

## THE PHOTOCHEMICAL DECOMPOSITION OF ALKYL AZIDES

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**Abstract**—A study has been made of the products resulting from the solution photolyses of n-butyl azide, n-octyl azide, 4-phenyl-1-butyl azide,  $\alpha$ -azidobutyric acid,  $\alpha$ -azidoisobutyric acid, azidodiphenylacetic acid, ethyl  $\alpha$ -azidobutyrate,  $\alpha$ -azidovaleric acid, and ethyl  $\alpha$ -azidovalerate. The effect of variations in solvent and temperature has been investigated as well as the influence of benzophenone photosensitization and iodine catalysis.

In the case of the first three azides the predominant product (besides nitrogen) under all photolytic conditions studied was the aldimine formed by 1,2-hydrogen migration. Hydrogen abstraction probably from solvent accounted for small amounts of primary amine. 1,2 Alkyl migration accounted for the formation of some of the lower homologous amine. Also secondary amine (1–2%) formed by insertion into the solvent cyclohexane was observed. Photolysis of the  $\alpha$ -azido acids in methanol solution resulted in efficient decarboxylation and aldimine formation. Minor amounts of amino acid formed presumably *via* hydrogen abstraction from solvent were also obtained. In the case of azidodiphenylacetic acid, phenyl group migration occurs in competition with direct loss of carbon dioxide. Photolysis of the ethyl esters of the  $\alpha$ -azido acids yielded predominantly  $\alpha$ -imino esters.  $\alpha$ -Deuterio- $\alpha$ -azidobutyric acid has been synthesized and photolysed for the purpose of determining the sequence of steps in the photodecarboxylation reaction.

Intramolecular photocyclization of alkyl azides to form pyrrolidine derivatives has been found to be a highly irreproducible process.<sup>1</sup> In the systems studied this pathway accounted for only a very minor amount of product or none at all. The stability of pyrrolidine under the photolytic and work up conditions was established. In spite of the large number of experimental variations employed, the yield of cyclic product could not be improved. Conditions for high yield cyclization have not been defined in the present investigation; and based upon results obtained, the photochemical decomposition of alkyl azides does not appear to be a generally useful method for pyrrolidine synthesis.

<sup>1</sup> Since the original report of the photocyclization of alkyl azides to pyrrolidine derivatives by Barton and Morgan,<sup>2</sup> reference to unsuccessful attempts to repeat these experiments has been made recently by Smolinsky.<sup>3</sup> In initial experiments in our laboratory we succeeded in obtaining 2-n-butylpyrrolidine by irradiation of octyl azide. Subsequently we were unable to reproduce this result although as far as possible essentially identical reaction conditions were employed. In a private communication from Prof. D. H. R. Barton<sup>4</sup> we have learned that he so far had been unsuccessful in repeating the original photolytic cyclization of azides. In addition to the work reported in this paper, research continues in our laboratory directed towards resolving these ambiguities.

<sup>2</sup> D. H. R. Barton and L. R. Morgan, Jr., *Proc. Chem. Soc.* 206 (1961); *J. Chem. Soc.* 622 (1962).

<sup>3</sup> E. Wasserman, G. Smolinsky, W. A. Yager, *J. Amer. Chem. Soc.* **86**, 3166 (1964); <sup>4</sup> G. Smolinsky and B. I. Feuer, *Ibid.* **86**, 3085 (1964).

<sup>4</sup> D. H. R. Barton and A. N. Starratt, *J. Chem. Soc.* to appear. We wish to thank Prof. D. H. R. Barton for supplying us with a preprint of this paper.

The mechanism of the photolyses is discussed in terms of the possible formation of an alkyl nitrene and subsequent intervention of other intermediates. For the  $\alpha$ -azido acids, a dual mechanism for decarboxylation is discussed involving the  $\alpha$ -nitreno acid and  $\alpha$ -imino acid.

OVER the past few years the photochemical decomposition of organic azides has been the subject of considerable research.<sup>5</sup> The general pathway by which these reactions proceed involves absorption of radiant energy by the azido group followed by photodissociation to yield molecular nitrogen and a monovalent nitrogen radical, R—N, which is often called a nitrene. The electronic state of the nitrene may be either singlet or triplet; evidence from electron spin resonance studies on photochemically generated aryl,<sup>6</sup> sulphonyl<sup>6</sup> and alkyl nitrenes<sup>7</sup> stabilized at low temperatures indicates that these possess triplet ground state configurations. Among the reactions open to photochemically generated nitrenes are abstraction of hydrogen from solvent, insertion into solvent, 1,2-alkyl group migration, 1,2-aryl group migration, 1,2-hydrogen shift and dimerization to yield azo compounds.<sup>5a</sup> Intramolecular cyclization has been demonstrated for aryl azides and acyl azides.<sup>5a</sup> Also carboethoxynitrene has been shown to add to the double bond of cyclohexene to give an aziridine derivative<sup>8</sup> and to react similarly with benzene to give ultimately N-carboethoxy azepine.<sup>9</sup> In 1961 Barton and Morgan<sup>2</sup> reported on a series of photocyclization reactions which afford pyrrolidine derivatives *via* intramolecular attack of the nitrene at the  $\delta$ -carbon-hydrogen bond. The generality of this reaction was supported by several examples, and it was extended to serve as the basis for a remarkably simple synthesis of the steroidal alkaloid conessine. Formally this cyclization is related to other reactions which involve intramolecular functionalization at unactivated centres. Thus the Hofmann-Löffler-Freytag cyclization of N-haloamines,<sup>10</sup> the lead tetraacetate oxidation of monohydric alcohols<sup>11</sup> and the photochemical decomposition of hypohalites<sup>12</sup> afford saturated five-membered rings *via* reaction at an unactivated  $\delta$ -carbon-hydrogen bond. Preference for five-membered ring formation has been ascribed by Barton<sup>13</sup> to the stability of the six-membered transition state for hydrogen abstraction. Detailed mechanistic studies have been carried out on the Hofmann-Löffler-Freytag reaction,<sup>14,15</sup> and to a somewhat lesser degree the mechanism of the lead tetraacetate oxidation of monohydric alcohols has been elucidated.<sup>11,16</sup>

<sup>5</sup> For recent reviews dealing in part with the photochemical decomposition of alkyl azides see <sup>a</sup> R. A. Abramovitch and B. A. Davis, *Chem. Rev.* **64**, 149 (1964); <sup>b</sup> L. Horner and A. Christmann, *Angew. Chem.* **75**, 707 (1963).

<sup>6</sup> G. Smolinsky, E. Wasserman and W. A. Yager, *J. Amer. Chem. Soc.* **84**, 3220 (1962).

<sup>7</sup> E. Wasserman, G. Smolinsky and W. A. Yager, *J. Amer. Chem. Soc.* **86**, 3166 (1964).

<sup>8</sup> W. Lwowski, T. J. Maricich and T. W. Mattingly, Jr., *J. Amer. Chem. Soc.* **85**, 1200 (1963).

<sup>9</sup> K. Hafner and C. König, *Angew. Chem. Intern. Ed. Engl.* **2**, 96 (1963).

<sup>10</sup> For a review see M. E. Wolff, *Chem. Rev.* **63**, 55 (1963).

<sup>11</sup> For a review see K. Heusler and J. Kalvoda, *Angew. Chem.* **76**, 518 (1964).

<sup>12</sup> M. Akhtar and D. H. R. Barton, *J. Amer. Chem. Soc.* **83**, 2213 (1961).

<sup>13</sup> D. H. R. Barton, J. M. Beaton, L. E. Getler and M. M. Pechet, *J. Amer. Chem. Soc.* **82**, 2640 (1960).

<sup>14</sup> E. J. Corey and W. R. Hertler, *J. Amer. Chem. Soc.* **82**, 1657 (1960).

<sup>15</sup> R. S. Neale and M. R. Walsh, *J. Amer. Chem. Soc.* **87**, 1225 (1965).

