ENGINEERING RESEARCH INSTITUTE
THE UNIVERSITY OF MICHIGAN
ANN ARBOR

Quarterly Progress Report No. 15

THE INTERACTION OF THE AZIDE GROUP IN ORGANIC COMPOUNDS WITH ADJACENT FUNCTIONAL GROUPS

May 2 to August 2, 1957

P. A. S. Smith

Project 2202

U. S. ARMY, ORDNANCE CORPS, DETROIT ORDNANCE DISTRICT
CONTRACT NO. DA-20-018-ORD-13283, DA PROJECT NO. 299-01-004
ORD PROJECT NO. TB2-0001, OOR PROJECT NO. 965

September 1957

ABSTRACT

1. The nitration of 2-methoxy-8-acetamidonaphthalene has now been found to give three products: the 5-nitro, the x,5-dinitro, and the x-nitro, where x is probably 1.

2. 4-Nitro-7-methoxy-1-naphthyl azide has been prepared from the corresponding amine.

3. p-Methoxythiobenzoyl azide has been prepared and found to cyclize at once to 5-p-anisylthiatriazole.

4. p-Chlorothiobenzoyl hydrazide and cyclohexanethiocarbonyl hydrazide have been prepared for conversion to the azides.

5. The thermal decomposition of 5-phenylthiatriazole has been established as giving benzonitrile, sulfur, and nitrogen, and its reduction by lithium aluminum hydride has been found to give thiobenzamide.

6. Thiobenzoyl azide is insoluble in dilute acids, but dissolves without decomposition in concentrated bydrochloric and nitric acids and ca. 50% sulfuric acid; concentrated sulfuric acid brings about gas evolution.

7. ter-Butyl azide has been found in small amounts from the reaction of ter-butyl chloride with sodium azide in methylcellosolve, and from the reaction of ter-butyl-hydrazine with nitrous acid, but these reactions are of no use for synthesis.

8. 1-Methylcyclohexyl azide has been prepared in ca. 20% yield from the reaction of 1-methylcyclohexyl chloride with aqueous sodium azide in phosphate buffer.

9. The rates of the noncatalyzed thermal decomposition of a group of o-azidobiphenyls have been found to be first order, and to vary somewhat with structure. The decomposition of p-azidobiphenyl and other azides incapable of cyclization is apparently of complex order. The decomposition of azides is apparently accelerated by polar solvents.

10. A paper, "The Synthesis of Heterocyclic Compounds from Aryl Azides. IV. Chloro-, Methoxy-, and Benzo-Carbazoles," presenting some of the results of this project, has been sent to the Journal of Organic Chemistry.

OBJECTIVE

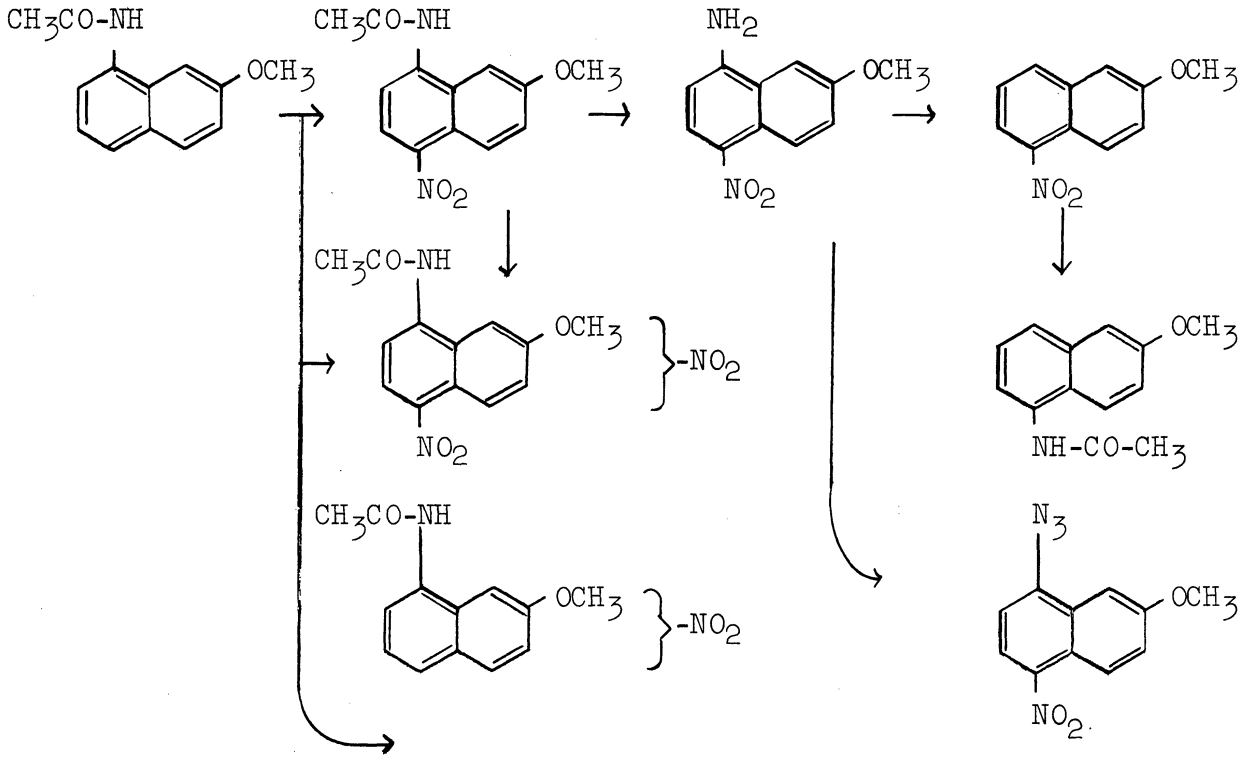
The objects of this investigation are the preparation and study of organic azides in which the azido group is adjacent to formal unsaturation, and tert-alkyl azides.

