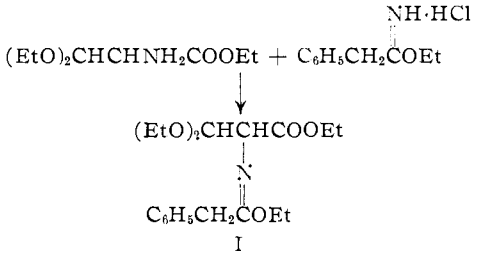

In some runs, phenylacetamide, which can arise from the decomposition of ethyl phenyliminoacetate hydrochloride,[5] was also found in the distillate.

Experimental

Ethyl α-(α′-Ethoxy-β′-phenylethylideneamino)-β,β-diethoxypropionate (I).—In a 500-ml. flask fitted with a Hershberg stirrer were placed 25 g. (0.122 mole) of ethyl β,β-diethoxyalanate[6] and 37 g. (0.175 mole) of ethyl phenyliminoacetate hydrochloride[7] in 200 ml. of ethylene dichloride. The mixture usually became warm at the start and was cooled in an ice-bath. The bath was then removed and stirring continued at room temperature for 24 hours. The ammonium chloride was filtered from the product, the solvent removed under reduced pressure, and the residue fractionated through a 12-cm. Vigreux column; b.p. 125–127° (0.04 mm.), yield 30 g. (70%). The product was a light yellow oil, soluble in ether and insoluble in 10% hydrochloric acid.

Anal. Calcd. for $C_{19}H_{29}O_5N$: N, 3.99; C_2H_5O, 51.28. Found: N (Kjeldahl), 4.01, 3.96, 3.95; C_2H_5O (Zeisel), 51.12, 50.80.

In some runs, small amounts of a white crystalline solid, m.p. 160–161°, codistilled with the product. A mixed melting point with an authentic sample of phenylacetamide showed no depression.

Anal. Calcd. for C_9H_9NO: C, 71.09; H, 6.71; N, 10.36. Found: C, 70.80; H, 6.69; N, 10.41.

(5) S. M. McElvain and B. E. Tate, THIS JOURNAL, **73**, 2233 (1951).

(6) "The Chemistry of Penicillin," Princeton University Press, Princeton, N. J., 1949, p. 512.

(7) S. M. McElvain and C. L. Stevens, THIS JOURNAL, **68**, 1917 (1946).

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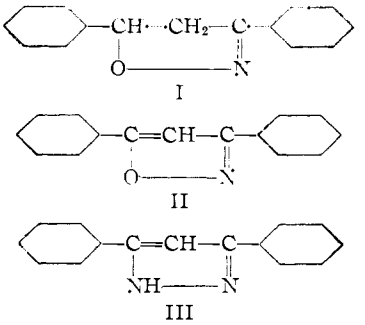
Spectroscopic Evidence for the Structure of Isoxazolines and the Mechanism of their Formation[1,2]

BY R. PERCY BARNES, GLADYS ESTELLE PINKNEY[3] AND GEORGE MCK. PHILLIPS[4]

RECEIVED JULY 31, 1953

In 1931 Blatt[5] showed that isoxazolines gave no methane on treatment with methylmagnesium iodide and on this basis assigned structure I to them. The same year Blatt and Stone[6] showed that isoxazolines derived from substituted chalcones had nitrogen attached to what had been the carbonyl carbon atom of the chalcone.

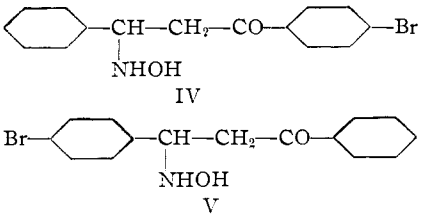


We have now examined the infrared spectra of a number of isoxoazolines, their related isoxazoles, and a pyrazole in the belief that additional information as to the structure of isoxazolines would thereby be obtained.

