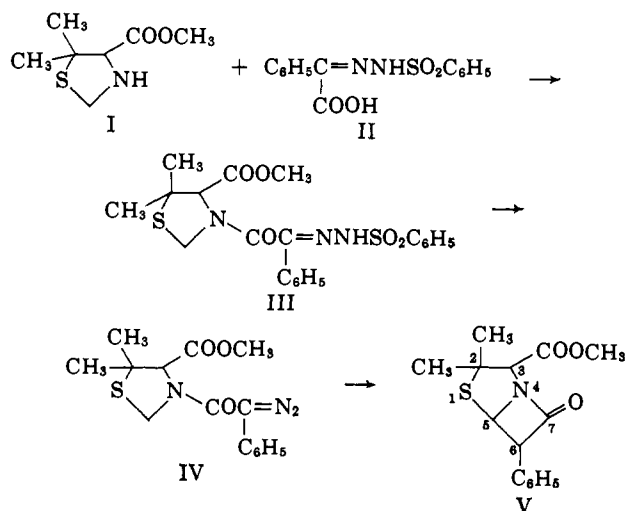


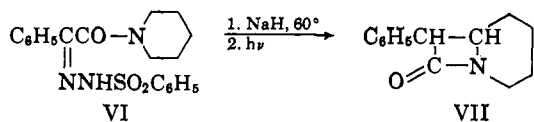
lamp with output mainly at 366 m μ (Westinghouse H38-4GS) led to rapid decomposition with evolution of nitrogen and formation of methyl 6-phenylpenicillanate (V) as the principal product, m.p. 95.0–95.5°, in-



frared peaks (in CCl₄) at 5.62 and 5.7 μ due to β -lactam and ester carbonyls. The molecular weight of the compound as determined by mass spectrometry⁴ was 291.0919 (calcd. 291.0929), and microanalysis gave C, 61.56; H, 5.88; N, 4.81, agreeing with V. The n.m.r spectrum (in CCl₄) showed two sharp peaks due to the methyl groups at C-2 at δ 1.42 (3 H) and 1.65 (3 H), a sharp peak due to carbomethoxy at 3.69 (3 H), a sharp singlet due to the proton at C-3 at 4.47 (1 H), a peak due to the aromatic protons at 7.24 (5 H), and doublets due to the protons attached to C-6 and C-5 at 4.34 and 5.18 (1 H each, $J = 2.0$ c.p.s.). These data are uniquely consistent with the formulation of the principal product as V, with the protons at C-5 and C-6 *trans* to one another. Although other isomers of V may be contained in the total reaction product, isolation has not been possible thus far.

These experiments demonstrate that the penicillanic acid system can be constructed in three operationally simple steps from the readily available thiazolidine (I). Furthermore, the approach is one which should allow access to a wide range of analogous β -lactam thiazolidine structures with variation of substituents at C-2, C-3, C-5, or C-6.

Other structures containing the β -lactam unit can also be synthesized by the α -diazo amide approach.⁵ For example, the bicyclic β -lactam VII, m.p. 85.5–86.0°, was obtained in 50% yield in two steps from the readily available amide hydrazone VI *via* the α -diazo amide as



described above. The assignment of structure VII to the product is supported by infrared (carbonyl ab-

(4) An Associated Electrical Industries MS-9 instrument was employed.

(5) To our knowledge there are no previous known examples of the synthesis of β -lactams from α -diazo amides. For a review of methods of β -lactam synthesis see J. C. Sheehan and E. J. Corey, *Org. Reactions*, **9**, 388 (1958). The α -diazo amides encountered in this work also undergo *thermal* conversion to β -lactams.

sorption at 5.72 μ in CCl₄) and n.m.r. spectra, and mass spectrometric, analytical, and chemical data. The β -lactam VII was formed stereospecifically.

There are a number of logical extensions of this work now under study in these laboratories, including the synthesis of the 6-acylaminopenicillanic acid system of the presently known biologically active penicillins and the study of the scope and utility of the new β -lactam synthesis (both thermal and photochemical modifications).

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The Photodecarboxylation of α -Azido Acids¹

Sir:

The photolysis of alkyl azides proceeds with loss of molecular nitrogen and formation of imines derived from 1,2-shift of hydrogen, alkyl, or aryl groups from carbon to nitrogen.^{2,3} We wish to report a new reaction pathway for the photochemical decomposition of alkyl azides. Ultraviolet irradiation of α -azido acids causes efficient decarboxylation and formation of the lower aldimine or ketimine and carbon dioxide. Typically, photolysis⁴ of α -azidobutyric acid in methanol yielded 60% carbon dioxide and 25% propionaldehyde imine which was isolated as the 2,4-dinitrophenylhydrazone (2,4-DNP). The yield of imine is not optimal due to partial decomposition under the photolytic conditions. Photolysis of α -azidovaleric acid led to decarboxylation to the extent of 60%. In addition to 20% of *n*-butyraldehyde imine, (\pm)- α -aminovaleric acid was also isolated, but (\pm)-proline, the product of intramolecular cyclization, was shown to be absent.⁵

In order to learn whether aryl or alkyl group migration to nitrogen³ could compete with loss of carbon dioxide the photolyses of α -azidoisobutyric acid and azidodiphenylacetic acid were studied. Irradiation of α -azidoisobutyric acid yielded carbon dioxide in 40% yield. Acetone imine was obtained in 20–25% yield

(1) We wish to thank the U. S. Army Engineer Research and Development Laboratories for support of this project under Contract DA44-009-AMC-861(T).

