

Direct Aromatic Amination by Azides: Reactions of Hydrazoic Acid and Butyl Azides with Aromatic Compounds in the Presence of Both Trifluoromethanesulfonic Acid and Trifluoroacetic Acid†

Hiroshi Takeuchi,* Taki Adachi, Hideaki Nishiguchi, Katsutaka Itou and Kikuhiko Koyama
Department of Chemistry and Material Engineering, Faculty of Engineering, Shinshu University, 500
Wakosato, Nagano 380, Japan

Reactions of hydrazoic acid with aromatic compounds in the presence of both trifluoromethanesulfonic acid (TFSA) and trifluoroacetic acid (TFA) efficiently gave primary arylamines without diamine contaminants. The reactions provide mainly the *ortho*- and *para*-monoamines even for readily oxidised aromatic compounds such as cumene, mesitylene, durene, isodurene and anisole. The mechanistic investigation demonstrates that the reactions proceed *via* a concerted process involving both arene attack on a conjugate acid of the azide and elimination of N₂ from the conjugate acid. The reaction of butyl azide with benzene and mesitylene in the presence of both TFSA and TFA produced *N*-butylarylamines in low yields together with high yields of butanal *via* a butylnitrenium ion intermediate; a similar reaction with *tert*-butyl azide gave no *tert*-butylarylamines.

Direct aromatic amination, other than by way of hydrogenation of the corresponding nitro compounds, is of great interest both synthetically and mechanistically. We have already reported the direct aromatic amination by ethoxycarbonylnitrenium ion,¹ arylnitrenium ions,² arylnitrenium-AlCl₃ complexes³ and parent nitrenium ion.⁴ However, the formation of primary arylamines by the parent nitrenium ion is contaminated by a side reaction occurring *via* the triplet nitrenium ion when the arene is a good H-atom donor such as durene or isodurene. Further, amination by the parent nitrenium⁴ ion needs expensive starting materials, *e.g.* 1-aminoquinolinium and 1-aminopyridinium salts. By contrast, from the less-expensive hydrazoic acid **1** we have now found that the title amination provides primary arylamines in good yields from a variety of arenes without side reactions. The azide **1** has earlier been used for direct aromatic amination in the presence of AlCl₃ or H₂SO₄,^{5,6} but the yields were not as high as those reported here because of side reactions resulting in the formation of tar or sulfonic acid and in hydrazine conversion.⁷

Results and Discussion

Reactions of Hydrazoic Acid 1 with Aromatic Compounds in the Presence of Both Trifluoromethanesulfonic Acid (TFSA) and Trifluoroacetic Acid (TFA).—Reactions of the azide **1** with benzene **2a**, toluene **2b**, ethylbenzene **2c**, cumene **2d**, anisole **2e**, bromobenzene **2f** and chlorobenzene **2g** in the presence of both TFSA and TFA yielded 2-, 3- and 4-substituted primary arylamines **3a–g**, **4b–g** and **5b–g** after work-up with aqueous Na₂CO₃ (Table 1 and Scheme 1). Similar reactions of **1** with *o*-, *m*- and *p*-xylenes **2i–k**, mesitylene **2l**, durene **2m** and isodurene **2n** gave 2,3- and 3,4-dimethylanilines **4i** and **6i**, 2,6-, 2,4- and 3,5-dimethylanilines **3j**, **5j** and **6j**, 2,5-dimethylaniline **3k**, 2,4,6-trimethylaniline **3l**, 2,3,5,6-tetramethylaniline **3m** and 2,3,4,6-tetramethylaniline **3n** (Table 1 and Scheme 1). The reactions of **1** with biphenyl **2o**, naphthalene **2p** and phenanthrene **2q** also afforded 2- and 4-aminobiphenyls **3o** and **5o**, 1- and 2-aminonaphthalenes **4p** and **5p** and 9-aminophenanthrene **3q** (Table 1 and Scheme 1). Since the reaction of **1** with nitrobenzene **2h** failed to decompose the azide at 60 °C, none of the corresponding arylamines was obtained (Table 1).

