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THE INTERACTION OF THE AZIDO GROUP IN ORGANIC
COMPONENTS WITH ADJACENT FUNCTIONAL GROUPS

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OBJECTIVES

The objectives of this research are the preparation and study of tertiary alkyl azides and of aryl azides in which the azido group is adjacent to formal unsaturation.

SUMMARY

1. 2-Hydroxycarbazole, prepared from 2-azido-4'-hydroxybiphenyl (Progress Report No. 2) has been methylated to give a product identical with the 2-methoxycarbazole obtained from 2-azido-4'-methoxybiphenyl.

2. Further work on the preparation and properties of 4'-azido-fluorenone is as yet inconclusive.

3. Ethyl azide has been converted to a solid derivative for identification by reaction with acetylenedicarboxylic acid. An initial attempt to prepare ethyl azide by nitrosation of N-ethyl-N-aminourea was unsuccessful.

4. O-Azido~~benzen~~arsonic acid has been prepared and selectively reduced to O-azidophenylarsenoxide, which inflames on contact with conc. sulfuric acid.

5. t-Butyl azide has been prepared from t-butyl chloride and sodium azide in neutral buffered solution.

6. O-Aminophenylhydroquinone diacetate has been prepared as an intermediate for the preparation of O-azidophenylquinone.

7. O-Azidodiphenyl sulfide has been oxidized to an azide believed to contain a sulfoxide group.

8. 8-Azido-2-naphthol has been prepared as an intermediate for the preparation of peri-substituted naphthyl azides.

9. Bicycloheptadiene has been investigated as an identification reagent for organic azides.

THE INTERACTION OF THE AZIDO GROUP IN ORGANIC
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INTRODUCTION

Research Assistants whose work is described in this report are William L. Berry, John M. Clegg, Joseph J. Lagowski, Richard K. Putney, and A. Charles Schoenthaler.

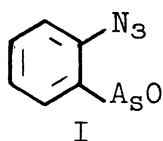
1. Earlier in this work, 2-hydroxycarbazole and 2-methoxycarbazole had been prepared by thermal cyclization of the corresponding o-azidobiphenyls. For purposes of structure confirmation, the 2-hydroxycarbazole has now been methylated with methyl sulfate to give a product identical with the 2-methoxycarbazole prepared previously.

2. 4-Azidofluorenone is being prepared in larger quantities than hetherto, in order to be able to examine its thermal-decomposition products more thoroughly. For this purpose, diphenic acid has been cyclized to fluorenone-4-carboxylic acid, from which 4-aminofluorenone is obtained by the Hofmann rearrangement.

3. N-Ethyl-N-aminourea had been prepared in small quantity for investigation of its nitrosation behavior which it was hoped might result in ethyl azide formation. Because of the small quantities anticipated and the difficulties of purifying and identifying a volatile liquid like ethyl azide, a solid derivative was sought. Reaction with dicyclopentadiene was incomplete and inconclusive, but acetylenedicarboxylic acid reacted readily in ether solution to give a good yield of crystalline 1-ethyl-1,2,3-triazole-4,5-dicarboxylic acid. The preparation of ethyl azide from N-ethyl-N-aminourea was then attempted, and the volatile products were treated with ethereal acetylenedicarboxylic acid, but no adduct could be isolated. Larger quantities of N-alkyl-N-aminoureas (2-Alkylsemicarbazides) are being prepared in order to try varied experimental conditions.

4. The known o-aminobenzenearsonic acid has been diazotized and converted to o-azidobenzenearsonic acid. Its dilute aqueous solution was reduced by sulfur dioxide in the presence of a trace of potassium iodide to a water-insoluble solid believed to be o-azidobenzenearsenoxide(I).

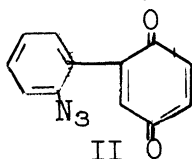
The infrared spectrum (Nujol mull)



shows the characteristic azide absorption at 4.75μ . and the substance decomposes violently on contact with conc. sulfuric acid and usually bursts into flame. It is proposed to couple this substance with benzenediazonium chloride in order to prepare o-azidodiphenylarsinic acid.

