

Figure 1. Dependence of  $\phi_{\text{Co}^{2+}}$  on [alcohol]:  $[\text{Co}(\text{NH}_3)_5\text{O}_2\text{CCH}_3^{2+}] = 5.0 \times 10^{-3} \text{ M}$ ;  $[\text{H}^+] = 0.1 \text{ M}$ ;  $I_a \approx 6.5 \times 10^{-3} \text{ einstein l}^{-1} \text{ min}^{-1}$ . Methanol, O; 2-propanol, ●.

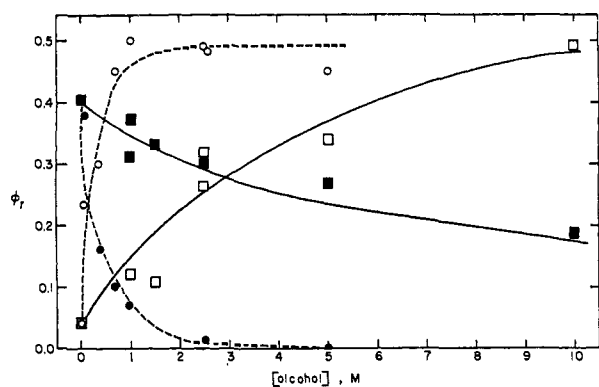
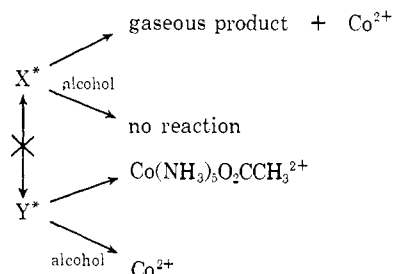


Figure 2. Dependence of the yields of  $\text{CH}_4$  and  $\text{C}_2\text{H}_6$  on [alcohol]:  $\phi_r = \phi_{\text{CH}_4}/\phi_{\text{Co}^{2+}}$  or  $\phi_{\text{C}_2\text{H}_6}/\phi_{\text{Co}^{2+}}$ ;  $[\text{Co}(\text{NH}_3)_5\text{O}_2\text{CCH}_3^{2+}] = 5.0 \times 10^{-3} \text{ M}$ ;  $[\text{H}^+] = 0.1 \text{ M}$ ;  $I_a \approx 6.5 \times 10^{-3} \text{ einstein l}^{-1} \text{ min}^{-1}$ . When alcohol = methanol, —;  $\text{CH}_4 = \square$ ,  $\text{C}_2\text{H}_6 = \blacksquare$ . When alcohol = 2-propanol, - - - - -;  $\text{CH}_4 = \circ$ ,  $\text{C}_2\text{H}_6 = \bullet$ .

turns to the ground state and has a sufficiently long lifetime to be reduced by the alcohols. The independence of the equivalent yields of gaseous product on [alcohol] shows that these two intermediate species are not interconvertible.



The intermediate leading to the gaseous products may well be a radical pair; if so, its lifetime is so short that it is not significantly scavenged by  $[\text{alcohol}] \leq 10 \text{ M}$ . Any precursor to this intermediate could not be scavenged without affecting the gas yields. Although the chemically important intermediates  $\text{X}^*$  and  $\text{Y}^*$  could derive from a common excited state, it is not unreasonable in this case to postulate that they arise from different excited states. In  $\text{Co}(\text{NH}_3)_5\text{O}_2\text{CCH}_3^{2+}$  the carbonyl and the acetate  $\rightarrow$  cobalt CT absorptions would be expected to occur in the same general spectral regions. Since the  $e_g$  acceptor orbital at the cobalt(III) center has approximately  $\sigma$  symmetry, interconversions between carbonyl and CT excited states would be symmetry forbidden.

These results represent the first unequivocal demonstration of the generation of more than one intermediate in the photochemistry of a cobalt(III) complex. It seems clear that the excited states populated do determine the course of reaction and must be taken into consideration in any mechanistic speculation.

