Most transition metal polypyrazolylborates are stable to air, water, dilute acids, and bases.

Analogs of pyrazaboles and poly(1-pyrazolyl)borates were also obtained from 1,2,4-triazole.

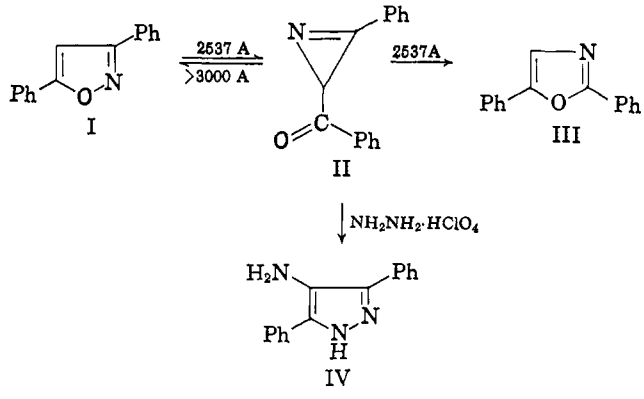
S. Trofimenko
Contribution No. 1196
Central Research Department, Experimental Station
E. I. du Pont de Nemours and Company
Wilmington, Delaware 19898
Received February 2, 1966

Photochemical Transposition of Ring Atoms in Five-Membered Heterocycles. The Photorearrangement of 3,5-Diphenylisoxazole

Sir:

Recently there have been described several examples of light-induced rearrangements of five-membered-ring heterocyclic compounds. In each case, the product could be formally derived by the transposition of two ring atoms together with their substituents. Thus, indazoles were found to rearrange to benzimidazoles,[1] pyrazoles to imidazoles,[1] and 2-substituted thiophenes to 3-substituted thiophenes.[2] An interesting suggestion has been made that these reactions may proceed by way of bridged valence tautomers[2] akin to those found as intermediates in the superficially similar phototransposition reactions of benzene derivatives.[3] We report here another example of the five-membered heterocyclic phototransposition reaction together with evidence concerning its mechanism.

Irradiation of 3,5-diphenylisoxazole[4] (I) ($\lambda\lambda_{max}^{ether}$ 245 mμ (ε 22,000); 265 mμ (ε 24,000)) in ether solution with 2537-A light[5] led to the formation of 2,5-diphenyloxazole[6] (III) ($\lambda\lambda_{max}^{ether}$ 302 mμ (ε 30,000); 315 mμ (ε 27,600)) in 50% yield. The reaction could conveniently be followed by ultraviolet spectroscopy and was found to proceed in yields of up to 84% under the spectroscopic conditions. However, spectra taken during the course of the reaction did not display isosbestic points as expected of a simple two-component system. Interruption of the reaction before completion led to isolation (silica chromatography) of a third substance, II (λ_{max}^{ether} 247 mμ (ε 24,300)) in 12% yield.[7] This compound was an oil which on further irradiation in ether with 2537-A light was converted to the oxazole III. When the reaction was followed spectroscopically the envelope of curves crossed at nearly one point, 267 mμ, and conversions of up to 82% were obtained. Additional prolonged irradiation of the oxazole III with >3000-A light[8] led to the gradual precipitation of a highly insoluble crystalline solid which reverted back to III on standing or heating in a solvent.



The analytical and mass spectral data for the oily compound II require that it be isomeric with the starting material. Its infared spectrum showed distinctive maxima at 5.63 and 5.99 μ which were in accord with the band positions expected for azirine C=N[9] and aromatic ketone stretching frequencies. The ultraviolet maximum of II at 247 mμ is close to the maxima of both phenyl cyclopropyl ketone[10] and N-phenylketimines,[9b,c] and the long wavelength tail of the band shows a shoulder at 350 mμ (ε 150) (partially obscured by traces of III) suggestive of an n → π* band of an aromatic ketone. Since longer wavelength absorption would be expected if the ketimine and ketone groupings were conjugated, only the azirine structure II is compatible with these facts. This structure is further supported by (a) the apprearance in the nmr of a single uncoupled proton signal at τ 6.25 (=NCHCO) together with signals at τ 1.8–2.6 (10 H, aromatic), (b) conversion of II to 4-amino-3,5-diphenylpyrazole[11] (IV) on warming with aqueous or alcoholic hydrazine perchlorate, (c) the thermal (200°) conversion of II in nonhydroxylic solvents to the isoxazole I, and (d) the near-quantitative conversion of II to the oxazole III in boiling methanol.[12]