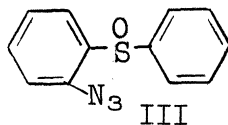
5. Initial attempts to prepare t-butyl azide by reaction of t-butyl chloride with sodium azide, dry or in aqueous solution, resulted in extensive dehydrohalogenation and dangerous accumulation of hydrogen azide. Partial success was obtained in neutral buffered solution, and a product has been obtained which gives t-butylamine on reduction with lithium aluminum hydride and has the boiling point (71°) estimated for t-butyl azide. It is being analyzed and otherwise investigated.

6. Difficulties had earlier been encountered in the handling of o-aminophenylhydroquinone, due to its great sensitivity to air and to nitrous acid. It was an intermediate in the projected synthesis of o-azidophenylquinone (II).



Consequently, o-nitrophenylhydroquinone diacetate was prepared and hydrogenated to o-aminophenylhydroquinone diacetate. This amine could not be diazotized without concurrent coupling, perhaps due to hydrolysis of the acetyl groups in the acidic diazotization solution. An attempt is now being made to oxidize it to o-aminophenylquinone, from which it may be possible to prepare the azide.

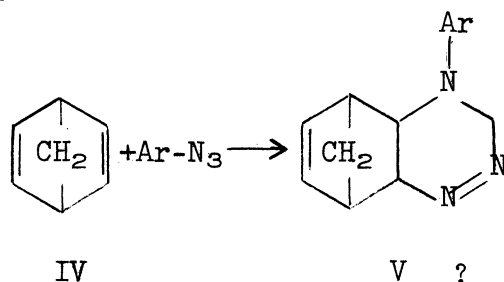
7. The preparation of o-azidodiphenylsulfoxide (III) was



started from o-azidodiphenyl sulfide by oxidation, and from o-nitrodiphenylsulfoxide by reduction of the nitro group, etc. The first method has resulted in the preparation of a substance apparently different from o-azidodiphenyl sulfone, and whose infrared spectrum shows the presence of an azido group. The second method, which has reached the stage of the successful preparation of o-nitrodiphenylsulfoxide, may not be continued if analysis confirms the nature of azide from the first route.

8. 8-Amino-2-naphthol, commercially available in technical purity, has been purified, and it was possible to prevent self-coupling during diazotization by including manganous sulfate in the reaction. The further addition of sodium azide has yielded a product with the characteristics to be expected of 8-azido-2-naphthol. It is hoped that peri-substituted α -naphthyl azides may be prepared from this product by suitable reactions at the reactive 1-position.

9 Bicyclo[2'2'1] heptadiene (IV) has been obtained from the Shell Development Company as a special favor. The presence of two bicyclic double bonds in this molecule make it of interest as a possible identification agent for organic azides, which generally add to such bonds to form triazolines. A reagent which would reliably give crystalline derivatives would be of great aid in characterizing azides too unstable to be purified by themselves, or liquid azides available in too small quantities to permit distillation. A single initial experiment shows that it reacts readily with phenyl azide, but that it may not be easy to recrystallize the solid adduct (V).



EXPERIMENTAL

Nitrosation of N-ethyl-N-aminourea

The aminourea was dissolved in an acidic solution to which was added dropwise a solution of sodium nitrite. The excess nitrous acid (slightly more than a 1:1 ratio was used) was destroyed with urea and the solution made basic. The mixture was steam distilled, the distillate was extracted into ether and dried, and acetylenedicarboxylic acid was added. After the solvent was heated and evaporated, only acetylenedicarboxylic acid remained.

2-Methoxycarbazole

In a 50-ml Erlenmeyer flask, 0.32 g (0.00175 mole) of 2-hydroxycarbazole was dissolved in 20 ml of sodium hydroxide. To this solution was added slowly 0.25 g (0.002 mole) of dimethyl sulfate, and the resulting mixture was heated on the steam bath for one hour. The yield of crude 2-methoxycarbazole obtained upon filtration of the cooled solution was 0.28 g, 81%, mp 225-230°.

