

Preparation of Azides from Hydrazines by using Dinitrogen Tetroxide as Nitrosonium Ion Source

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Various hydrazines such as aryl-, carbonyl-, and sulfonyl-hydrazine were reacted with dinitrogen tetroxide to give the corresponding azides in excellent yields under mild conditions at low temperature (-20–-40°C) in acetonitrile. The reaction appears to be initiated by formation of the β -nitroso hydrazine intermediate which converts into the azide product.

Key words: Dinitrogen tetroxide, Nitrosation, Hydrazine, Hydrazide, Azide, Nitrosonium ion

INTRODUCTION

All the known organic azides are synthesized chemically, and there is no example in the literature to reports on a naturally occurring compound in this class (Sheradsky, 1971). The first organic azide, phenyl azide, was synthesized by Peter Griess from benzene diazonium perbromide and ammonia (Sheradsky, 1971). The discovery by Curtius of the rearrangement of acyl azide to isocyanate stimulated interests in organic azides and most of the general synthetic methods were soon developed (Smith, 1949). Intensive studies on organic synthesis using organic azides have been reported for the important preparation of amines (Corey *et al.*, 1975), azo compounds (Bayley *et al.*, 1978), azomethines (Bayley *et al.*, 1978), Iminosulphuranes (Horner and Christman, 1983), isocyanates (Hine, 1956), and aziridines (Ittah *et al.*, 1956). Azides are essential intermediates in organic synthesis and have been prepared by substitution on carbon of sodium azide (Kuzuhara and Emoto, 1973), trimethyl silyl azide (Kricheldorf, 1972; MacMillan and Washburne, 1973) or by nitrosation of hydrazine derivatives (Honzl and Rudinger, 1961) using nitrous acid (Roesky and Glemser, 1964), nitrosyl chloride (Neunhoffer *et al.*, 1968), organic nitrites (Smart *et al.*, 1960) and ferric nitrate (Laszlo and Polla, 1984). Previously we reported that dinitrogen te-

troxide is a good nitrosation reagent for activating thiols to convert into the thionitrites (Oae *et al.*, 1977, Kim *et al.*, 1978), and hydrazines to convert into azides as a communication (Kim *et al.*, 1986). Now we report that various hydrazines reacted rapidly with dinitrogen tetroxide to give the corresponding azides in mostly quantitative yields under mild conditions at low reaction temperature (-20–-40°C) in aprotic polar solvents such as acetonitrile and tetrahydrofuran. Although dinitrogen tetroxide (N_2O_4) is commercially available, in our study it was easily prepared in situ (Pedler and Pollard, 1957). N_2O_4 gas was trapped in a cold flask containing P_2O_5 below -20°C. The solid N_2O_4 was dissolved in cold CCl_4 , and this solution titrated was used for the reaction.

MATERIALS AND METHODS

Materials and Instruments

The organic solvents and reagents for the reaction were obtained from Oriental Chemical Inc. (Seoul, Korea) and purified by the appropriate methods before use. The commercially available hydrazines such as phenyl hydrazine, 4-nitro phenyl hydrazine, 2,4-dinitro phenyl hydrazine, 4-toluenesulfonic acid hydrazide, and 2-furoic acid hydrazide were obtained from Aldrich Chemical Inc. (Milwaky, U.S.A.). And the other carboxylic acid hydrazides such as benzoic acid hydrazide, 4-nitro benzoic acid hydrazide, 4-chloro benzoic acid hydrazide, and terephthalic acid dihydrazide were synthesized by the following general procedure; Carboxylic acid ester (0.1 mole) was dissolved in 50 ml of metha-

