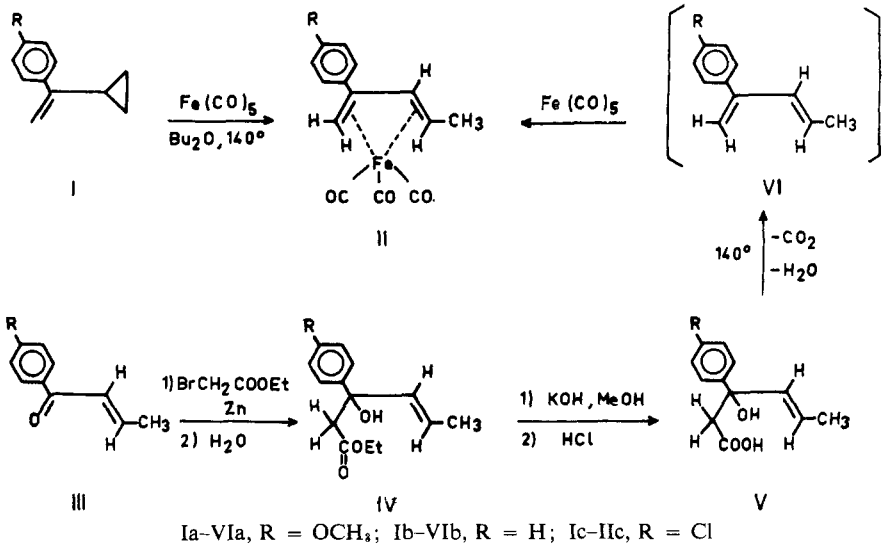
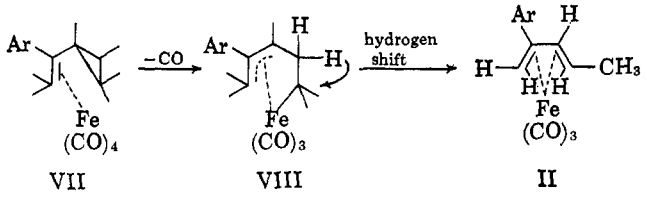
Chart I



Ia–VIa, R = OCH_3; Ib–VIb, R = H; Ic–IIc, R = Cl

conclusive evidence for the structural assignment, but also suggest the possible use of β-hydroxy γ,δ-unsaturated acids as convenient precusors for the formation of diene–iron tricarbonyl complexes in cases where the diene is highly unstable. Examination of the infrared data permits the conclusion that carbonyl bond orders in IIa–IIc vary according to the polar characteristics of substituents at the *para* position in the phenyl group and that the electrons in the whole complex system are considerably delocalized, in harmony with theory.[13]

Chart II



This study shows that vinylcyclopropanes, when properly activated, afford a novel source of four π-electrons suitable for complexing with iron pentacarbonyl. A schematic description for the mechanism of the reaction is given in Chart II. It postulates an initial complexing[14] at the vinyl group, VII, followed by cyclopropane ring opening, to yield a four-electron-donor complex intermediate, VIII, in which the organic moiety is bound to the metal by both a π-allyl and a σ-component. The formation of the final compound, II, involves a hydrogen shift toward the terminal carbon atom, σ-bonded to the metal, to obtain the more stable *trans*-dienic π-complex (VIII → II). Complete discussion of the mechanism will be given in the full paper.

Acknowledgment. We wish to thank Dr. Yuval Shvo of the Department of Organic Chemistry, Weizmann Institute of Science, Rehovoth, for determining the n.m.r. spectra, and to Professor M. Cais for helpful discussions.

Shalom Sarel
Department of Pharmaceutical Chemistry
Raphael Ben-Shoshan, Benjamin Kirson
Department of Inorganic and Analytical Chemistry
The Hebrew University, Jerusalem, Israel
Received January 12, 1965

(13) See D. A. Brown and H. Sloan, *J. Chem. Soc.*, 3849 (1962).

(14) In exclusion of iron pentacarbonyl, the free ligand shows no tendency to undergo isomerization into VI, since quantitative recovery of I could be obtained upon its subjection to comparable reaction conditions.

