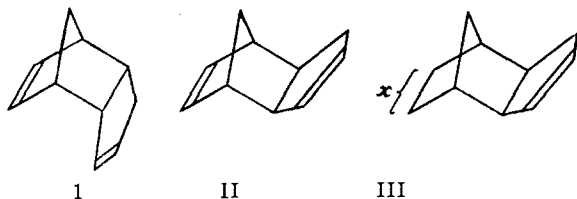


NOTES

exo-Dicyclopentadiene

BY PAUL D. BARTLETT AND IRVING S. GOLDSTEIN

It was discovered by Bruson and Riener¹ that ordinary dicyclopentadiene (I) on addition of hydrogen chloride and other reagents is converted by rearrangement into a set of products (III) later shown² to be derived from the *exo*-isomer of dicyclopentadiene (II). The presence of this isomer in heated dicyclopentadiene was established by Alder and Stein,³ who characterized it by means of its phenyl azide derivative and established its configuration by relating it to the well-studied isomers of the addition product of maleic anhydride to cyclopentadiene.



The isolation of *exo*-dicyclopentadiene, however, was not successfully accomplished. It was of interest to us to isolate this missing member of the series, in view of the great availability of its isomer and of the many hundreds of its derivatives made available by the method of Bruson and Riener.

exo-Dicyclopentadiene (II) was obtained in 57% yield by the reaction of alcoholic potassium hydroxide with the product of addition of hydrogen iodide to *endo*-dicyclopentadiene. The product boils at 170–172° at 763 mm. and at 51–53° under 12 mm. pressure. It has d_{20} 0.977 and n_D^{25} 1.5070. It does not solidify at 0°. It adds hydrogen chloride and (in the presence of sulfuric acid) water, less cleanly than the *endo*-isomer, yielding the same product as the *endo*-isomer in each case. It reacts with phenyl azide, apparently more vigorously than the *endo*-isomer, to yield a derivative melting at 123–124°.

Experimental

Iodo-dihydro-*exo*-dicyclopentadiene¹ was obtained in a yield of 97 g. (44%) from six hours of stirring on the steam-bath of 110 g. of ordinary (*endo*) dicyclopentadiene with 227 g. of 47% hydriodic acid. The product was distilled at 8–9 mm. and the fraction boiling from 120–130° was taken.

exo-Dicyclopentadiene.—To 97 g. of iodo-dihydro-*exo*-dicyclopentadiene was added a solution of 50 g. of potassium hydroxide in 200 cc. of 95% ethyl alcohol. The mixture was heated under reflux on a steam-bath for twenty-

four hours, then diluted with water and extracted with ether. The ether extract was dried with calcium chloride and distilled, yielding a fraction of 28.5 g. (57% yield) boiling at 43–46° under 6–7 mm. pressure. On redistillation the fraction boiling at 51–53° at 12 mm. was retained. This boiled under atmospheric pressure (763 mm.) at 170–172° and did not solidify at 0°. It decolorized bromine water and permanganate solution. It had n_D^{25} 1.5070 and d_{20} 0.977. The original distillation, continued at 5 mm., yielded 16.5 g. of a light yellow oil boiling from 95 to 101° and having an odor like that of hydroxydihydro-*exo*-dicyclopentadiene.

Reaction of *exo*-Dicyclopentadiene with Sulfuric Acid.—Five grams of *exo*-dicyclopentadiene and 15 g. of 25% sulfuric acid were heated on the steam-bath with stirring for five hours. After dilution, extraction with ether, washing with alkali, drying, and distillation there was recovered about 2 g. of starting material and 2 cc. of a colorless viscous oil with a very sweet odor. This product yielded a phenylurethan which, after recrystallization from alcohol, melted at 163–165° alone and at 162–165° when mixed with the phenylurethan of authentic hydroxydihydro-*exo*-dicyclopentadiene.

Reaction with Hydrochloric Acid.—Five grams of the *exo*-dicyclopentadiene and 10 cc. of 37% hydrochloric acid were stirred for five hours on the steam-bath. The mixture turned black. The ether extract was washed with alkali, dried, and distilled, yielding almost 5 cc. of a colorless oil boiling under 10 mm. pressure at 96–98° and having n_D^{25} 1.5206. Chlorodihydro-*exo*-dicyclopentadiene¹ boils under 12 mm. pressure at 100–102°, with n_D^{25} 1.5208. The compound gave slight precipitation of potassium chloride after a day on the steam-bath with alcoholic potassium hydroxide.

Reactions of *exo*- and *endo*-Dicyclopentadienes with Phenyl Azide.—To a 3-g. sample of *exo*-dicyclopentadiene and a similar sample of the *endo* isomer, 2 cc. of phenyl azide was added. After a few minutes the solutions grew warm, the warming being more marked with the *exo* than with the *endo* form. The reaction was moderated by surrounding with water. After standing overnight the flasks both contained crystal cakes. After three recrystallizations from ethanol, in which the *exo* derivative was the more soluble of the two, and decolorization with charcoal, the phenyl azide derivative of the *endo* isomer was obtained as white needles melting at 128–129° and that of the *exo* isomer as white prisms melting at 123–124°. The mixture of the two melted at 95–105°. Alder and Stein³ report the melting points of both the *endo* and *exo* derivatives as 127–128°.

In a second preparation of the *exo* derivative it was obtained in a yield of 80.6% from *exo*-dicyclopentadiene.

Anal. Calcd. for $C_{10}H_{17}N_3$: C, 76.46; H, 6.82. Found: C, 76.15; H, 6.48.

CONVERSE MEMORIAL LABORATORY
HARVARD UNIVERSITY

CAMBRIDGE 38, MASSACHUSETTS RECEIVED JUNE 10, 1947

The Synthesis of Some New Pteridines

BY GERTRUDE B. ELION AND GEORGE H. HITCHINGS

The condensation of 4,5-diaminopyrimidines with di-carbonyl reagents, such as diketones,¹ dicarboxylic acids² and α -keto-esters³ are known

(1) Bruson and Riener, *THIS JOURNAL*, **67**, 723, 1178 (1945).
(2) Bartlett and Schneider, *ibid.*, **68**, 6 (1946); Bruson and Riener, *ibid.*, **68**, 8 (1946).
(3) Alder and Stein, *Ann.*, **594**, 219 (1933).

(1) Kuhn and Cook, *Ber.*, **70**, 761 (1937).
(2) Purrmann, *Ann.*, **544**, 182 (1940).
(3) Purrmann, *ibid.*, **548**, 284 (1941).

methods for the synthesis of pteridines. Oxomalonate ester condenses with 2,4,5-triamino-6-hydroxypyrimidine to form isoxanthopterin-6-carboxylic acid and xanthopterin-7-carboxylic acid. In *N* acetic acid the former isomer is obtained in 85% yield; in 2 *N* sulfuric acid the yield of this isomer is only 29% and, in addition, 42% of xanthopterin-7-carboxylic acid is formed.³

Both 6-methylisoxanthopterin and 7-methylxanthopterin have now been prepared by condensing 2,4,5-triamino-6-hydroxypyrimidine with pyruvic acid. The formation of the xanthopterin derivative is favored both in 2 *N* sulfuric acid and in dilute acetic acid; the isoxanthopterin derivative is formed in poor yield only during the condensation in acetic acid. The two isomers are separable by their different solubilities in hot 2 *N* hydrochloric acid and are distinguishable by their ultraviolet absorption spectra.

A new pyrimidine, 2-mercapto-4,5-diaminopyrimidine, was synthesized and used as an intermediate in the preparation of 2-mercaptopteridine. Isay⁴ attempted to reduce 2-chloro-4-amino-5-nitropyrimidine with hydrogen sulfide without success. However, it was found that an excess of potassium hydrosulfide reduces the nitro group and simultaneously replaces the chlorine by a sulfhydryl group. The 2-mercapto-4,5-diaminopyrimidine was condensed with glyoxal to give 2-mercaptopteridine.

2-Mercapto-4,6,7-trihydroxypteridine was synthesized by the condensation of 2-mercapto-4,5-diamino-6-hydroxypyrimidine with oxalic acid. Both mercaptopteridine derivatives were found by analysis to contain water of crystallization which is not lost at 140°. Water of crystallization which is not lost on heating is not uncommon among purine derivatives (*e. g.*, refs. 5, 9). Since the physical properties and ultraviolet absorption spectra of the mercapto compounds are consistent with the pteridine structure and differ from those of substituted pyrimidines one is justified in assuming closure of the pyrazine ring to have occurred.

Experimental

7-Methylxanthopterin.—Two and one-half grams of 2,4,5-triamino-6-hydroxypyrimidine sulfate monohydrate⁷ and 2 g. of pyruvic acid were boiled in 200 ml. of 2 *N* sulfuric acid for one hour, cooled and the undissolved crystalline material filtered off (0.55 g.). The filtrate was heated to 90° and brought to about pH 6. The orange-brown precipitate was recrystallized twice by solution in 250 parts of hot 2 *N* hydrochloric acid, treatment with carbon and neutralization with ammonium hydroxide. On slow cooling, bunches of microscopic orange-brown crystals were formed; yield, 1.48 g. (75.8%). The compound does not melt and is insoluble in organic solvents and in hot water. The crystals contain one-half mole of water of crystallization, which is lost at 130°.

Anal. Calcd. for $C_7H_7N_5O_2 \cdot \frac{1}{2}H_2O$: C, 41.58; H, 3.96; H_2O , 4.45. Found: C, 42.07; H, 4.14; H_2O , 4.49.

(4) Isay, *Ber.*, **39**, 250 (1906).

(5) Fischer, *ibid.*, **30**, 2246 (1897).

(6) Kenner, Lythgoe and Todd, *J. Chem. Soc.*, 656 (1944).

(7) Traube and Dudley, *Ber.*, **46**, 3839 (1913).