DISTRIBUTION LIST

Office of Ordnance Research Box CM, Duke Station Durham, North Carolina	3
Office, Chief of Ordnance Washington 25, D. C. Attn: ORDTB PS	2
Commanding Officer Redstone Arsenal Huntsville, Alabama	2
Commanding Officer Frankford Arsenal Bridesburg Station Philadelphia 37, Pennsylvania	2
Chief, Detroit Ordnance District 574 East Woodbridge Detroit 31, Michigan Attn: ORDEF-IM	2

DISCUSSION

The nitration of 2-methoxy-8-acetamidonaphthalene has been reported in Progress Reports Nos. 13 and 14 as part of a projected route to peri-substituted naphthyl azides. The major product, mp 235-236°, has now been proven to be 2-methoxy-5-nitro-8-acetamidonaphthalene, by determining that hydrolysis and deamination give 2-methoxy-5-nitronaphthalene. This was itself characterized by conversion to known 2-methoxy-5- acetamidonaphthalene.



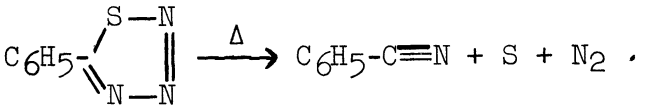
Since the 5-nitro, which was not the desired product, was obtained in only about 50% yield, the nitration mixture was investigated for other products. An isomeric nitro compound, mp 198-202°, was found in much lower yield, and a dinitro compound, mp 284-286°. Since the dinitro compound could also be obtained from further nitration of the compound now proven to be 2-methoxy-5-nitro-8-acetamidonaphthalene, one of its two nitro groups must be in the 5-position. The second nitro group in this substance, as well as the nitro group in the minor mononitration product, may perhaps be in the desired 1-position. Their structures will be determined.

As an alternate method for determining the position of the nitro group, 2-methoxy-5-nitro-8-naphthylamine was converted to 2-methoxy-5-nitro-8- naphthyl azide, the nature of whose decomposition (ease and product) would depend

on the relative positions of the nitro and azido groups. However, with the success of the deamination structure proof, the pertinence of this approach has largely disappeared.

In Progress Report No. 13, the preparation of thio-benzoyl azide was reported, together with evidence that it had cyclized immediately upon formation to give 5-phenylthiatriazole. The same observation has now been made on the p-methoxy derivative, which has been prepared by an analogous route from dithioanisic acid via thioanisoyl hydrazide. p-Chlorothiobenzoyl and cyclohexanecarbonyl hydrazide have now been prepared for conversion to additional representatives of this new class of compound.