Upon recrystallization from acetone-water, 0.15 g, mp 231.5-234.5° and 0.06 g, mp 224-230° was obtained. A mixed melting point with material prepared from 2-azido-4'-methoxybiphenyl gave no depression.

Diphenic Acid

Prepared by the method given in Org. Syn., Coll. Vol. I, 2nd edition, p. 222.

4-Fluorenonecarboxylic Acid

Prepared by the method of Graebe and Aubin, Ann., 247, 283 (1888).

Ethyl Azide

Prepared by the method of E. Oliveri-Mandalá and G. Caronna, Gazz. chim. ital., 71, 188 (1941).

Acetylenedicarboxylic Acid

Prepared by the method given in Org. Syn., Coll. Vol. II, p. 10.

1-Ethyl-1,2,3-triazole-4,5-dicarboxylic Acid

In a 50-ml round-bottomed flask were placed 4 g (0.0565 mole) of ethyl azide, 6.4 g (0.0565 mole) of acetylenedicarboxylic acid and 10 of ether; the resulting solution was allowed to reflux under the heat of the reaction, and then heated on a steam bath for about 15 minutes longer. Upon evaporation of the solvent, the hydrated triazole was obtained as a white solid, 7.57 g, 66%, which started to soften at 85° when heated slowly.

o-Azidobenzenearsonic Acid

A chilled solution of 2.18 g (0.01 mole) of o-arsanilic acid in 3.0 ml of conc. hydrochloric acid diluted with water was diazotized with 0.75 g of sodium nitrite, the excess nitrous acid was destroyed with sulfamic acid, and 0.75 g of sodium azide was added. There was immediate frothing and formation of a creamy precipitate. The solid was filtered off, washed with water, and allowed to dry in air overnight, wt. 1.95 g (80%), mp 188° with effervescence to form a black-brown froth. Recrystallization from 150 ml of boiling water gave 1.13 g of long, light-tan needles having the same melting behavior. This sample is being analyzed. This compound appears to be unaffected by diffuse daylight or fluorescent light, but is slowly darkened by direct sunlight filtered through glass. With conc. sulfuric acid, there is immediate gentle effervescence, but no color is developed.

o-Azidophenylarsenoxide

The filtrate from the recrystallization of the o-azidobenzene-o-arsonic acid, presumably containing ca 0.8 g, was acidified with 25 ml of 10% sulfuric acid. A small crystal of potassium iodide was added, and sulfur dioxide was bubbled through. After about two hours, a precipitate began to appear, and after about four hours, the sulfur dioxide stream was stopped and the reaction mixture was filtered. The creamy white solid, presumably o-azidophenylarsenoxide, weighed 0.30 g (45%), and melted at 167° to a black-brown liquid with effervescence. From the filtrate, a further 0.05 g of product was obtained as nodules of small crystals. This compound is not noticeably soluble in acetone, ethanol, ethyl acetate, or chloroform at room temperature, and it is denser than all of them. The

infrared spectrum in Nujol mull is very clean, showing bands only at 3.5μ (C-H), 4.76μ ($-\text{N}_3$), 6.45μ , 6.9μ , 7.0μ , 7.75μ , 7.85μ , 8.0μ (all perhaps phenyl), 8.8μ and 9.05μ (both weak), and 12.7μ and 13.3μ . The compound reacts with conc. sulfuric acid with a hiss and sometimes a flash of flame, leaving a dark green or brown solution. The compound is being analyzed.

t-Butyl Azide

t-Butyl chloride (0.53 mole) and reprecipitated sodium azide (0.53 mole) were mixed together with mechanical stirring for varying amounts of time. In all cases only t-butyl chloride was recovered from the reaction mixture.

A series of experiments was attempted in which t-butyl chloride (0.5 mole) was mixed, with mechanical stirring for 48 hours, with a saturation solution of sodium azide (100 ml). During this time the aqueous phase turned orange, but no amine was formed upon treatment of the organic phase with LiAlH_4 .