6-Methylisoxanthopterin.—Two and one-half grams of 2,4,5-triamino-6-hydroxypyrimidine were dissolved in 200 ml. of hot 5% aqueous acetic acid containing 2 ml. of pyruvic acid. The solution was brought to a boil and then permitted to stand at room temperature for several hours. A copious orange precipitate began to form in a few minutes. After standing overnight at 10°, the precipitate was filtered off, washed with water and alcohol and dried *in vacuo*. The crude product (2.38 g.) was dissolved in 150 ml. of 0.25 *N* sodium hydroxide solution, treated with carbon and filtered into 250 cc. of boiling 2 *N* hydrochloric acid. A light-colored amorphous precipitate formed, leaving an orange-colored supernatant liquid. Re-solution and precipitation in the same way resulted in a pale pink product, weighing 0.35 g. (10%), and having no melting point. This compound closely resembles isoxanthopterin in color and insolubility in hot mineral acids.

Anal. Calcd. for $C_7H_7N_5O_2$: C, 43.52; H, 3.63. Found: C, 43.42; H, 3.35.

By neutralization of the orange-colored acidic filtrates from the purification of 6-methylisoxanthopterin, 1.43 g. (42%) of 7-methylxanthopterin was obtained.

2-Mercapto-4,5-diaminopyrimidine.—A mixture of 5 g. of 2-chloro-4-amino-5-nitropyrimidine⁴ and 150 ml. of *N* potassium hydrosulfide solution was heated on the steam-bath for two and one-half hours. The solution was filtered hot to remove a small amount of sulfur and the filtrate was acidified with acetic acid. The crude yellow precipitate was recrystallized from 700 ml. of hot water. After cooling, fluffy yellow needles formed slowly (1.9 g.). Evaporation of the mother liquors to 200 ml. yielded another 0.65 g. of product. Recrystallization from 250 parts of hot water, using carbon, gave white needles, darkening at 230° and decomposing at 250°.

Anal. Calcd. for $C_4H_6N_4S$: C, 33.80; H, 4.22. Found: C, 33.84; H, 4.27.

2-Mercaptopteridine.—A solution of 1.42 g. of 2-mercapto-4,5-diaminopyrimidine in 400 ml. of hot water and 1 g. of glyoxal (as 35% commercial solution) was boiled for fifteen minutes; orange prisms precipitated on cooling. After recrystallization from 400 ml. of water, the yield was 0.95 g. (52%), dec. 200°–205°. The product crystallizes with 1 mole of water, which is not lost at 140° after four hours.

Anal. Calcd. for $C_6H_4N_4S \cdot H_2O$: C, 39.60; H, 3.26. Found: C, 39.61; H, 3.23.

2-Mercapto-4,6,7-trihydroxypteridine.—A finely divided mixture of 0.5 g. of 2-mercapto-4,5-diamino-6-hydroxypyrimidine⁸ and 2.5 g. of oxalic acid was heated to 140°. A slight vacuum was applied and the temperature was raised gradually to 260°, where it was maintained for ten minutes. The reaction mixture was dissolved in 85 ml. of 0.3 *N* sodium hydroxide solution, treated with carbon and filtered into 50 ml. of hot 2 *N* hydrochloric acid. The yellow precipitate was recrystallized by the same procedure. Yield was 0.4 g. (60%). The compound crystallizes with 1 mole of water, which is not lost at 140° after eight hours; it has no melting point.

Anal. Calcd. for $C_8H_4N_4O_8S \cdot H_2O$: C, 31.30; H, 2.60. Found: C, 31.51; H, 2.64.

Ultraviolet Absorption Spectra.—The spectra of the new pteridines were determined in 0.1 *N* hydrochloric acid

TABLE I

Compound	ULTRAVIOLET ABSORPTION MAXIMA AT pH 1.0	
	Absorption maxima in Å.	
Xanthopterin	2300, 2600	3520
7-Methylxanthopterin	2320, 2700	3580
Isoxanthopterin		2880 3420
6-Methylisoxanthopterin		2900 3360
2-Mercaptopteridine		2700 3150
2-Mercapto-4,6,7-trihydroxypteridine		2400 3140

(8) Traube, *Ann.*, **331**, 64 (1904).

with the Beckmann spectrophotometer. The absorption maxima are given in Table I, together with those of xanthopterin and isoxanthopterin determined in the same way.

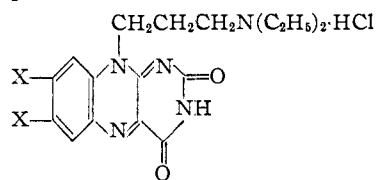
The authors wish to express their gratitude to Mr. Samuel W. Blackman for the microanalyses recorded here.

THE WELLCOME RESEARCH LABORATORIES
TUCKAHOE 7, NEW YORK RECEIVED JUNE 14, 1947

Basically-substituted Isoalloxazines

BY HOWARD BURKETT

The structural similarity of atebtrin to riboflavin suggested the synthesis of basically-substituted isoalloxazine derivatives, such as I, II and III, as possible antimalarials.



I, X = CH₃—
II, X = CH₃O—
III, X = Cl—

After this work was begun, other series of compounds very closely related to these were reported.^{1,2,3} As a result the preparation of related compounds which had been planned was not carried out. The synthesis of compound III was attempted using a procedure similar to that employed for I and II and also according to the method of Kuhn and Weygand,⁴ in which acetic acid served as the solvent and boric acid as the catalyst. That the product in very dilute solution gave a yellow-green fluorescence, typical of isoalloxazines, would indicate that the desired product was present, but the analyses indicated considerable contamination and cast some doubt that the expected compound was obtained. Consequently, this product was not submitted for biological testing and it is not reported in this note.

Compounds I and II were devoid of antimalarial activity, when tested on ducks infected with *Plasmodium lophuræ*.

The author thanks Dr. K. K. Chen and Dr. C. L. Rose of Eli Lilly and Company for the pharmacological tests, Mr. Howard Hunter also of Eli Lilly and Company for the microanalyses and Eli Lilly and Company for financial assistance.

Experimental

7,8-Dimethoxy-10-(γ -diethylaminopropyl)-isoalloxazine Hydrochloride.—Four grams of 4,5-dinitroveratrole⁵ was mixed with 4 ml. of γ -diethylaminopropylamine and 5 ml. of ethanol. After the mixture had refluxed for twenty hours, it was poured into water and acidified with hydrochloric acid. This solution was extracted with ether. The aqueous solution was made basic with sodium hydroxide and extracted with ether. The ethereal solution was dried over anhydrous magnesium sulfate, filtered and

saturated with anhydrous hydrogen chloride, forming an oily precipitate of crude 4-nitro-5-(γ -diethylaminopropylamino)-veratrole hydrochloride,⁶ which could not be made to crystallize. The hydrobromide, sulfate and free-base could not be obtained in solid form and the base could not be distilled. Consequently, the oily hydrochloride was dissolved in 40 ml. of methanol and hydrogenated at atmospheric pressure and room temperature, using 0.10 g. of Adams platinum oxide catalyst. After the catalyst had been removed by filtration, the methanol was evaporated under reduced pressure with slight warming. Twenty milliliters of methanol was added and again evaporated. Ether was added to the residue and the mixture was saturated with anhydrous hydrogen chloride. After the ether had been decanted, the oil which remained was dissolved in 40 ml. of boiling methanol and 2.5 g. of alloxan monohydrate in 15 ml. of methanol was added. After refluxing for thirty minutes, the mixture was cooled and filtered. Recrystallization of the yellow solid from a water-acetone solution gave 1.04 g. (13.1%) of product melting at 220–222° with decomposition.

Anal. Calcd. for C₁₉H₂₆N₆O₄·HCl·2H₂O: C, 49.70; H, 6.58; N, 15.25. Found: C, 49.76; H, 6.22; N, 15.70.

4-Nitro-5-(γ -diethylaminopropylamino)-*o*-xylene.

Three grams of 4,5-dinitro-*o*-xylene,⁷ 4 ml. of γ -diethylaminopropylamine and 8 ml. of ethanol were refluxed on the steam-bath for four days. The reaction mixture was cooled, poured into water, acidified with concentrated hydrochloric acid and extracted with ether. In a short time, as the dissolved ether evaporated spontaneously from the aqueous solution, yellow needles precipitated. Filtering and washing with a small amount of water yielded 2.89 g. of product melting at 211–212.5°.

Anal. Calcd. for C₁₅H₂₅N₃O₂: C, 57.00; H, 7.99; N, 13.33. Found: C, 56.73; H, 8.03; N, 13.17.

Evaporation of the filtrate to two-thirds of its original volume and cooling yielded an additional 0.4 g. of slightly less pure product, making the total yield 3.29 g. (77%).

7,8-Dimethyl-10-(γ -diethylaminopropyl)-isoalloxazine Hydrochloride.—Treatment of the 4-nitro-5-(γ -diethylaminopropylamino)-*o*-xylene in the same way as the 4-nitro-5-(γ -diethylaminopropylamino)-veratrole hydrochloride was treated above, yielded 37.5% of a yellow, crystalline product melting at 289–289.5° with decomposition.

Anal. Calcd. for C₁₉H₂₆N₆O₂·HCl·2.5H₂O: C, 52.20; H, 6.86; N, 16.01. Found: C, 52.26; H, 6.66; N, 16.23.

(6) The procedure for the synthesis of this compound has been discussed by Parijs, *Rec. trav. chim.*, **49**, 45 (1930), and by Kipnis, Weiner and Spoerri, *THIS JOURNAL*, **66**, 1446 (1944). The latter authors give other references to applications of this reaction.

(7) Prepared according to the method of Crossley and Renouf, *J. Chem. Soc.*, **95**, 212 (1909).