5-Phenylthiatriazole has been found to be much more stable than the related acylazides. A temperature near 200° is required to bring about loss of nitrogen. Sulfur precipitates, and the solution contains benzonitrile, as shown by its infrared absorption (Progress Report No. 13), and now by the identification of benzoic acid obtained by hydrolysis.



$$C_6H_5\text{-}\underset{\displaystyle N=N}{\overset{\displaystyle S-N}{\overset{/}{\underset{\backslash}{\overset{\|}{\underset{\|}{}}}}}} \xrightarrow{\Delta} C_6H_5\text{-}C\equiv N + S + N_2 \,.$$

5-Phenylthiatriazole is not sufficiently basic to dissolve in dilute strong mineral acids, but it dissolves in concentrated acids. Concentrated sulfuric acid causes decomposition (loss of nitrogen), but hydrochloric and nitric do not. It is possible that the conjugate acid of the thiatriazole ring is in equilibrium with an appreciable amount of the protonated thioazide, which would be expected to decompose readily. The other products are being investigated.

ter-Butyl azide was once obtained by the reaction of ter-butyl chloride with sodium azide in buffered aqueous solution, but the product could not be freed entirely from ter-butyl alcohol (Progress Report No. 3). An alternative method for carrying out this reaction was recently suggested which might avoid the contaminant. The aqueous buffer solution was replaced by anhydrous methylcellosolve. Reaction occurred, but the amount of azide produced was so small that it could only be identified by infrared spectroscopy or vapor-phase chromatography.

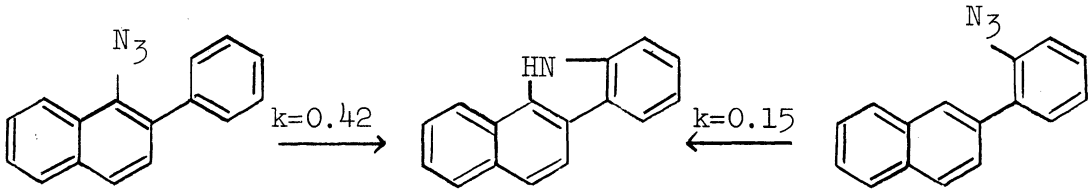
We were recently able to prepare ter-butyl hydrazine in useful quantities in connection with another problem. The reaction of alkylhydrazines with nitrous acid normally gives N-alkyl-N-nitroso-hydrazines and not alkyl azides, but it was thought that the steric effect of the ter-butyl group might cause N'-nitrosation to give azide instead. ter-Butyl-hydrazine was found to react with nitrous acid, but the products were a complex mixture, of which ter-butyl azide was only a very minor constituent, identifiable by infrared spectroscopy and vapor-phase chromatography.

The aqueous buffer method was moderately successful in converting 1-methyl-

cyclohexyl chloride into its azide. Careful distillation of the products through a good fractionating column gave 1-methylcyclohexyl azide in about 20% yield, contaminated with a very small amount of spectroscopically detectable hydroxylic substance.

Qualitative observations of the thermal decomposition of various aryl azides, particularly o-azidobiaryls, had shown that very similar temperatures (ca. 180°) are required for their breakdown. This general observation suggested that the loss of nitrogen from o-azidobiaryls is not a concerted process, and should be influenced little or not at all by the nature of the second ring. Recently, however, the isomeric o-azidobiaryls 1-azido-2-phenylnaphthalene and 2-(o-azidophenyl) naphthalene were prepared and studied, and a small but clear difference in the temperature required for their decomposition was noticed. Because of this, a limited kinetic investigation of azide decomposition has been begun.

The loss of nitrogen from o-azidobiphenyl, 2 azido-4'-nitrobiphenyl, and the pair of isomeric azides previously mentioned obeyed a first-order kinetic law rather well, except for an initial retardation. This was at first thought to be due to slow attainment of thermal equilibrium following addition of the sample to the apparatus, but this possibility has since been eliminated. However, from the straight-line portions of the plots of the logarithm of the azide concentration against time, reproducible rate constants can be determined. In general, only small differences were observed from one azide to another, but 1-azido-2-phenylnaphthalene was unusually fast, its constant being 0.42 at 178.8° compared to 0.15 for its isomer. The significance of this should be clearer when some additional azides have been examined kinetically.



Phenyl azide, p-xenyl azide, and p-anisyl azide, which cannot cyclize on decomposition, nevertheless decomposed at rates very close to those of the o-azidobiaryls. Their rate laws, however, were noticeably different, and did not correspond to either a simple first- or second-order expression.