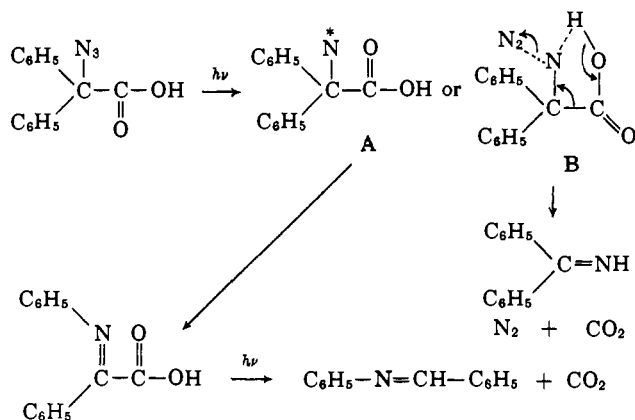
(2) For a splendid review of the photochemical decomposition of organic azides see R. A. Abramovitch and B. A. Davis, *Chem. Rev.*, **64**, 149 (1964).

(3) W. H. Saunders, Jr., and E. A. Caress, *J. Am. Chem. Soc.*, **86**, 861 (1964).

(4) Photolyses were carried out using a Hanau high-pressure (Q81) immersion lamp surrounded by a quartz water-cooled heat exchanger. Filter solutions were circulated as coolants. α -Azido acids undergo two electronic excitations: the $sp_x \rightarrow \pi_y^*$ ($^1\Sigma_g^+ \rightarrow ^1\Delta_u$) at 2160 Å. and the $\pi_y \rightarrow \pi_x^*$ ($^1\Sigma_g^+ \rightarrow ^1\Delta_u$) at 2870 Å. Radiation above 3000 Å. was removed by use of a nickel sulfate heptahydrate-cobalt sulfate heptahydrate aqueous solution filter. Since the decarboxylation reaction occurs in benzene solution the longer wave length excitation $\pi_y \rightarrow \pi_x^*$ appears to be implicated. Photolyses proceeded to about 85% as determined by loss of the asymmetric stretching frequency absorption at 4.75 μ in the infrared. Carbon dioxide evolved was determined as barium carbonate or by absorption in potassium hydroxide. No correction has been made for the solubility of carbon dioxide in methanol. α -Azidobutyric, α -azidoisobutyric, and α -azidovaleric acids were prepared by the method of M. O. Forster and R. Muller, *J. Chem. Soc.*, 191 (1909). Azidodiphenylacetic acid was prepared by the method of K. Hohenlohe-Oehringen, *Monatsh.*, **89**, 562 (1958).

(5) D. H. R. Barton and L. R. Morgan, Jr., *J. Chem. Soc.*, 622 (1962).

(as the 2,4-DNP), but no acetaldehyde 2,4-DNP could be detected. Photolysis of azidodiphenylacetic acid yielded carbon dioxide in 60% yield. Treatment of the photolysate with 2,4-dinitrophenylhydrazine in acid solution yielded a mixture of benzophenone 2,4-DNP (20%) and benzaldehyde 2,4-DNP (30%). Yields are based on the starting azido acid. Thus, in this system phenyl group migration competes effectively with loss of carbon dioxide. The origin of the benzaldehyde was established by the fact that separate irradiation of benzoylformic acid phenylimine leads to 80% decarboxylation.⁶ Hydrolytic work-up of the photolysate yielded benzaldehyde (45% as the 2,4-DNP) and aniline (60% as benzaniline). Benzaldehyde phenylimine was detected spectroscopically as a product of this photolysis. The photodecarboxylation of azidodiphenylacetic acid probably proceeds *via* a dual mechanism involving both direct loss of carbon dioxide and also phenyl group migration followed by decarboxylation.