(a) *Decomposition via a Conjugate Acid of Hydrazoic Acid.*—In the absence of TFSA, hydrazoic acid **1** failed to decompose in the presence of aromatic compound, but completely decomposed in the presence of TFSA (Table 1). This suggests that the reaction requires an acid such as TFSA which is stronger than TFA. The selectivity factor, $S_f = \log[2 \times (\%para)/(\%meta)]$, for the formation of toluidines did not depend upon the acid participating in the reaction; the reaction of **1** with toluene at 20 °C in the presence of both TFA and fluorosulfonic acid (FSA) provided almost the same S_f value (0.95) as that (0.94) for the reaction using TFSA instead of FSA. The result indicates that the reaction proceeds *via* an intermediate which is independent of the acid. Thus, the intermediate should be the conjugate acid of **1**, not a hydrogen-bonding complex between **1** and the acid (Scheme 1).

(b) *Concerted Process involving Nucleophilic Attack of the Conjugate Acid and the Elimination of N₂.*—The azide almost quantitatively decomposed at a relatively high temperature (40–60 °C) in the reactions of benzene, bromobenzene or chlorobenzene, but the denitrogenation is completed at a lower temperature (25 °C) in the reactions with alkylbenzenes, biphenyl, naphthalene and phenanthrene. In detailed experiments, the reaction with toluene for 2 h at 20 °C under the conditions detailed in Table 1 results in 75% decomposition of **1** while that with benzene instead of toluene showed only 13% decomposition of **1**. The results suggest that the denitrogenation proceeds *via* a concerted process involving both nucleophilic attack of the arene on the conjugate acid of **1** and an elimination of N₂ from the conjugate acid (Scheme 1).

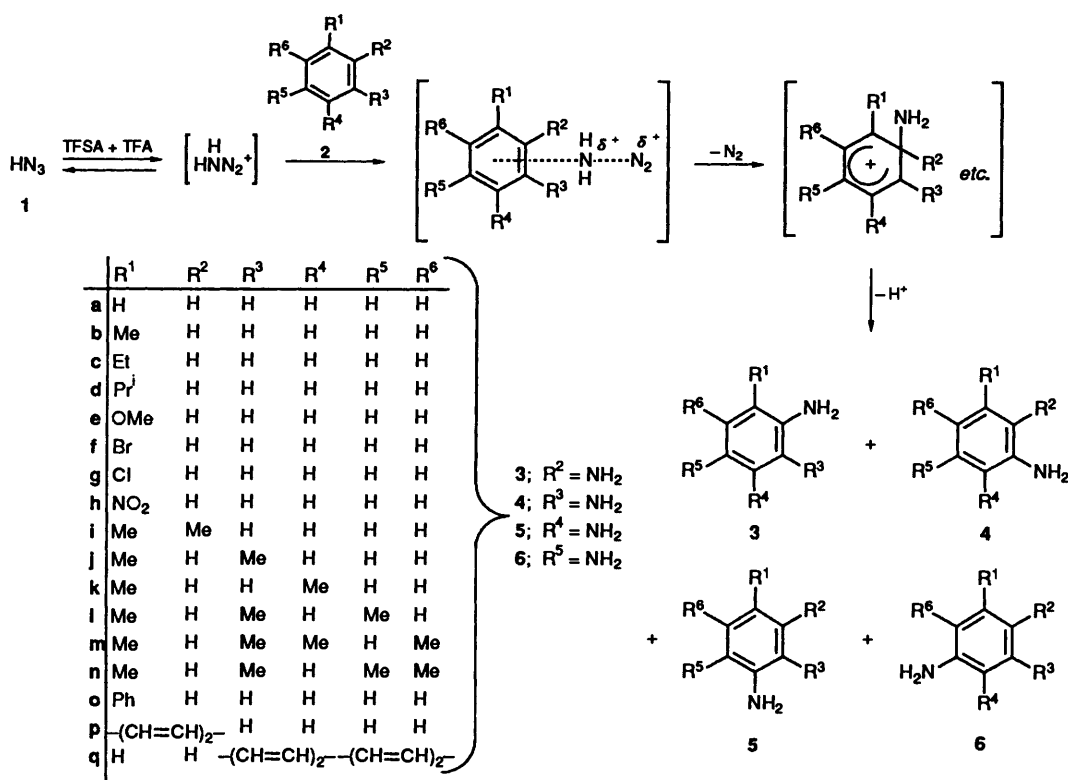
(c) *Exclusion of the Other Mechanisms.*—The high *ortho*- and *para*-direction for the amination of toluene, ethylbenzene, cumene, bromobenzene and chlorobenzene (the low *meta*-selectivity) excludes a nitrenium ion mechanism; if the free H₂N⁺ fragment⁶ formed by a spontaneous decomposition of the conjugate acid of **1** were the actual electrophile, one would expect a higher *meta*-formation (*i.e.* much lower S_f values) since a relatively high *meta*-content suggests that the attacking species are highly active.⁷ Both Schmidt⁸ and Bertho⁹ postulated the nitrene route for the amination by **1** in the presence of H₂SO₄. The route can be ruled out since the rate of denitrogenation depends upon the nucleophilic character of the arene; if the reaction proceeded *via* the nitrene, the rate should be inde-

