TABLE I

ACTIVATION ENERGIES FOR CYCLOBUTENE ISOMERIZATIONS

Compd	E_A (kcal/mole)	Ref
1	39	This work
	32.5	*a*
	33	*b*

[a] W. Cooper and W. D. Walters, *J. Am. Chem. Soc.*, **80**, 4220 (1958). [b] See ref 3c.

gated cyclobutenes. Presumably this reflects the conjugated nature of **1**, and the relative instability of **2** compared with more typical butadienes. While the additional ring strain in **1** should work in the opposite direction, it is not surprising that this effect is relatively small.

Experimental Section[7]

A. **2,5-Dimethylhexa-1,3,4-triene** (**2**). **From 1-Methyl-3-isopropylidenecyclobutene.**—Samples of **1** (*ca.* 20 μl) were introduced by syringe into the injector (340°) of an Aerograph A-90-P_2 gas chromatograph. Using a 10-ft Cyanosilicone column maintained at 60°, a single peak (retention time 9.5 min) was observed. This component was trapped in a collector held at Dry Ice–acetone temperature. From 0.285 g of **1** there was obtained 0.151 g of **2**, $n^{25}\text{D}$ 1.4617.

Anal. Calcd for C_8H_{12}: C, 88.82; H, 11.18. Found: C, 88.68; H, 11.20. Spectral properties of **2** are reported in the text.

B. **From 2,5-Dimethylhexa-2,3,4-triene.**—A freshly prepared sample of **3**[1] (100 g) was dissolved in 3 ml of carefully purified and degassed triglyme. Sodium hydride (0.08 g) was added and the suspension stirred under nitrogen for 20 min at 100°. The cooled solution was decanted and examined by glpc showing only one peak with a retention time identical with that of **2** prepared by method A. Preparative glpc of a 0.5-ml aliquot resulted in the collection of 0.009 g of **2** which showed infrared and ultraviolet absorption identical with that of **2** prepared by method A.

Catalytic Reduction of 2.—A sample (0.100 g) of pyrolytically prepared **2** was dissolved in 3 ml of 95% ethanol and hydrogenated for 1 hr in a microapparatus using 0.100 g of 5% Pd–C catalyst. The uptake of hydrogen was 106% of that calculated for three double bonds. The filtered solution was taken up in 10 ml of pentane, washed four times with water, and dried. Most of the pentane was removed through a Vigreux column. Preparative glpc of the residue afforded 0.041 g of 2,5-dimethylhexane, the infrared and nmr spectra of which were identical with those of an authentic sample.

Kinetics of the Pyrolysis.—Carefully washed and dried capillary tubes were filled with dilute (3%) solutions of **1** in carefully purified *n*-hexane. The tubes were cooled, purged with purified nitrogn, and sealed. Pyrolyses were carried out in a thermostated Woods metal bath (±0.3°). For analysis, samples were removed, cooled, opened, and the amount of **1** (relative to *n*-hexane standard) remaining determined by the areas of the relative glpc peaks. The injector and detector of the glpc for analysis were maintained at 120° and the 10-ft cyanosilicone column at 60°, conditions which were shown not to isomerize **1**. Rates obtained from good first-order plots were $k_{200°} = 1.58 \times 10^{-4}\ \text{sec}^{-1}$ and $k_{200°} = 8.60 \times 10^{-4}\ \text{sec}^{-1}$.

Acknowledgment.—This work was supported by a grant from the Petroleum Research Fund administered by the American Chemical Society. We are extremely grateful to Dr. W. H. Sharkey for the sample of **1** which made this study possible.

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[7] The analysis was by Galbraith Laboratories Inc. Infrared spectra were run on a Beckman IR-8, ultraviolet spectra on a Cary 15, and nmr spectra on a Varian A-60 instrument in carbon tetrachloride using TMS as an internal standard.

The Oxidative Decarboxylation of α-Halo Acids by Pyridine N-Oxide. A Degradative Method for Carboxylic Acids[1]

