There are two molecules per asymmetric unit and we expected the two chlorine and two sulfur atoms to be useful as "heavy atoms." However, only three heavy atoms could be located in both a three-dimensional Patterson function and in an E map computed with phases determined by the symbolic addition method. Subsequent Fourier syntheses located the light atoms and indicated that one of the thiophene rings was disordered. A least-squares refinement[5] using isotropic and then anisotropic thermal parameters reduced R (the usual residual) to 0.091. A difference Fourier synthesis was used to locate the hydrogen atoms and a subsequent refinement reduced the R to 0.055.

The differences between chemically equivalent bonds in the two molecules are not statistically significant and the average bond lengths are close to the expected values. A view down the carbon–carbon bond of the dimethylaminoethyl side chain in both molecules is illustrated in Figure 1, where the difference in the orientation of the thiophene rings is easily seen. The conformation in Histadyl is similar to that found in histamine[3] with the dimethylamino group being *trans* to the substituent on C-2 of the dimethylaminoethyl chain. In contrast a partially eclipsed conformation was found in histidine which exhibits neither the physiological behavior of a histamine nor of an antihistamine.[6] Since the dimethylamino group is more basic than the NH_2 group of histamine, the antihistamine can compete favorably with histamine for a receptor site. The *trans* configuration must be essential to antihistamine activity and must be related to the steric requirements of the receptor site. The function of the bulky pyridine and thiophene groups is not understood at the present time.

The above arguments depend upon the conformation being retained *in vivo;* however, the hypothesis is consistent with the structural data available to date. Furthermore, our results explain the radically different physiological behavior of histidine compared to histamine and Histadyl in terms of the conformational differences in the three molecules.

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(5) All the calculations used an average C plus S f-curve for the two disordered ring atoms.

(6) The crystal structure of histidine was refined by J. Donohue and A. Caron, *Acta Crystallogr.*, 17, 1178 (1964), but the conformation about the C–C bond is given in ref 3.

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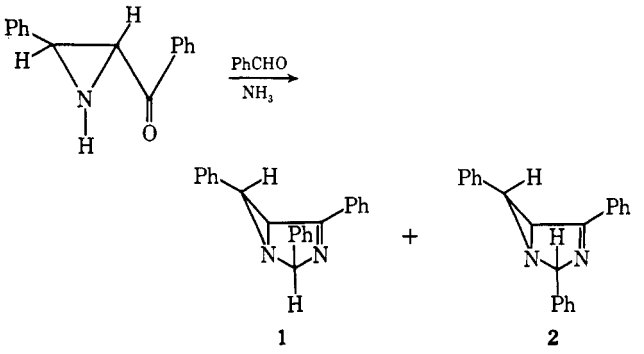
On the Photoisomerization of the Triphenyl-1,3-diazabicyclo[3.1.0]hex-3-ene System[1]

Sir:

The photochemistry of substituted 1,3,5-hexatrienes has been the subject of extensive investigation.[2-6] Current interest in these reactions has been heightened by the awareness that orbital symmetry factors may control the various bond reorganizations to a substantial degree.[7] The influence of substituents on the course of the photoisomerization of 1,3,5-hexatrienes to bicyclo[3.1.0]hex-2-enes has been reported,[8] but no information has been available concerning the stereochemistry of the photoisomerization.[6] In the hope of providing some data for understanding the stereochemical course of this reaction, we have investigated the photochemistry of the related 1,3-diazabicyclo[3.1.0]hex-3-ene system, with the results described below.

endo- and *exo*-2,4,6-triphenyl-1,3-diazabicyclo[3.1.0]-hex-3-ene (**1** and **2**) were prepared by treating *trans*-2-phenyl-3-benzoylaziridine with benzaldehyde in an ethanolic solution saturated with ammonia and containing small quantities of ammonium bromide.[9] Fractional crystallization gave **1**, mp 143–144°, and **2**, mp 154–155°. Spectral data and elemental analyses were in complete agreement with the structures.[10] Of particular relevance is the fact that compound **2** showed a strong intramolecular nuclear Overhauser effect (NOE).[11] In the nmr spectrum of **2**, application of an intense radiofrequency field at the transition energy of proton H_2 produced a NOE at proton H_6 (31% intensity increase), whereas similar irradiation of the H_2 proton in the other isomer had no effect.