† Preliminary report, H. Takeuchi, T. Adachi and H. Nishiguchi, *J. Chem. Soc., Chem. Commun.*, 1991, 1524.

Table 1 Reactions of hydrazoic acid **1**^a with arenes **2a–q** in the presence of acid

Arene 2	<i>T</i> /°C	<i>t</i> /h	TFSA (%) v/v	TFA (%) v/v	Yield ^b (%)			
					3	4	5	6
a ; Benzene	40	12	10	34	100			
a ; Benzene ^c	40	12	0	38	0			
b ; Toluene	25	3	10	34	57	8	35	
c ; Ethylbenzene	25	4	10	34	47	8	34	
d ; Cumene	25	5	10	34	48	9	37	
e ; Anisole	25	8	10	34	38	2	46	
f ; Bromobenzene	60	3	10	34	30	10	25	
g ; Chlorobenzene	60	3	10	34	17	3	22	
h ; Nitrobenzene ^d	60	12	10	34	0	0	0	
i ; <i>o</i> -Xylene	25	1	10	34		30		44
j ; <i>m</i> -Xylene	25	1	10	34	15		58	2
k ; <i>p</i> -Xylene	25	1	10	34	43			
l ; Mesitylene	25	1	10	34	99			
m ; Durene	50	1	13	33	37			
n ; Isodurene	25	1	10	34	73			
n ; Isodurene ^e	25	12	0	38	0			
o ; Biphenyl ^e	40	3	10	34	57		38	
p ; Naphthalene ^f	25	12	10	34		77	10	
q ; Phenanthrene ^f	40	3	10	34	43			

^a A solution containing **1** (1.7 mol dm⁻³) in CHCl₃ (3.0 cm³) was added to a mixture of TFA (5.0 cm³) and the arene (5.0 cm³). ^b The yields are based on **1** used. ^c On using TFA instead of both TFSA and TFA, **1** failed to decompose. ^d On using **2h**, denitrogenation failed to occur. ^e **2o** of 1.0 g was used. ^f 1.5 g of arene was used.

**Scheme 1**

pendent of the nucleophilic nature of arene. The reaction of aminyl radical with benzene or toluene may give a mixture of amines which are decomposed to NH₄⁺, biphenyl and arylamine (low yield) by distillation,^{10,11} and so the route *via* aminyl radical can be ruled out.

(d) *Feature of the Direct Aromatic Amination.*—This direct aromatic amination provided primary arylamines in high yields even for the reaction of readily oxidised compounds such as alkylbenzenes **2d** and **2l–n** and anisole **2e**. The high yield results from a favourable concerted process and from the non-oxidising

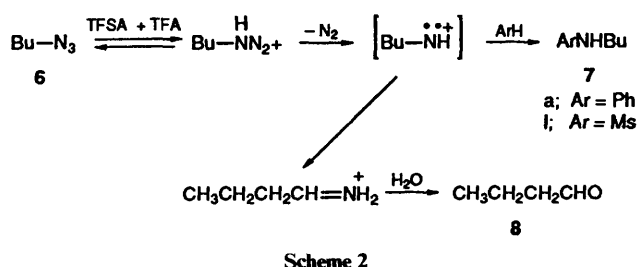
nature of TFSA and TFA. There was no contamination by diamination because the product is a salt before treatment with Na₂CO₃ and is less nucleophilic than the starting arene.

Preferential *ortho*- and *para*-direction is characteristic for this aromatic amination. The *para*:*ortho* ratio increased as the bulk of the alkyl group increased: the ratios were 0.61, 0.72 and 0.77 for the reactions of toluene, ethylbenzene and cumene, respectively. Further, the yield of 1-aminonaphthalene **4p** was higher than that of 2-aminonaphthalene **5p**. These results are similar to those for the more customary aromatic nitration.