DEPARTMENT OF CHEMISTRY
DEPAUW UNIVERSITY
GREENCASTLE, INDIANA

RECEIVED MAY 7, 1947

The Reduction of Allylic Quaternary Ammonium Bromides

BY DAVID R. HOWTON

In connection with other work, we have studied the reduction of 2-cyclohexenyltrimethylammonium bromide (I). The catalytic hydrogenation of I at room temperature and atmospheric pressure over Adams platinum, Raney nickel, palladium-on-barium-sulfate, or palladium-on-charcoal proceeds with the uptake of more than one molecular equivalent of hydrogen and the forma-

(1) Adams, Weisel and Mosher, *THIS JOURNAL*, **68**, 883 (1946).

(2) King and Acheson, *J. Chem. Soc.*, 681 (1946).

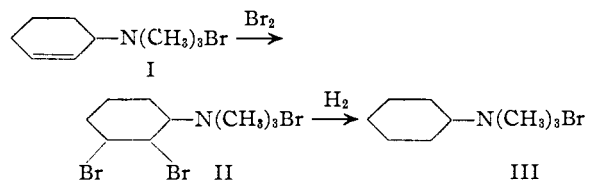
(3) Kipnis, Weiner and Spoerri, *THIS JOURNAL*, **69**, 799 (1947).

(4) Kuhn and Weygand, *Ber.*, **68**, 1282 (1935).

(5) Prepared according to the method of Vermeulen, *Rec. trav. chim.*, **48**, 969 (1929).

tion of trimethylamine hydrobromide. With the palladium catalysts, small amounts of the intact reduction product (III) are formed.¹

We wish to report that the reduction $I \rightarrow III$ can be accomplished smoothly by addition of bromine to I^2 followed by hydrogenation of the intermediate dibromoquaternary bromide (II) at room temperature and pressure over palladium-on-barium sulfate.³



We have also applied this procedure, which is presumably of general applicability, to the conversion of allyltrimethylammonium bromide into *n*-propyltrimethylammonium bromide; further examples of its use⁴ will be published in the near future.

The author wishes to thank Dr. Edwin R. Buchman for his interest in, and The Research Corporation for its financial support of, this work.

Experimental⁵

2-Cyclohexenyltrimethylammonium bromide (I) was prepared in 82% yield by adding somewhat more than the theoretical amount of an 18% solution of trimethylamine in benzene to 3-bromocyclohexene⁶ and allowing the mixture to stand overnight at room temperature. Recrystallized from ethyl acetate-ethanol or by rapidly diluting a concentrated methanol solution with acetone, I formed colorless needles or flat blades, m. p. 179.5–180.0° dec. Harries,⁷ who prepared this salt by another method, gives m. p. 181°. The quaternary picrate cor-

(1) Emde and Kull (*Congr. intern. chim. pura applicada*, **4**, 290 (1934) [*C. A.*, **30**, 2932 (1936)]; *Arch. Pharm.*, **274**, 173 (1936) [*C. A.*, **30**, 4829 (1936)]) have observed similar results in the hydrogenation of other allylic trimethylammonium halides; apparently Raney nickel has not been shown previously to cause this type of hydrogenolytic fission of the carbon-nitrogen bond.

(2) Brominations of this type have been carried out by Partheil (*Ann.*, **268**, 155 (1892)) and others; the statement by Robertson, Clare, McNaught and Paul (*J. Chem. Soc.*, 335 (1937); cited by Williams, *Trans. Faraday Soc.*, **37**, 750 (1941)) that allylammonium ions are unreactive toward bromine is unqualified and unsupported by any evidence in their paper.

(3) These conditions have been used by Rosenmund and Zetzsche (*Ber.*, **51**, 578 (1918)) to replace halogen with hydrogen in vicinal dihalides of another type.

(4) Buchman and Howton, work in progress; an allylic rearrangement has been observed to take place during one bromination of this type.

(5) All melting points are corrected. Microanalytical work was done by Dr. G. Oppenheimer and G. A. Swinehart. Except as described otherwise, quaternary picrates reported in this paper were prepared by addition of a hot 10% aqueous solution of sodium picrate to a concentrated solution of the corresponding quaternary halide in water. Occasionally we have noted that picrates prepared in this way are apparently double salts containing, in addition to the expected quaternary picrate, an equivalent amount of sodium picrate. In order to detect these anomalies, salts prepared by this method should be subjected to carbon-hydrogen analysis to reveal any ash content; nitrogen analyses may not discern such anomalies in some cases.

(6) Ziegler, Späth, Schaaf, Schumann and Winkelmann, *Ann.*, **551**, 80 (1942); see also Howton, *THIS JOURNAL*, **69**, 2060 (1947).

(7) Harries, *Ber.*, **45**, 813 (1912).

responding to I formed long bright yellow needles from ethanol, m. p. 129.7–130.1°.

Anal. Calcd. for $C_{15}H_{20}N_4O_7$: C, 48.91; H, 5.47. Found: C, 49.12; H, 5.53.

Direct catalytic hydrogenation of I over pre-reduced platinum oxide resulted in the absorption of 1.62 molecular equivalents of hydrogen; trimethylamine hydrobromide (identified by m. p. and mixed m. p. with an authentic sample) was isolated in good yield from the reaction mixture. The use of Raney nickel as a catalyst in the hydrogenation gave very similar results. The principal product of an experiment using palladium-on-charcoal was again trimethylamine hydrobromide; by virtue of the volatility of free trimethylamine, a 6% yield of III (identified by m. p. and mixed m. p. of the picrate double salt described below) was also obtained; hydrogenation over palladium-on-barium sulfate⁸ also gave small amounts of III.

(2,3-Dibromocyclohexyl)-trimethylammonium Bromide (II).—A solution of 1.10 g. (0.005 mole) of I in about 5 ml. of chloroform was treated with one molecular equivalent (0.80 g.) of bromine. On standing overnight at room temperature, the initially-precipitated heavy orange oil lost most of its color and redissolved. After removing the chloroform on a steam-bath, the solid residuc was taken up in a little warm ethanol and diluted with acetone, giving 1.54 g. (81%)⁹ of II, crude m. p. 144–149° dec.; recrystallization from methanol diluted with acetone gave well-formed colorless rhombs, m. p. 152° dec.

Anal. Calcd. for $C_9H_{18}Br_2N$: N, 3.69. Found: N, 3.26.

The picrate of II, after two recrystallizations from ethanol-water, formed glistening aggregates of yellow needles, m. p. 148.9–149.2°.

Anal. Calcd. for $C_{15}H_{20}Br_2N_4O_7$: C, 34.11; H, 3.82. Found: C, 34.38; H, 4.16.

Hydrogenation of II.—Shaking a solution of 0.91 g. of II in 10 ml. of water with 0.50 g. of palladium-on-barium-sulfate⁸ and moist hydrogen resulted in the absorption of 113.6 ml. (calcd. for two mole-equivalents, 123 ml.) of the gas in about two hours. Two recrystallizations of the crude product (0.47 g., calcd. 0.53 g.) from acetone-methanol gave sparse clusters of colorless needles (III), m. p. 281° dec., in good yield.

Anal. Calcd. for $C_9H_{20}BrN$: N, 6.30. Found: N, 6.47.

Treatment of this salt with sodium picrate gave a product identical (m. p. and mixed m. p.) with that prepared in the same way from an authentic sample of cyclohexyltrimethylammonium iodide¹⁰; analysis of this derivative (clusters of long orange-yellow needles from ethanol, m. p. 188.2–188.5°) indicated that it was a hydrated double salt composed of cyclohexyltrimethylammonium picrate and sodium picrate.

Anal. Calcd. for $C_{15}H_{22}N_4O_7 \cdot C_6H_2N_3O_7 \cdot Na \cdot 1.5H_2O$: C, 38.89; H, 4.20; N, 15.12; Na, 3.55. Found: C, 38.87; H, 4.27; N, 15.33; Na, 3.68.

The sodium-free picrate corresponding to III was obtained by shaking an aqueous solution of the iodide with silver oxide and adding an equivalent amount of picric

(8) Catalyst prepared according to Schmidt, *Ber.*, **52**, 409 (1919).

(9) An experiment of the same size in which bromine was added until it was no longer taken up and the excess bromine destroyed almost at once by heating with ethanol gave a 66% yield of II and 13% of recovered I.

(10) Obtained in 85% yield by the exhaustive methylation of cyclohexylamine, massive striated colorless bars from acetone-methanol, m. p. 271.5–271.8° dec. Wallach, *Ann.*, **340**, 46 (1905), gives m. p. 260°; Breuer and Schnitzer, *Monatsh.*, **68**, 301 (1936), m. p. 263°. Catalytic (platinum) hydrogenation of the methbromide of *N,N*-dimethylaniline (from the base, plus methyl bromide in benzene, pale blue jagged clusters from ethyl acetate-ethanol, m. p. 212° dec.; Vorländer and Siebert, *Ber.*, **52**, 283 (1919), give m. p. ca. 214°, gave an almost quantitative yield of trimethylamine hydrobromide, as reported in a similar case by Emde and Kull (*cf.* ref. 1).

acid to the resulting solution of the quaternary hydroxide, clusters of yellow needles from ethanol, m. p. 125.4°.

Anal. Calcd. for $C_{15}H_{22}N_4O_7$: C, 48.64; H, 5.99; N, 15.13. Found: C, 48.92; H, 5.98; N, 15.04.

Mixing an aqueous solution of this salt with another of sodium picrate gave the mixed salt, m. p. 188°.

Allyltrimethylammonium bromide (IV), obtained by the method used to prepare I, formed a picrate, long yellow needles from ethanol-water, m. p. 220.3–220.5° dec.

Anal. Calcd. for $C_{12}H_{16}N_4O_7$: C, 43.90; H, 4.91. Found: C, 43.92; H, 4.71.

The action of sodium styphnate on IV in aqueous solution gave a styphnate, long slender yellow bars from water, m. p. ca. 155° dec.