Investigation of the effect of different wavelengths of light on the azirine II revealed a striking dependence of its photochemistry with wavelength. Irradiation of ether solutions of II with >3000-A light[8] led to near-quantitative conversion to the isoxazole I (nearly perfect isosbestic point at 258 mμ). This contrasts sharply with the observed 82% conversion of the azirine II to the oxazole III with 2537-A light. Two interpretations of these observations must be considered. Either (1) different wavelengths of light produce different reactions of the azirine II, or (2) the conversion of the azirine II to the oxazole III actually proceeds by way of the isoxazole I, but with >3000-A light the

(1) H. Tiefenthaler, W. Dörscheln, H. Göth, and H. Schmid, *Tetrahedron Letters*, 2999 (1964).
(2) H. Wynberg and H. van Driel, *J. Am. Chem. Soc.*, **87**, 3998 (1965).
(3) K. E. Wilzbach and L. Kaplan, *ibid.*, **86**, 2307 (1964); **87**, 4004 (1965); A. W. Burgstahler and P. L. Chien, *ibid.*, **86**, 2940, 5281 (1964); E. M. Arnett and J. M. Bollinger, *Tetrahedron Letters*, 3803 (1964); L. Kaplan, K. E. Wilzbach, W. G. Brown, and S. S. Yang, *J. Am. Chem. Soc.*, **87**, 675 (1965).
(4) C. Goldschmidt, *Ber.*, **28**, 2540 (1895).
(5) An Hanovia 100-w medium-pressure U-shaped mercury vapor arc was used together with Kasha's filter combination E; M. Kasha, *J. Opt. Soc. Am.*, **38**, 929 (1948).
(6) R. Robinson, *J. Chem. Soc.*, **95**, 2167 (1909).
(7) Up to 38% yields of II could be obtained by irradiation of ether solutions of I in Pyrex glass flasks with a GE B-H6 lamp with no filter (<1.0% of light transmitted to solution below 2800 A).
(8) A 6-mm thick Pyrex glass filter was used together with a GE B-H6 lamp (<1.0% of light transmitted below 3000 A).
(9) (a) D. J. Cram and M. J. Hatch, *J. Am. Chem. Soc.*, **75**, 33 (1953); (b) G. Smolinsky, *ibid.*, **83**, 4483 (1961); (c) R. F. Parcell, *Chem. Ind.* (London), 1396 (1963).
(10) R. P. Mariella and R. R. Raube, *J. Am. Chem. Soc.*, **74**, 518, 525 (1952).
(11) M. Ruccia, *Ann. Chim.* (Rome) **49**, 720 (1959); *Chem. Abstr.*, **53**, 21892*i* (1959).
(12) This reaction also occurred at 25° in weakly alkaline methanol.

reaction is suppressed at the isoxazole stage due to the failure of I to absorb this light. If this latter alternative were correct then the oxazole III should be formed more rapidly by irradiation of the isoxazole I than by irradiation of the azirine II with 2537-A light. Since the contrary is true (the oxazole III is initially formed over eight times as efficiently from the azirine) III cannot be formed to a significant extent by direct rearrangement of the isoxazole I. Accordingly, *the azirine III is truly an intermediate in the phototransposition reaction, and its photochemical reactivity is dramatically sensitive to different wavelengths of light; the oxazole III is formed with 2537-A light while the isoxazole I is formed with >3000-A light.* Although it was not possible to determine accurately the degree of specificity of these reactions, the fact that perfect isosbestic points were not obtained suggests that the two reactions of II are not quite mutually exclusive. Thus, the spectra suggest that as much as 4% of the isoxazole may temporarily accumulate during 2537-A irradiation of II, while temporary buildup of about 2% of the oxazole III was observed during >3000-A irradiation of II.

We believe this wavelength dependence is probably caused by selective excitation of one of the two isolated chromophores in the azirine II followed by a molecular rearrangement which proceeds more rapidly than energy transfer between the two chromophores. Excitation of the benzoyl chromophore, which should contribute most heavily to the long wavelength tail due to its $n \rightarrow \pi^*$ transition, should occur quite selectively with >3000-A light. Thus, excitation of this grouping is probably responsible for the rearrangement to the isoxazole I. On the other hand, both chromophores should absorb the 2537-A light, and thus it is probably excitation of the ketimine chromophore which leads to the formation of the oxazole III.