This reaction was attempted a second time. There resulted in explosion upon fractionation of the organic phase. It is thought that dehydrohalogenation of t-butyl chloride led to the formation of HN_3 . The explosion was traced to the first fraction collected which boiled at 36 – 37°C (bp of HN_3 is 37°C). The accumulation of HN_3 suggested that the aqueous phase be buffered to suppress dehydrohalogenation, and that the organic phase be washed with sodium bicarbonate before any further operations.

Accordingly, 0.5 mole of t-butyl chloride was mixed with 100 ml of a saturated solution of sodium azide which was buffered at pH 7. The buffer was a standard Clark and Lubs phosphate buffer mixture, which consists of 0.1185 g of sodium hydroxide and 0.6804 g of potassium dihydrogen phosphate dissolved and diluted to 100 cc with saturated aqueous sodium azide solution. This buffered reaction mixture was mechanically stirred for 76 hours; the reaction mixture remained water white. The organic phase was then washed with sodium bicarbonate solution until the wash water was basic to litmus. This washing greatly reduced the volume of the organic phase. The organic phase was dried over anhydrous sodium sulfate, reduced with LiAlH_4 and extracted with aqueous hydrochloric acid. The aqueous phase was made strongly basic with sodium hydroxide solution and steam distilled into aqueous HCl. This aqueous solution yielded impure t-butylamine hydrochloride upon evaporation on a steam bath under reduced pressure. The dried, impure solid was extracted with absolute ethanol and the extract evaporated to dryness on a steam bath; 3.5 g of pure t-butylamine hydrochloride was obtained.

The benzoyl derivative was prepared according to Cheronis and Entrikin; it melted at 140-142°. An authentic sample of N-t-butylbenzamide melted at 139-141°, and the mixed melting point was 140-142°.

In an attempt to obtain pure t-butyl azide, the same procedure was used on a larger scale (1.0 mole of t-butyl chloride and 200 ml of buffered sodium azide solution). The washed and dried organic phase was fractionated with a 15 cm Vigreux column and cuts were taken at 2° intervals from 67 to 75°. The largest fraction came over at 73-75°. All fractions contained nitrogen. Redistillation of the 73-75° fraction gave a product boiling sharply at 71°, which is being analyzed and otherwise investigated.

o-Nitrophenylhydroquinone

The procedure of Dobas was modified as follows: The filtered diazonium solution was used directly without neutralization, ether was substituted for amyl alcohol in the extraction, the final acid solution was allowed to stand for several days, and the product was collected in several crops of orange needles, m; 165-7° (reported, 167°). Best yields (25-30%) were obtained with the addition of octyl alcohol to reduce frothing, accompanied by vigorous stirring to insure immediate mixing of the solutions. This substance was prepared by chromic oxide oxidation² of o-nitrophenylhydroquinone in 84-96% yield, with mp 100-101°C (reported 101-2°). Attempts at preparation by direct reaction of o-nitrobenzene-diazonium chloride with quinone in alcohol⁴ with or without the presence of copper salts⁵ or in basic aqueous solution,⁴ resulted only in tarry residues from which unreacted quinone was the only pure substance isolated.

o-Nitrophenylhydroquinone diacetate

By the method of Chattaway⁶, nearly quantitative yields were obtained, mp 148-9° (reported, 150°), after two recrystallizations from acetonitrile (which solvent gave better recovery than the previously suggested²¹ ethanol).

o-Aminophenylhydroquinone diacetate

The o-nitrophenylhydroquinone diacetate above (6.66 g, 0.0635 mole) was reduced catalytically over platinum oxide in benzene, the theoretical amount of hydrogen being absorbed in forty-five minutes at room temperature and sixty pounds pressure. Most of the amine separated from

solution, and after filtration it was dissolved away from the admixed catalyst by means of acetone. Removal of the acetone from this fraction and of the benzene from the original filtrate under nitrogen at reduced pressure afforded 5.13 g (85.3%) of tan powder mp 162.5-164.5°. The substance was insoluble in dilute mineral acids, slightly soluble in ether and benzene, soluble in glacial acetic and concentrated mineral acids. When treated with dilute sodium hydroxide, the amine rapidly dissolved to give a dark-orange solution changing to a pale orange upon acidification, indicating hydrolysis of the acetyl groups, perhaps accompanied by air oxidation.