All the azides were measured in dilute solution, using kerosene, decalin, nitrobenzene, or ethylene glycol. The observed differences were very small with the first three solvents, but nitrobenzene seemed to exert a just noticeable acceleration. Ethylene glycol, in the one experiment in which it was used, gave a poorer fit to first-order kinetics, and a rate constant twice that of the constant determined from nitrobenzene solutions.

Those who have participated in the above work are: Donald Erickson, J. Herbert Hall, David H. Kenny, Thomas vanden Bosch, and Julian Lakritz.

EXPERIMENTAL

S-p-CHLOROTHIOBENZOYLTHIOGLYCOLIC ACID

A solution of 120 ml of carbon disulfide (reagent grade) in 200 ml of anhydrous ether was added to the ethereal Grignard reagent prepared from 192 g (1 mole) of p-chlorobromobenzene and 27.2 g of magnesium. After 16 hours, the mixture was hydrolyzed with ice and water, and the aqueous layer was filtered, washed with ether, and treated with 152 g of sodium carbonate and 100 g of chloroacetic acid. After standing overnight, the precipitated solid was collected and the filtrate was acidified with 80 ml concentrated hydrochloric acid. Orange crystals, wt 2.0 g, mp 114-117°, were collected. Three recrystallizations from benzene gave an analytical sample, mp 118-119°.

Analysis: Calcd. for $C_9H_7O_2ClS_2$: C, 43.80, H, 2.86.
Found: C, 43.82; H, 2.88.

p-CHLOROTHIOBENZHYDRAZIDE

One milliliter of hydrazine hydrate was added to a solution of 2.32 g of S-p-chlorothiogenzoylthioglycolic acid in 10 ml of 1 N sodium hydroxide. The hydrazide precipitated rapidly; after 15 minutes, 1 ml of acetic acid was added, and the product was collected; wt 1.38 g, mp 122-123°. Three recrystallizations from benzene gave an analytical sample, mp 123-124°.

Analysis: Calcd. for $C_7H_7N_2ClS$: C, 45.04; H, 3.78; N, 15.01.
Found: C, 45.40; H, 3.99; N, 15.40.

p-NITROBENZAL DERIVATIVE

From 80 mg of the foregoing hydrazide and 65 mg of p-nitrobenzaldehyde was obtained 114 mg of p-nitrobenzaldehyde p-chlorothiobenzoylhydrazone, mp 168-170°. Two recrystallizations from methanol gave an analytical sample, mp 168° (analysis pending).

CYCLOHEXANETHIONCARBONYLTHIOGLYCOLIC ACID AND CYCLOHEXANETHIONCARBOHYDRAZIDE

Carbon disulfide (120 g) was added carefully to the Grignard reagent prepared from 163 g of cyclohexyl bromide, 27.2 g of magnesium, and 500 ml of

ether. After standing overnight, the mixture was hydrolyzed with ice and water, filtered, and the aqueous layer was washed with ether and treated with 152 g of sodium carbonate and 100 g of chloroacetic acid. The next day the mixture was filtered and then acidified with hydrochloric acid, which caused the product to separate as an oil.

A solution of 9 g of the oily acid in 50 ml of 1 N sodium hydroxide precipitated the solid hydrazide almost immediately after the addition of 5 ml of hydrazine hydrate. After 1/2 hour, 5 ml of glacial acetic acid was added, causing some further precipitation, and the product was filtered off; wt 5.0 g, mp 75-81°. Four recrystallizations from benzene gave an analytical sample, mp 106-107°.

Analysis: Calcd. for $C_7H_{14}N_2S$: C, 53.12; H, 8.91; N, 17.71.
Found: C, 53.39; N, 8.94; N, 17.30.

p-NITROBENZAL DERIVATIVE

This compound was obtained in the usual manner, albeit in poor yield, and had mp 125-126° crude, and 124° after two recrystallizations from aqueous methanol (analysis pending).

5-p-ANISYLTHIATRIAZOLE

A solution of 10 g of p-anisoyl thiohydrazide in 200 ml of ca. 7% hydrochloric acid was filtered and diazotized; the precipitate of 5-p-anisylthiatriazole, which formed rapidly, weighed 5 g and had mp 92-95°. Three recrystallizations gave a colorless product of mp 102°.

Analysis: Calcd. for $C_8H_7ON_3S$: C, 49.73; H, 3.65; N, 21.75.
Found: C, 49.83; H, 3.89; N, 21.84.