The reaction with durene **2m** and isodurene **2n** brought about

dealkylation of the starting arenes; in fact, pentamethylbenzene was formed by reaction of the starting material with methyl cation generated by the dealkylation. The dealkylation probably decreases the yield of the aromatic amination. At the present time, we cannot explain the reason for the low yield of phenanthrene product **3q**.

Reactions of Butyl Azide with Benzene and Mesitylene in the Presence of both TFSA and TFA.—Reactions of butyl azide **6** with benzene and mesitylene gave *N*-butylaniline **7a** (5%) and *N*-butyl-2,4,6-trimethylaniline **7l** (21%) along with butanal **8** in yields of 80 and 30%, respectively. The denitrogenation of the azide **6** required the presence of acid, and was not accelerated in the presence of benzene. These facts suggest that the azide **6** decomposes *via* the conjugate acid of **6**, the latter spontaneously decomposing to give a butylnitrenium ion. Thus, the aromatic amination by the nitrenium ion yields *N*-butylanilines **7**, and aldehyde **8** was formed by hydrolysis of butyliminium ion given by a hydride migration of the alkylnitrenium ion¹² (Scheme 2). Since such a rapid migration competes with the aromatic amination, the yield of amination increased with the use of more



nucleophilic mesitylene rather than benzene, and the yield of aldehyde **8** decreased in the following order: 85% for the reaction in the absence of aromatic compound, >80% for the reaction with benzene, >30% for the reaction with mesitylene. In the reaction of *tert*-butyl azide with benzene, we expected the aromatic amination by *tert*-butylnitrenium ion which has no capacity for the above hydride migration. But, the reaction did not give *N*-*tert*-butylaniline, and acetone was detected; the latter might be formed by hydrolysis of $\text{Me}_2\text{C}=\text{N}^+\text{HMe}$ given by a fast migration of methyl anion from *tert*-butylnitrenium ion. We think that the aromatic amination by butyl azides is not successful because the rapid migration cannot be avoided.

Experimental

IR spectra were recorded using a Hitachi EPI-G3 spectrometer. NMR spectra (¹H and ¹³C) were taken with a Nippondensi JNM-FX-60Q instrument. Mass spectra were recorded with a Hitachi M-80B spectrometer. GLC analyses were performed with Shimadzu GC-6A chromatography using a glass column (2 m × 3 mm) [column A, 10% polyethylene glycol (20 M) on Chromosorb W AW DMCS (60–80 mesh), column B, 10% SE-30 on the above Chromosorb], and with a Hewlett Packard 5896 chromatograph using a J & W Fused Silica Megabore column (30 m) DB 225. Two runs within ±3% for the yields of the products which were determined by replicate GLC analyses. Preparative GLC was carried out with a Hitachi model 063-0012 unit using a column (2 m × 3 mm) packed with 10% polyethylene glycol (20 M) on the Chromosorb.

Chloroform, dichloromethane, benzene, toluene, ethylbenzene, cumene, anisole, bromobenzene, chlorobenzene, *o*-, *m*- and *p*-xylenes, biphenyl and naphthalene were purified by standard methods before use. Mesitylene, durene, isodurene and trifluoroacetic acid (TFA) were purified by distillation. The fol-

lowing compounds were reagent grade (Wako), and used without further purification: Phenanthrene, trifluoromethanesulfonic acid (TFSA), fluorosulfonic acid (FSA), aniline **3a**, *o*-, *m*-, and *p*-toluidines **3b**, **4b** and **5b**, 2-, 3- and 4-ethylanilines **3c**, **4c** and **5c**, 2- and 4-isopropylanilines **3d** and **5d**, *o*-, *m*- and *p*-anisidines **3e**, **4e** and **5e**, 2-, 3- and 4-bromoanilines **3f**, **4f** and **5f**, and 2-, 3- and 4-chloroanilines **3g**, **4g** and **5g**, 2-, 3- and 4-nitroanilines **3h**, **4h** and **5h**, 2,3- and 3,4-dimethylanilines **4i** and **6i**, 2,6-, 2,4- and 3,5-dimethylanilines **3j**, **5j** and **6j**, 2,5-dimethylaniline **3k**, 2,4,6-trimethylaniline **3l**, 2-aminobiphenyl **3o**, 1- and 2-aminonaphthalenes **4p** and **5p**, 9-aminophenanthrene **3q**, pentamethylbenzene, *N*-butylaniline **7a** and butanal **8**.