A decision concerning the generality of this mechanism in phototransposition reactions of other five-membered ring heterocycles must await further study.

Edwin F. Ullman, Balwant Singh

Chemical Department
Central Research Division
American Cyanamid Company, Stamford, Connecticut

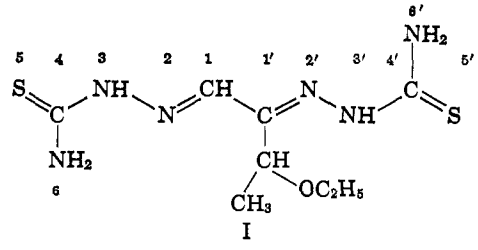
Received February 18, 1966

The Crystal Structures of Compounds with Antitumor Activity. 2-Keto-3-ethoxybutyraldehyde Bis(thiosemicarbazone) and Its Cupric Complex[1]

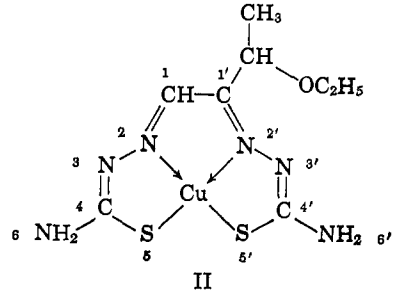
Sir:

2-Keto-3-ethoxybutyraldehyde bis(thiosemicarbazone) (I) has been shown to be effective as an antitumor agent in certain animals[2] and is currently being tested clinically. Its activity is dependent on the presence of certain metal ions in the diet,[3] and in *in vitro* test systems the cupric complex II has been found to be the most active form.[4]

The crystal structures of I and II have been determined by X-ray diffraction methods[5] in order to obtain information about any electronic and sterochemical differences between them that could account for the increased activity of II.



I



II

I crystallizes in the monoclinic space group $P2_1/c$ with $a = 20.846$, $b = 13.809$, $c = 9.557$ A, $\beta = 95° 30'$, and $Z = 8$. There are two molecules of $C_8H_{16}N_6OS_2$ per asymmetric unit. The intensities of 6018 unique reflections from a crystal ground as a sphere were measured on a G.E. XRD-5 diffractometer, using nickel-filtered Cu Kα radiation. Of these reflections 3831 were significantly above the background intensity. Absorption corrections were applied. The structure was solved by an application of the symbolic addition procedure.[6] Refinement by differential syntheses and least-squares techniques using the observed data has reduced R to 0.052. All 32 hydrogen atoms were located in a difference map at $R = 0.076$ and they were included in the calculations from that point, but their parameters have not yet been refined.

II may be prepared by dissolving freshly precipitated cupric hydroxide in an aqueous solution of I. It crystallizes from hot aqueous solution as dark red-brown, soft, triclinic plates[7] with $a = 9.306$, $b = 10.443$, $c = 7.479$ A, $\alpha = 90° 38'$, $\beta = 114° 15'$, $\gamma = 98° 25'$, and $Z = 2$. The space group is probably $P\bar{1}$. The intensities of 2874 unique reflections were measured as for I and 2454 were significantly above the background. Absorption corrections were applied.

(1) Research financed by Grants 1-SO1-FR-05539, AM 02884, and CA 06927 from the National Institutes of Health, U. S. Public Health Service.

(2) H. G. Petering, H. H. Buskirk, and G. E. Underwood, *Cancer Res.*, 24, 367 (1964).

(3) H. G. Petering, H. H. Buskirk, J. A. Crim, and G. J. Van Giessen, *Pharmacologist*, 5, 271 (1963).

(4) G. J. Van Giessen and H. G. Petering, Abstracts, 149th National Meeting of the American Chemical Society, Detroit, Mich., April 1965, Paper P-13N.

(5) We are indebted to Dr. H. G. Petering for a generous sample of the pure ligand I.

(6) *E.g.*, I. L. Karle and J. Karle, *Acta Cryst.*, **16**, 969 (1963).

(7) An orthorhombic modification of II crystallizes from the same solution at room temperature, $a = 10.45$, $b = 13.83$, $c = 9.32$ A, and $Z = 4$. The space group is probably $Pmn2_1$. These crystals could not be grown large enough for X-ray data collection purposes.