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### Conformational Influences on Antihistamine Activity. The Crystal Structure of 2-[(2-Dimethylaminoethyl)-2-thenylamino]pyridine Hydrochloride, an Antihistamine

Sir:

Antihistamines are believed to compete with histamine for an ill-defined receptor site.<sup>1</sup> One of the requirements for antihistamine activity was assumed to be a conformational similarity with histamine. However, no structural data have been available to test this hypothesis. We have completed the first crystal structure study of an antihistamine, 2-[(2-dimethylaminoethyl)-2-thenylamino]pyridine hydrochloride, Histadyl,<sup>2</sup> and have found a conformation similar to that observed recently in the histamine cation.<sup>3</sup>

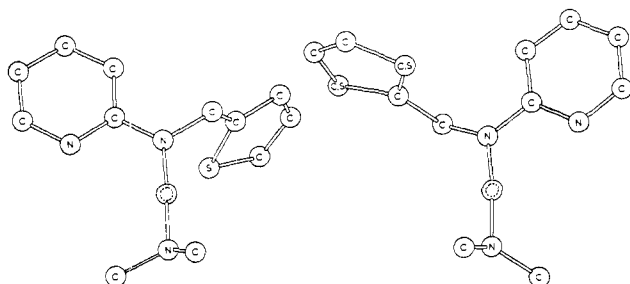


Figure 1. A view down the C-C bond of the dimethylaminoethyl group in the two molecules in the asymmetric unit. The disordered thiophene ring atoms are labeled C,S.

Histadyl was reported to crystallize in the monoclinic space group  $P2_1/n$  with cell dimensions of  $a = 27.35$ ,  $b = 10.38$ ,  $c = 10.96 \text{ \AA}$ , and  $\beta = 96^\circ$ .<sup>4</sup> The density calculated for eight molecules (mol wt = 297.85) per unit cell is  $1.281 \text{ g/cm}^3$  and the observed density is  $1.273 \text{ g/cm}^3$ . We used the standard setting  $P2_1/c$  with  $a = 10.936 \pm 0.003$ ,  $b = 10.417 \pm 0.003$ ,  $c = 28.256 \pm 0.008 \text{ \AA}$ , and  $\beta = 106.21 \pm 0.02^\circ$ . The intensity data were measured using the stationary crystal-stationary counter method with a G.E. automatic diffractometer. A total of 3023 nonzero reflections with  $2\theta \leq 135^\circ$  (Cu radiation) were used in the analysis.

(1) (a) R. E. Wilhelm, *Med. Clin. N. Amer.*, **45**, 887 (1961); (b) C. Botré, M. Marchetti, C. Del Vecchio, G. Lionetti, and A. Memoli, *J. Med. Chem.*, **12**, 832 (1969).

(2) Histadyl is the registered trade name of Eli Lilly and Co. for the compound 2-[(2-dimethylaminoethyl)-2-thenylamino]pyridine hydrochloride.

(3) M. V. Veidis and G. J. Palenik, *Chem. Commun.*, 196 (1969).

(4) H. A. Rose and J. G. Williams, *J. Amer. Pharm. Assoc.*, **48**, 487 (1959).

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<sup>5</sup> 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<sup>3</sup> 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.<sup>6</sup> Since the dimethylamino group is more basic than the NH<sub>2</sub> 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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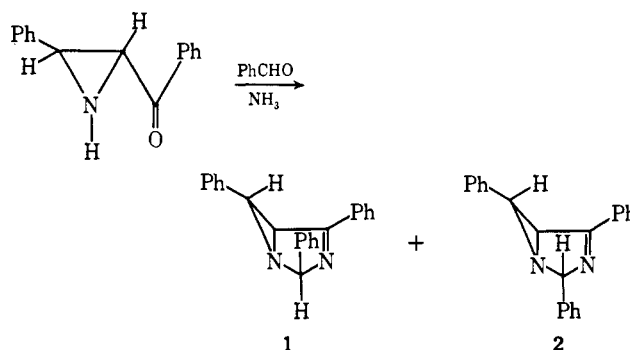
### On the Photoisomerization of the Triphenyl-1,3-diazabicyclo[3.1.0]hex-3-ene System<sup>1</sup>

Sir:

The photochemistry of substituted 1,3,5-hexatrienes has been the subject of extensive investigation.<sup>2-6</sup>

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.<sup>7</sup> 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,<sup>8</sup> but no information has been available concerning the stereochemistry of the photoisomerization.<sup>8</sup> 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.<sup>9</sup> Fractional crystallization gave **1**, mp 143-144°, and **2**, mp 154-155°. Spectral data and elemental analyses were in complete agreement with the structures.<sup>10</sup> Of par-



ticular relevance is the fact that compound **2** showed a strong intramolecular nuclear Overhauser effect (NOE).<sup>11</sup> In the nmr spectrum of **2**, application of an intense radiofrequency field at the transition energy of proton H<sub>2</sub> produced a NOE at proton H<sub>6</sub> (31% intensity increase), whereas similar irradiation of the H<sub>2</sub> 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).