Pergamon

Tetrahedron Letters 39 (1998) 4533–4536

TETRAHEDRON
LETTERS

Nitrogen dioxide - sodium iodide as an efficient reagent for the one-pot conversion of aryl amines to aryl iodides under nonaqueous conditions

Hitomi Suzuki*, Nobuaki Nonoyama

Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo-ku, Kyoto 606-8224, Japan

Received 2 March 1998; revised 15 April 1998; accepted 17 April 1998

Abstract

Successive treatment of aromatic amines with liquid nitrogen dioxide and powdered sodium iodide in acetonitrile at −20 ℃, followed by usual work-up, gave the corresponding aryl iodides in good yield. This method worked especially well for less basic amines bearing electron-withdrawing substituents.

Keywords: Halogenation; Amines; Diazo compounds; Nitrogen oxides

Nitrogen dioxide (NO_2) is important as an industrial chemical for the production of a wide variety of nitrogen-containing organic and inorganic compounds, but in laboratory its use for preparative purpose is rather limited at present. This compound is commercially supplied at low price in a cylinder, and can be used direct in a gaseous state or in the form of liquid (b.p. 21 ℃) collected by transfer distillation into an ice-cooled vessel. We have already shown that NO_2 in combination with ozone can act as an excellent nitrating agent for aromatic compounds under non-acid conditions (*kyodai*-nitration) [1,2]. We now report that NO_2 in combination with sodium iodide (NaI) can be used conveniently for the single-pot conversion of aromatic amines to the corresponding iodides under nonaqueous conditions. Due to the versatile utility of aromatic iodides in organic synthesis, the transformation of aromatic amines into iodides constitutes one of important laboratory processes [3].

It has long been known that secondary amines are readily nitrosated by NO_2 to form *N*-nitrosoamines. This is because dimeric NO_2 exists in part in the ionized form $NO^+NO_3^-$ under polar conditions. Thus the action of NO_2 on aromatic amines in polar environments can reasonably be expected to lead to arenediazonium nitrates according to the following equations;

$$2\,NO_2 \rightleftharpoons N_2O_4 \rightleftharpoons NO^+NO_3^-$$

$$Ar\text{-}NH_2 + NO^+NO_3^- \longrightarrow [Ar\text{–}NH_2NO]^+NO_3^- \longrightarrow Ar\text{-}N_2^+NO_3^- + H_2O$$

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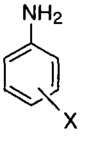
* Corresponding author. E-mail: suzuki@kuchem.kyoto-u.ac.jp

0040-4039/98/$19.00
PII: S0040-4039(98)00824-7



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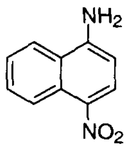
a X = 4-OMe
b X = 4-Me
c X = 4-I
d X = 2-Cl
e X = 4-CO_2Et
f X = 2-NO_2
g X = 4-NO_2
h X = 2,4-$(NO)_2$
i X = 4-NH_2
j X = 3-$NH_3^+HSO_4^-$



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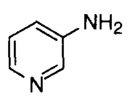


1l

Table 1
Aromatic iodides **3a-g**, **i-l** obtained

Amine	Iodide	Yield[a] (lit.)(%)
1a	**4a**	58 (78[7], $\underline{51}$[8], 82[9], 43[10])
1b	**4b**	68 ($\underline{79}$[8], $\underline{88}$[9], 84[10], 56[11])
1c	**4c**	85 (64[11],62[12], 78[13])
1d	**4d**	83 ($\underline{77}$[9], 81[12])
1e	**4e**	98
1f	**4f**	92 (65[7], $\underline{64}$[8])
1g	**4g**	98 (90[7], $\underline{80}$[8], 72[9], 61[10], 74[14])
1h	**4c**	81
1i	**4i**[b]	40
1j	**4j**	21
1k	**4k**	80 (80[15])
1l	**4l**	72 (50[16])

[a] Yields refer to the compounds, isolated and purified by silica gel chromatography. Underlined numerals in parentheses denote GLC yield.
[b] *m*-Diiodobenzene.

This idea now has been successfully exploited in the single-pot conversion of several aromatic amines to the corresponding iodides under non-aqueous conditions. The present method is especially attractive when aromatic amines bear electron-withdrawing group and/or the reaction needs neutral or nonaqueous conditions [4]. Conventional diazotization of weak amines such as **1f-h** with sodium nitrite is usually carried out by using concentrated sulfuric acid or hydrochloric acid as the reaction media [5,6], while the corresponding reaction under nonaqueous conditions requires prolonged heating with isoamyl nitrite [7].