(2,3-Dibromo-*n*-propyl)-trimethylammonium bromide (V) was prepared from IV as described above in the preparation of II, colorless flossy sheaves from ethanol, m. p. 178° dec. (Partheil (see ref. 2) gives m. p. 173°). The picrate was recrystallized from ethanol, brilliant yellow needles, m. p. 127.5–128.5°.

Anal. Calcd. for $C_{12}H_{16}Br_2N_4O_7$: C, 29.53; H, 3.30. Found: C, 29.56; H, 3.31.

Hydrogenation of V (0.68 g.) was carried out as with II. After one hour, the hydrogen-uptake was negligible and 109.6 ml. had been absorbed (theory 103.5 ml.). The light brown crystalline residue obtained by evaporation of the catalyst-freed solution weighed 0.36 g. (calcd. 0.36 g.). The picrate prepared from this crude product was identical with an authentic sample of *n*-propyltrimethylammonium picrate (m. p. and mixed m. p., see below).

Authentic *n*-propyltrimethylammonium bromide was prepared from *n*-propyl bromide by the action of trimethylamine in benzene; the crude product was dissolved in a small amount of warm ethanol and diluted with acetone, irregular etched colorless bars or parallelograms, m. p. 242.5–243.0° dec.

Anal. Calcd. for $C_6H_{16}BrN$: C, 39.57; H, 8.86; N, 7.69. Found: C, 39.42; H, 8.73; N, 7.77.

The corresponding picrate formed opaque yellow striated bars from water, m. p. 200–201°.¹¹

(11) Hanhart and Ingold, *J. Chem. Soc.*, 1014 (1927), give m. p. 195–196°; Ries, *Z. Kryst. und Min.*, **55**, 485 (1915–1920), m. p. 207°.

GATES AND CRELLIN LABORATORIES OF CHEMISTRY
CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA 4, CALIFORNIA RECEIVED JUNE 3, 1947

Diffusion Coefficients and Molecular Radii of Hydrogen Cyanide, Cyanogen Chloride, Phosgene and Chloropicrin¹

BY I. M. KLOTZ AND D. K. MILLER

In studies of the mechanism of removal of gases by porous adsorbents such as charcoal, it is necessary to have information on the diffusion coefficients of these molecules in air.² While approximate methods are available for estimating these coefficients³ it was considered desirable to obtain accurate information for a number of substances of historical interest as toxic agents. Since classical kinetic theory correlates the molecular radius with the diffusion coefficient of a gas, it is also possible to use the data obtained to calculate radii for the substances investigated. These radii may be of particular interest in connection with the

(1) This work was performed under OSRD contract OEMsr-282 between Northwestern University and the Office of Scientific Research and Development, Washington, D. C.

(2) I. M. Klotz, *Chem. Rev.*, **39**, 241 (1946).

(3) E. R. Gilliland, *Ind. Eng. Chem.*, **26**, 681 (1934).

determination of surface areas from adsorption methods.

Experimental

The rate of evaporation of the substance in the liquid state was measured with an apparatus which is essentially the Winkelmann modification of Stefan's method.⁴ In brief the diffusion coefficient is determined by following the rate of fall of the meniscus of a column of the liquid in a small glass tube across the top of which a current of fresh air is blown. Experiments were carried out at a number of different rates of flow in order to be certain that zero concentration of toxic gas was maintained at the open end of the small glass tube. All experiments were carried out in duplicate. Temperatures were constant within $\pm 0.05^\circ$.

Results and Calculations

The diffusion coefficient, D , was calculated from the equation

$$D = \frac{x \Delta \rho RT}{M \bar{p}} \frac{1}{\ln \left[\frac{\bar{p}}{\bar{p} - p_s} \right]} \quad (1)$$

where

- x = average distance, in cm., from the level of the meniscus to the top of the tube during the experiment
- Δx = change in the level of the meniscus in the time t
- ρ = density of the liquid
- R = gas constant
- T = absolute temperature
- M = molecular weight of the vapor
- \bar{p} = total pressure
- p_s = saturation pressure of the vapor at the temperature T

The results obtained are summarized in Table I.

TABLE I
DIFFUSION COEFFICIENTS

Vapor	Temperature, °C.	D (sq. cm./sec.)
CCl_3NO_2	25	0.088
$COCl_2$	0	.095
$CNCl$	0	.111
HCN	0	.173

From Table I, it is evident that the diffusion coefficient rises with decreasing molecular weight, as would be expected from the kinetic theory of gases. It is also of interest to note that the values obtained fall quite close to the approximate curve used previously for general calculations.²

Estimates of the radii of these vapor molecules have been made from the measured diffusion coefficients with the aid of the equation^{5,6}

$$(r + 1.54 \times 10^{-8})^2 = \frac{\sqrt{\bar{C}_1^2 + \bar{C}_2^2}}{3\pi D n (1 + \alpha)} \quad (2)$$

where

- r = the radius of the vapor molecule
- \bar{C}_1 = the mean velocity of the vapor molecule
- \bar{C}_2 = the mean velocity of an air molecule
- $\bar{C} = 0.921 \sqrt{3RT/M}$
- n = the number of molecules in one cc. of air at 760 mm. and the temperature T
- α = a correction factor depending on the relative masses of the vapor and air molecules^{5,6}

(4) K. Jellinek, "Lehrbuch der physikalischen Chemie," Vol. II, 2nd ed., F. Enke, Stuttgart, 1928, pp. 615–618.

(5) J. H. Jeans, "The Dynamical Theory of Gases," Cambridge University Press, Cambridge, 1921, p. 316.

(6) E. Mack, Jr., *THIS JOURNAL*, **47**, 2468 (1925).

The average radius of an air molecule was taken as 1.54×10^{-8} cm.⁶ and is the second term in the parentheses on the left-hand side of the equation.

The radii so calculated are listed in Table II, together with molecular radii calculated from the densities of the corresponding liquids on the assumption that the molecule occupies a volume equal to that of a cube with a side whose length equals the diameter of the molecule. The agreement between the two methods is excellent.

TABLE II
MOLECULAR RADII

Vapor	From diffusion coefficient, in Å.	From liquid density, in Å.
CCl ₃ NO ₂	2.78	2.75
COCl ₂	2.42	2.45
CNCl	2.31	2.19
HCN	2.03	2.00

DEPARTMENT OF CHEMISTRY
NORTHWESTERN UNIVERSITY
EVANSTON, ILLINOIS

RECEIVED MAY 28, 1947

Dielectric Studies. VIII. Dipole Moments of Solvents in Nonpolar Solvents of Unknown Molecular Weights¹

BY NORMAN C. C. LI,² C. V. AN AND W. H. WU

In a recent paper Li and Chu³ reported the dipole moment of acetonitrile in three solvents of unknown and variable molecular weights, namely, gasoline, kerosene and petroleum ether. It was shown that in determining the molar polarization at infinite dilution, graphical extrapolation is not necessary and the molecular weight of the non-polar solvent used need not be known, if the dielectric constant and density of dilute solutions are linear functions of weight fractions of the solute. In this study we report dipole moment values of two polar solvents, namely, acetone and chloroform in two different samples of gasoline of different physical properties.

Acetone of tested purity was refluxed over potassium permanganate, placed over anhydrous calcium chloride and subsequently carefully fractionated. The fraction boiling between 56 and 56.5° was taken, its refractive index being n_D^{25} 1.3567. Chloroform of U.S.P. grade was purified from alcohol by one thorough extraction with 9 *M* sulfuric acid followed by six extractions with water. The product was dried over freshly-fused calcium chloride and distilled, b. p. 61–61.5°. Gasoline, colorless grade, was used without further purification. The samples came from different sources with different refractive indices: sample A, n_D^{25} 1.4242; sample B, n_D^{25} 1.4287.

(1) Presented before the Division of Physical and Inorganic Chemistry of the American Chemical Society, Atlantic City Meeting, April, 1947.

(2) Present address: Department of Chemistry, St. Louis University.

(3) Li and Chu, *THIS JOURNAL*, **69**, 558 (1947).

The apparatus for determinations of dielectric constant, density and refractive index have been described by Li and Chu.²

The results of the experimental work are presented in Tables I and II. The dielectric constant data are accurate to about 0.1%.

TABLE I

Acetone in gasoline (sample A) 25°			Chloroform in gasoline (sample B) 15°		
W_2	E	d	W_2	E	d
0.0000	2.032	0.7452	0.0000	2.051	0.7525
.0182	2.253	.7461	.0384	2.097	.7708
.0330	2.452	.7466	.0582	2.119	.7795
.0541	2.700	.7475	.0719	2.136	.7856
.0615	2.778	.7479	.0933	2.163	.7943
.0861	3.111	.7489			

In Table I the headings W_2 , E , d are the weight fraction of solute, dielectric constant and density, respectively.

TABLE II

CONSTANTS OF THE GASOLINE

	Sample A	Sample B
$C (= 3/d_1(E_1 + 2)^2)$	0.2476	0.2430
$p_1 = (E_1 - 1)/(E_1 + 2)d_1$.3435	.3447

Subscript 1 refers to solvent.

Data in Table I indicate that dielectric constant and density are linear functions of weight fractions W_2 , and therefore the method and formulas described by Li and Chu² can be used and a knowledge of the molecular weight of the non-polar solvent is not necessary. The formulas used are

$$P_{2(\infty)} = [p_1(1 - b) + CaE_1]M_2 \quad (1)$$

$$\mu = 0.01273 \times 10^{-18} \sqrt{(P_{2(\infty)} - P_{2D})T} \quad (2)$$

where $P_{2(\infty)}$ is the molar polarization of the solvents at infinite dilution, p_1 is the specific polarization of the solvent $\left(\frac{E_1 - 1}{E_1 + 2} \frac{1}{d_1}\right)$, a and b are the dielectric constant and density coefficients in the equations $E = E_1(1 + aW_2)$ and $d = d_1(1 + bW_2)$, respectively, $C = 3/d_1(E_1 + 2)^2$, M_2 is the molecular weight of the solute. The dipole moments for acetone and chloroform in gasoline are calculated to be 2.8 and 1.16×10^{-18} , respectively. These values are in good agreement with the values given in the literature, namely, 2.72 and 1.15×10^{-18} , respectively, when solvents of known and definite molecular weights were used.