Irradiation of a solution of **1** (0.15 g) in benzene at 50° in a Pyrex immersion apparatus with a 450-W Hanovia lamp for 4 hr led to complete disappearance of starting material. Conventional isolation procedures

(1) Photochemical Transformations of Small-Ring Heterocyclic Compounds. XXIV. For part XXIII see A. Padwa and R. Gruber, *J. Amer. Chem. Soc.*, 92, 107 (1970).

(2) J. Meinwald and P. H. Mazzocchi, *ibid.*, 88, 2851 (1966); 89, 696 (1967).

(3) M. Pomerantz, *ibid.*, 89, 694 (1967).

(4) R. N. Warrener and J. B. Bremner, *Rev. Pure Appl. Chem.*, 16, 117 (1966).

(5) K. R. Huffman and E. F. Ullman, *J. Amer. Chem. Soc.*, 89, 5629 (1967).

(6) W. G. Dauben, *Pure Appl. Chem.*, 9, 539 (1969); W. G. Dauben and J. H. Smith, *J. Org. Chem.*, 32, 3244 (1967).

(7) See G. B. Gill, *Quart. Rev.* (London), 22, 338 (1968), for leading references.

(8) J. Meinwald and P. H. Mazzocchi, *J. Amer. Chem. Soc.*, 89, 1755 (1967).

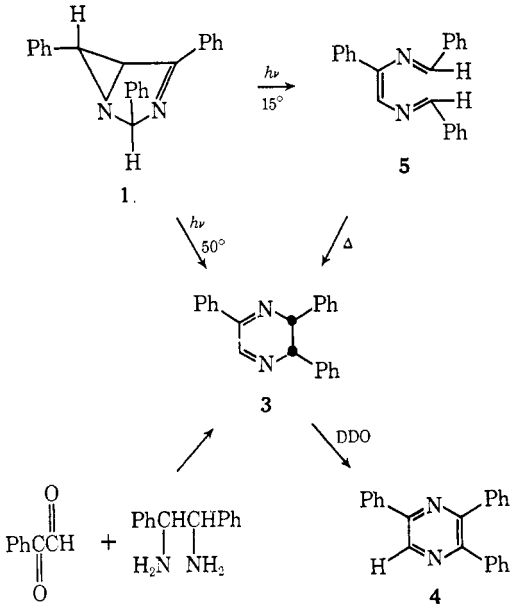
(9) H. Heine, R. Weese, R. Cooper, and A. Durbetaki, *J. Org. Chem.*, 32, 2708 (1967). These authors were the first to synthesize the diazabicyclo[3.1.0]hex-3-ene system. They report only the formation of **2** from the above reaction.

(10) All compounds analyzed satisfactorily. Complete spectroscopic and degradative details will be given in our full publication.

(11) F. A. L. Anet and A. J. R. Bourn, *J. Amer. Chem. Soc.*, 87, 5250 (1965).

afforded 0.14 g (94%) of a solid, mp 145–146°, whose structure is assigned as *cis*-2,3-dihydro-2,3,5-triphenylpyrazine (**3**) on the basis of the chemical and physical data cited: λ_{max} (KBr) 6.40, 6.70, 6.90, 10.50, 13.10, 14.35, 14.55 μ; λ_{max} (95% ethanol) 274 mμ (ϵ 7500); nmr, 4.94 (broad s, 2 H), 2.89 (m, 13 H), 1.98 (m, 2 H), 1.34 (d, 1 H). Chemical confirmation was obtained by the oxidation of **3** with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) to 2,3,5-triphenylpyrazine (**4**). Structure **3** was further confirmed by its unequivocal synthesis from phenylglyoxal and *meso*-stilbenediamine.

Irradiation of a solution of **1** at 15° for the same period gave virtually no dihydropyrazine (**3**). Instead, formation of a new product occurred. At 50°, thermal rearrangement of the labile photoproduct took place. These reactions are reproducible and clearly require that some photochemically generated precursor of **3** persists after the light source is extinguished which then rearranges upon heating to *cis*-2,3-dihydropyrazine **3**. From its absorption spectra (ir, 6.14 μ; uv, λ_{max} 360 mμ (ϵ 12,000); nmr, 2.50 (m, 16 H), 1.50 (s, 2 H)), its thermal instability, and behavior on hydrolysis, this compound is most reasonably assigned ene diimine structure **5**.