The success of the reduction appeared to be sensitive to the purity of the nitro compound; runs on lower melting material gave an orange glass which could be rendered crystalline, but still impure, by treating with Norit in benzenepetroleum ether and allowing the solution to stand several days.

Attempted Preparation of o-Azidophenylhydroquinone

A small amount of the above amine was dissolved in glacial acetic acid, 2 ml of dilute hydrochloric acid was added, and the solution was diazotized in the usual manner₁, the excess nitrous acid being destroyed with sulfamic acid. The diazonium solution was then filtered and excess sodium azide added. After 36 hours in the cold, tan crystals, mp 184-6°, separated in an amount insufficient to permit further characterization.

o-Nitrodiphenylsulfide

o-Nitrodiphenylsulfide was prepared in 86% recrystallized yield essentially according to the directions of Cullinane and Davies.⁷ A higher yield and a cleaner product results if the bath temperature is kept at 170-180°C for four hours.

o-Aminodiphenylsulfide

A. Catalytic hydrogenation of o-nitrodiphenylsulfide at approximately 1.5 atmospheres using Adams catalyst gave the amino-sulfide quantitatively.

B. One hundred and twenty-five ml of 95% ethanol containing 1 g of the nitro-sulfide and 2 ml of 99% hydrazine hydrate was heated 4 hours under reflux with a spatula-tip of Raney nickel. Filtration, followed by evaporation under nitrogen, gave 0.82 g (90%) of o-aminodiphenylsulfide, mp 43-45°C. Recrystallization from 30-40° petroleum ether gave light-yellow plates, mp 44-45.5°C.

o-Azidodiphenylsulfide

Prepared according to the directions of Smith, et al,²

o-Azidoiphenylsulfoxide

Thirty percent hydrogen peroxide (0.66 g, 5.9 m moles) of o-azidodiphenylsulfide in 15 ml of glacial acetic acid. The light-yellow solution was stored in the dark at room temperature for 76 hours. Pouring into ice-water precipitated a white solid, weight 1.17 g (91%) mp 120-123.5° dec. Three recrystallizations from aqueous ethanol gave small white rods, mp 123-124.3° dec. The infrared spectrum is consistent with that of reported sulfoxides, and the characteristic azide frequency at 4.75μ is present. Elementary analysis is pending.

o-Nitrodiphenylsulfoxide

Essentially according to the method of Hinsberg,⁹ 30% hydrogen peroxide (1.5 g) was added to 3.0 g of o-nitrodiphenylsulfide dissolved in 60 ml of glacial acetic acid. After standing in the dark at room temperature for 112 hours, the solution was poured into ice-water and extracted with three 25-ml portions of chloroform. Following washings with dilute soda solutions and water, the chloroform solution was taken to dryness with nitrogen, leaving a residue of wt. 1.6 g (97%). Three recrystallizations from aqueous ethanol gave a light-yellow powder, mp 94.5-95.7°C. The infrared spectrum was obtained. Analysis: Calcd for $C_{12}H_9O_3NS$: C, 58.29; H, 3.67. Found: C, 58.52; H, 3.72.

Sodium p-Toluenesulfinate

Preceding the investigation of the system $R-S-N_3$, sodium p-toluenesulfinate was prepared in 86% yield using directions described in Org. Syn., Coll. Vol. I, p. 492.

8-Azido-2-Naphthol

A. 8-Amino-2-naphthol, dissolved in 50% sulfuric acid, and then diluted to 30% sulfuric acid, was diazotized by the direct method. Two such attempts to obtain a stable diazonium solution at 0° to -5°C gave chiefly decomposition products. Filtration and sodium azide addition followed by several days standing led only to intractable tars. Stabilization

of the diazonium solution was accomplished by the addition of stannous chloride, but the reaction of the resulting suspension with sodium azide was extremely slow if it occurred at all.