A New Synthetic Approach to the Penicillins

Sir:

For several years we have been engaged in the investigation of new synthetic routes to the penicillins with the ultimate objective of developing efficient syntheses of known antibiotics in this series and various types of structural analogs.[1] In this communication we describe an approach which has been applied successfully to the formation of simple model structures and which appears to offer considerable promise as a general method of penicillin synthesis.

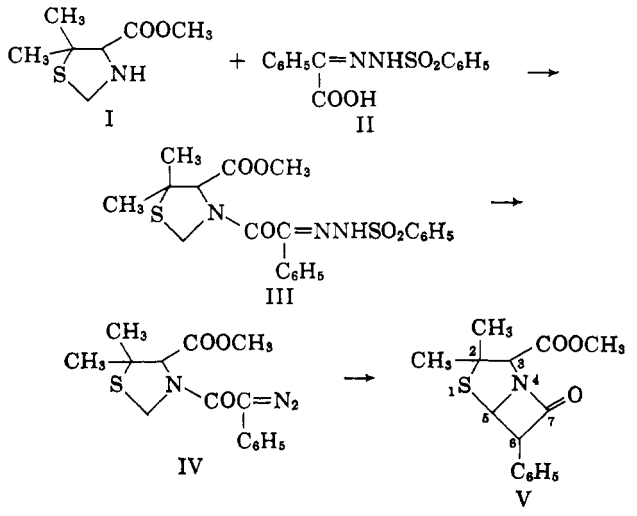
Acylation of *dl*-5,5-dimethyl-4-carbomethoxythiazolidine (I)[2] by the benzenesulfonylhydrazone of benzoylformic acid (II)[3] was carried out using N,N′-dicyclohexylcarbodiimide as reagent to give the ester amide III. Reaction of III with 1 equiv. of sodium hydride in dry 1,2-dimethoxyethane at 60–65° for 15 min. produced the corresponding α-diazo amide (IV) and sodium benzenesulfinate. The diazo compound IV, obtained as a solid foam, manifested infrared absorption (in CCl_4) at 4.82 and 4.83 μ (shoulder) due to the diazo function and at 5.82 and 6.18 μ due to ester and amide carbonyl groups, respectively, and ultraviolet absorption maxima (in ethanol) at 265 mμ (ϵ 11,100), 335 (1500), and 425 (55). Irradiation of the α-diazo amide IV at 10° in methylene chloride solution using a 100-w.

(1) For a recent review of the penicillins including the pioneering synthetic studies of J. C. Sheehan, see F. P. Doyle and J. H. C. Nayler, *Advan. Drug. Res.*, 1, 1 (1964).

(2) H. T. Clark, J. R. Johnson, and R. Robinson, Ed., "Chemistry of Penicillin," Princeton University Press, Princeton, N. J., 1949, p. 958.

(3) Prepared from benzoylformic acid and benzenesulfonylhydrazine in acetic acid. The structures assigned to this and other key intermediates described herein are fully supported by spectroscopic and analytical data.

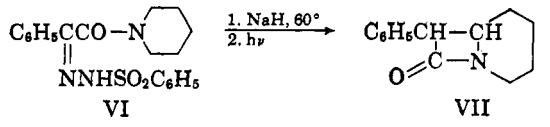
lamp with output mainly at 366 mμ (Westinghouse H38-4GS) led to rapid decomposition with evolution of nitrogen and formation of methyl 6-phenylpenicillanate (V) as the principal product, m.p. 95.0–95.5°, in-



frared peaks (in CCl_4) at 5.62 and 5.7 μ due to β-lactam and ester carbonyls. The molecular weight of the compound as determined by mass spectrometry[4] 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 CCl_4) 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 absorption at 5.72 μ in CCl_4) 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).

Acknowledgment. We thank the National Institutes of Health for generous support of this work.

E. J. Corey and Arthur M. Felix
Department of Chemistry, Harvard University
Cambridge, Massachusetts 02138
Received April 14, 1965

(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.

The Photodecarboxylation of α-Azido Acids[1]

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, photolysis[4] 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, (±)-α-aminovaleric acid was also isolated, but (±)-proline, the product of intramolecular cyclization, was shown to be absent.[5]

In order to learn whether aryl or alkyl group migration to nitrogen[3] 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 $\pi_y \rightarrow \pi_z^*$ ($^1\Sigma g^+ \rightarrow {}^1\Delta_u$) 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 $\pi_y \rightarrow \pi_z^*$ 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).