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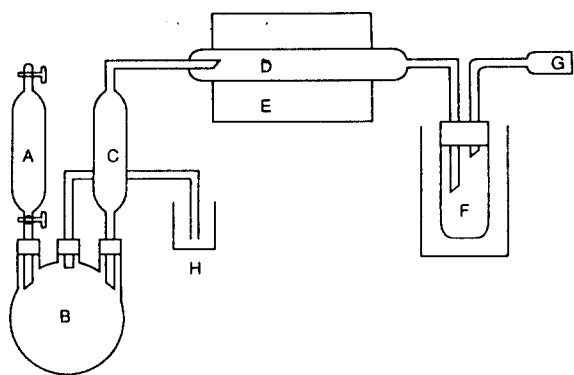


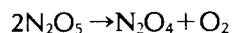
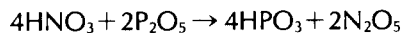
Fig. 1. Apparatus for the preparation of N_2O_4 .

nol solution, then hydrazine hydrate (85%, 25 ml, 0.4 mole) was added. The reaction mixture was heated to reflux. After 3-5 hours, the reaction mixture was cooled to $0^\circ C$, and the resulting acid hydrazide was crystallized on the standing. The hydrazides were obtained by filtration, washing with water and small amount of methanol, and recrystallization from methanol or acetonitrile depending on their solubility.

Melting points were taken on a Electrochemical Melting Point Apparatus (Electrothermal Engineering Ltd.). Infrared Spectra were recorded on a Perkin Elmer 283 B Spectrophotometer. 1H nmr spectra were determined on Varian T-60 A, and the chemical shifts are reported in ppm relative to internal tetramethylsilane. TLC was carried out on silicagel, Merck GF₂₅₄, 20×20 cm glass plates with 1.0 mm thickness.

Preparation of Dinitrogen Tetroxide

Dinitrogen pentoxide was prepared by dehydrating nitric acid. The strong affinity of N_2O_5 for H_2O requires the use of a very strong dehydrating agent such as phosphorous pentoxide, which is sufficiently deliquescent to remove H_2O from nitric acid.



In the gas phase, N_2O_5 is thermodynamically unstable and loses O_2 to form the equilibrium mixture of NO_2 and N_2O_4 . While this decomposition occurs slowly even at room temperature, elevated temperatures are more convenient for synthetic purposes. Apparatus for the preparation of N_2O_4 is depicted in Fig. 1.

Decomposition tube D was filled with glass beads. The drying column C and drying tube G were loosely filled with the mixture of phosphorous pentoxide and glass wool. A safety bubbler H was filled with silicon oil. Trap E was then surrounded with a Dewar bottle containing a mixture of dry ice and acetone. Trap F was sunk in Dewar bottle like the Fig. 1 to prevent the tube connected to trap F blocked by generated

N_2O_4 solid. Phosphorous pentoxide (200 g, 0.88 mole) was placed in 1 l-3-necked round bottomed flask B, and 105 ml of fuming nitric acid (2.25 mole) was placed in a dropping funnel A. The temperature of electric furnace E was adjusted to $260^\circ C$. Then, nitric acid was added dropwise where the addition was sufficiently slow to avoid an introduction of the acid into the connecting tubes. White solid of N_2O_4 was trapped in Trap E. The obtained N_2O_4 solid was well dissolved in the appropriate amount of dried CCl_4 . The resulting N_2O_4 in CCl_4 solution was stored in the refrigerator and its concentration was determined by titration before USE (Pedler and Pollard, 1957).

Determination of Concentration of N_2O_4 in CCl_4

The N_2O_4 solution (0.1 ml) was quenched in ice water (10 ml) and then gradually warmed to room temperature.



The molar concentration of N_2O_4 was calculated from the amount of sodium hydroxide used to neutralize the generated nitric acid according to the above stoichiometric equation by titration using phenobarbital as indicator.