The general procedure of our method is as follows; to a stirred solution of aromatic amine **1** (2.0 mmol) in acetonitrile (20 cm^3) was introduced liquid nitrogen dioxide (0.14 cm^3, 4.4 mmol) at −20 ℃ (*Fume hood*). After 5 min, powdered sodium iodide (0.45 g, 3.0 mmol) was added in one portion. A slight gas evolution was observed and a white solid soon precipitated. After stirring for additional 10 min, the mixture was diluted with water (20 cm^3) and the organic phase was extracted with dichloromethane or ethyl acetate (20 cm^3 × 2). The combined extracts were washed with aqueous $Na_2S_2O_3$ and dried over Na_2SO_4. Removal of the solvent under reduced pressure left a pale yellow to light brown oil or solid, which was chromatographed on silica gel using hexane-ethyl acetate as the eluent to give the expected iodide **4**.

Representative results obtained are summarized in Table 1. The yields were not optimized but, in most cases examined, they were comparable or better than those previously reported. Especially, the present method proved to be effective for less basic amines **1c-h,k** bearing electron-withdrawing group or groups. For electron-rich amines **1a,b**, the yields were modest, probably due to concurrent side reactions involving the diazotized species or nitrogen dioxide. Minor products isolated therefrom were ring nitrated compound, deaminated substrate, or highly colored nitrogen-containing substance. Direct conversion of aromatic diamines to the corresponding diiodides was less satisfactory; *p*-phenylenediamine **1i** and *m*-phenylenediamine monosulfate **1j** gave the expected diiodides **4c,j** in low to moderate yields, while *o*- and *m*-phenylenediamines led to a complicated mixture of products.

In order to get an insight into the pathway of this reaction, the progress of diazotization was monitored by ^{1}H-

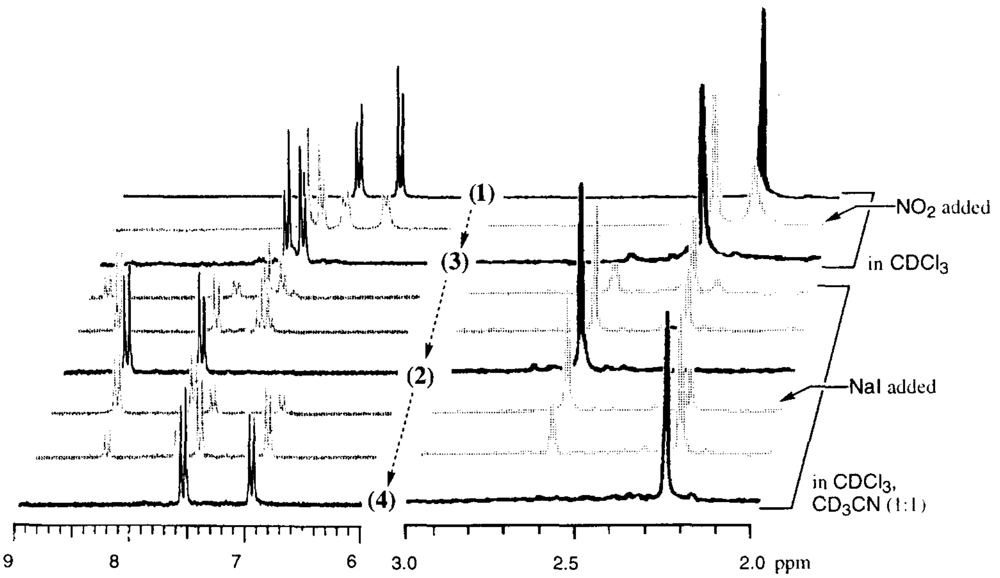
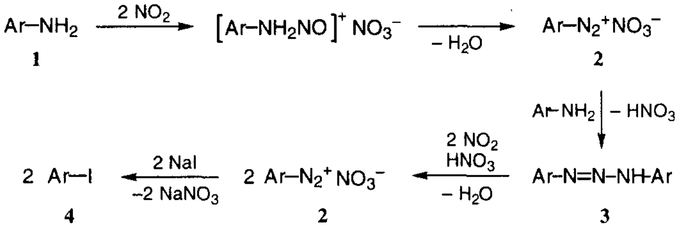


Fig. 1 Conversion of 4-methylaniline **1b** to iodide **4b**, monitored by ^{1}H-NMR.



Scheme 1 Pathway from aromatic amine **1** to iodide **4** via triazene **3**.

