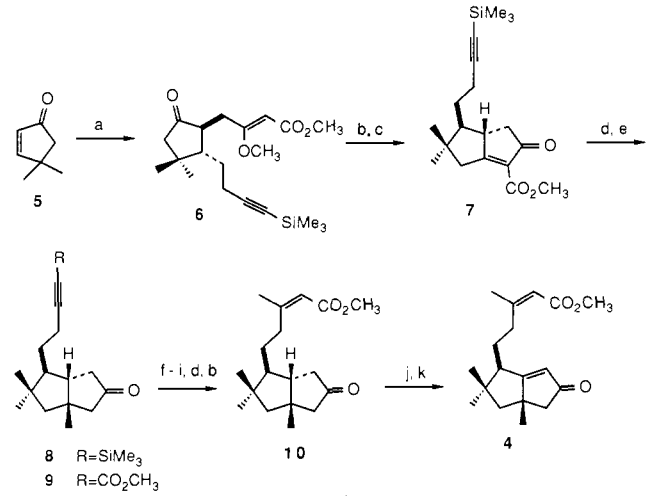


**1**

nation of chemical and spectroscopic methods and further confirmed by X-ray crystallography on a brominated derivative.[2] It is a member of the class of angularly fused triquinanes which have recently stimulated much synthetic activity.[3] Laurenene itself, although the subject of much synthetic effort,[4] has not previously yielded to total synthesis. We report here the first total synthesis of this unusual molecule.[4c]

Several salient features of the laurenene system must be considered in any synthetic approach to this molecule: (1) the tetracyclic skeleton of three five-membered rings and one seven-membered ring attached to a central quaternary carbon atom, (2) the stereochemistry of the C-15 secondary methyl, (3) the regiochemistry of the C-1,2 double bond, and most critically (4) the three contiguous quaternary centers at C-4,8,9 which create a severely sterically crowded region wherein the two methyl groups at C-4 and C-9 point directly at one another. Retrosynthetically, it was anticipated that **1** could be obtained from unsaturated ketone **2**. Ketone **2** could be derived from cyclobutane **3** through reductive cleavage of the cyclobutane and refunctionalization. The cyclobutane **3** might be prepared through a [2 + 2] photocycloaddition[5] of enone **4** since we had previously demonstrated in a model system that the three contiguous quaternary centers could be introduced through an elevated temperature intramolecular photocycloaddition.[6] Enone **4** could be prepared from the readily available 4,4-dimethylcyclopent-2-en-1-one (**5**).[7]

**Scheme I**[a]




[a] (a) $BrMgCH_2CH_2CCSiMe_3$, $[CuIPBu_3]_4$, THF, −50 °C, 2 h; then HMPA, $ICH_2C(OCH_3)=CHCO_2CH_3$, 25 °C, 1 h; (b) 10% HCl, acetone, 6 h; (c) NaOMe, MeOH, 0 °C, 30 min; (d) $Me_2CuLi$, $Et_2O$, −78 °C, 30 min; (e) LiCl, $H_2O$, DMSO, 140 °C, 15 min; (f) *p*-TsOH, $(CH_2OH)_2$, $C_6H_6$, 80 °C, 5 h; (g) KF, $Bu_4N^+F^-$, $CH_3CN$, 80 °C, 2 h; (h) BuLi, THF, $CO_2$, −78 °C; (i) 10% HCl, then $CH_2N_2$, $Et_2O$; (j) $Me_3SiCH_2CO_2Et$, THF, $Bu_4NF$ (catalyst), −78 °C, 1 h; then 25 °C, 1 h; (k) $Pd(OAc)_2$, $CH_3CN$, *p*-benzoquinone, 6 h.

Thus, our attention was initially focused on the preparation of the keto ester **4**. Copper-catalyzed conjugate addition of the Grignard reagent prepared from 4-bromo-1-(trimethylsilyl)-1-butyne[8] to dimethylcyclopentenone **5** (Scheme I) followed by alkylation of the regiospecifically generated enolate with methyl 4-iodo-3-methoxycrotonate[9] provided the crystalline (mp 46–48 °C) trans substituted cyclopentanone **6**[10] in 60% yield. Hydrolysis of the enol ether of **6** (10% HCl; acetone) followed by base-induced cyclization (NaOMe; MeOH; 0 °C; 15 min)[6] provided the diquinane **7** (mp 65–68 °C). Exposure of **7** to lithium dimethylcopper and subsequent decarbomethoxylation (DMSO, $H_2O$, LiCl)[11] gave ketone **8**[10] in 71% overall yield from **6**. Conversion of **8** to **9** was readily achieved by protection of the ketone [$(CH_2OH)_2$, *p*-TsOH, $C_6H_6$, 80 °C], removal of the trimethylsilyl group [KF; $Bu_4N^+F^-$ (catalyst); $CH_3CN$; 80 °C, 2 h], and carbomethoxylation of the terminal acetylene to produce **9** in 90%

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