<sup>16</sup> For recent contributions to the mechanism see <sup>a</sup> D. Hauser, K. Schaffner and O. Jeger, *Helv. Chim. Acta* **47**, 1883 (1964); <sup>b</sup> V. M. Micovic, R. I. Maumuzic and M. Lj. Mihailovic, *Tetrahedron Letters* No. **29**, 2091 (1963).

In order to learn whether the formal resemblance between the photodecomposition of alkyl azides and the above-mentioned reactions reflected a mechanistic relation we undertook a detailed study of the azide reaction. Our projected goals included (a) a test of the preference for five *versus* six-membered ring formation in systems where either could form, (b) an examination of the steric course of the reaction at the centre undergoing functionalization, (c) a test of the order of reactivity of primary *versus* secondary *versus* tertiary carbon-hydrogen bonds towards intramolecular abstraction by nitrene and, finally, (d) detection of a possible deuterium isotope effect in the abstraction process.

As a starting point for these studies an attempt was made to standardize the conditions for photodecomposition of *n*-butyl azide and *n*-octyl azide in terms of isolation of the cyclic products. Repetition of the photolyses as described by Barton and Morgan<sup>2</sup> proved to be somewhat more complex than was implied in their original experimental procedure. In the meantime, Smolinsky<sup>3</sup> of Bell Telephone Laboratories found it impossible to duplicate the photocyclization of *n*-butyl azide to pyrrolidine and *n*-octyl azide to 2-*n*-butylpyrrolidine. Furthermore, in subsequent investigations by Barton and Starratt,<sup>4</sup> the reactions of Barton and Morgan<sup>2</sup> could not be repeated. With these uncertainties in mind, we decided to postpone our original mechanistic study and rather concentrate upon the goal of obtaining a pyrrolidine derivative by photolysis of an alkyl azide. Although an inevitable product in all the photolyses was the aldimine, variable amounts of amines were obtained. The percentages of these compounds depended upon the reaction conditions, but unfortunately the variations were erratic. The uncertain nature of this reaction is further exemplified by our inability to reproduce our own earlier successful photochemical transformation of *n*-octyl azide to 2-*n*-butylpyrrolidine.<sup>17</sup>

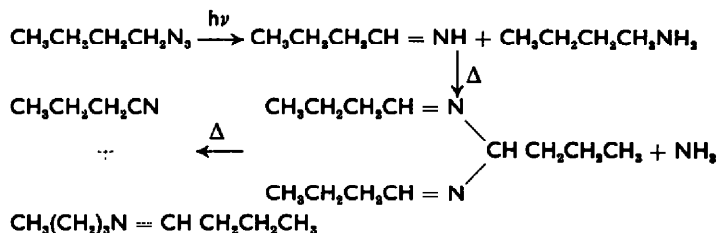
## RESULTS

In most cases the azides were prepared by two different methods. Their purity was established by application of the usual criteria, and the physical properties agreed in all cases with published data.

*Photolysis of n-Butyl Azide.* In typical experiments diethyl ether was used as solvent and solutions varying between 1 to 5% of azide were photolysed at 25–30° in a nitrogen atmosphere. Irradiation with a high pressure Hanau Immersion lamp was continued until disappearance of the azido asymmetric stretching vibration absorption in the IR at 4.70  $\mu$  (from one to two hr). Several work up procedures were employed. Saturation of the ethereal solution after photolysis with hydrogen chloride yielded a precipitate which was largely ammonium chloride. From this precipitate about a 5% yield of *n*-butyl amine was identified by means of vapour phase chromatography. No pyrrolidine was detected within the limits of our vapour phase chromatographic method (<1%). Treatment of the amine fraction with *p*-toluenesulphonyl chloride or picric acid failed to yield the corresponding pyrrolidine derivative as assayed by thin layer chromatography. In another experiment direct treatment of the photolysate with 2,4-dinitrophenylhydrazine in acid solution yielded about 70% of *n*-butyraldehyde-2,4-dinitrophenylhydrazone. In a separate series of runs, the concentrated photolysate was subjected to vapour phase chromatographic (VPC) analysis

<sup>17</sup> These earlier experiments were communicated to D. H. R. Barton in a letter on February 11, 1964.

and *n*-butyl amine, *n*-butyraldehyde, propyl cyanide were identified. Also about 30% of polymeric material was obtained. Since no nitrile absorption was observed in the IR of the photolysate prior to VPC, we infer that propyl cyanide forms by a secondary thermal process. Also attempted vacuum distillation of the photolysate led to extensive formation of nonvolatile higher mol. wt. products. Thermally induced condensation of *n*-butyl imine could account for these secondary products:



It is known<sup>18</sup> that isobutyraldehyde imine trimerizes to yield *N,N*-diisobutylidene-1,1-isobutyldiamine. Distillation leads to elimination of ammonia and formation of *N*-isobutylidene-isobutylamine. Similarly neopentaldehyde imine gives *N*-neopentylidene-neopentylamine and *t*-butyl cyanide upon heating.<sup>18</sup>

The above reactions led us to consider the possibility that pyrrolidine was perhaps formed in the photolysis but consumed by subsequent condensation with imine. This was shown not to be the case, however, for in an experiment in which pyrrolidine and a three fold excess of *n*-butyl azide were photolysed together, the pyrrolidine was recovered unchanged and in essentially quantitative yield. Use of benzophenone as a possible photosensitizer did not lead any change in the distribution of products relative to the unphotosensitized process. Analysis of the photolysate by VPC definitely excluded pyrrolidine as a product. Using cyclohexane as solvent and an acid hydrolytic work up, *n*-propyl amine, *n*-butyl amine and *n*-butylcyclohexylamine were identified by TLC and VPC. Each was formed in about 1% yield.

*n*-Octyl azide. In a typical experiment, a 1% solution of *n*-octyl azide was irradiated as described above. In various runs diethyl ether, *n*-hexane and cyclohexane were used as solvents. Photolyses in cyclohexane were carried out at several concentrations and a variety of work up procedures were used. Distillation of the photolysate gave about 12.5% of *n*-octyl amine as the main volatile product. A small amount of product (about 3–5%) which possessed the same retention time in the VPC as 2-*n*-butyl-pyrrolidine was also obtained. The yield of this fraction varied from run to run but in no case did it exceed 5%. Extensive polymerization of the higher boiling part of the photolysate occurred during distillation possibly due to self condensation of *n*-octaldehyde imine as discussed earlier. Direct treatment of the photolysate solution in cyclohexane with 2,4-dinitrophenylhydrazine in acid solution afforded a 50% yield of *n*-octaldehyde-2,4-dinitrophenylhydrazone. Vapour phase chromatographic analysis of the photolysate showed that the major products were *n*-octaldehyde, *n*-octyl amine, *n*-heptyl cyanide and dimeric material. In another experiment the basic fraction after acid hydrolysis was separated and analysed by TLC and VPC *n*-octylamine (8.5%), *n*-octyl cyclohexylamine (1.0%) and a trace of 2-butylpyrrolidine were identified.

<sup>18</sup> R. H. Hasek, E. U. Elam and J. C. Martin, *J. Org. Chem.* **26**, 1882 (1961).

Additional photochemical experiments were carried out in order to learn the possible effect of impurities which might be present in the azides as trace contaminants. Conceivably alkyl iodide or molecular iodine carried over in the synthesis of the azide might act as catalysts for intersystem crossing of the intermediary nitrene. Others have attempted to catalyse singlet-triplet interconversion of methylene with iodine (methyl iodide solution).<sup>19</sup> While this possibility was extremely unlikely in the present system, since such catalysis requires collision for spin inversion and trace quantities hardly could be efficient in this process, experiments were carried out with solution of 1% azide and 0.004% to 0.01% iodine in cyclohexane. The results obtained were qualitatively similar to the uncatalysed reaction in that the imine was the main product, however, small (3%) and fairly reproducible amounts of 2-n-butyl pyrrolidine were indicated in the VPC. However, photochemical production of iodine atoms could change the mechanism of the reaction. Similarly, photodecomposition of n-octyl azide in the presence of methyl iodide yielded n-octaldehyde imine as the main product and minor amounts of n-octyl amine along with material having a similar retention time in the VPC as 2-n-butylpyrrolidine. Irradiation of n-octyl azide as a pure solid at  $-50^{\circ}$  was not very useful due to poor absorption of light. Only low conversions to n-octaldehyde imine were observed; no other product was isolated.