NMR using 4-methylaniline **1b** as the substrate. Addition of NO_2 to a solution of **1b** in chloroform-*d* gave an orange-colored solution, ^{1}H-NMR spectrum of which showed a singlet at δ 2.3 and two doublet peaks at δ 7.1 and 7.2, attributable to an initial product (Fig. 1, (**3**)). At this stage, addition of NaI did not lead to any iodide. When allowed to stand further, the solution slowly turned red in parallel with the disappearance of this intermediate and a red powder began to deposit on the wall of an NMR tube, which, on treatment with NaI, gave the expected iodide **4b**. When NO_2 was added to a solution of **1b** in a mixture of acetonitrile-d_3 and chloroform-*d* (1:1) containing nitromethane as an internal standard (δ 4.3), a whole range of the ^{1}H-NMR changes resulting from the conversion of amine **1b** to iodide **4b** was observable in well-resolved spectral patterns within an appropriate time span, as shown in Fig. 1 ((**1**) to (**4**)). The initial product was identified as 1,3-bis(4-methylphenyl)triazene **3b** by direct comparison with the authentic specimen [17]. This means that 1,3-diaryltriazenes **3** are also accessible from aromatic amines **1** in one-pot way by the present procedure. The spectrum (**2**) of the second product showed a singlet at δ2.6 and two doublets at δ 7.7 and 8.3, attributable to the diazonium compound **2b**, and its yield estimated from peak area integration was 93%. On subsequent treatment with NaI, the solution evolved nitrogen gas to give iodide **4b** in 90% yield (Spectrum (**4**)).

In acetonitrile-d_3, addition of NO_2 immediately led to a yellow solution, ^{1}H NMR spectrum of which was identical with that of compound **2**, showing that the diazotization reaction in polar environments proceeds much faster than in nonpolar environments. On the basis of these observations, we can depict the pathway of the one-pot conversion of amine **1** to the corresponding iodide **4**, as shown in Scheme 1. Thus, under polar nonaqueous conditions, the diazotization of aromatic amines with NO_2 has been found to proceed via two distinct stages involving triazene **3** as the intermediate.

In conclusion, a combination of NO_2 and NaI proved to be an efficient reagent for converting aromatic amines to the corresponding iodides in one-pot way under nonaqueous conditions. The mild conditions, high yield, simplicity of manipulation, rapidity, ease of product isolation, and effectiveness for weak aromatic amines are among distinct advantages of the present method.

CAUTION. Nitrogen dioxide is poisonous. With the exception of tetrafluoroborates and hexafluorophosphates, arenediazonium salts are potentially explosive and should be handled with care, keeping the compounds out of *dry solid* state.

Acknowledgements

Financial support of this work by a Grant-in-Aid for Specially Promoted Scientific Research (No. 08101003) of the Ministry of Education, Science, Sports and Culture of Japan is gratefully acknowledged. N.N. thanks the Japan Society for the Promotion of Science for the Fellowship (No. 9191).

References

[1] For a survey, see: Suzuki T, Noyori R. Chemtracts 1997;**10**:813-817.
[2] Mori T, Suzuki H. Synlett 1995:383-392.
[3] For a review, see: Merkushev EB. Synthesis. 1988:923-937.
[4] Engel A. Methoden der Organischen Chemie vol. E16a/2, Stuttgart: Georg Thieme Verlag, 1990:1052-1087.
[5] Bartle M, Gore ST, Mackie RK, Tedder JM. J. Chem. Soc., Perkin Trans. 1. 1976:1636-1638.
[6] Beaton HG, Willey GR, Drew MGB. J. Chem. Soc., Perkin Trans. 2. 1987:469-472.
[7] SmithWB, Ho OC. J. Org. Chem. 1990;**55**:2543-2545.
[8] Oae S, Shinhama K, Kim YH. Chem. Lett. 1979:939-942.
[9] Korzeniowski SH, Gokel GW. Tetrahedron Lett. 1977;**18**:3519-3522.
[10] Evans MJ, Christiaens LE, Guillaume MR, Renson MJ. J. Org. Chem. 1985;**50**:1779-1780.
[11] Friedman L, Chlebowski JF. J. Org. Chem. 1968;**33**:1636-1638.
[12] Lee JG, Cha HT. Tetrahedron Lett. 1992;**33**:3167-3168.
[13] Fry HS, Grote IW. J. Am. Chem. Soc. 1926;**48**:710-714.
[14] Bartsch RA, Yang IW. Tetrahedron Lett. 1979;**20**:2503-2504.
[15] Hodgson HH, Walker JW. J. Chem. Soc. 1933:1620-1621.
[16] Binz A, Räth C. Liebigs Ann. Chem. 1931;**486**:95-106.
[17] Vernin G, Siv C, Metzger J, Párkányi C. Synthesis. 1977:691-693.