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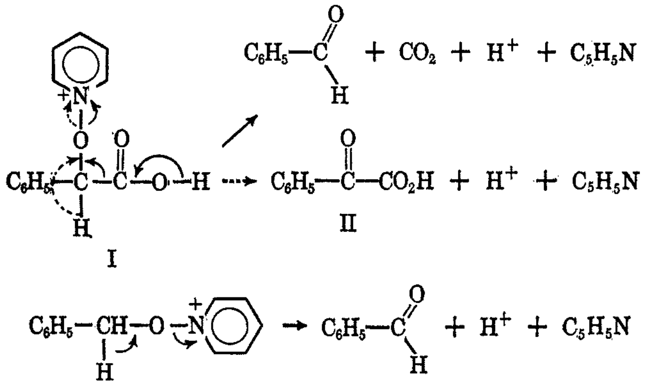
It has been reported that a number of carboxylic acid anhydrides can be oxidatively decarboxylated to aldehydes and ketones by pyridine N-oxide.[2,3] In order to account for the benzaldehyde and the small quantity of phenylglyoxylic acid (II) produced in the oxidative decarboxylation of phenylacetic acid, it was postulated that a key reaction intermediate is the N-(α-carboxybenzyloxy)pyridinium ion (I).[2] The β elimination of a proton and a pyridine nucleus, as shown (dotted arrows) would produce phenylglyoxylic acid. This reaction is directly analogous to the base-promoted decomposition of the N-benzyloxypyridinium ion (III) which produces benzaldehyde.[4] The ion I could also decompose in the carboxylogous[5] fashion (solid arrows) to yield benzaldehyde, carbon dioxide, and the elements of the pyridinium ion.



III

This scheme suggests that the nucleophilic attack of pyridine N-oxide on α-bromophenylacetic acid should produce benzaldehyde and phenylglyoxylic acid *via* the intermediate I. This postulated reaction sequence has in fact been realized. The reaction of excess pyridine N-oxide with α-bromophenylacetic acid in refluxing benzene produces benzaldehyde (49% yield), carbon dioxide (46%), and phenylglyoxylic acid (5%). Pyridine is produced but was not quantitatively determined. In refluxing toluene, the yields are improved to 58%, 58%, and 11%, respectively.

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[1] (a) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research. (b) Taken from the Ph.D. thesis of I. H. Song, University of Pittsburgh, 1966.

[2] T. Cohen, I. H. Song, and J. H. Fager, *Tetrahedron Letters*, 237 (1965).

[3] C. Rüchardt, S. Eichler, and O. Krätz, *ibid.*, 233 (1965); T. Koenig, *ibid.*, 3127 (1965).

[4] W. Feely, W. L. Lehn, and V. Boekelheide, *J. Org. Chem.*, **22**, 1135 (1957).

[5] This convenient term takes cognizance of the fact that for most reactions which involve proton removal there are analogous reactions of the corresponding carboxylic acid which involve loss of both a proton and carbon dioxide. The latter reactions, which are carboxylogs of the former, invariably occur more rapidly.

TABLE I

PRODUCT YIELDS IN REACTIONS OF α-HALO ACIDS WITH PYRIDINE N-OXIDE

α-Halo acids[a]	Solvent	Reaction time, hr	Products	% Yields: Aldehyde or ketone	% Yields: Carbon dioxide
α-Bromophenylacetic[b]	Benzene	6	Benzaldehyde	48.6[c]	46.4
α-Bromophenylacetic[d]	Toluene	8	Benzaldehyde	58.3[c]	57.7
α-Bromobutyric	Benzene	24	Propionaldehyde	45.4[e]	50.5
α-Bromoisobutyric	Xylene	9	Acetone	77.6[e]	100
α-Bromovaleric	Xylene	24	*n*-Butyraldehyde	67.4[e]	84.1
Chloroacetic	Xylene	4	Formaldehyde	65.0[e]	100

[a] Four moles of pyridine N-oxide per mole of acid was used. [b] Yield of phenylglyoxylic acid was 5%. [c] Yield determined by vpc. [d] Yield of phenylglyoxylic acid was 10.6%. [e] Yield determined as the 2,4-dinitrophenylhydrazine derivative.

Other α-halocarboxylic acids are also smoothly oxidatively decarboxylated by pyridine N-oxide. α-Bromobutyric, α-bromoisobutyric, α-bromovaleric, and chloroacetic acids yield propionaldehyde, acetone, *n*-butyraldehyde, and formaldehyde, respectively. The yields and reaction conditions are summarized in Table I.

It is apparent that this type of reaction is quite general. The ready availability of α-halocarboxylic acids *via* the Hell-Volhard-Zelinsky reaction should make this oxidative decarboxylation a useful process. Two obvious applications are the preparation of certain aldehydes and possibly ketones and the systematic degradation of carboxylic acids for purposes of structural identification. The latter procedure would involve α bromination and treatment with pyridine N-oxide. If the product is an aldehyde, it is clear that the carboxylic acid must have had two hydrogen atoms on the α carbon. The aldehyde can be oxidized and the procedure repeated until a ketone is obtained. This would indicate that the last carboxylic acid bears only one α hydrogen. Such a sequence appears considerably simpler than the traditional Barbier-Wieland degradation and should be successful in many cases in which the latter is precluded.