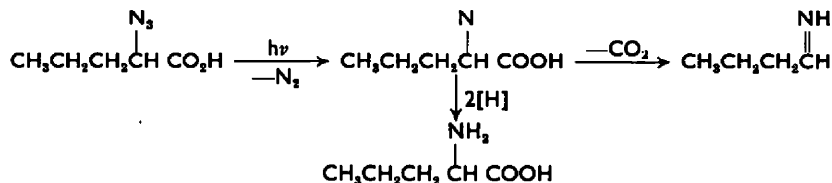
*4-Phenyl-1-butyl azide.* Intramolecular insertion of a nitrene into a benzylic carbon-hydrogen bond should have a lower activation energy compared to insertion into the primary and secondary aliphatic ones present in n-butyl and n-octyl azides. Therefore, a series of photolyses of 4-phenyl-1-butyl azide was carried out in various solvents. Separation of the photolysate into a basic fraction and neutral fraction was performed. Examination of the basic fraction by VPC revealed the presence of no material with the same retention time as synthetic 2-phenylpyrrolidine. Tosylation of the basic part followed by thin layer chromatographic (TLC) analysis revealed that no detectable amount of 2-phenylpyrrolidine was present. The neutral part was subjected to acid hydrolysis and a 25% yield of 4-phenylbutyraldehyde was isolated as its semicarbazone. From the acidic portion of the hydrolysate, a 7-8% yield of an amine was isolated which had the same retention time in the VPC as 2-phenylpyrrolidine and also yielded a picrate derivative which was indistinguishable from authentic 2-phenylpyrrolidine picrate. That this product was not obtained by direct acidification of the photolysate, but only after hydrolytic treatment in which 4-phenylbutyraldehyde was obtained, suggested that 2-phenylpyrrolidine may form in the photolysis but then condense with 4-phenylbutyraldehyde-imine. It is conceivable that subsequent hydrolysis of this proposed condensation product releases 4-phenylbutyraldehyde and 2-phenylpyrrolidine.

In addition to 4-phenyl-1-butyl amine and 2-phenylpyrrolidine, tetrahydrobenzazepine may, in principle, form *via* insertion into an aromatic carbon-hydrogen bond. This latter compound was not detected.

*$\alpha$ -Azido acids and  $\alpha$ -azido esters.* Photolysis of  $\alpha$ -azidobutyric acid in methanol proceeded with 60% evolution of carbon dioxide. Propionaldehyde imine was formed in 25% yield and identified by conversion to its 2,4-dinitrophenylhydrazone derivative. No other 2,4-dinitrophenylhydrazone was detected by TLC. Similar photolysis of  $\alpha$ -azidovaleric acid yielded 60% carbon dioxide and 20% of n-butyraldehyde imine

<sup>19</sup> H. M. McConnell, *J. Chem. Phys.* **20**, 1043 (1952); **23**, 2440 (1955).

identified as the 2,4-dinitrophenylhydrazone. Also ( $\pm$ )- $\alpha$ -aminovaleric acid was shown to be present while ( $\pm$ ) proline was not detected. The photodecomposition of the latter  $\alpha$ -azido acid may be represented as follows:



A concerted loss of nitrogen and carbon dioxide is both attractive and possible. However, no conclusive evidence to this point has been obtained in the present study.

The above description of the photodecarboxylation is not unequivocal. Instead of loss of carbon dioxide directly from the nitrene,<sup>20</sup> 1,2-hydrogen migration might take precedence. The resulting  $\alpha$ -imino acid conceivably could undergo photodecarboxylation to yield the aldimine and carbon dioxide. We have shown that pyruvic acid N-methylimine and benzoylformic acid N-phenylimine undergo photodecarboxylation.<sup>21</sup> Leermakers and Vesley<sup>22</sup> have shown that photolysis of pyruvic acid in water leads to formation of carbon dioxide and acetoin. The most direct experimental method for testing the intermediacy of the  $\alpha$ -imino acid would obviously be irradiation of a pure sample in a separate experiment. Unfortunately  $\alpha$ -ketobutyric acid imine and  $\alpha$ -ketovaleric acid imine could not be synthesized due to their inherent instability.

In order to determine to what extent the direct mechanism was operative, the photolysis of  $\alpha$ -deuterio- $\alpha$ -azidobutyric acid was studied. The propionaldehyde-2,4-dinitrophenylhydrazone which was obtained was found to contain 58% deuterium.<sup>23</sup> NMR analysis revealed that the deuterium was at the aldehydic carbon atom. Since formation of the  $\alpha$ -imino acid requires migration of the  $\alpha$ -hydrogen or  $\alpha$ -deuterium from carbon to nitrogen it may be concluded that direct decarboxylation occurs at least to the extent of 50%. The undeuterated propionaldehyde-2,4-dinitrophenylhydrazone may originate from photodecarboxylation of the  $\alpha$ -imino acid. Clarification of this point awaits the synthesis of pure  $\alpha$ -imino derivatives of  $\alpha$ -ketobutyric and  $\alpha$ -ketovaleric acids.

<sup>20</sup> Intervention of a discrete nitrene is assumed. Of course a concerted mechanism need not require a nitrene. In MeOH solution, the  $\alpha$ -azido acids would be expected to be partially dissociated. The question arises whether the conjugate base or undissociated acid is the species which undergoes decarboxylation. However, since photodecarboxylation occurs in benzene solution, it is clear that the carboxylate anion is not required. Also, one must recognize the possibility of photosensitization occurring with benzene as solvent. We thank the referees for calling both points to our attention.

<sup>21</sup> The photochemically induced decarboxylation of N-alkyl and N-aryl  $\alpha$ -imino acids will be discussed in a separate publication.

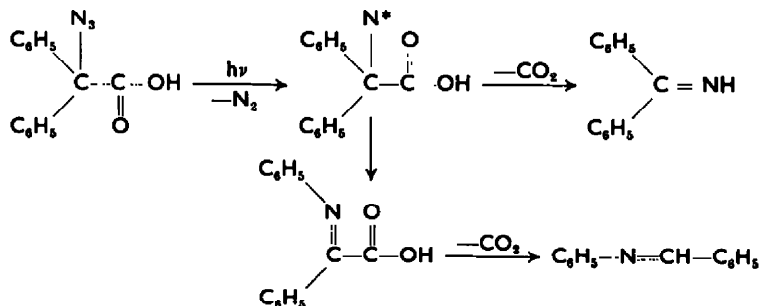
<sup>22</sup> P. A. Leermakers and G. F. Vesley, *J. Amer. Chem. Soc.* **85**, 3776 (1963).

<sup>23</sup> Deuterium analyses were carried out by J. Nemeth, Urbana, Illinois.

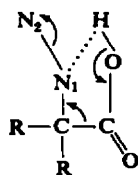
In order to learn whether alkyl or aryl group migration to nitrogen could compete with loss of carbon dioxide, the photolyses of  $\alpha$ -azidoisobutyric acid and azido-diphenylacetic acid were studied.