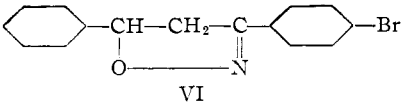
3,5-Diphenyl-, 3-*p*-bromophenyl-5-phenyl-, 3-phenyl-5-*p*-bromophenylisoxazolines and their corresponding isoxazoles all showed strong absorption at 5.8μ, attributable to the –C=N– grouping, but no absorption in the 2–9μ region. In contrast, 3,5-diphenylpyrazole shows absorption at 2.9μ owing to the presence of an –NH– grouping. These findings confirm the assignment of structure I to the isoxazolines, and Barnes and Dodson were in error in assigning to 3-*p*-bromophenyl-5-phenylisoxazoline and the corresponding isoxazole the 3-phenyl-5-*p*-bromophenyl structure.[7]

In recent studies by Barnes and co-worker[8] it was found that chalcones with highly hindered carbonyls such as benzalacetomesitylene do not form isoxazolines but yield substituted hydroxylamines instead. They isolated the substituted hydroxylamine hydrochloride which upon rearrangement and hydrolysis[9] yielded benzylmesitylglyoxal, as Blatt's corresponding methoxy derivatives rearrange and hydrolyze to alpha diketones.

From the isomeric benzal-*p*-bromoacetophenone and *p*-bromobenzalacetophenone we prepared the isomeric hydroxylamino ketones IV and V, respectively, isolating them as their hydrochlorides.



The hydrochlorides of the hydroxylamino ketones IV and V were subjected to treatment with hydroxylamine hydrochloride and excess potassium hydroxide, and they yielded isoxazolines VI and VII, respectively.



(1) This work was supported by a grant from the Research Corporation of New York for the purchase of a Perkin–Elmer 12C infrared spectrometer.

(2) The authors wish to acknowledge the invaluable aid of Mr. Jonas Carroll of the Food and Drug Administration, U. S. Department of Health, Education and Welfare, and the use of their Perkin–Elmer 21 infrared spectrometer.

(3) Research Associate in Chemistry, Howard University, Washington, D. C.

(4) In partial fulfillment of the requirements for the master's degree in chemistry.

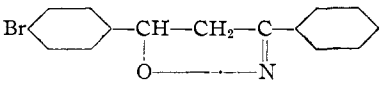
(5) A. H. Blatt, THIS JOURNAL, **53**, 1133 (1931).

(6) A. H. Blatt and J. F. Stone, *ibid.*, **58**, 4180 (1936).

(7) R. P. Barnes and L. M. Dodson, *ibid.*, **67**, 132 (1945).

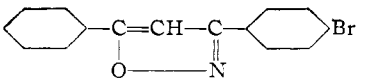
(8) Nancita Robinson, unpublished master's thesis, Department of Chemistry, Howard University, 1949.

(9) A. H. Blatt, THIS JOURNAL, **61**, 3494 (1939).

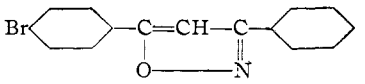


VII

Isoxazolines VI and VII when oxidized with chromic acid yield isoxazoles VIII and IX, respectively.



VIII



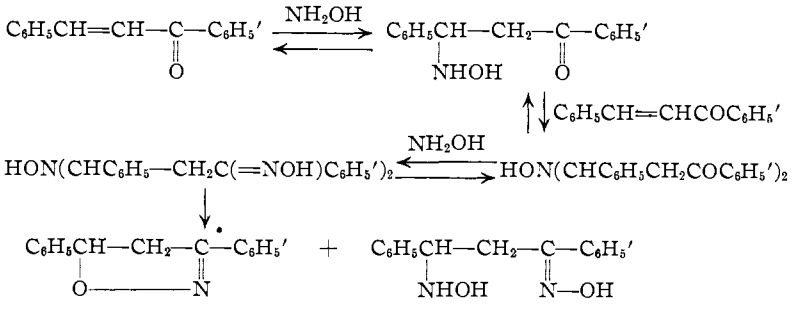
IX

We also studied the behavior of the substituted hydroxylamines IV and V toward Fehling solution. These hydroxylamines IV and V thus yield isoxazoles IX and VIII, respectively.

We prepared the oximinohydroxylamine of v. Auwers and Muller[10] and found that when treated with hydroxylamine hydrochloride and excess alkali it did *not* yield the isoxazaline, but instead yielded the high-melting dioxime as these authors report it behaves in alkaline solution. Thus the hydroxylamines are intermediates in the isoxazoline reaction, but the oximinohydroxylamines are *not*.