Benzoyl azide

Dinitrogen tetroxide solution (2 mmole, CCl_4 : 0.3 ml) was slowly added to the benzoic acid hydrazide (0.138 g, 1 mmole, anhydrous CH_3CN : 5 ml) at $-30^\circ C$ with good stirring under argon atmosphere. The reaction was monitored by t.l.c. (Merck; Kiesegel 60F₂₅₄, $CHCl_3$). After being stirred for 10 minutes, 25 ml of ethyl ether was added to the reaction mixture and this ether layer was washed with 10 ml of saturated sodium bicarbonate and 10 ml of brine, and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave the highly pure azide (0.141 g, 96%) (Laszlo and Polla, 1984), which were further purified by column chromatography (silicagel; Wakogel 300, ether: n-hexane=1:1, 0.133 g, 91%): IR (neat, cm^{-1}) 2340 (w), 2160 (sh), 2130 (s), 1690 (s), 1230 (s), 1175 (s); 1H nmr ($CDCl_3$, 60 MHz) 8.00 (d, 2H), 7.77-7.23 (m, 3H).

4-Toluenesulfonyl azide

Toluenesulfonic acid hydrazide (0.187 g, 1 mmole) was reacted with dinitrogen tetroxide (2 mmole, CCl_4 : 0.3 ml) in 6 ml of anhydrous acetonitrile at $-20^\circ C$ under argon atmosphere. After being stirred for 10 minutes, the work-up was carried out as previously described for the preparation of benzoyl azide to give crude toluenesulfonyl azide (0.193 g, 97%) (Laszlo and Polla, 1984), which were further purified by column

chromatography (silicagel; Wakogel 300, ether:n-hexane=2:3, 0.182 g, 95%): IR (neat, cm^{-1}) 2340 (w), 2130 (s), 1170 (s); ^1H nmr (CDCl_3 , 60 MHz) 7.80 (d, 2H), 7.33 (d, 2H), 2.45 (s, 3H).

Phenyl azide

Phenyl hydrazine (0.108 g, 1 mmole) was reacted with dinitrogen tetroxide (2 mmole, CCl_4 : 0.3 ml) in 6 ml of anhydrous acetonitrile at -20°C under argon atmosphere. After being stirred for 20 minutes, the solvent and excess dinitrogen tetroxide rapidly evaporated under the reduced pressure. The resulting residue was chromatographed (silicagel; Wakogel 300, ether:n-hexane=11:1) in the cold chamber (5°C) to give the pure product (96 mg, 91%) (Laszlo and Polla, 1984): IR (neat, cm^{-1}) 2140(w), 2110(s), 2090(s); ^1H nmr (CDCl_3 , 60 MHz) 7.60-6.91(m, 5H).

2-Furoyl azide

2-Furoic acid hydrazide (0.128 g, 1 mmole) was reacted with dinitrogen tetroxide (2 mmole, CCl_4 : 0.3 ml) in anhydrous acetonitrile at -25°C under argon atmosphere. After being stirred for 20 minutes, the work-up was carried out as previously described for the preparation of benzoyl azide. Crude 2-furoyl azide (d. 123 g, 91%) was chromatographed (silicagel; Wakogel 300, ether:n-hexane=1:1) to give the pure azide (0.109 g, 85%) (Kuhn and Kruger, 1956): IR (KBr, cm^{-1}) 2250 (w), 2210(sh), 2160(s), 1700(s), 1300(s); ^1H nmr (CDCl_3 , 60 MHz) 6.5(m, 1H), 7.2(d, 1H), 7.5(d, 1H).

Terephthaloyl diazide

Terephthalic acid dihydrazide (0.194 g, 1 mmole) was reacted with dinitrogen tetroxide (4 mmole, CCl_4 : 0.6 ml) in anhydrous acetonitrile at -10°C under argon atmosphere. After 10 minutes, the work-up was carried out as previously described for the preparation of benzoyl azide. Crude terephthaloyl diazide (0.198 g, 92%) was chromatographed (silicagel; Wakogel 300, ether:n-hexane=1:1) to give the pure azide (0.193 g, 89%) (Munekata and Kikuchi, 1968): IR (KBr, cm^{-1}) 2290 (w), 2185 (sh), 2140 (s), 1690 (s), 1235 (s); ^1H nmr (CDCl_3 , 60 MHz) 8.7 (s, 4H).