$\alpha$ -Azidoisobutyric acid was irradiated and found to undergo decarboxylation to the extent of 30%. Treatment of the photolysate with 2,4-dinitrophenylhydrazine in acid solution yielded 25% acetone-2,4-dinitrophenylhydrazone but no acetaldehyde-2,4-dinitrophenylhydrazone. No trace of the latter could be detected by TLC analysis of the total 2,4-dinitrophenylhydrazone portion or by NMR analysis. In a separate experiment pyruvic acid methylimine, the product of 1,2-methyl shift in an assumed  $\alpha$ -nitreno-isobutyric acid intermediate, was irradiated and found to undergo decarboxylation to yield carbon dioxide and acetaldehyde-imine (isolated as the 2,4-dinitrophenylhydrazone).<sup>21</sup>

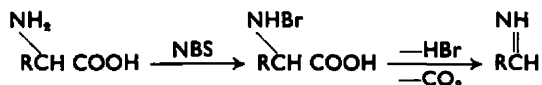
In the case of azidodiphenylacetic acid, however, phenyl group migration to nitrogen did occur to a significant extent. Photolysis of this acid yielded 75% of carbon dioxide. Treatment of the photolysate with 2,4-dinitrophenylhydrazine in acid solution yielded a mixture of benzophenone-2,4-dinitrophenylhydrazone (20%) and benzaldehyde-2,4-dinitrophenylhydrazone (30%). The yields are based upon the starting azido acid. Benzophenone is considered to result from direct photodecarboxylation at the nitrene stage. Benzaldehyde could derive from initial migration of a phenyl group to the nitrene nitrogen to yield benzoylformic acid phenylimine. Subsequent photodecarboxylation could yield benzaldehyde phenylimine. That this in fact is a valid presupposition was demonstrated by showing in a separate experiment that irradiation of benzoylformic acid phenylimine yielded carbon dioxide and benzaldehyde phenylimine.<sup>21</sup> Hydrolysis yielded aniline and benzaldehyde. The photodecarboxylation of  $\alpha$ -azidodiphenylacetic acid may be considered to proceed *via* a dual mechanism involving both direct loss of carbon dioxide from the nitrene and also phenyl group migration followed by decarboxylation:



As mentioned earlier it is possible that concerted loss of nitrogen and carbon dioxide occurs. One could envision a bridged transition state involving a hydrogen bond between  $N_1$  and the carboxyl group proton:



This representation of the transition state for the reaction raises the basic question of whether a discrete nitrene is involved at all in these decarboxylation reactions.<sup>20</sup> The system under investigation represents a special case of the general category of reactions for which simultaneity of reaction steps in a cyclic process cannot be decided. We have no evidence in support of a discrete nitrene or concerted reaction pathway. The representation of a free nitrene is a convenient formalism. It is not required by our results nor can it be definitely excluded. The photodecarboxylation of  $\alpha$ -azido acids resembles the bromodecarboxylation reaction of amino acids.<sup>24</sup>



Boyer and Stocker<sup>25</sup> have found that acid-catalysed decomposition of  $\alpha$ -azidoisobutyric acid and  $\alpha$ -azidophenyl acetic acid proceeds with methyl group migration and 1,2 hydrogen shift, respectively; no decarboxylation was reported by these workers.

Photolysis of ethyl  $\alpha$ -azidobutyrate in anhydrous ether did not yield carbon dioxide. A 15% yield of ethyl  $\alpha$ -ketobutyrate imine was obtained as the 2,4-dinitrophenylhydrazone derivative after hydrolysis. No propionaldehyde-2,4-dinitrophenylhydrazone was obtained. Similarly photolysis of ethyl  $\alpha$ -azidovalerate proceeded without loss of carbon dioxide and with formation of 15% of ethyl  $\alpha$ -ketovalerate imine (isolated as the 2,4-dinitrophenylhydrazone). Isolation of the amino acid part by hydrolysis gave a small yield of ( $\pm$ )  $\alpha$ -aminovaleric acid but no ( $\pm$ )-proline could be obtained. In agreement with these results Barton and Morgan have reported that photolysis of ethyl  $\alpha$ -azidopropionate<sup>2</sup> yields 34% of ethyl pyruvate imine.

## DISCUSSION

A starting point for the discussion of the photolysis of alkyl azides is the excitation process and subsequent dissipation of absorbed energy. Two electronic absorption bands occur in alkyl azides around 2160 Å ( $\epsilon \cong 500$ ) and 2870 Å ( $\epsilon \cong 25$ ). The low intensity of the latter is due to the fact that it is a "perpendicular" transition<sup>26</sup> and hence a forbidden one. Under the photolytic conditions used in the present investigation the longer wavelength  $\pi \rightarrow \pi^*$  transition is the one of concern. The initially formed excited singlet azide could convert to an excited triplet. Dissociation could result from either the excited singlet or triplet azide.

The incident radiation has energy in the range of 100 kcal/mole. The bond dissociation energy for RN—N<sub>2</sub> is probably no more than 40 kcal/mole. Thus dissociation of the excited singlet azide to singlet nitrene and singlet nitrogen molecule in the gas phase produces these species with about 60 kcal/mole excess energy shared between them.<sup>27</sup> In solution collisional deactivation certainly would remove part of this excess energy, however the excited nitrene would be expected to be in a high energy state. Reaction could occur from either singlet or triplet excited state or, less likely, from a vibrationally excited ground singlet state. No fluorescence could be detected

<sup>24</sup> N. Konigsberg, G. Stevenson and J. M. Luck, *J. Biol. Chem.* **235**, 1341 (1960).

<sup>25</sup> J. H. Boyer and J. Stocker, *J. Org. Chem.* **21**, 1030 (1956).

<sup>26</sup> W. D. Closson and H. B. Gray, *J. Amer. Chem. Soc.* **85**, 290 (1963).

<sup>27</sup> C. L. Curry and B. de B. Darwent, *Canad. J. Chem.* **41**, 1552 (1963).



at 77°K for either n-octyl azide or  $\alpha$ -azidovaleric acid as pure solids.<sup>28</sup> The cyclic arrangement of the alkyl azide which is required for  $\delta$ -hydrogen abstraction places rather strict conformational requirements upon the component carbon atoms. In contrast, 1,2-hydrogen migration would appear to be a much more favourable process. The activated nitrene would possess more than enough energy for the carbon-hydrogen bond cleavage, and also partial bridging of the hydrogen between carbon and nitrogen would further lower the energy requirement for hydrogen transfer. It would appear that the lifetime of the excited state is too short to allow ring formation and that the extremely facile hydrogen migration takes precedence over the cyclization process. In other words, the fastest process of chemical significance which occurs in the deactivation of the excited state in the condensed phase is 1,2-hydrogen migration. Since internal conversion from the excited singlet to a vibrationally excited ground state singlet would be extremely rapid ( $10^{-11}$  sec), it is difficult to identify the electronic state responsible for reaction.

The high reactivity of the alkyl nitrene is probably due to the instability associated with the presence of two unpaired electrons localized on nitrogen. Relatively little overlap with the alkyl  $\sigma$  bonds is possible. If a group is attached to nitrogen which is capable of delocalizing one of the unpaired electrons, then a more stable nitrene occurs. Thus, it has been observed that aryl nitrene and arylsulphonyl nitrene exist as stable triplets at 77°K.<sup>6</sup> We have found that alkyl nitrenes such as n-octyl and triphenylmethyl cannot be observed in the ESR at 77°K.<sup>29</sup> Wasserman *et al.*<sup>7</sup> have shown that at 4°K alkyl nitrenes are stable. Also we have found that methanesulphonyl nitrene, in the solid state, is observable as a triplet in the ESR up to 253°K.<sup>29</sup> The kind of reactivity shown by "delocalized nitrenes" differs from that of the alkyl nitrene. Typically o-azidobiphenyl upon photolysis yields carbazole while  $\beta$ -phenylethyl azide upon similar treatment did not yield dihydroindole.<sup>30</sup> Photo-addition of delocalized nitrene to double bonds is known<sup>8</sup> and intramolecular insertion of acyl nitrenes occurs.<sup>31-33</sup>

This heightened selectivity displayed by "delocalized nitrenes" probably is a result of their longer lifetime. Furthermore the very facile imine formation cannot occur in these cases since no  $\alpha$ -hydrogen is present for 1,2-shift.