THERMAL DECOMPOSITION OF 5-PHENYLTHIATRIAZOLE

A solution of 2.6 g of 5-phenylthiatriazole in 26 ml of tetralin was boiled until gas evolution ceased; 360 ml of nitrogen was collected. Steam distillation separated all organic materials from a residue of sulfur. The nonaqueous phase of the steam distillate was mixed with concentrated sulfuric acid and refluxed for several hours, after which the cooled mixture was alkalized with sodium hydroxide and extracted with benzene. Acidification of the aqueous phase precipitated 0.75 g of benzoic acid, identified by mixed melting point.

REDUCTION OF 5-PHENYLTHIATRIAZOLE WITH LITHIUM ALUMINUM HYDRIDE

A solution of 7.48 g of 5-phenylthiatriazole in 150 ml of dry ether was added to 2.1 g of lithium aluminum hydride in 60 ml of ether; vigorous reaction occurred. After 10 minutes, 2.1 ml of water was added, followed by 2.1 ml of 15% sodium hydroxide solution and then 6.3 ml of water. The ether layer was separated from the filtered solution and dried over magnesium sulfate. Distillation of the solvent left 4.77 g of brown oil, which gave colorless crystals from petroleum ether, mp 109-115°. Recrystallization raised this to 116° (reported for thiobenzamide, 115-116°). Sodium fusion showed sulfur present.

ter-BUTYL AZIDE FROM ter-BUTYL CHLORIDE

A mixture of 100 g of ter-butyl chloride, 91 g of sodium azide and 200 ml of methylcellosolve was refluxed for 63 hours. Some ether was added to prevent fractionation of pure hydrogen azide, and the filtered mixture was distilled through a good fractionating column. The cuts from 76° to 100°, wt 14.7 g, were redistilled. No sharp fractions were obtained, and only a few tenths of a gram distilled in the range expected for ter-butyl azide. A vapor-phse chromatogram showed the presence of ter-butyl azide in a concentration of about 70%, but the total amount was too small to justify attempts at further purification.

ter-BUTYL AZIDE FROM ter-BUTYLHYDRAZINE

A. With Nitrous Acid.—A solution of 20 g of ter-butylhydrazine hydrochloride in 55 ml of water was added to 52 g of sodium nitrite dissolved in 50 ml of water. The mixture was chilled in an ice bath and stirred while 115 ml of 5 N hydrochloric acid was added dropwise. After 18 hours in a refrigerator, the now two-phase mixture was steam-distilled. A little urea was added to the distillate to destroy nitrous acid, and salt was added to saturation. The yellowish, oily organic layer was separated and dried over magnesium sulfate. It weighed 1.54 g, and vapor-phase chromatography showed it to contain 32% of ter-butyl azide, which was also identified by the infrared spectra of the separate chromatogram fractions.

B. With Nitrogen Tetroxide.—ter-Butylhydrazine (5.0 g) was added in small portions with stirring to a mixture of 5.8 g of nitrogen tetroxide, 5.65 g of sodium acetate, 4.0 g of magnesium sulfate, and a quantity of glacial acetic acid, while kept in an ice bath. The mixture was filtered after 3-1/2 hours. Two extractions of the solid portion with hot, absolute alcohol removed 1.65 g of a white, crystalline material, mp 169-171°, which reduced Fehling's solution but gave a negative Liebermann nitroso test. It is presumably ter-butylhydrazine acetate.

Fractional distillation of the filtrate gave only 0.28 g of material boiling below 98°. It showed strong infrared absorption due to azide, plus absorption due to appreciable amounts of contaminants such as acetic acid. Since the amount was so small, it was not considered worth further study.

1-METHYLCYCLOHEXYL AZIDE

1-Methylcyclohexyl chloride was prepared by the action of hydrochloric acid on 1-methylcyclohexanol obtained by the Grignard reaction on cyclohexanone [J. Am. Chem. Soc., 73, 219 (1951)].