For the past four years the senior author of this paper and his students have examined over ten different compounds dissolved in non-polar solvents of unknown molecular weights. In each case they have found that the dielectric constant and density of the mixture are linear functions of weight fractions for solutions whose concentrations are less than 8%, and that the values of the dipole moments thus obtained are correct. Many different samples of gasoline, kerosene and petroleum

ether have been used as solvents without any purification, and the results are the same.

DEPARTMENT OF CHEMISTRY
CATHOLIC UNIVERSITY
PEIPING, CHINA, AND
ST. LOUIS UNIVERSITY
ST. LOUIS, MO.

RECEIVED MAY 15, 1947

Thermal Decomposition of Ammonium Nitrate

By J. T. KUMMER

Recent interest in the decomposition of ammonium nitrate seems to make it worthwhile to call attention to an observation made recently during the preparation of a $N^{14}N^{14}$, $N^{14}N^{15}$, $N^{15}N^{15}$ mixture from a sample of NH_4NO_3 (Eastman Kodak Co.) in which the ammonium group contained 62 atom per cent. N^{15} and 38 atom per cent N^{14} and the nitrate group contained the 0.38% N^{16} of normal nitrogen. This NH_4NO_3 was decomposed, after it had melted, at 290° to give nitrous oxide. The nitrous oxide was then permitted to react quantitatively with a reduced iron catalyst at room temperature to give nitrogen and iron oxide. The nitrogen, when analyzed by a mass spectroscopy, was found to contain 0.35% $N^{15}N^{15}$. If the ammonium nitrate molecule decomposed by the reaction of the ammonium group with the nitrate group, the percentage of $N^{15}N^{15}$ would be 0.24; whereas if all the nitrogen atoms present in the ammonium nitrate combined at random, the percentage of $N^{15}N^{15}$ would be 9.6. These results show that the decomposition of the ammonium nitrate to give N_2O proceeds practically entirely by a bond formation between the two nitrogen atoms of the two different groups present, and not by the interaction of similar groups.

GULF RESEARCH AND DEVELOPMENT Co. FELLOWSHIP
MELLON INSTITUTE
PITTSBURGH, PA.

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An Extension of the Scope of the Hammick Reaction

By KURT MISLOW

The synthesis of α -pyridylcarbinols by the decarboxylation of picolinic acid in an excess of aldehyde or ketone was first reported by Hammick and co-workers.^{1,2} These authors, after an apparently exhaustive investigation of a large number of decarboxylating acids, reported that "... the decarboxylation of pyridine and quinoline acids other than those containing the carboxyl group α to the nitrogen atom yielded no products of interaction with aldehydes and ketones."²

The similarity of the reactivity of the α - and γ -positions on the pyridine ring suggested, however,

(1) Dyson and Hammick, *J. Chem. Soc.*, 1724 (1937).

(2) Ashworth, Daffern and Hammick, *ibid.*, 809 (1939).

that this reaction might not necessarily be restricted to picolinic, quinaldinic and isoquinaldinic acids, but that it might be extended to include acids such as isonicotinic acid.

When isonicotinic acid was decarboxylated in boiling benzophenone, a small yield of diphenyl- γ -pyridylcarbinol was indeed realized. Benzophenone was selected as the solvent reagent because it had been shown² to react with decarboxylating picolinic acid and because its boiling point roughly coincides with the decarboxylating temperature of isonicotinic acid.

This result indicates that the Hammick reaction is of greater generality than has hithertofore been assumed.

Experimental³

A mixture of 19.8 g. (0.16 mole) of recrystallized isonicotinic acid and 250 g. (1.37 mole) of benzophenone was refluxed for nine and one-half hours, an air condenser being employed. A sealed-in plunger arrangement helped to scrape sublimed crystals of isonicotinic acid back into the reaction mixture. After five hours, 3600 ml. of carbon dioxide had been evolved (90% of the theory), and in the subsequent four and one-half hours, only 50 ml. more of the gas was evolved. The dark brown solution was allowed to cool to room temperature, diluted with 500 ml. of benzene and extracted with 2.5 *N* hydrochloric acid (more concentrated acid precipitates a tar, which redissolves on dilution). The acid extracts were made alkaline and extracted with benzene. The solid A at the interface was removed by centrifugation and the benzene layer was evaporated to dryness. The partially crystalline residue was freed of oil by washing with acetone, leaving 0.85 g. of crystals, m. p. 192–232°; recrystallization of A from benzene-pyridine gave an additional 0.6 g. of tan prisms, m. p. 205–232°. The total yield of crude carbinol thus amounted to 3.5%. Further recrystallization from benzene-pyridine afforded colorless microscopic prisms, m. p. 237–238°.

Anal. Calcd. for $C_{11}H_{13}ON$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.94; H, 5.79; N, 5.09.

Tschitschibabin and Benewolenskaja,⁴ who prepared this compound by the action of phenylmagnesium bromide on phenyl- γ -pyridylketone, report a melting point of 235°.

(3) All melting points are corrected; microanalysis by Dr. G. Oppenheimer and Mr. G. A. Swinehart.

(4) Tschitschibabin and Benewolenskaja, *Ber.*, 61, 547 (1928).

GATES AND CRELLIN LABORATORIES OF CHEMISTRY
CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA 4, CALIFORNIA

RECEIVED MAY 31, 1947

Correlation of Surface Area and Dehydrogenation Activity for a Chromia-Alumina Catalyst

By J. R. OWEN

In connection with dehydrogenation of normal butane at Plains Butadiene Plant, which is operated by Phillips Petroleum Company for Reconstruction Finance Corporation—Office of Rubber Reserve, a laboratory study was made of dehydrogenation activity and surface area of several samples of chromia-alumina catalyst A¹ that were used in the plant.

(1) G. H. Hanson and H. L. Hays, *Chem. Eng. Progress*, to be published.

Methods and Results.—Dehydrogenation activity was determined by passing normal butane (Pure Grade) through a portion of catalyst supported vertically in an electrically heated tube furnace, under the following conditions: hydrocarbon space velocity of 500 volumes (STP) per volume of catalyst per hour, pressure of one atmosphere (absolute), average internal catalyst temperature of 1100° F., and on-stream period of sixty minutes. The catalyst was flushed for two minutes before and after each dehydrogenation period with nitrogen, and was revived for fifty-six minutes with air at a space velocity of 1000 volumes per volume of catalyst per hour. The single-pass conversion to normal butenes plus butadiene during each of 5 to 8 cycles was determined with a hydrogen-sensitive, thermal-conductivity gas analyzer and these values were averaged. The gas analyzer was calibrated by data from low-temperature fractional analyses of total dehydrogenation effluent.

Surface area of each catalyst was determined after the dehydrogenation test by the low-temperature nitrogen-adsorption method developed by Brunauer and Emmett,² in an apparatus similar to that described by Krieger.³ The area was calculated by a two-point substitution in the BET equation. The data obtained are in Fig. 1; they show that there is a definite correlation between surface area and dehydrogenation activity for the chromia-alumina catalyst.

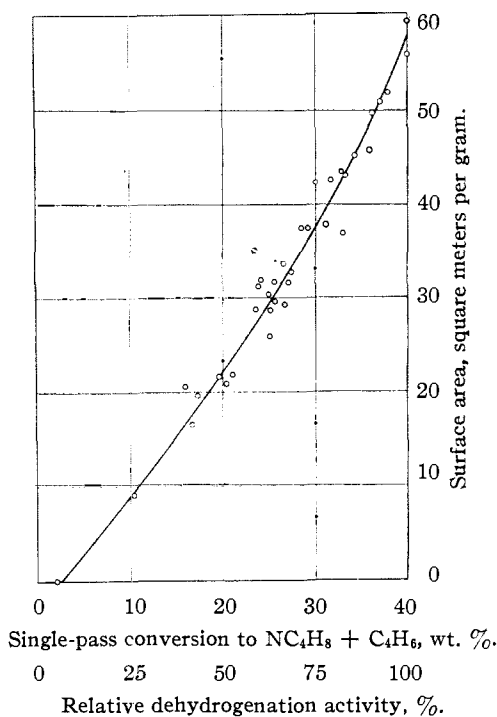


Fig. 1.—Correlation of surface area and dehydrogenation activity for chromia-alumina catalyst A.

Acknowledgment.—The author wishes to thank Phillips Petroleum Company and Reconstruction Finance Corporation—Office of Rubber Reserve for permission to publish these data.

PHILLIPS PETROLEUM COMPANY
RESEARCH DEPARTMENT
BARTLESVILLE, OKLAHOMA

RECEIVED MAY 24, 1947

(2) S. Brunauer and P. H. Emmett, *THIS JOURNAL*, **57**, 1754 (1935); *et seq.*

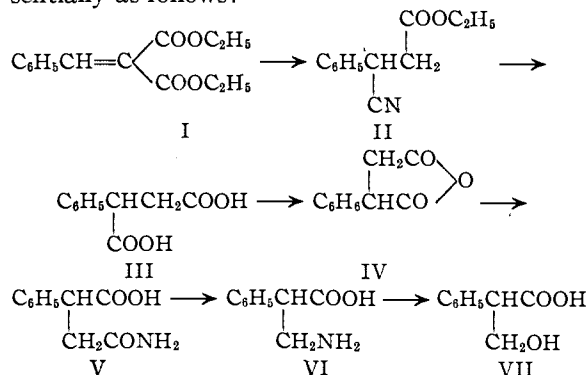
(3) K. A. Krieger, *Ind. Eng. Chem., Anal. Ed.*, **16**, 398 (1944).