Recalling that Blatt[9] synthesized β,β'-methoxyamino-bis-[-β-phenylpropiophenone] by treating β-phenyl-β-methoxyaminopropiophenone with benzalacetophenone in alcoholic solution, we decided to modify the procedure of Auwers and Muller[10] in preparing their bis-compound. Accordingly we used molar quantities of the chalcone and hydroxylamine hydrochloride in slightly excessively basic alcoholic solution, and obtained an almost quantitative pure product. When this bis-compound was subjected to treatment with hydroxylamine hydrochloride in excessively alkaline solution, the isoxazoline was formed in excellent and practically pure yield.

We conclude that isoxazolines are formed according to the following scheme and that the oximinohydroxylamines are by-products of isoxazoline formation



Experimental

1. Preparation of the Substituted Hydroxylamines (IV) and (V).—To 0.02 mole of benzal-*p*-bromoacetophenone and *p*-bromobenzalacetophenone in 130 cc. of methanol in separate containers was added slowly and with stirring 20 cc. of a solution of 4.17 g. (0.06 mole) of hydroxylamine hydrochloride and 3.36 g. (0.06 mole) of potassium hydroxide (the amine hydrochloride and potassium hydroxide were each dissolved in 10 cc. of cold water and mixed). The temperature of the reaction mixture was maintained at 60–63°. The mixture was allowed to stand at room temperature for six hours. An equal volume of ether was added and portions of 500 cc. of 1 *N* hydrochloride acid added until the precipitate which was formed redissolved. The mixture was placed in a separatory funnel and the ether layer discarded. The water layer was poured into the remainder of the acidic solution. The solutions were chilled overnight, filtered and washed with small amounts of ether.

Benzal-*p*-bromoacetophenone gave a colorless substance IV melting at 135°. The other chalcone gave a colorless material (V) melting at 145°.

Anal. Calcd. for $C_{15}H_{15}O_2BrCl$: C, 50.4; H, 4.20. Found: IV, C, 50.3; H, 4.17; V, C, 50.59; H, 4.65.

The hydrochlorides of IV and V were treated with hydroxylamine hydrochloride and alkali resulting in the formation of isoxazolines VI and VII, respectively. These isoxazolines mix-melted sharply at 138–139° and 130–131°, respectively, with those obtained directly from benzal-*p*-bromoacetophenone and *p*-bromobenzalacetophenone. They showed strong absorption at 5.85 μ in 0.01 *M* solution in dioxane.

2. Preparation of Isoxazoles IX and VIII from Hydroxylamine Hydrochlorides IV and V.—To 2 g. of the substituted hydroxylamine hydrochlorides IV and V, suspended in small amounts of water, was added slowly and with warming Fehling solution until the blue color persisted. The suspensions were filtered and recrystallized from methanol. The hydroxylamine hydrochloride IV yielded isoxazole IX, and the hydroxylamine hydrochloride V yielded isoxazole VIII, identified by mixed-melting point with the isoxazoles obtained from the oxidation of the isoxazolines VII and VI, respectively, and confirmed by conversion into their respective isoxazolium–ferric chloride salts.[11] These isoxazoles show strong absorption at 5.85 μ in 0.01 *M* solution in dioxane.

3. Preparation of β,β'-Hydroxylamino-bis-[β-phenylpropiophenone].—To a solution of 2.1 g. (1.5 moles) of potassium hydroxide in 100 cc. of methanol was added 1.8 g. (1.0 mole) of hydroxylamine hydrochloride dissolved in 3 cc. of water. When the reaction was complete, this solution was filtered slowly onto 10.4 g. (2 moles) of dry finely crystalline benzalacetophenone, and the potassium chloride on the filter was washed with 10 cc. of methanol. The chalcone dissolved. After standing for 16 hours at room temperature, the contents of the flask appeared to be a solid mass of fine colorless filmy needles arranged in definite star-like patterns. The material was filtered, washed with cold methanol and dried. This crop melted sharply at 190° and weighed 5.0 g. Upon concentrating the filtrate by applying suction, 3.5 g. more of the 190° material was obtained.