## EXPERIMENTAL

M.ps are uncorrected. IR spectra were recorded on a Perkin-Elmer Infracord Spectrophotometer. UV spectra were determined on a Bausch and Lomb Model 505 recording spectrophotometer. NMR spectra were taken using a Varian A-60 spectrophotometer operating at 60.0 Mc/s, CCl<sub>4</sub> was used as solvent unless otherwise stated. An F and M Model 500 gas chromatograph was used. MgSO<sub>4</sub> served as drying agent. Microanalyses were carried out by George Robertson, Florham Park, New Jersey. VPC analyses of the amine mixtures were carried out on a 7'  $\times$  0.25" column of 30% SE-30 methyl silicone rubber gum 60/80 mesh gas-chrom P. The column packing was suggested and kindly supplied by Dr. H. Fales, National Institutes of Health, Bethesda 14, Maryland.

*General procedure for irradiation.* A Hanau high press. (Q81, 0.5 watt at 2,800 Å) immersion lamp surrounded by a quartz water-cooled heat exchanger was placed directly into the solution to

<sup>28</sup> We wish to thank Miss Sandra A. Mancewicz, National Naval Medical Center, Washington, D.C.

<sup>29</sup> Unpublished results with G. King, Fort Belvoir, Virginia.

<sup>30</sup> P. A. S. Smith and B. B. Brown, *J. Amer. Chem. Soc.* **73**, 2435 (1951).

<sup>31</sup> J. W. ApSimon and O. E. Edwards, *Canad. J. Chem.* **40**, 896 (1962).

<sup>32</sup> W. L. Meyers and A. S. Levinson, *J. Org. Chem.* **28**, 2856 (1963).

<sup>33</sup> S. Masamune, *J. Amer. Chem. Soc.* **86**, 290 (1964).

be irradiated.  $N_2$  was constantly bubbled through the solution during the photolysis. In quantitative determinations of  $CO_2$  the evolved gases were passed into an aqueous solution of  $Ba(OH)_2$ . Also the  $CO_2$  evolution was followed by absorption in standard KOH aq and determining the change in pH. The disappearance of the azide was followed by the diminution of azide absorption ( $4.69 \mu$ ) in the IR as the photolyses progressed.

*n-Butyl azide.* This compound was prepared by the method of Lieber, *et al.*,<sup>34</sup> and it had b.p.  $65-69^\circ$  (220 mm),  $n_D^{25}$  1.4193; lit.<sup>34</sup>, b.p.  $71^\circ$  (225 mm)  $n_D^{20}$  1.4192. The NMR showed the  $\underline{CH_2}-CH_2$  triplet centered at  $9.00 \tau$ ,  $J = 7$  c/s and the  $\underline{CH_2}-N_3$  triplet centered at  $6.64 \tau$ ,  $J = 6.5$  c/s.

*n-Octyl azide.* This azide was prepared by the method of Lieber *et al.*<sup>34</sup> and it had b.p.  $75^\circ$  (6 mm),  $n_D^{25}$  1.4359; lit.<sup>34</sup>, b.p.  $62^\circ$  (3.3 mm),  $n_D^{20}$  1.4368, the NMR showed the  $\underline{CH_2}-CH_2$  triplet centered at  $9.10 \tau$ ,  $J = 5.5$  c/s and the  $\underline{CH_2}-N_3$  triplet at  $6.70 \tau$ ,  $J = 6$  c/s.

*4-Phenyl-1-butyl azide.* 4-Phenyl-1-butyl alcohol was prepared by the method of Oae *et al.*<sup>35</sup> and had b.p.  $103-104^\circ$  (6 mm), lit.  $124-125^\circ$  (14 mm). 4-Phenyl-1-butyl bromide was prepared from the alcohol by the method of Badger and Kimber<sup>36</sup> and had b.p.  $119-121^\circ$  (8 mm),  $n_D^{24}$  1.5390, lit. b.p.  $132^\circ$  (12 mm),  $n_D^{19}$  1.5408. The bromide was converted to the azide by two different methods:

A. A mixture of 4-phenyl-1-butyl bromide (10.7 g, 0.05 mole), 15 ml 95% EtOH,  $NaN_3$  (7.0 g, 0.11 mole) and 10 ml water was kept at reflux for 3-4 hr. At the end of this time the reaction mixture was diluted with water, extracted with ether, and the dried extracts were concentrated *in vacuo*. Distillation of the crude product afforded 7.1 g (81%) pure azide, b.p.  $114-116^\circ$  (4 mm),  $n_D^{25}$  1.5188. The NMR showed aromatic protons at  $2.28 \tau$  (5H) singlet and  $\underline{CH_2}-N_3$  triplet centered at  $6.67 \tau$ ,  $J = 6.5$  c/s.

B. 4-Phenyl-1-butyl bromide (19.2 g; 0.09 mole) was added in one portion with stirring to a solution of  $NaN_3$  (10.0 g, 0.15 mole) dissolved in 130 ml methyl carbitol and 23 ml water. The mixture was heated at  $95^\circ$  for 24 hr. The resulting solution was diluted with water extracted with ether and the combined extracts were dried and concentrated *in vacuo*. Distillation yielded the pure azide, 11.4 g (71%), b.p.  $93-94^\circ$  (2 mm),  $n_D^{25}$  1.5180. The IR and NMR spectra were essentially identical with those of a sample prepared by Method A.

*Ethyl  $\alpha$ -azidobutyrate.* Treatment of ethyl  $\alpha$ -bromobutyrate with  $NaN_3$  in aqueous EtOH yielded the  $\alpha$ -azido ester,<sup>37</sup> b.p.  $59-60^\circ$  (6 mm), lit.<sup>37</sup>  $63-64^\circ$  (6.5 mm). The NMR showed  $-\underline{CH}-N_3$  triplet at  $6.17 \tau$ ;  $J$ , 7.0 c/s.

*$\alpha$ -Azidobutyric acid.* Saponification of the above ester yielded the acid, b.p.  $64^\circ$  (0.08 mm), lit.<sup>37</sup>  $81^\circ$  (0.11 mm); NMR showed  $-\underline{CH}-N_3$  triplet at  $6.01 \tau$ ;  $J$ , 7.0 c/s.

*Ethyl  $\alpha$ -azidovalerate.* This compound was prepared as described above from the  $\alpha$ -bromo ester in a yield of 80% and had b.p.  $65-70^\circ$  (2.8 mm). The NMR showed  $\underline{CH}-N_3$  triplet at  $6.14 \tau$ ;  $J$ , 6.5 c/s.

*$\alpha$ -Azidovaleric acid.* The ester was hydrolysed as described above to give the acid in 77% yield. The acid had b.p.  $80-81^\circ$  (0.4 mm), and the NMR possessed absorption at  $6.00 \tau$  (triplet);  $J$ , 6.5 c/s.

*Ethyl  $\alpha$ -azidoisobutyrate.* Treatment of ethyl  $\alpha$ -bromoisobutyrate with  $NaN_3$  in aqueous EtOH yielded the  $\alpha$ -azido ester b.p.  $48.5^\circ$  (6.5 mm), lit.<sup>37</sup>  $52-53^\circ$  (6.5 mm).

*$\alpha$ -Azidoisobutyric acid.* Saponification of the above ester yielded the corresponding acid, b.p.  $59-61^\circ$  (0.05-0.1 mm), lit.<sup>37</sup>  $75^\circ$  (0.15 mm).

