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FACILE SYNTHESIS OF AZIDES: CONVERSION OF HYDRAZINES USING DINITROGEN TETROXIDE

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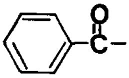
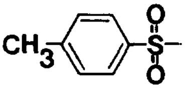
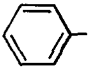
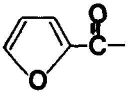
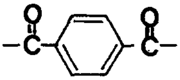
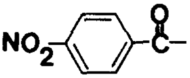
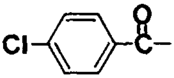
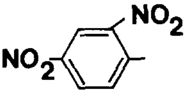
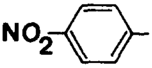
Abstract : Various hydrazines such as aryl-, carbonyl-, and sulfonylhydrazine were reacted with dinitrogen tetroxide to give the corresponding azides in excellent yields under mild conditions at low temperature(-20~-40 °C) in acetonitrile.

Intensive studies on organic syntheses[1] using organic azides have been reported for the important preparation of amines[1,2], azo compounds[1,3], azomethines[1,3], iminophosphoranes[4], iminosulphuranes[5], isocyanates[6], and aziridines[7]. Azides are essential intermediates in organic synthesis and have been prepared by substitution on carbon of sodium azide[8], trimethyl silyl azide[9] or by nitrosation of hydrazine derivatives[10] using nitrous acid[11], nitrosyl chloride[12], organic nitrites[13] and ferric nitrate[14]. Previously we reported that dinitrogen tetroxide is a good nitrosation reagent for activating thiols to convert into the thionitrites[15]. We have now found that various hydrazines reacted rapidly with dinitrogen tetroxide[16] to give the corresponding azides in mostly quantitative yields under mild conditions at low temprature(-20~-40 °C) in acetonitrile. In a typical procedure, dinitrogen tetroxide solution(2 mmole, CCl_4: 300 μ l) was slowly added to the benzoyl hydrazide(0.138g,1 mmole, anhydrous CH_3CN : 5ml) at -10 °C with stirring. The reaction was monitored by t.l.c. (Merck; Kiesegel $60F_{254}$, $CHCl_3$). After being stirred for 10 minutes, 25 ml of ether was added to the reaction mixture and this ether layer was twice washed with 10 ml of saturated sodium bicarbonate solution and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave the highly pure azide(0.141g, 96%), which were further purified by column chromatography(Silicagel; Wako gel 300, ether:n-hexane=1:1, 0.133g, 91%). All the products thus obtained were identified by comparing their ir, ^1H nmr spectra and melting points with those from the authentic samples. The results obtained are summarized in Table 1.

Table 1. Conversion of Hydrazines into Azides

$$R\text{-}NH\text{-}NH_2 \xrightarrow[CH_3CN]{N_2O_4} R\text{-}N_3$$

Run	R	Reactn. Temp.(^{o}C)	Reactn. time(min.)	Yield(%)[a]	Ref. No[b]
1		-30	10	91[c]	14
2		-20	10	95[c]	14
3		-20	20	87	14
4		-25	20	86	20
5		-10	10	92	21
6		-30	10	89	22
7		-40	20	84	22
8		-30	10	90	23
9		-30	10	95	24

a : Isolated and purified yield.

b : References for the known products of azides are cited in the reference section.

c : When the reaction was carried out at ca. 0 ^{o}C, the yield of azide was about the same.

N_2O_4 is known to be in equilibrium with NO^+ and NO_3^- in solution by its self ionization[18]. Probably the electrophilic attack of NO^+ on the nitrogen atom of the amine forms the corresponding β-nitroso hydrazine intermediate ($\underset{\sim}{2}$) which may finally convert into the products, azides($\underset{\sim}{3}$). Nitrosation of secondary amines with dinitrogen tetroxide are well known by isolation of the stable secondary nitroso compounds[19].

$$N_2O_4 \rightleftharpoons NO^+ + NO_3^-$$

$$\underset{\underset{\sim}{1}}{R\text{-}NHNH_2} + N_2O_4 \longrightarrow \underset{\underset{\sim}{2}}{[R\text{-}NH\text{-}NH\text{-}N{=}O]} + HNO_3$$

$$\longrightarrow \underset{\underset{\sim}{3}}{R\text{-}N{=}\overset{+}{N}{=}\overset{-}{N}} + H_2O + HNO_3$$

The yields of the azides are markedly high when the reaction temperatures are controlled at lower than -20 °C. While, p-nitrophenyl- and phenyl azides appear to rearrange to the heterocycles[14] due to their instability at high temperature. Our method can be carried out in the wide range of low reaction temperature (-10~-40 °C) for short reaction time (10-20 min) and is simple for work up after the completion of the reaction. Thus, this facile method seems to be widely available for the preparation of various azides from hydrazines.

Acknowledgment

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16) N_2O_4 is commerially available or can be easily prepared[17]. N_2O_4 gas was trapped in a cold flask containing P_2O_5 at -20 °C. The liquid N_2O_4 was trapped in cold CCl_4, and this solution titrated was used for the reaction.

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