1 5 3 4

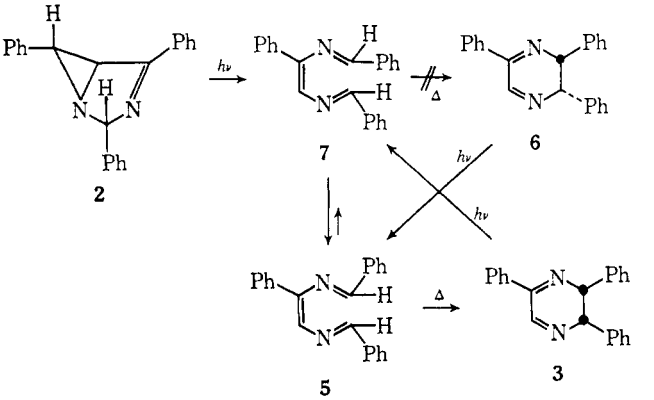
According to orbital symmetry considerations, ring opening of an electronically excited *exo,endo*-disubstituted bicyclo[3.1.0]hex-2-ene (such as **1**) to a *trans,cis,trans*-hexatriene is an allowed process.[12,13] Orbital symmetry further predicts that the hexatriene would undergo ring closure by disrotatory motion. Complete stereospecific formation of **3** from **1** is in accord with the Woodward–Hoffmann selection rules.[14] In order to further test the validity of this interpretation we have investigated the photochemistry of **2**. Formation of *trans*-2,3-dihydro-2,3,5-triphenylpyrazine (**6**) from **2** was expected. However, irradiation of **2** at 50° resulted in the exclusive formation of *cis*-dihydropyrazine (**3**).

(12) R. Hoffmann and R. B. Woodward, *Accounts Chem. Res.*, **1**, 17 (1968).

(13) The stereospecificity of the 1,3,5-hexatriene to bicyclo[3.1.0]-hex-2-ene system is under study and will be the subject of a future publication.

(14) It should be emphasized that although orbital symmetry control is implicated, these results do not prove such control because several geometries of uncertain reactivity are available to the ene–diimine intermediate.

The most direct explanation of the above result is that the ene–diimine exists as an equilibrium mixture of two isomers **5** and **7**, the more prevelant isomer being **5**. The formation of *cis*-dihydropyrazine from the irradiation of **2** may then be pictured as occurring *via* a three-step process. The first step involves ring opening of **2** to an ene diimine (**7**). The second step of the reaction involves rapid *syn–anti* isomerization of **7** to **5** which then undergoes disrotatory closure to give **3**. *syn–anti* isomerizations of N-arylimines are known to occur rapidly[15,16] and provide reasonable chemical analogy for the second step.



2 7 6 5 3

In support of this sequence we find that irradiation of *trans*-dihydropyrazine **6**[17] at 15° gives a labile ene diimine which thermally cyclizes to give **3**. On the other hand, irradiation of *cis*-dihydropyrazine **3** at 15° affords an ene diimine which regenerates starting material on warming. These results indicate that **5** is an important intermediate in the isomerization of **6** to **3** and that irradiation of **3** results in conrotatory opening to give **7** which rapidly isomerizes to **5**. The above data demonstrate the limitations of the orbital symmetry rules in interpreting a pericyclic transformation without knowledge of the number and sequence of steps involved.

Beak and Miesel have reported earlier that 2,3-dihydropyrazines rearrange to imidazoles upon irradiation.[18] The authors suggest that the reaction proceeds through an irreversibly formed ene diimine intermediate. It is interesting to note that we do not detect any 1-benzyl-2,5-diphenylimidazole in our system and that the isomerization *trans*- (**6**) to *cis*-dihydropyrazine (**3**) does occur. At this time we have no ready explanation which satisfactorily accounts for the differences noted. We prefer to postpone further discussion of this point until a more thorough study can be undertaken.

Acknowledgment. We gratefully acknowledge support of this work by the National Science Foundation (Grant GP-9385).

(15) D. Y. Curtin and J. W. Hausser, *J. Amer. Chem. Soc.*, **83**, 3474 (1961).

(16) D. Y. Curtin, E. J. Grubbs, and C. G. McCarty, *ibid.*, **88**, 2775 (1966).

(17) Compound **6**, mp 117–118°, was prepared by the action of racemic stilbenediamine on phenylglyoxal.

(18) P. Beak and J. L. Miesel, *J. Amer. Chem. Soc.*, **89**, 2375 (1967).

(19) Alfred P. Sloan Fellow, 1968–1970.

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