Experimental Section

Oxidation of α-Bromophenylacetic Acid in Refluxing Toluene.—A solution of 10.8 g (50.0 mmoles) of α-bromophenylacetic acid[6] and 20 g (21.0 mmoles) of pyridine N-oxide in 160 ml of anhydrous toluene was heated at reflux under nitrogen for 8.5 hr. The nitrogen stream which had flowed over the reaction mixture was conducted through an ice-water trap, a tube containing Drierite, and finally two tubes in series containing Caroxite (Fisher Scientific Co.) where carbon dioxide was quantitatively absorbed. Most of the gas was evolved during the first 2 hr of the heating period. The total weight of carbon dioxide absorbed was 1.27 g (57.7%).

The cooled reaction mixture, which smelled strongly of pyridine, consisted of a supernatent liquid and a solid, presumably mostly pyridine hydrobromide. Quantitative vpc analysis of an aliquot of the liquid indicated the presence of a 58.3% yield of benzaldehyde. The latter was qualitatively determined by the identity of its vpc retention time and infrared spectrum with those of an authentic sample, by the melting point (156–157°; lit.[7] mp 158°) of its phenylhydrazone, and by its autoxidation to benzoic acid

Phenylglyoxylic acid was quantitatively determined in the following way. A 10-ml aliquot of the original 155 ml of liquid reaction product was extracted with aqueous 10% hydrochloric acid (four 10-ml portions). The combined extract was extracted with ether (four 20-ml portions). To a solution of the oily residue from evaporation of the ether in 10 ml of water was added with stirring 10 ml of an aqueous solution containing 1.3 g of mercuric acetate. The white mercuric salt (0.085 g, 10.6%) of phenylglyoxylic acid, which formed immediately, had mp 165–166° (lit.[8] mp 164°). The mercuric salt of an authentic sample[9] of phenylglyoxylic acid was shown to be formed essentially quantitatively under these conditions. Confirmation of the identity of the phenylglyoxylic acid product was obtained by a comparison of the infrared spectrum of a specimen obtained in a similar way from another aliquot with that of an authentic sample and by preparing a 2,4-dinitrophenylhydrazone (mp 195–196°; lit.[7] mp 196–197°) in the usual way.

Oxidation of α-Bromophenylacetic Acid in Refluxing Benzene.—The procedure was the same as for the above reaction. A solution of 9.50 g (100 mmoles) of pyridine N-oxide and 5.38 g (25.0 mmoles) of α-bromophenylacetic acid in 125 ml of benzene was heated at reflux for 6 hr. Most of the carbon dioxide was given off during the first 4 hr of heating.

The yields were carbon dioxide, 46.4%; benzaldehyde, 48.6%; and phenylglyoxylic acid (as its mercuric salt), 5%.

Oxidation of α-Bromobutyric Acid in Refluxing Benzene.—A solution of 8.35 g (50.0 mmoles) of α-bromobutyric acid and 19.0 g (200 mmoles) of pyridine N-oxide in 150 ml of benzene was heated at reflux for 24 hr.

The propionaldehyde formed in the reaction was carried by the effluent nitrogen stream to a trap containing 125 ml of ice-cold water. The effluent from the trap was dried with Drierite before being passed into the Caroxite tube for carbon dioxide absorption. The yield of carbon dioxide was 50.5%.

At the end of the heating period, the water in the trap was divided into three equal parts. One of these portions was mixed with ethanol (50 ml) and then 150 ml of 2,4-dinitrophenylhydrazine reagent was added. The yield of propionaldehyde as its 2,4-dinitrophenylhydrazone was 45.4%. After recrystallization from ethanol, the derivative had mp 150–152° (lit.[7] mp 154°).

An unsuccessful attempt was made to prepare a 2,4-dinitrophenylhydrazone of α-ketobutyric acid from the acid fraction of the reaction product.

Oxidation of α-Bromovaleric Acid in Refluxing Xylene.—A solution of 9.05 g (50.0 mmoles) of α-bromovaleric acid and 19.0 g (200 mmoles) of pyridine N-oxide in 150 ml of xylene was heated at reflux for 24 hr. The procedure and work-up of the reaction mixture were the same as those for the α-bromobutyric acid reaction, except that the *n*-butyraldehyde formed by the reaction was trapped in an ethanol solution due to its low solubility in water.