A New Synthesis of *dl*-Tropic Acid

BY M. R. NATARAJAN AND S. SWAMINATHAN¹

Tropic acid (VII) is formed through hydrolysis of atropine and related alkaloids. The earliest synthesis of this acid was by Ladenburg and Rügheimer² and this preparation was later improved by McKenzie and Wood.³ In addition, syntheses have been reported by Müller⁴ and by Chambon.⁵

The scheme of synthesis herein reported is essentially as follows:



β -Amino- α -phenylpropionic acid (VI) was obtained by McKenzie and Strathern⁶ by interaction of atropic acid and hydroxylamine in alcoholic solution, and, more recently, by Craig and Henze⁷ through reduction of β -amino- α -hydroxy- α -phenylpropionic acid. The conversion of VI to tropic acid was achieved by adopting the method outlined by McKenzie and Strathern.⁶

Experimental

Phenylsuccinic acid was prepared from benzalmalonic ester,⁸ and the anhydride obtained therefrom either by distilling under reduced pressure,⁸ or by treating with three equivalents of acetyl chloride at 110° for three hours and subsequently distilling after removal of acetic acid, acetic anhydride and acetyl chloride at reduced pressure. The pure product distilled at 191–192° (12 mm.). The ammonium salt of α -phenylsuccinamic acid was obtained by interaction of dry ammonia and an ether solution of phenylsuccinic anhydride; the amido acid was precipitated in almost quantitative yield by addition of hydrochloric acid;⁹ it melted at 145–146°.

β -Amino- α -phenylpropionic Acid.—To a cooled solution of 11.6 g. of potassium hydroxide in 105 cc. of water, 4 g. of bromine was added gradually with thorough stirring, the temperature being maintained at 0–5°. Four and one-half grams of α -phenylsuccinamic acid was added portion-wise, and the mixture was warmed at 70° for four hours. After neutralization with hydrochloric acid, the solution was evaporated, the residue shaken with 60 cc. of water, and separated by filtration. The undissolved portion was

(1) Lady Tata Research Scholar, Indian Institute of Science.

(2) Ladenburg and Rügheimer, *Ber.*, **13**, 2041 (1880); **23**, 2590 (1889).

(3) McKenzie and Wood, *J. Chem. Soc.*, **115**, 830 (1919).

(4) Müller, *Ber.*, **51**, 252 (1918); Wislicenus and Bilhuber, *ibid.*, **51**, 1237 (1918).

(5) Chambon, *Compt. rend.*, **186**, 1630 (1928).

(6) McKenzie and Strathern, *J. Chem. Soc.*, **127**, 85 (1925).

(7) Craig and Henze, *J. Org. Chem.*, **10**, 19 (1945).

(8) Bredt and Kallen, *Ann.*, **293**, 344–349 (1896); Wegscheider and Hecht, *Monatsh.*, **24**, 418 (1903).

(9) Hahn and Walter, *Ann.*, **354**, 132 (1907).

crystallized from hot water with aid of norite; m. p. 222–223°; yield 2.5 g.

Anal. Calcd. for $C_9H_{11}NO_2$: N, 8.48. Found: N, 8.35.

Tropic Acid.—The procedure adopted for conversion of VI to tropic acid was essentially that described by McKenzie and Strathern.⁶ A concentrated aqueous solution of potassium nitrite (3 g.) was added gradually to 3 g. of β -amino- α -phenylpropionic acid dissolved in 55 cc. of normal hydrochloric acid. The reaction mixture was warmed on the water-bath for fifteen minutes; the oil which settled was separated. The aqueous solution was extracted with ether; the solvent was removed, and the residue was twice recrystallized from benzene; m. p. 116–117°; yield 0.2 g.

Anal. Calcd. for $C_9H_{10}O$: C, 65.06; H, 6.02. Found: C, 65.9; H, 6.1.

MAHARAJA'S COLLEGE
ERNAKULAM, INDIA
DEPARTMENT OF PURE AND APPLIED CHEMISTRY
INDIAN INSTITUTE OF SCIENCE
BANGALORE, INDIA

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(10) Manuscript originally received November 4, 1946

Derivatives of Taurine and β -Alanine¹

BY M. M. RAPPORT, J. F. MEAD, J. T. MAYNARD, A. E. SENEAR AND J. B. KOEPLI

During an investigation of derivatives of pantoyltaurine as potential antimalarials,² a number of somewhat related compounds, derivatives of either taurine or β -alanine, were prepared and tested for antimalarial activity.³

Experimental⁴

Sodium γ -Hydroxybutyryltaurate⁵ (I).—The sodium salt of taurine was heated with an excess of γ -butyrolactone for five hours at 115°. The product was extracted with boiling ethanol and treated with Norite and the solvent removed *in vacuo*. The residue after washing with acetone to remove unreacted lactone was crystallized from ethanol from which it separated as deliquescent plates, m. p. 204–210°.

Anal. Calcd. for $C_6H_{12}O_5NSNa$: N, 6.0; Na, 9.8. Found: N, 5.8; Na, 9.8.

γ -Hydroxybutyryltaurine (II).—The taurinamide obtained from 25 g. of taurinamide hydrochloride² was heated with 14 g. of γ -butyrolactone for twelve hours at 120°. The resulting oil crystallized after standing at 4° under acetone-ether solution and was recrystallized from absolute ethanol to give colorless rosetts of prisms, m. p. 66–69°.

Anal. Calcd. for $C_8H_{14}O_4N_2S$: C, 34.3; H, 6.7. Found: C, 34.2; H, 6.7.

Analytical results, etc., when not given for a compound in the running text, are recorded in Table I.

(1) This work was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the California Institute of Technology.

(2) Mead, Rapport, Senear and Koepfli, *J. Biol. Chem.*, **163**, 465 (1946).

(3) The survey number, designated SN, identifies a drug in the records of the Survey of Antimalarial Drugs. The antimalarial activity is tabulated in a monograph entitled "A Survey of Antimalarial Drugs, 1941–1945," F. Y. Wiselogle, Editor, J. W. Edwards, Ann Arbor, Michigan, 1946.

(4) All melting points have been corrected for exposed stem. The microanalyses reported have been carried out by Dr. Gertrud Oppenheimer and Mr. G. A. Swinehart.

(5) Compare Winterbottom, Clapp, Miller, English and Roblin, *This Journal*, **69**, 1393 (1947).

***p*-Nitrobenzoyltaurine (III).**—To 10 g. of taurinamide hydrochloride dissolved in 150 ml. of water containing 78 g. of sodium carbonate was added 11 g. of *p*-nitrobenzoyl chloride. The mixture was shaken and warmed on the steam-bath for two hours and then filtered. The product was washed with dilute sodium carbonate solution and water and dried *in vacuo* to give 10.5 g.

***p*-Aminobenzoyltaurine (IV).**—Twelve grams of III was reduced with hydrogen at 2000 pounds pressure in dioxane over Raney nickel catalyst at 80°. After removal of the catalyst and evaporation of the solvent 8 g. of a light colored oil was obtained which crystallized on standing.

***p*-Nitrobenzenesulfonyltaurine (V).**—Treatment of 4.1 g. of taurinamide hydrochloride with 6.8 g. of *p*-nitrobenzenesulfonyl chloride in a similar manner to that described for the preparation of III, yielded 8 g. of V.

***p*-Aminobenzenesulfonyltaurine (VI).**—Eleven and one-half grams of V, reduced under the conditions employed to obtain IV, yielded 8.6 g. of VI.

***O*-Acetylmandeloyltaurine (VII).**—To a solution of 10 g. of taurinamide hydrochloride and 13 g. of sodium bicarbonate in 100 ml. of water there was added 14.5 g. of acetylmandeloyl chloride.⁶ The mixture was stirred for one hour after the evolution of gas had ceased and the precipitate filtered off, washed with sodium bicarbonate solution and water and dried *in vacuo*. The 18 g. of material thus obtained was pure enough for the next reaction, but was crystallized for analysis.

Mandeloyltaurine (VIII).—To 10.7 g. of VII dissolved in the minimum amount of methanol at 4° there was added 10 ml. of 2.2 *N* barium methylate⁷ and the solution allowed to stand at 4° for two days. The solution was then treated with the required amount of 2 *N* sulfuric acid and centrifuged to remove the barium sulfate. The resulting solution was taken to dryness, dissolved in a little ethanol and poured into mixture of equal parts of ether and petroleum ether (30–60°). A crystalline solid was thus obtained which was recrystallized in the same way to give 8 g. of product.

***N*-Carbobenzoxy- β -amino- β -phenylpropionyl Chloride (IX).**—To 5 g. of *N*-carbobenzoxy- β -phenyl- β -alanine⁸ suspended in 50 ml. of dry ether there was added 3.9 g. of phosphorus pentachloride and the mixture shaken with cooling for twenty minutes. The reactants went into solution and the acid chloride began to crystallize out in long colorless needles. Two hundred milliliters of petroleum ether (30–60°) was added to complete the separation, and the mixture allowed to stand at 4° for one-half hour. The product was filtered off and washed with petroleum ether to give 4.9 g. of colorless needles, m. p. 89–91°.

Anal. Calcd. for $C_{17}H_{15}O_3NCl$: Cl, 11.2. Found: Cl, 11.8.

***N*-Carbobenzoxy- β -amino- β -phenylpropionyltaurine (X).**—To 22.9 g. of IX there was added a solution of 13 g. of taurinamide hydrochloride and 18 g. of sodium bicarbonate dissolved in one liter of water. The mixture was stirred for one hour and then allowed to stand at 4° overnight. The precipitate was collected and washed with water to give 25.6 g. of product.