A solution of 32 g of sodium azide and 25 g of sodium dihydrogen phosphate monohydrate in 65 ml of water was brought to pH 6.2 by the addition of 10% sodium hydroxide solution (about 40 ml). A solution of 1-methylcyclohexyl chloride in 200 ml of carbitol was added, and the mixture was refluxed with stirring for 24 hours. The cooled mixture was then diluted with two liters of water and extracted five times with ether. Distillation of the dried (calcium chloride) extracts at 115-mm pressure gave the following fractions:

bp	wt	
50-54°	1.63 g	all decolorized bromine
54-55°	6.12 g	
54-35°	0.83 g	
100-105°	7.34 g	$n_D^{23.5°} = 1.4593$

The last fraction, presumably fairly pure 1-methylcyclohexyl azide, showed strong azide absorption in its infrared spectrum plus a small O-H band which could not be removed by redistillation.

RATE OF DECOMPOSITION OF AROMATIC AZIDES

The rate of decomposition of aromatic azides was determined by following the rate of evolution of nitrogen. The moles of nitrogen evolved were calculated from the volume of nitrogen collected. The moles of unreacted azide at a given time were calculated by subtracting the moles of nitrogen evolved at that time from the total moles of nitrogen ultimately evolved. The first-order rate constants were calculated from the slope of a plot of log (moles of azide) versus time. Two procedures were used. One procedure consisted of dissolving the azide in the solvent and then immersing it in a constant temperature bath. The second procedure involved the addition of a small volume of a concentrated solution of the azide to a large volume of a preheated solvent.

Procedure A.—Approximately 0.1 g of the azide was accurately weighed and placed in a 15-ml one-neck flask. Twelve ml of solvent were added to dissolve the azide. Cargille boiling chips (0.15 g) were added. The flask was attached

to an outlet tube by means of a Standard-Taper joint. The nitrogen evolved was collected over water in an inverted buret. The reaction vessel was immersed in a constant temperature bath (temperature regulation ±0.2°). About 6 minutes were required for the reaction mixture to reach the temperature of the oil bath. Since at the time of immersion of the reaction vessel in the bath there is an expansion of the air in the vessel which forces air into the buret, it was necessary to run a blank and apply a correction to the buret readings.

Procedure B.—The reaction vessel had a capacity of 115 ml. It had three necks: one for a thermometer, one for introducing the azide, and the third was a capillary outlet tube. A magnetic stirring bar was placed in the flask and 100 ml of the solvent added. A serum cap was placed on one neck of the flask so that the azide could be introduced by means of a syringe. The reaction vessel was then immersed in a constant temperature oil bath. The solution in the reaction flask was stirred by means of a magnetic stirrer placed under the oil bath. The nitrogen evolved was collected over water in a water-jacketed buret A standard solution of the azide in m-dimethoxybenzene (ca. 0.25 g/ml) was prepared. As soon as the system reached temperature equilibrium, 0.40 ml of the azide solution was injected into the solvent with a syringe. Introduction of the cold syringe into the air space of the reaction flask appeared to cause a small amount of cooling of the air space, which required 5 to 8 minutes before the new temperature equilibrium was established and reliable data could be obtained. The temperature control in the reaction vessel was ±0.05°.

Results.—All the azides which cyclize to give carbazole derivatives gave first-order kinetics. Those azides which do not cyclize showed deviations from first-order kinetics. If one calculates the order of reaction from the data, it turns out to be 1.1 to 1.2. The rate constants given below for these latter azides were obtained from first-order plots and initial rates.

TABLE I

RATES OF THERMAL DECOMPOSITION OF ARYL AZIDES

Azide	k, min^{-1}	Solvent	Temp	Procedure
2-Azidobiphenyl	0.0732	Kerosene	173.3	A
2-Azidobiphenyl	0.0759	Nitrobenzene	173.3	A
2-Azidobiphenyl	0.0747	Decalin	173.3	A
2-Azido-4'-nitrobiphenyl	0.0643	Kerosene	173.3	A
2'-Azido-2-phenylnaphthalene	0.0739	Kerosene	173.3	A
2'-Azido-2-phenylnaphthalene	0.15	Kerosene	178.8	A
1-Azido-2-phenylnaphthalene	0.42	Kerosene	178.8	A
Phenyl Azide	0.0591[a]	Decalin	173.3	A
4-Azidobiphenyl	0.0745[a]	Decalin	173.3	A
4-Methoxyphenyl Azide	0.102[a]	Decalin	173.3	A
2-Azidobiphenyl	0.0813[b]	Decalin	173.9	B
2-Azidobiphenyl	0.0882	Nitrobenzene	173.9	B
2-Azidobiphenyl	0.173	Ethylene Glycol	173.9	B

[a]Calculated from initial rates.
[b]Average of four values. Average deviation 2.5%.