The yield of carbon dioxide was 84.1% and that of *n*-butyraldehyde as its 2,4-dinitrophenylhydrazone was 67.4%. After three recrystallizations from ethanol, the derivative had mp 120–122° (lit.[7] mp 122°). The weight of black, hard, water-soluble solid (salt) separated from the reaction mixture was 1.53 g.

Oxidation of α-Bromoisobutyric Acid in Refluxing Xylene.—A solution of 8.35 g (50.0 mmoles) of α-bromoisobutyric acid and 19.0 g (200 mmoles) of pyridine N-oxide in 150 ml of xylene was heated at reflux for 9 hr. The procedure and work-up of the reaction mixture were the same as those for the α-bromobutyric acid reaction.

The yield of carbon dioxide was 100% and that of acetone as its 2,4-dinitrophenylhydrazone was 77.6%. After two recrystallizations from ethanol, the derivative had mp 125.5–126° (lit.[7] mp 126°). The weight of black, water-soluble solid (salt) that separated from the reaction mixture was 9.2 g.

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[6] J. M. Bruce and F. K. Sutcliffe, *J. Chem. Soc.*, 4789 (1957).

[7] R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th ed, John Wiley and Sons, Inc., New York, N. Y., 1956.

[8] M. S. Kharasch and F. W. Staveley, *J. Am. Chem. Soc.*, **45**, 2961 (1923).

[9] K and K Laboratories, Inc., Jamaica, N. Y.

Oxidation of Chloroacetic Acid in Refluxing Xylene.—A solution of 4.73 g (50.0 mmoles) of chloroacetic acid and 19.0 g (200 mmoles) of pyridine N-oxide in 150 ml of xylene was heated at reflux for 3.5 hr. The procedure and work-up of the reaction mixture were the same as those for the α-bromobutyric acid reaction.

The yield of carbon dioxide was 100% and that of formaldehyde as its 2,4-dinitrophenylhydrazone was 65.0%. After three recrystallizations from ethanol, the derivative had mp 160–163° (lit.[7] mp 166°). The weight of black, hard, water-soluble solid (salt) that separated from the reaction mixture was 11.8 g.

Reactions of Phenyl Isothiocyanate with Metal Derivatives of Pyrrole[1]

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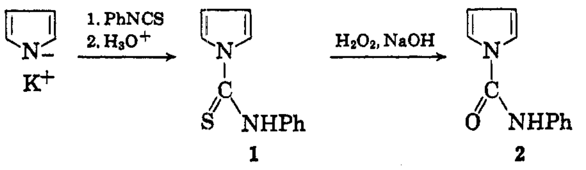
Received May 13, 1966

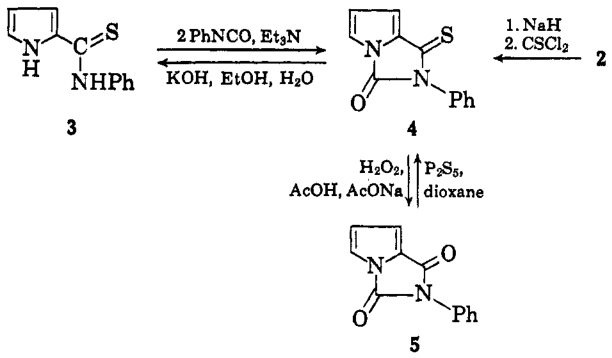
Phenyl isothiocyanate is known to react with aromatic compounds (in the presence of Lewis acids),[3,4] Grignard reagents,[5,6] and alkali metal derivatives of active methylene compounds,[3,6,7] acetylenes,[6] amides,[8] and sulfonamides[6] to form the corresponding thioanilides. With pyrrole and its homologs,[9] 2-pyrrolethiocarbanilides are formed, unless both α positions are occupied. Then reaction occurs at a β position, and when all carbon atoms are occupied, there is no reaction.

In view of the results of reactions of phenyl isocyanate with metal derivatives of pyrrole,[10] a brief investigation was undertaken of similar reactions of phenyl isothiocyanate. Pyrrolylpotassium reacts with phenyl isothiocyanate in tetrahydrofuran to give 1-pyrrolethiocarbanilide (1). Whereas the potassium salt of 1-pyrrolecarboxanilide (2) is hydrolyzed readily,[10] that of 1 is apparently stable in aqueous solution, and precipitation of 1 occurs only after acidification. The structure formulated for 1 is supported by its oxidation to 2 with alkaline hydrogen peroxide.