4. Conversion of β,β'-Hydroxylamino-bis-[β-phenylpropiophenone] to 3,5-Diphenylisoxazoline.—To a suspension of 2.25 g. (1.0 mole) of the bis-compound in 50 cc. of methanol was added 0.70 g. (2.0 moles) of hydroxylamine hydrochloride dissolved in 3 cc. of water. This addition was followed immediately by the addition of 0.85 g. (3.0 moles) of potassium hydroxide dissolved in 3 cc. of water. The suspension was refluxed for one hour. This bis-compound slowly dissolved with the production of a pale yellow solution. The solution was concentrated to small volume by evaporation, and diluted slowly with water. On chilling, colorless crystals separated. The solid was filtered, washed with dilute aqueous methanol and finally recrystallized from methanol, yielding 3,5-diphenylisoxazoline, identified by mix-melting at 75° with an authentic sample. The aqueous alkaline alcoholic mother liquor upon neutralization with dilute hydrochloric acid gave a white precipitate which, when dried and recrystallized from ben-

(10) K. von Auwers and H. Muller, *J. prakt. Chem.*, **137**, 57 (1933).

(11) A. H. Blatt, THIS JOURNAL, **71**, 1861 (1949).

zene, gave a colorless solid which, melting and mix-melting with an authentic sample at 147°, proved to be the oximinohydroxylamino compound of Auwers and Muller.[10] 3,5-Diphenylisoxazoline shows strong absorption at 5.85 μ in 0.01 M solution in dioxane.

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The Synthesis of Dimethyl β-(Carboxymethoxy)-propionate

BY WARREN J. BREHM[1] AND THEODORE LEVENSON

RECEIVED JULY 31, 1953

In connection with another problem we had need of the dimethyl ester of β-(carboxymethoxy)-propionic acid. While this material was known, the reported[2,3] syntheses were inconvenient for our purposes and an improved synthesis was sought.

Attempts to cyanoethylate glycolonitrile or to add methyl glycolate to methyl acrylate according to the procedures of Hansley[4] or Woodward and Eastman[5] were failures. The desired ester was obtained in small yield through the diazoketone rearrangement applied to the half methyl ester acid chloride of diglycolic acid. However, the reaction of methyl glycolate with β-propiolactone[6] is to be considered the preferred method of synthesis.

Experimental

α-(Carbomethoxymethoxy)-acetyl Chloride.—Following the procedure of Anschütz and Jaeger[7] diglycolic acid was converted into its half methyl ester and, with an excess of thionyl chloride, into the desired product, b.p. 104–108° (11 mm.) (78% yield based on diglycolic acid).

α-(Carbomethoxymethoxy)-α-diazoacetone.—A solution of 10 g. of α-(carbomethoxymethoxy)-acetyl chloride in 100 ml. of anhydrous ether was slowly dropped into a cold stirred solution of excess diazomethane in ether. After standing overnight at room temperature protected from atmospheric moisture the ether was removed from the reaction mixture *in vacuo*. The residual yellow oil crystallized on standing. A portion melted at 35° after recrystallization from carbon tetrachloride–petroleum ether.

Dimethyl β-(Carboxymethoxy)-propionate.—The main portion of the crude diazoketone was dissolved in 125 ml. of methanol and 2.0 g. of freshly prepared silver oxide was added. The suspension was stirred mechanically and heated under reflux for about one hour until evolution of nitrogen ceased. The gases evolved had a strong "acrylate" odor. Using charcoal and Hiflo Supercel the mixture was filtered and the filtrate fractionated *in vacuo*. After removing methanol the high boiling material was separated into two fractions. The first, b.p. under 30° (0.2 mm.), 1.2 g., was methyl glycolate and gave glycolamide, m.p. 117–119°, on treatment with ammonia. The second, b.p. 40–87° (1.5 mm.), 2.3 g., was redistilled to give 1.1 g. of product, b.p. 87° (1.5 mm.). With ammonia this gave a solid, m.p. 175.5–177.5°, identical with authentic diamide of β-(carboxymethoxy)-propionic acid, and is considered to be dimethyl β-(carboxymethoxy)-propionate.