β -Amino- β -phenylpropionyltaurine (XI).—A suspension of 12 g. of X in anhydrous methanol was reduced over palladium black catalyst with hydrogen at 2500 pounds pressure for twenty-three hours. Filtration and evaporation yielded 4.5 g. of a colorless oil which crystallized on scratching.

***N*-Carbobenzoxy- β -amino- β -(4-nitrophenyl)-propionic Acid (XII).**—A solution of β -amino- β -(4-nitrophenyl)-propionic acid⁹ (14 g.) and sodium hydroxide (2.7 g.) in 400 ml. of water was chilled in an ice-salt-bath and 17.5 ml. of carbobenzoxy chloride (sp. gr. 1.16) added with continuous shaking over a period of one hour. During the reaction the solution was kept alkaline to phenol-

(6) Thayer, "Organic Syntheses," Coll. Vol. I, p. 12.

(7) Weltzien and Singer, *Ann.*, **443**, 104 (1925).

(8) Dyer, *This Journal*, **63**, 265 (1941).

(9) Posner, *Ann.*, **389**, 40 (1912).

TABLE I

Compound ^a	SN	Formula	Solvent	M. p., °C.	Percentage composition			
					Carbon		Hydrogen	
					Calcd.	Found	Calcd.	Found
II	3274	C ₈ H ₁₄ O ₄ N ₂ S	Absolute E ^b	66-69	34.3	34.2	6.7	6.7
III	3284	C ₈ H ₁₁ O ₅ N ₂ S	Cellosolve	197-198	39.6	39.8	4.1	4.2
IV	3283	C ₉ H ₁₃ O ₃ N ₃ S	75% E	152-153	44.4	44.5	5.4	5.3
V	3291	C ₈ H ₁₁ O ₆ N ₃ S ₂	I ^c	139-141	31.1	31.4	3.6	3.5
VI	3285	C ₈ H ₁₃ O ₄ N ₂ S ₂	I	121-123	34.4	34.4	4.7	4.8
VII	3290	C ₁₂ H ₁₆ O ₅ N ₂ S	I	145-147	48.0	47.8	5.4	5.3
VIII	3286	C ₁₀ H ₁₄ O ₄ N ₂ S	...	100-102	46.5	46.3	5.5	5.5
X	..	C ₁₀ H ₂₀ O ₅ N ₂ S	80% E	183-186	57.5	57.4	5.9	6.2
XI	3289	C ₁₁ H ₁₇ O ₃ N ₂ S	E	152-154	48.8	48.8	6.3	6.0
XII	..	C ₁₇ H ₁₆ O ₆ N ₂	60% E	150-151	59.3	59.3	4.7	4.4
XIII	..	C ₁₉ H ₂₄ O ₇ N ₄ S	80% E	200-202	50.7	51.0	4.9	4.7
XIV	..	C ₁₉ H ₂₂ O ₃ N ₄ S	E	177-179	54.3	54.5	5.7	5.5
XVA	..	C ₁₃ H ₂₂ O ₅ N ₄ S	Absolute E	150-151	45.1	45.3	6.4	6.5
XV	3632	C ₁₁ H ₁₈ O ₃ N ₄ S	Absolute E	135-136	46.2	46.3	6.3	6.1
XVIII	4469	C ₉ H ₁₂ O ₂ N ₂	60% E	210-211 ^d	60.0	60.3	6.7	6.6

^a All compounds were crystalline and colorless. ^b E, ethanol. ^c I, Isopropyl alcohol. ^d Decomposes.

phthalein by the addition of 6 *N* sodium hydroxide when necessary. The solution was shaken an additional twenty minutes at room temperature and then extracted with three 200-ml. portions of ether, filtered and made acid to congo red with concentrated hydrochloric acid. After standing in the cold room the precipitate was filtered off and taken up in boiling ethanol, from which 13.5 g. crystallized out on addition of water.

N-Carbobenzoxy- β -amino- β -(4-nitrophenyl)-propionyltaurineamide (XIII).—A solution of 12 g. of XII and 8 g. of phosphorus pentachloride in 150 ml. of dry ether was shaken with cooling for one-half hour. The product which had precipitated was filtered off and washed with petroleum ether. The yield of acid chloride was 12.2 g., m. p. 89-91°, which was added to a solution of 5.6 g. of taurineamide hydrochloride and 7 g. of sodium bicarbonate in 300 ml. of water. After stirring for two hours, the product (13 g.) was filtered off.

N-Carbobenzoxy- β -amino- β -(4-aminophenyl)-propionyltaurineamide (XIV).—Five grams of XIII was suspended in 200 ml. of absolute methanol and reduced over palladium black with hydrogen at 3000 pounds pressure for sixteen hours. The product (3 g.) crystallized from the filtered solution after concentration. The reason that hydrogenolysis of the carbobenzoxy group did not occur to an appreciable extent in this single experiment has not been investigated.

β -Amino- β -(4-aminophenyl)-propionyltaurineamide (XV).—To a suspension of 22.7 g. of XIII in 150 ml. of 80% methanol containing 6 ml. of glacial acetic acid was added 0.5 g. of palladium black catalyst. The mixture was shaken under 40 pounds pressure of hydrogen until the pressure had dropped the amount calculated for the reduction of the nitro group. The stopper of the reduction bottle was then replaced with a two-hole stopper having an inlet tube for hydrogen leading almost to the bottom of the bottle and an outlet tube leading to a bubbler for determination of carbon dioxide. Hydrogen was passed into the solution slowly with vigorous shaking for three hours, at which time the formation of carbon dioxide had ceased. The solution was filtered and concentrated under reduced pressure to dryness. The residue was taken up in a small quantity of absolute ethanol and after one hour at 4° a crystalline precipitate (14.5 g.) was collected and dried at room temperature which proved to be the acetate (XVA).

The acetate, after long drying *in vacuo* and recrystallization from absolute ethanol, gave XV.

N-Carbobenzoxy- β -alanineamide (XVI) (SN 3272).—A suspension of 15 g. of N-carbobenzoxy- β -alanine¹⁰ (SN 3278) and 15 g. of phosphorus pentachloride in 150 ml.

of dry ether was shaken for one-half hour. After filtration and concentration under diminished pressure, the residual oil was dissolved in 200 ml. of dry ether and ammonia passed into the solution for one-half hour. The precipitated amide was collected, washed with hot dilute sodium bicarbonate and then ice-water and then crystallized from ethyl acetate to give 13 g. of colorless crystals, m. p. 163-164°.

Anal. Calcd. for C₁₁H₁₄O₂N₂: N, 12.6. Found: N, 12.4.

(+)-Pantoyldiethylaspartate¹¹ (XVII) (SN 3292).—Fifteen grams of *l*-pantolactone was dissolved in 21.8 g. of diethyl *l*-aspartate¹² and the solution heated for three days at 55-65°. The reaction mixture was distilled and 26.9 g. of a fraction, b. p. 118° (9 mm.), was collected; [α]_D²⁰ +9.5° (6.2% in absolute ethanol).

Anal. Calcd. for C₁₄H₂₆O₇N: C, 52.7; H, 7.9; N, 4.4. Found: C, 53.2; H, 8.1; N, 4.3.

β -Amino- β -(4-aminophenyl)-propionic Acid (XVIII).—Prepared in almost quantitative yield by the reduction of β -amino- β -(4-nitrophenyl)-propionic acid⁹ in glacial acetic acid with platinum oxide catalyst and hydrogen at 40 pounds pressure; m. p. 210-211° (dec.), from aqueous ethanol.

Anal. Calcd. for C₉H₁₂O₂N₂: C, 60.0; H, 6.7. Found: C, 60.3; H, 6.6.

(+)-Sodium β -Pantoylamido- β -(4-nitrophenyl)-propionate XIX.—Fifteen grams of the finely powdered and carefully dried sodium salt of β -amino- β -(4-nitrophenyl)-propionic acid⁹ was heated with 10 g. of *l*-pantolactone and a few drops of absolute ethanol at 105° for two hours. After adding 60 ml. of absolute ethanol, the mixture was refluxed for four hours, cooled, filtered from 3.5 g. of unreacted sodium salt and poured into 700 ml. of isopropyl ether to precipitate the product. A sample was twice reprecipitated for analysis.

Anal. Calcd. for C₁₅H₁₉O₇N₂Na: N, 7.7; Na, 6.35. Found: N, 8.1; Na, 6.89.

(+)-Sodium β -Pantoylamido- β -(4-aminophenyl)-propionate (SN 3633).—Ten grams of XIX in 250 ml. of 80% ethanol was reduced with hydrogen at 40 pounds pressure over 0.38 g. of platinum oxide catalyst. When the calculated amount of hydrogen had been absorbed, the solution was filtered, evaporated to dryness *in vacuo* and the residual oil crystallized by treatment with 10 volumes of ethyl acetate and one volume of absolute ethanol. The white powder (9 g.) was further purified by precipitation from absolute ethanol with isopropyl ether; [α]_D²⁰ +8.5° (1.41% in water).

(11) Compare Weinstock, *et al.*, *J. Biol. Chem.*, **136**, 343 (1940).

(12) Fischer, *Ber.*, **37**, 4599 (1904).

(10) Siffard and du Vigneaud, *J. Biol. Chem.*, **100**, 753 (1935).

Anal. Calcd. for $C_{16}H_{21}O_2N_2Na$: Na, 6.92. Found: Na, 6.99.