*Azidodiphenylacetic acid.* Bromodiphenylacetone nitrile was prepared according to the method of Kaufmann *et al.*<sup>38</sup> and had b.p.  $137^\circ$  (0.08-0.1 mm). Azidodiphenylacetone nitrile was prepared by treatment of bromodiphenylacetone nitrile with  $NaN_3$  in aqueous acetone and it had m.p.  $41^\circ$ , lit.<sup>39</sup>  $41^\circ$ . The nitrile was hydrolysed to the corresponding acid by reaction with 20% alcoholic KOH aq, and had m.p.  $143-145^\circ$ , lit.<sup>39</sup>  $147-150^\circ$ .

*2-n-Butylpyrrolidine (A).* Following the method of Hess<sup>40</sup> pyrrol propyl ketone was reduced with Na in EtOH to 1-( $\alpha$ -pyrrolidyl)-butan-1-ol. The NMR spectrum showed no olefinic proton absorption. Reduction of this alcohol with HI and red P yielded 2-n-butylpyrrolidine, b.p.  $70-80^\circ$

<sup>34</sup> E. Lieber, T. S. Chao and C. N. R. Rao, *J. Org. Chem.* **22**, 238 (1957).

<sup>35</sup> S. Oae and C. A. van der Werf, *J. Amer. Chem. Soc.* **75**, 5037 (1953).

<sup>36</sup> G. M. Badger and R. W. L. Kimber, *J. Chem. Soc.* 2455 (1958).

<sup>37</sup> M. O. Forster and R. Muller, *J. Chem. Soc.* 191 (1909).

<sup>38</sup> P. Kaufmann, M. B. Frankel and H. S. Mosher, *J. Amer. Chem. Soc.* **76**, 5794 (1954).

<sup>39</sup> K. Hohenlohe-Oehringen, *Monatsh.* **89**, 557 (1958).

<sup>40</sup> K. Hess, *Ber. Dtsch. Chem. Ges.* **52**, 1633 (1919).

at 30–35 mm lit.<sup>40</sup>, 154–156° (753 mm). This material was further purified by VPC. The chloroplatinate of the purified material had m.p. 178–180°, lit.<sup>40,41</sup> 178°.

(B) An alternative procedure due to Cantor and van der Werf<sup>41</sup> was also employed for the preparation of 2-n-butylpyrrolidine. 2-n-Butylpyrrole was prepared by the action of n-butyl bromide upon pyrrol magnesium bromide. Catalytic reduction of this compound yielded 2-n-butylpyrrolidine. The NMR spectrum was in complete agreement with the assigned structure. The spectrum possessed a signal at 9.08 ( $J = 5$  c/s) for the terminal methyl group. Complex methylene absorption at 8.66  $\tau$  (6H) and at 8.26  $\tau$  (4H) was observed. Additional absorption occurred at 7.12  $\tau$  (4H). No olefinic proton absorption was present. The *p*-toluene-sulfonamide had m.p. 52–53° (purified by recrystallization from EtOH).

*$\alpha$ -Phenylpyrrolidine.* Following the method of Knott<sup>42</sup> acetophenone was treated with formaldehyde and dimethylamine hydrochloride to yield  $\beta$ -dimethylamino propiophenone hydrochloride. Treatment with KCN yielded  $\beta$ -benzoylpropionitrile which was treated with Raney Ni to yield 2-phenylpyrrolidine. LAH reduction yielded 2-phenylpyrrolidine, b.p. 50° (0.1 mm), picrate 148–149°.

*n-Octaldehyde-imine.* Anhydrous  $\text{NH}_3$  was passed into a mixture of n-octaldehyde (27 g, 0.21 mole) and 1 g anhydrous  $\text{K}_2\text{CO}_3$ . The mixture was analysed by VPC (SE-30 on Gas-Chrom. P column at 150°). Two main peaks were observed and they corresponded to n-octaldehyde and n-heptyl cyanide.

*Benzoylformic acid N-phenylamine.* To a solution of 1.0 g benzoylformic acid in 20 ml dry benzene was added 1.0 g aniline dissolved in 5 ml benzene. After 0.5 hr the imino acid precipitated in 80% yield; m.p. 149–150°, lit.<sup>43</sup> 150°.

#### Photolytic experiments

*n-Butyl azide.* A solution of n-butyl azide (1.0 g, 0.0101 mole) dissolved in 100 ml ether was irradiated for 3 hr. Addition of HCl gas resulted in the precipitation of  $\text{NH}_4\text{Cl}$ , 0.487 g (90%). The ether filtrate was refluxed with 300 ml saturated solution of 2,4-dinitrophenylhydrazine in 2 N HCl for 2 hr. Ether was evaporated from the two-phase system and the 2,4-dinitrophenylhydrazone derivative of butyraldehyde was collected by filtration, 1.18 g (77%). Its identity was established by m.p. and m.m.p. (120–122°), lit.<sup>43</sup> 122°, and also by TLC using benzene as the solvent.

In another experiment, n-butyl azide (1.0 g, 0.0101 mole) was dissolved in 100 ml anhydrous ether and irradiated for 3 hr. Distillation of ether through a fractionating column yielded a residue ca. 3 g (containing ether). The residue was subjected to VPC analysis on a 30% SE 30 column on Gas Chrom P, kept at 65°. The VPC chromatogram revealed the presence of n-butyraldehyde, n-butyronitrile and two other products of higher retention times and variable compositions (dimeric or trimeric forms of butyraldehyde imine). The identities of the aldehyde and the nitrile were established by comparison of peak positions in the VPC and IR spectra of the authentic compounds. In other experiments, solutions containing 2.0 g n-butyl azide in 120 ml of dry cyclohexane were irradiated for 3 hr. The photolysate was shaken with 50 ml 2N HCl overnight. The aq. layer was separated, washed with ether, concentrated under vacuum, cooled and basified with 50% NaOH aq. The liberated bases were taken up in ether, dried and concentrated by distillation at atm. press. using packed column up to a temp of 36–37. TLC of the concentrate using butanol-acetic acid-water (80:10:20 by volume) revealed the presence of n-propyl amine as the major component ( $R_f = 0.24$ ) and n-butylamine as the minor component ( $R_f = 0.37$ ). Another component appeared with  $R_f = 0.63$  which corresponds to N-n-butylcyclohexylamine. Quantitative VPC analyses showed this latter compound to the extent of 1.5% (based on starting azide). Identities of these amines were established by using a different proportion of the above solvent combination, namely 60:20:20. Authentic pyrrolidine appears as a bright yellow elongated spot ( $R_f = 0.16$ ) on TLC (ninhydrin as chromogen), others are purple to brown. Only a trailing appeared corresponding to pyrrolidine from the irradiation products.

*n-Butyl azide and pyrrolidine.* A solution containing n-butyl azide (1.5 g, 0.015 mole) and pyrrolidine (0.4 g, 0.006 mole) in 100 ml ether was irradiated for 3 hr. The ether was carefully removed

<sup>41</sup> P. A. Cantor and C. A. van der Werf, *J. Amer. Chem. Soc.* **80**, 970 (1958).

<sup>42</sup> E. B. Knott, *J. Chem. Soc.* 186 (1948).

<sup>43</sup> C. F. H. Allen, *J. Amer. Chem. Soc.* **52**, 2955 (1930).

by distillation and the concentrated photolysate was examined by means of VPC at 65° column temp. The pyrrolidine peak was clearly resolved along with the other peaks observed in the irradiation product of *n*-butyl azide in ether. Furthermore, pure pyrrolidine was quantitatively recovered after irradiation in ether under typical conditions used for the azide photolyses. The reaction mixture was analysed by a quantitative VPC method at a column temp of 65°.

*n*-Butyl azide and benzophenone. A solution containing *n*-butyl azide (2.0 g, 0.02 mole) and benzophenone (1.82 g, 0.01 mole) in 250 ml ether was irradiated for 5 hr with a pyrex filter. VPC analysis of the photolysate revealed a pattern quite similar to the unphotosensitized reaction. The absence of pyrrolidine was proven by addition of pure pyrrolidine to the photolysate and VPC analysis at 65°. The added pyrrolidine was well resolved and clearly not present in the original photolysate.