B. Five grams of the amine bisulfate was added to a dilute solution of sulfuric acid and followed by 3 g of manganous sulfate dissolved in 20 ml of water. Diazotization was carried out as usual at 0 to -5°C . Two grams of sodium azide dissolved in 15 ml of water was added and the solution stored for 14 hours in the cold. Filtration at the end of this period gave a dark brown solid, mp $124-127^{\circ}$, dec., which decomposed with a puff on heating in a flame. The infrared spectrum showed the presence of both hydroxyl and azide groups. Conc. sulfuric acid became colored dark green after one drop decomposed a few needles instantaneously.

Preliminary Investigation of the Synthesis of 2-Nitro-2'5'-Dihydroxydiphenylsulfone

o-Nitrobenzenesulfinic acid was prepared according to the method of Gatterman¹⁰ in discouraging yield (15%).

A hot alcoholic solution of p-benzoquinone was added to a hot, dilute alcoholic solution of o-nitrobenzenesulfinic acid. The solution surrendered a reddish solid after several days storage in the cold. Purification is anticipated.

Benzo-1,2,3-thiadiazole

Benzo-1,2,3-thiadiazole has failed to undergo any reaction with sodium azide in concentrated hydrochloric acid or concentrated sulfuric acid with hydroxylamine or hydrazine in ethanol or pyridine.

Naphthalene-1-diazo-2-oxide

Naphthalene-1-diazo-2-oxide has so far failed to give any identifiable product on treatment in the cold with sodium azide in hydrochloric acid solution or with hydroxylamine or hydrazine in pyridine or aqueous ethanol.

Bicyclo-[2,2,1]-heptadiene Derivative of Phenyl Azide

One ml (0.01 mole) of phenylazide was added to a warm solution of 1.0 ml (0.01 mole) of bicyclo-[2,2,1]-heptadiene-2,5 (b₇₄₆ $88.6-89.6^{\circ}\text{C}$) at such a rate that the mixture refluxes gently. One ml of benzene was added

and the solution was boiled for five minutes and allowed to cool. The colorless, crystalline product was washed with several small portions of benzene and dried at 30°C. Yield: 0.5 g (25% on the basis of a 1:1 addition product) mp 227° with decomposition (gas evolution). The compound darkens on prolonged heating at 75°C, alone or suspended in a variety of organic solvents. It is insoluble in all the low-boiling solvents tried and probably cannot be purified by recrystallization. It dissolves in glacial acetic acid at room temperature to give a deep violet solution which, when diluted and neutralized with sodium hydroxide, turns yellow and deposits a brown solid, mp 135-140°, which is soluble in benzene, ethanol, and ether and has not yet been purified and identified. Acidification of the filtrate with acetic acid does not regenerate the violet color. The adduct is being analyzed.

REFERENCES

1. J. Dobas, Chem. Listy, 46, 247 (1952) [C.A., 47, 8669d (1953)].
2. A. I. Vogel, Textbook of Practical Organic Chemistry, Second Edition, Longmans, Green and Co., Inc., New York, 1951, p. 709.
3. T. K. Schimmelschmidt, Ann., 566, 184 (1950).
4. D. E. Qualnes, J. Am. Chem. Soc., 56, 2478 (1934).
5. C. F. Koelsch and V. Vockelheide, J. Am. Chem. Soc., 66, 412 (1944).
6. F. D. Chattaway, J. Chem. Soc., 2495, (1931).
7. N. M. Cullinane and C. G. Davies, Rec. trav. chim., 55, 881 (1936).
8. P. A. S. Smith, B. B. Brown, R. K. Putney, and R. L. Reinisch, J.A.C.S., 75, 6355 (1953).
9. O. Hinsberg, Ber., 43, 289 (1910).
10. L. Gatterman, Ber., 32, 1136 (1899).

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