A concerted loss of nitrogen and carbon dioxide is possible although not required by the present results. The operational difference between A and B is that A is an intermediate and B is a transition state. If nitrogen and carbon dioxide are lost in the same transition state then a discrete alkyl nitrene such as A need not occur.⁷

Related photolyses of the ethyl esters of the α -azido acids were also carried out. No decarboxylation was observed with the esters; the principal products were α -imino esters and small yields of α -amino esters. Thus ethyl α -azidobutyrate yielded ethyl α -ketobutyrate (25% as the 2,4-DNP from the imine) and ethyl α -azidovalerate yielded ethyl α -ketovalerate imine (25%) along with ethyl (\pm)- α -aminovalerate (5%). No ethyl (\pm)-proline was observed.^{5,8}

The question of whether the photodecarboxylation of α -azido acids bearing an α -hydrogen proceeds *via*

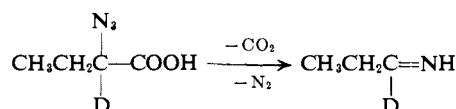
(6) The photochemically induced decarboxylation of N-alkyl- and N-aryl- α -imino acids will be discussed in a separate publication. Irradiation of benzaldehyde phenylimine in 98% sulfuric acid yields phenanthridine (G. M. Badger, C. P. Joshua, and G. E. Lewis, *Tetrahedron Letters*, No. 49, 3711 (1964)).

(7) In methanol solution, the α -azido acids would be expected to be partially dissociated. The question arises whether the conjugate base or undissociated acid is the species which undergoes decarboxylation. However, since photodecarboxylation occurs in benzene solution it is clear that the carboxylate anion is not required. Also, one must recognize the possibility of photosensitization occurring with benzene as solvent. We thank the referees for calling both points to our attention.

(8) Barton and Morgan⁵ have found that photolysis of ethyl (\pm)- α -azidopropionate yielded ethyl pyruvate imine (34%). Kuhn⁹ studied the irradiation of racemic N,N-dimethyl- α -azidopropionamide with dextro and levo circularly polarized light as a model experiment for the formation of optically active compounds *de novo*.

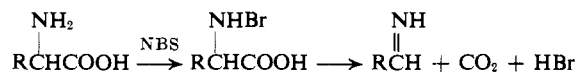
(9) W. Kuhn and E. Knopf, *Z. physik. Chem.*, 7B, 292 (1930); *Naturwiss.*, 18, 183 (1930).

direct loss of carbon dioxide or, alternatively, by photolysis of an intermediary α -imino acid is complicated by the fact that either pathway leads to the same products. The latter route is plausible both on the basis of the observed photodecarboxylation of N-aryl- α -imino acids and also due to the known photochemical decarboxylation reaction of α -keto acid.¹⁰ In order to learn to what extent photodecarboxylation of α -azido acids bearing an α -hydrogen proceeds by direct loss of carbon dioxide, the photolysis of α -deuterio- α -azidobutyric acid¹¹ was studied. The propionaldehyde 2,4-DNP obtained in this photolysis was found to contain 58% deuterium.¹² Nuclear magnetic resonance analysis indicated that the deuterium was at the aldehydic carbon atom. Intermediacy of an α -imino acid requires loss of deuterium in the 1,2-shift from carbon to nitrogen.



The observed result indicates that the direct mechanism is operative at least to the extent of 50%. It is possible that the undeuterated propionaldehyde may result from photodecarboxylation of the α -imino acid; this point is currently under investigation.

Finally, it may be noted that the photodecarboxylation of α -azido acids resembles the bromodecarboxylation reaction observed upon treatment of α -amino acids with N-bromosuccinimide.¹³



(10) P. A. Leermakers and P. A. Vesley, *J. Am. Chem. Soc.*, 85, 3776 (1963).

(11) α -Deuterio- α -azidobutyric acid was synthesized
 $C_2H_5CH(COOH)_2 \rightarrow C_2H_5CBr(COOH)_2 \xrightarrow{D_2O} C_2H_5CBr(COCl)_2 \xrightarrow{\Delta} C_2H_5CDBrCOOD \rightarrow C_2H_5CDBrCOOC_2H_5 \rightarrow C_2H_5CDN_3COOC_2H_5 \rightarrow C_2H_5CDN_3COOH$

(12) Deuterium analysis was performed by J. Nemeth, Urbana, Ill.
 (13) N. Konigsberg, G. Stevenson, and J. M. Luck, *J. Biol. Chem.*, 235, 1341 (1960).

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Evidence for the Conversion of *o,p*-DDT (1,1,1-Trichloro-2-*o*-chlorophenyl-2-*p*-chlorophenylethane) to *p,p'*-DDT (1,1,1-Trichloro-2,2-bis(*p*-chlorophenyl)ethane) in Rats

Sir:

In a recent report¹ it was shown that reductive dechlorination of DDT to DDD (1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethane) occurs in the liver of the rat consuming a diet to which DDT had been added. In these experiments both *ortho,para* and *para,para'* isomers of DDT were fed. It was noted that irrespective of the isomer fed only *p,p'*-DDD was found in

(1) A. K. Klein, E. P. Laug, P. R. Datta, J. O. Watts, and J. T. Chen, *J. Assoc. Offic. Agr. Chemists*, 47, 1129 (1964).