*n*-Octyl azide. In a typical experiment a solution of 1.0 g azide in 100 ml cyclohexane was irradiated at 22–23° for 3 hr. The solvent was removed by distillation at atm. press. through an efficient column. Further distillation at 200 mm yielded a distillate, 0.105 g, from which *n*-octylamine could be separated (12.5% from starting azide). Its identity was established by VPC analysis at 140° column temp and also by formation of the chloroplatinate derivative, m.p. 198–200°, lit. 200°. Another portion of the residue was treated with 2,4-dinitrophenylhydrazine and an amount of *n*-octanaldehyde-2,4-dinitrophenylhydrazone corresponding to a 50% yield was obtained, (1.0 g), m.p. 105–106°, lit.<sup>43</sup> 106°.

VPC analysis of the photolysate upon 30% SE 30 column at 140° revealed the presence of 3 fractions which were collected and identified as *n*-octaldehyde, *n*-heptyl cyanide and butyl carbitol (solvent in which *n*-octyl azide was prepared). In other experiments, solutions containing 2.0 g (12.9 mmole) of *n*-octyl azide in 120 ml cyclohexane were irradiated for 3–3.5 hr using a quartz window or pyrex filter. Hydrolytic work up followed by TLC and VPC analyses as detailed under butyl azide, definitely established the presence of *N*-cyclohexyl-*n*-octylamine to the extent of 0.5–1.1%, together with other amines. These other amines are probably a mixture of *n*-heptyl and *n*-octyl amines which could not be well resolved in either form of chromatography. Also 2-butylpyrrolidine was found to be present in minor amounts in the TLC as evidenced by a bright yellow color reaction when ninhydrin was used as chromogen. EtOH-NH<sub>4</sub>-OH (4:1) was also used as solvent system for the amine-TLC with Dragendorff-Munier reagent as chromogen. The different conditions of photolyses did not affect the nature of the products, but slightly affected their distribution; namely, with quartz window, total primary amine was obtained in 8.4% yield and cyclohexyloctylamine in 1.03% and with pyrex filter the corresponding amounts were 15.5% and ca. 0.5%.

*In the presence of iodine.* A solution of 3.0 g *n*-octyl azide and 0.100 g I<sub>2</sub> in 250 ml cyclohexane was irradiated for 3 hr. At the end of this time 8 ml 5 N HCl was added and the mixture was stirred at room temp overnight. The layers were separated and the cyclohexane portion was washed with water and then dried and distilled at red. press. After most of the cyclohexane had been removed, the residual liquid was treated with 2,4-dinitrophenylhydrazine in methanolic HCl. A precipitate of *n*-octaldehyde-2,4-dinitrophenylhydrazone was obtained.

The aqueous acidic layer was basified in the cold with 5 N NaOH and the liberated base were extracted with ether. The ether was dried and distilled to give a residue, 0.12 g (5%) which gave a chloroplatinate derivative, m.p. 188–190° (recrystallized from EtOH). In other experiments chloroplatinate derivatives of m.p. 175–180° were obtained. The m.p. of 2-*n*-butylpyrrolidine chloroplatinate is 177–178°. The identity of the synthetic 2-*n*-butylpyrrolidine chloroplatinate was established by comparison of its IR spectrum with that of an authentic sample.

*4-Phenyl-1-butyl azide.* 4-Phenyl-1-butyl azide (1 g) in 100 ml dry cyclohexane was irradiated for 10 hr. Dry HCl was then passed through the solution and the precipitate was collected and quickly basified and extracted with ether. The combined ether extracts were dried and the ether was removed *in vacuo* to yield a residue, 0.250 g. This material was treated with *p*-toluenesulphonyl chloride and aqueous alkali. Subsequent chromatography upon alumina failed to yield a crystalline product. Similarly no crystalline picrate could be obtained from this basic fraction. The basic fraction was subjected to VPC (SE-30, 130°), TLC, IR and UV analysis in conjunction with synthetic 2-phenylpyrrolidine. No similarity was observed in these comparisons. The cyclohexane filtrate was washed with water dried and concentrated to dryness to yield 0.500 g of a gum. This material was treated with 5 N HCl for 4 hr at room temp. Extraction with ether, concentration of ether

extracts to dryness, and treatment of the residue with semicarbazide hydrochloride yielded 0.250 g 4-phenylbutyraldehyde, semicarbazone m.p. 104–106°, lit.<sup>44,45</sup> m.p. 104–105°. The above aqueous part contained quite a bit of gummy material which was insoluble in ether but soluble in  $\text{CHCl}_3$ . The aqueous portion was basified and extracted with ether. The ether extracts were dried and concentrated to dryness. Treatment with picric acid yielded a crystalline derivative, 80 mg, m.p. 144–146° lit.<sup>44</sup> 2-phenylpyrrolidine picrate, m.p. 148–149°.

*$\alpha$ -Azidobutyric acid.* A solution of  $\alpha$ -azidobutyric acid (2.0 g, 0.0155 mole) dissolved in 120 ml MeOH was irradiated for 6 hr. The evolved  $\text{CO}_2$  was led into an aqueous solution of  $\text{Ba(OH)}_2$ . The precipitated  $\text{BaCO}_3$  was washed with water and MeOH and dried at 110° to yield 1.25 g; this amount corresponds to 42% decarboxylation. An aliquot of the photolysate solution was treated with 2,4-dinitrophenylhydrazine and a precipitate of propionaldehyde-2,4-DNP was obtained (0.170 g) which corresponded to 21% based upon the starting azide. Thin layer chromatography revealed the presence of no other 2,4-dinitrophenylhydrazone.

A second aliquot was stirred with 2,4-dinitrophenylhydrazine in 2 N HCl for several hr. The solution was then extracted continuously with  $\text{CH}_2\text{Cl}_2$  for a period of 24 hr. Evaporation of the  $\text{CH}_2\text{Cl}_2$  and subsequent chromatography upon acid washed grade III alumina using low boiling pet ether and benzene (1:1) as solvent yielded propionaldehyde 2,4-dinitrophenylhydrazone in 20% yield. No other 2,4-dinitrophenylhydrazone was obtained.

*Ethyl  $\alpha$ -azidobutyrate.* A solution containing 2.0 g (0.0127 moles) ester in 120 ml anhydrous ether was irradiated for 4 hr. No significant amount of  $\text{CO}_2$  was evolved. After this period 25 ml 5 N HCl was added and the two phase system was stirred at 35° for 1 hr. The layers were separated and the ether portion was concentrated to dryness and treated with 2,4-dinitrophenylhydrazine. A yield of 520 mg (15%) ethyl  $\alpha$ -ketobutyrate-2,4-dinitrophenylhydrazone was obtained, m.p. 135–136°. Also the IR spectrum of this compound and that of an authentic sample were superimposable. The aqueous portion from the hydrolysis was neutralized with KOH aq and extracted with ether. The ether extracts were concentrated to dryness to yield 1.0 g oil. Attempts to prepare derivatives with *p*-toluenesulphonyl chloride, in pyridine and also benzoyl chloride failed to yield a crystalline product. The identity of these products is still under investigation.

*$\alpha$ -Azidovaleric acid.* A solution of 1.2 g (0.0084 mole) of the acid in 120 ml MeOH was irradiated for 6 hr. The evolved  $\text{CO}_2$  was precipitated as  $\text{BaCO}_3$  (0.985 g, 54% decarboxylation). An aliquot was treated with 2,4-dinitrophenylhydrazine. A yield of *n*-butyraldehyde 2,4-dinitrophenylhydrazone corresponding to 20% was obtained. TLC of the total 2,4-dinitrophenylhydrazone precipitate prior to isolation of the above pure material revealed the presence of 3 other components in minor amounts. None was isolated and identified. Another aliquot was analysed for amino acids by TLC (propanol–water, 64:36, w/w; ninhydrin or isatin was used as stain). ( $\pm$ )  $\alpha$ -Aminovaleric acid was definitely identified while proline was shown to be absent. A similar result was obtained using *n*-butanol–acetic acid–water, 60:20:20 (w/w).