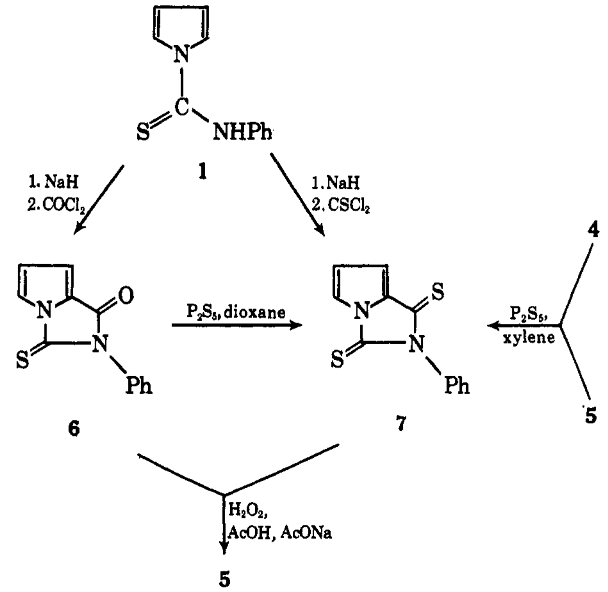


The reaction of pyrrolylmagnesium bromide with phenyl isothiocyanate in ethyl ether yields a mixture of 1- (75%) and 2-pyrrolethiocarbanilide (3) (25%). When tetrahydrofuran is used as the solvent, the results are very similar. A 70:30 mixture of 1- and 2-pyrrolethiocarbanilide is obtained both at room and at reflux temperature.

In the presence of triethylamine, 2-pyrrolethiocarbanilide (3)[9] reacts spontaneously with 2 equiv of phenyl isocyanate to produce 2-phenylpyrrolo[1,2-*c*]-1-thiohydantoin (4) and N,N′-diphenylurea. This reaction takes place much more easily than the corresponding reaction of 2-pyrrolecarboxanilide,[10] and resembles the conversion of enamine thioanilides into thiouracils by the action of phenyl isocyanate.[11] The structure assigned to 4 is confirmed by its oxidation to 2-phenylpyrrolo[1,2-*c*]hydantoin (5)[10] with hydrogen peroxide, and by its formation from 5 by the action of phosphorus pentasulfide. Further, 4 was obtained from the sodium salt of 1-pyrrolecarboxanilide (2) and thiophosgene, and, in small amounts, from the products of the reaction of the potassium and sodium salts of 2-pyrrolethiocarbanilide (3) with phosgene. Finally, alkaline hydrolysis of 4 afforded the expected 3.



Probably because of the lower reactivity of phenyl isothiocyanate toward nucleophiles, as compared with phenyl isocyanate,[3] attempts to cause the former reagent to react with 2-pyrrolecarboxanilide[12] and 2-pyrrolethiocarbanilide, in the presence of triethylamine, did not yield the desired products 6 and 7. Also unsuccessful were attempts to prepare these compounds from thiophosgene and the potassium or sodium salts



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[1] This study was supported by the National Institutes of Health Grant CA 01696-14.

[2] On leave (1965–1966) from the Department of Chemistry of the American University of Beirut, Beirut, Lebanon.

[3] P. A. S. Smith, "The Chemistry of Open-Chain Organic Nitrogen Compounds," Vol. I, W. A. Benjamin, Inc., New York, N. Y., 1965, pp 241–243.

[4] K. K. Ginwala and J. P. Trivedi, *J. Indian Chem. Soc.*, **40**, 897 (1963).

[5] M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall Co., Inc., New York, N. Y., 1954, p 1200.

[6] S. J. Assony, "Organic Sulfur Compounds," Vol. I, N. Kharasch, Ed., Pergamon Press, Inc., New York, N. Y., 1961, pp 332–336.

[7] G. Barnikow and H. Kunzek, *J. Prakt. Chem.*, **29**, 323 (1965).

[8] J. Goerdeler and U. Keuser, *Ber.*, **97**, 3106 (1964).

[9] E. Bullock and R. J. Abraham, *Can. J. Chem.*, **37**, 1391 (1959). The yield of 2-pyrrolethiocarbanilide (3) reported by these authors (3–10%) was improved as described in the Experimental Section.

[10] E. P. Papadopoulos and H. S. Habiby, *J. Org. Chem.*, **31**, 327 (1966).

[11] G. Bianchetti, P. Dalla Croce, and D. Pocar, *Gazz. Chim. Ital.*, **94**, 606 (1964).

[12] A. Treibs and W. Ott, *Ann.*, **577**, 119 (1952).