4-Nitro benzoyl azide

4-Nitro benzoic acid hydrazide was reacted with dinitrogen tetroxide (2 mmole, CCl_4 : 0.3 ml) in anhydrous acetonitrile at -30°C . After 10 minutes, the work-up was carried out as previously described for the preparation of benzoyl azide. Crude 4-nitro benzoyl azide (0.175 g, 91%) was chromatographed (silicagel, Wakogel 300, ether:n-hexane=2:1) to give the pure azide (0.170 g, 89%) (Yukawa and Tsuno *et al.*, 1957): IR (KBr, cm^{-1}) 2290 (w), 2195 (sh), 2120 (s), 1795 (s),

1250 (s); ^1H nmr (CDCl_3 , 60 MHz) 7.80-8.50 (m, 5H).

4-Chloro benzoyl azide

4-Chloro benzoic acid hydrazide (0.170 g, 1 mmole) was reacted with dinitrogen tetroxide (2 mmole, CCl_4 : 0.3 ml) in anhydrous acetonitrile at -40°C . After 20 minutes, the work-up was carried out as previously described for the preparation of benzoyl azide. Crude 4-chloro azide (0.156 g, 86%) was chromatographed (silicagel, Wakogel 300, ether:n-hexane=1:1) to give the pure azide (0.152 g, 84%) (Bailey and Case, 1958): IR (KBr, cm^{-1}) 2280 (w), 2175 (sh), 2140 (s), 1690 (s), 1255 (s), 1180 (s); ^1H nmr (CDCl_3 , 60 MHz) 7.41 (d, 2H), 8.00 (d, 2H).

2,4-Dinitro phenyl azide

2,4-dinitro phenyl hydrazine (0.194 g, 1 mmole) was reacted with dinitrogen tetroxide (2 mmole, CCl_4 : 0.3 ml) in anhydrous acetonitrile at -30°C under argon atmosphere. After 10 minutes, the solvent and excess dinitrogen tetroxide was rapidly evaporated under the reduced pressure. The resulting residue was rapidly chromatographed (silicagel; Wakogel 300, ether:n-hexane=2:1) in the cold chamber (5°C) to give the pure azide (0.185 g, 90%) (Lieber *et al.*, 1957): IR (neat, cm^{-1}) 2420 (w), 2240 (sh), 2120 (s); ^1H nmr (CDCl_3 , 60 MHz) 8.82 (d, 1H), 8.52 (q, 1H), 7.62 (d, 1H).

4-Nitro phenyl azide

4-Nitro phenyl hydrazine (0.154 g, 1 mmole) was reacted with dinitrogen tetroxide (2 mmole, CCl_4 : 0.3 ml) in acetonitrile at -30°C under argon atmosphere. After 10 minutes, the solvent and excess dinitrogen tetroxide was rapidly evaporated under the reduced pressure. The resulting residue was chromatographed (silicagel; Wakogel 300, ether:n-hexane=2:1) to give the pure azide (0.149 g, 95%) (Lieber *et al.*, 1957): IR (neat, cm^{-1}) 2410 (w), 2260 (w), 2220 (ms), 2140 (s), 2120 (s); ^1H nmr (CDCl_3 , 60 MHz) 8.27 (d, 2H), 7.18 (d, 2H).

RESULTS AND DISCUSSION

Despite of their toxicity and their instability, azides are essential intermediates in organic synthesis (Sheradsky, 1971). We report that various hydrazines such as aryl-, carbonyl-, and sulfonyl hydrazines were reacted with dinitrogen tetroxide to give the corresponding azides in excellent yields under mild conditions at low temperature (-20 – -40°C) in acetonitrile as shown in Table 1.

All the products obtained were identified by comparing their i.r., ^1H nmr spectra and melting points with those of the authentic samples. References for the

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