*$\alpha$ -Azidoisobutyric acid.* A solution containing 2.0 g (0.0155 mole)  $\alpha$ -azidoisobutyric acid in 250 ml MeOH was irradiated for 6 hr. The evolved  $\text{CO}_2$  was estimated as  $\text{BaCO}_3$  (0.80 g, 0.0041 mole, 26.2% decarboxylation).

An aliquot of the photolysate was treated with excess 2,4-dinitrophenylhydrazine reagent and a 25% yield of acetone 2,4-dinitrophenylhydrazone was obtained by direct crystallization. TLC of the total crude 2,4-dinitrophenylhydrazone using nitromethane, pet. ether and benzene as solvent system revealed that no other 2,4-dinitrophenylhydrazone was present. Co-chromatography of the crude 2,4-dinitrophenylhydrazone with authentic acetaldehyde 2,4-dinitrophenylhydrazone established the absence of this compound.

*Azidodiphenylacetic acid.* A solution of azidodiphenylacetic acid (1.0 g, 0.0040 mole) in 250 ml MeOH was irradiated for 6 hr. The  $\text{CO}_2$  evolved amounted to 73% (0.57 g of  $\text{BaCO}_3$ ). An aliquot of the photolysate equivalent to one half was treated with 200 ml sat. solution of 2,4-dinitrophenylhydrazine in 2 N HCl and 0.360 g product was obtained. This product was analysed by preparative TLC and benzophenone-2,4-dinitrophenylhydrazone and benzaldehyde-2,4-dinitrophenylhydrazone were obtained in a molar ratio of 2:3, respectively.

<sup>44</sup> J. v. Braun and O. Krumer, *Ber. Dtsch. Chem. Ges.* **45**, 384 (1912).

<sup>45</sup> *Dictionary of Organic Compounds* (Edited by I. M. Heilbron and H. M. Bunbury) Vol. III; p. 390. Oxford University Press (1943).

The filtrate from the 2,4-dinitrophenylhydrazone preparation was treated with acetone to remove excess reagent. The resulting aqueous solution was extracted thoroughly with  $\text{CH}_2\text{Cl}_2$ . The aqueous part was basified with cold 50% KOH and the liberated base was extracted with ether. The ether solution was dried and concentrated to dryness to yield an oily residue which was treated with benzoyl chloride.

Crystallization of the solid residue from EtOH afforded 50 mg benzanilide, m.p. and m.m.p. with an authentic sample was 155–157°.

*Ethyl  $\alpha$ -azidovalerate.* A solution containing 1.0 g (0.0059 mole) ethyl- $\alpha$ -azidovalerate dissolved in 100 ml ether was irradiated for 6 hr. No decarboxylation occurred. Aqueous 5 N HCl (20 ml) was added to the ethereal solution and the resulting two phase system was shaken for 1 hr. Concentration of the ether solution to dryness and treatment with 2,4-dinitrophenylhydrazine yielded 0.150 g (7%) ethyl  $\alpha$ -ketovalerate-2,4-dinitrophenylhydrazone. The aqueous portion was basified and extracted with ether. The ether extracts were concentrated to dryness and the residue was stirred for 4 hr with 1 N NaOH. The hydrolysed solution was acidified with 2 N HCl and the aqueous acidic solution was concentrated to  $\frac{1}{3}$ th of its original volume. From this concentrated solution ( $\pm$ )- $\alpha$ -aminovaleric acid was definitely identified by TLC in the two solvent systems mentioned earlier and proline was again shown to be absent.

*Pyruvic acid.* 2.0 g in 250 ml MeOH was irradiated for 6 hr and the evolved  $\text{CO}_2$  was determined quantitatively as  $\text{BaCO}_3$  (1.22 g, 27.2% decarboxylation).

*$\alpha$ -Ketobutyric acid.* 0.49 g in 250 ml MeOH was irradiated for 6 hr and 0.39 g (41.2%)  $\text{BaCO}_3$  was obtained.

*$\alpha$ -Deuterio- $\alpha$ -azidobutyric acid.* Saponification of diethyl ethylmalonate (63.8 g; 0.35 mole) by KOH (75 g; 1.34 mole) in 60 ml water, followed by acidification with HCl and solvent extraction yielded ethylmalonic acid in ether.<sup>46</sup>

The above ether solution (200 ml) was dried and brominated with 17 ml  $\text{Br}_2$ .<sup>46</sup> Excess  $\text{Br}_2$  was removed from the ether solution with thiosulphate and water. The ether solution of the ethyl-bromomalonic acid was dried and concentrated to give 53.0 g *crude acid*.

The crude bromoethylmalonic acid (48.0 g; 0.227 mole) was mixed with  $\text{SOCl}_2$  (135.6 g; 1.114 mole) and refluxed for 20 hr.<sup>49</sup> Excess  $\text{SOCl}_2$  was removed by distillation. Attempted distillation of the residue under vacuum resulted in apparent decomposition. Therefore, the crude chloride was directly used for the subsequent reactions.

A mixture of bromoethylmalonyl chloride (24.1 g; 0.09 mole) and  $\text{D}_2\text{O}$  (99.7%, 15 g; 0.75 mole) was stirred at room temp for 2 hr, then at 80–85° for 2 hr and then at 130° for 5 hr until no more  $\text{CO}_2$  was evolved.<sup>49</sup> The black residue was directly distilled under vacuum to give  $\alpha$ -bromo- $\alpha$ -deuteriobutyric acid, 9.0 g, b.p. 87–90° (5 mm). IR and NMR spectra were in agreement with the structure.

The above acid (7.5 g) was esterified by EtOH (2.3 g) and conc.  $\text{H}_2\text{SO}_4$  (5 drops). Work up and distillation yielded ethyl  $\alpha$ -bromo- $\alpha$ -deuteriobutyrate, 3.5 g, b.p. 85–87° (6 mm). The IR and NMR were in agreement with expectation.

The ethyl ester (3.5 g) was mixed with 2.0 g  $\text{NaN}_3$  and 2.0 g EtOH and refluxed for 28 hr. Work up and distillation gave the azido ester, 1.6 g, b.p. 60° (6 mm).

The azidoester (1.25 g) was hydrolysed with 2.25 ml KOH aq containing 0.48 g. Work up and distillation yielded  $\alpha$ -deuterio- $\alpha$ -azidobutyric acid, 0.61 g, b.p. 57.5–58° (0.05 mm). IR and NMR were in agreement with expectation.

*Photolysis of  $\alpha$ -deuterio- $\alpha$ -azidobutyric acid.* Five hundred milligrams of  $\alpha$ -Deuterio- $\alpha$ -azidobutyric acid (500 mg; 3.85 mmoles) dissolved in 250 ml MeOH was irradiated for 7 hr. The evolved  $\text{CO}_2$  was determined quantitatively as  $\text{BaCO}_3$  yielding 410 mg, corresponding to 54.0% decarboxylation.

The photolysate solution was treated with 2,4-dinitrophenylhydrazine (600 mg; 3 mmoles) dissolved in 150 ml 2 N HCl. The first crop of precipitated 2,4-dinitrophenylhydrazone (60 mg, 7%) was purified by preparative TLC and pure propionaldehyde-2,4-dinitrophenylhydrazone (40 mg, 4.4%) was isolated

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and identified by m.p. and m.m.p. 146–148°. The NMR spectra in both  $\text{CH}_2\text{Cl}_2$  and  $\text{CDCl}_3$  showed almost complete absence of aldehydic proton at 2.12  $\tau$ .<sup>50</sup> Analysis showed the retention of about 58% of starting deuterium.<sup>23</sup>

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