β-(Carbomethoxymethoxy)-propionic Acid.—A mixture of 17.3 g. (0.24 mole) of β-propiolactone and 50.0 g. (0.55 mole) of methyl glycolate was kept at 80° for 72 hours. At this time, titration of an aliquot with standard thiosulfate indicated that 90% of the β-propiolactone had been consumed. Fractionation gave 35 g., b.p. 47° (9 mm.), of unreacted methyl glycolate. There was also isolated 16 g., b.p. 129–131° (0.6 mm.) (41% of theory), of material with a neutral equivalent of 174 (theory is 162 indicating 93% purity). Redistillation of the second fraction gave an analytical sample, b.p. 138° (1.5 mm.).

Anal. Calcd. for $C_6H_{10}O_5$: C, 44.4; H, 6.17. Found: C, 45.2, 45.5; H, 6.37, 6.53.

Dimethyl β-(Carboxymethoxy)-propionate.—Esterification of the half ester with diazomethane gave an 88% yield of material, b.p. 82–83° (0.8 mm.).

Anal. Calcd. for $C_7H_{12}O_5$: C, 47.7; H, 6.87. Found: C, 47.9; H, 6.89.

The **diamide**, prepared by saturating a methanol solution of the diester with ammonia, was a white solid, m.p. 174–176°. Baker[3] reports m.p. 174° for this compound.

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(1) Polychemicals Department, E. I. du Pont de Nemours & Co., Inc., Wilmington, Del.

(2) W. Borsche and K. Thiele, *Ber.*, **56B**, 2012 (1923).

(3) J. W. Baker, *J. Chem. Soc.*, 296 (1944).

(4) V. L. Hansley, U. S. Patent 2,333,782.

(5) R. B. Woodward and R. H. Eastman, THIS JOURNAL, **68**, 2229 (1946).

(6) T. L. Gresham, J. E. Jansen, F. W. Shaver, J. T. Gregory and W. L. Bears, *ibid.*, **70**, 1004 (1948).

(7) R. Anschütz and S. Jaeger, *Ber.*, **55B**, 670 (1922).

Cleavage of Hexaphenyldisilane by Sodium and Lithium

BY A. G. BROOK AND HENRY GILMAN

RECEIVED JULY 6, 1953

The solvent for the preparation of triphenylsilylpotassium in this Laboratory has until recently been restricted to diethyl ether. In this medium, the triphenylsilylpotassium, derived by cleavage of hexaphenyldisilane with sodium–potassium alloy,[1] is an almost completely insoluble yellow-brown solid.

Recent studies of other organometallic systems[2] have indicated that ethylene glycol dimethyl ether is an excellent solvent for these reactions and consequently tests using this solvent as a medium were carried out with the triphenylsilylpotassium preparation.

We have found that hexaphenyldisilane is readily cleaved by sodium–potassium alloy in ethylene glycol dimethyl ether and further that the triphenylsilylpotassium formed is soluble in this solvent, a marked advantage over the suspensions obtained in diethyl ether. However not only is hexaphenyldisilane cleaved by sodium–potassium alloy in this ether, but it is also readily cleaved by sodium and by lithium. These cleavages are the first reported successful cleavages of the silicon–silicon bond by these metals.[3] Attempts to cleave hexaphenyldisilane with magnesium in this solvent have been made, but have not been successful as yet.

The cleavages of hexaphenyldisilane with sodium–potassium alloy and with lithium occur quite rapidly and are complete in a period of 2–4 hours, as indicated by the absence of any undissolved material. With sodium the reaction is much slower, due to the lumping of the metal. All the

$$(C_6H_5)_3Si\text{–}Si(C_6H_5)_3 \xrightarrow{Li} (C_6H_5)_3SiLi \xrightarrow{(CH_3)_3SiCl} (C_6H_5)_3Si\text{–}Si(CH_3)_3$$

(1) H. Gilman, T. C. Wu, H. A. Hartzfeld, G. A. Guter, J. J. Goodman and S. H. Eidt, THIS JOURNAL, **74**, 561 (1952).

(2) A. G. Brook, H. L. Cohen and G. F. Wright, *J. Org. Chem.*, **18**, 447 (1953); N. D. Scott, J. F. Walker and V. L. Hansley, THIS JOURNAL, **58**, 2442 (1936).

(3) H. Gilman and T. C. Wu, *ibid.*, **73**, 4031 (1951); H. Gilman and T. C. Wu, *J. Org. Chem.*, **18**, 753 (1953).