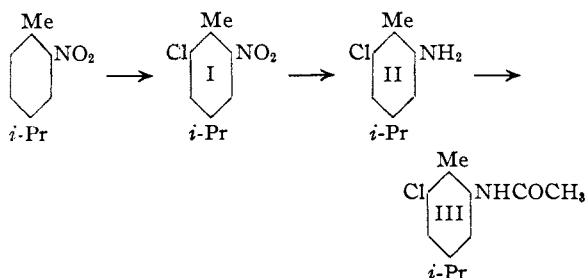
CONTRIBUTION NO. 1127

GATES AND CRELLIN LABORATORIES OF CHEMISTRY
CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA, CALIFORNIA

RECEIVED APRIL 18, 1947

The Chlorination of 2-Nitro-*p*-cymene. I. Monosubstitution¹

BY ALVIN S. WHEELER, J. M. EARLY AND JOSEPH N. LECONTE



The chlorination of 2-nitro-*p*-cymene yielded 2-nitro-6-chloro-*p*-cymene (I). There was evidence of the formation of 2-chloro-*p*-toluic acid, m. p. 195°, and an aldehyde fraction, b. p. 110–120°. The 2-nitro-6-chloro-*p*-cymene was reduced to 2-amino-6-chloro-*p*-cymene (II), and its acetate (III) and hydrochloride were prepared and studied. The structure of the chlorinated product was proved by reduction, diazotization to remove the amino group, and subsequent oxidation to 2-chloro-*p*-toluic acid.

attached to a reflux condenser, and 150 cc. of concentrated hydrochloric acid was added in 10-cc. portions, precautions being taken to prevent overheating. When the initial reaction subsided, the mixture was heated on a steam-bath for four hours. The reaction mixture was then distilled with steam and the unreacted nitro compound retrieved. The mixture was now made basic with sodium hydroxide, the amine steam distilled, extracted with ether, dried over solid sodium hydroxide, the ether evaporated and the residual oil distilled under diminished pressure. The water white oil which distilled at 137–138° at 27 mm. pressure was saved; yield was 25.2 g.

Derivatives. (1) **Hydrochloride.**—Dry hydrogen chloride was passed into an ethereal solution of the amine. The precipitate was dried in a desiccator. The white solid melted 200–205° dec. It was soluble in acetone, hydrolyzed by cold water, and was insoluble in concentrated hydrochloric acid.

(2) **2-Acetamino-6-chloro-*p*-cymene.**—The compound was prepared in the usual way. Four parts of acetic anhydride, one part of the amine and pyridine (2% of the anhydride) were heated for a period of two hours, poured into water, excess anhydride destroyed by heating and the acetamino compound purified by recrystallization from ethanol; m. p. 59–60°; white needles from alcohol and from acetic acid.

UNIVERSITY OF GEORGIA
ATHENS, GEORGIA

RECEIVED MAY 23, 1947

The Oxidation of Acetic Acid with Selenium Dioxide

BY R. B. THOMPSON AND J. A. CHENICEK

The oxidation of compounds that contain an activated hydrogen with selenium dioxide is now a standard preparative method.¹ The reaction is usually carried out by heating the material to be oxidized under reflux with selenium dioxide while employing a suitable inert solvent. Under these

TABLE I

Compound	Formula	M. p., °C.	B. p., °C.	Refractive index		% Chlorine	
				20°C.	26°	Calcd.	Found
2-Nitro-6-chloro- <i>p</i> -cymene (I)	$C_{16}H_{12}O_2NCl$	152–153 (26 mm.)	1.1965	1.4934	16.61	16.42
2-Amino-6-chloro- <i>p</i> -cymene (II)	$C_{16}H_{14}NCl$	137–138 (27 mm.)	1.0968	1.5583	19.32	19.88
Derivatives of II							
Acetate	$C_{12}H_{16}ONCl$	59–60	15.74	15.66
Hydrochloride	$C_{16}H_{16}NCl_2$	206–208 dec.	32.24	32.10

Experimental

Preparation of 2-Nitro-6-chloro-*p*-cymene.—Dry chlorine gas was led into 100 g. of redistilled nitrocymene and 0.5 g. of aluminum-mercury couple until the system had gained the necessary weight for mono-substitution. The mixture was poured into water, washed first with sodium hydroxide solution, and then with sodium bisulfite solution, and finally with water. It was extracted with ether and the ethereal solution dried over calcium chloride. The ether was evaporated and the residual oil distilled under diminished pressure. That portion boiling between 152 and 153° at 26 mm. pressure was the nitrochlorocymene; yield 45.5 g. of a pale yellow, sweet aromatic odored oil.

Preparation of 2-Amino-6-chloro-*p*-cymene.—Forty-five grams of mossy tin, 39.5 g. of nitrochlorocymene, and 25 cc. of 95% ethanol were placed in a 500-cc. balloon flask,

conditions acetic acid is frequently used as the inert solvent. However, it has been found that under more drastic conditions acetic acid undergoes an unexpected reaction with selenium dioxide, namely, oxidation in a small yield to succinic acid. Thus selenium dioxide (14 g.), acetic acid (75 cc.), and water (2.2 cc.), were sealed in a rotating autoclave and heated in an atmosphere of nitrogen at 200° for twelve hours. Selenium (9.7 g.) was separated by filtration. The liquid product was evaporated *in vacuo* and deposited 2 g. of solid material which was identified as succinic acid by mixed melting point with an authentic sample. Conversion to the anhydride gave a product which did not depress the melting point of an authentic sample of succinic anhydride. The only other oxidized material which could be identified was carbon di-

(1) This paper is an abstract of a thesis submitted by J. M. Early in partial fulfillment of the requirements for the degree of Master of Science at the University of North Carolina, with completion of work by J. N. LeConte now of the University of Georgia. Alvin S. Wheeler is now deceased.

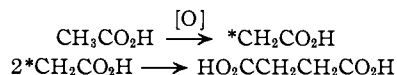
(1) G. R. Waitkins and C. W. Clark, *Chem. Rev.*, **36**, 235 (1945).

oxide; presumably the formation of carbon dioxide must also be accompanied by the formation of water. By approximate measurement the amount of carbon dioxide was that which should be expected from the amount of selenium dioxide used in excess of that required for the condensation reaction.

This reaction resembles those which Kharasch²

(2) M. S. Kharasch and M. T. Gladstone, *THIS JOURNAL*, **65**, 15 (1943).

has carried out with peroxides and it appears likely that it proceeds by a similar mechanism



RESEARCH AND DEVELOPMENT LABORATORIES
UNIVERSAL OIL PRODUCTS COMPANY
RIVERSIDE, ILLINOIS

RECEIVED MAY 10, 1947

COMMUNICATIONS TO THE EDITOR

A RAPID METHOD OF PREPARING NaC^{14}N FROM $\text{BaC}^{14}\text{O}_3$

Sir:

Studies on the exchange of radiocyanide ion with cyanide complexes have been initiated recently in this Laboratory. Since radiocarbon is presently available only in the form of barium carbonate, it was necessary to investigate various means of converting it into a soluble cyanide.

A possible procedure is that of Cramer and Kistiakowsky.^{1,2} This makes use of the reaction of gaseous ammonia and carbon dioxide with a potassium mirror. The procedure is somewhat elaborate and requires the use of a vacuum apparatus. For this reason, some simpler method of accomplishing the conversion would be highly desirable.

Several exploratory experiments were carried out on the use of electro-positive metals as reductants.³ It was found that insignificant yields of cyanide resulted on heating zinc, aluminum, magnesium or sodium with barium carbonate, in a nitrogen atmosphere. This is in agreement with Loftfield's report.²

Preliminary results indicate, however, that yields of 75–80% can be obtained by heating sodium azide and barium carbonate in a nitrogen atmosphere. The method has the advantage of requiring only about thirty minutes and not necessitating the use of any special apparatus.

The procedure is: 0.1 g. of barium carbonate is mixed with 1 g. of sodium azide (Amend Drug and Chemical Co., N. Y.) in a six-inch test-tube, and a slow stream of nitrogen is directed into the mouth of the tube. The mixture is then heated carefully so as to maintain a steady but not too rapid decomposition of the azide. The fumes of sodium oxide may be drawn off into a hood or through a funnel connected to an aspirator.

(1) Cramer and Kistiakowsky, *J. Biol. Chem.*, **137**, 549 (1941).

(2) Loftfield, "The Preparation of Carbon-fourteen Labelled Hydrogen Cyanide, Alanine and Glycine," Circular C-3, Isotopes Branch, United States Atomic Energy Commission, June, 1947.

(3) A portion of these experiments was carried out by Mr. M. Volpe.

When the decomposition is complete, the test-tube is heated at a dull red heat for ten minutes. After cooling, water is added dropwise until all of the sodium present has reacted. The solution is then diluted, acidified with sulfuric acid, and the hydrogen cyanide distilled over into a slight excess of sodium hydroxide solution.

Four experiments were made with inactive barium carbonate. The resulting cyanide was determined by adding ammonia and potassium iodide and titrating with silver nitrate solution. The average yield was $78 \pm 2\%$. In addition, two runs were made with added $\text{BaC}^{14}\text{O}_3$.⁴ The specific gravity of the radiocyanide, counted as silver cyanide, was within experimental error of the calculated value, indicating that the radiochemical yield is the same as the analytical yield.

Much of the cyanide is formed during the final heating when no sodium azide is present. This suggests that the actual reaction may involve not the sodium azide, but the sodium nitride formed by its decomposition.

Support of this investigation by a grant-in-aid from The Research Corporation is gratefully acknowledged.

(4) Supplied by the U. S. Atomic Energy Commission.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF SOUTHERN CALIFORNIA
LOS ANGELES, CALIFORNIA ARTHUR W. ADAMSON
RECEIVED SEPTEMBER 10, 1947

POLY-LYSINE

Sir:

On extending experiments concerning polymerization of amino acids¹ to basic amino acids, we succeeded in preparing poly-lysine. This polymer represents the first synthetic basic α -poly-amide and as it is water soluble, it may serve as a suitable model in protein research.

A suitable monomer was found in ϵ -carboxybenzoxy- α -carboxyl-1-lysine anhydride (I)² which

(1) Frankel and Katchalski, *THIS JOURNAL*, **64**, 2264 (1942); **64**, 2268 (1942).

(2) Bergmann, Zervas and Ross, *J. Biol. Chem.*, **111**, 245 (1935).