4-Aminobiphenyl **5p**,¹³ hydrazoic acid **1**¹⁴ and butyl azide **6**¹⁵ were prepared by the methods described in the literature. The preparation of *tert*-butyl azide was carried out by the reaction of *tert*-butyl chloride with sodium azide in the presence of tetrabutylammonium perchlorate in water; *tert*-butyl azide had b.p. 68–71 °C,¹⁶ and its identity was confirmed by ¹H and ¹³C NMR spectroscopic analysis.

Reactions of Hydrazoic Acid 1 with Aromatic Compounds in the Presence of TFSA and TFA.—The azide was almost completely decomposed under the conditions employed, the results for which are shown in Table 1. Extreme conditions were needed to complete the decomposition with anisole (*cf.* those for toluene or cumene) because, presumably, its strong interaction with acid prevents formation of the conjugate acid of the azide. After the reaction, TFA and volatile aromatic compounds were evaporated from the reaction mixture, and aqueous Na_2CO_3 was added until the solution reached pH > 7. The organic layer was extracted with benzene, the products being isolated by preparative GLC and identified by comparison with the IR and ¹H NMR spectra of authentic specimens. The yields of the products for the reactions of **2a** and **2l-o** were determined by GLC analysis using column A. However, the yields for the reactions of **2b-k** were determined by GLC analysis using the above-mentioned Megabore column; the *m*-isomers **4b-g** could be resolved from the *p*- or the *o*-isomers, and **4i** and **6i** also showed separate peaks as well as **3j**, **5j** and **6j**. Product **4d** was not commercially available, but its identity was confirmed by GLC mass analysis; its GLC peak has a longer retention time than that for **3d** or **5d**, and its mass spectra were as follows: *m/z* (EI method) 135 (M^+), 120, 107, 93, 77, 65, 51 and 39. The yield of **4d** was determined by the assumption that **4d** has the same GLC area-sensitivity as **3d**. The yields of 1- and 2-aminonaphthalenes **4p** and **5p**, 9-aminophenanthrene **3q** and nitroanilines were determined by GLC analysis using column B. The identities of the following compounds were confirmed from their spectroscopic data rather than by individual preparation.

2,3,5,6-Tetramethylaniline 3m. M.p. 23 °C;¹⁷ $\delta_{\text{H}}(\text{CCl}_4\text{-CDCl}_3)$ 2.0–2.6 (12 H, br, Me), 3.1–3.7 (2 H, br, NH_2) and 6.85 (1 H, s, phenyl H); $\delta_{\text{C}}(\text{CCl}_4\text{-CDCl}_3)$ 13.3, 15.8, 17.3 and 20.0 (Me) and 118.5, 120.3, 125.4, 128.9 and 140.8 (C-6, -2, -4, -3, -5 and -1); *m/z* 149 (M^+), 134, 117, 105, 91, 77, 65, 53, 39 and 27.

2,3,4,6-Tetramethylaniline 3n. M.p. 75 °C;¹⁸ $\nu_{\text{max}}(\text{Nujol})/\text{cm}^{-1}$ 3420, 3300, 1620, 1310, 1265, 1100, 1020 and 800; $\delta_{\text{H}}(\text{CCl}_4\text{-CDCl}_3)$ 2.1 (6 H, s, Me), 2.25 (6 H, s, Me), 2.05–3.05 (2 H, NH_2) and 6.55 (1 H, s, phenyl H); *m/z* 149 (M^+), 134, 117, 105, 91, 77, 65, 53, 39 and 27.

Selectivity Factors (S_f) for Toluene.—The S_f value for the reaction of **1** (1.7 mol dm^{-3} in CHCl_3 , 3.0 cm^3) with toluene (5 cm^3) in the presence of TFSA (1.5 cm^3) and TFA (5.0 cm^3) was 0.94, and the value S_f 0.95 was obtained for the reaction using fluorosulfonic acid (FSA) (0.98 cm^3) instead of TFSA. The S_f values did not vary by treatment of a mixture of *o*-, *m*- and *p*-toluidines under the reaction conditions. The S_f values were determined by GLC analysis using column A.

Reactions of Butyl Azide 6 with Benzene and Mesitylene in the Presence of Both TFSA and TFA.—The reaction of **6** (6.0 mmol) with benzene (5.0 cm³) or mesitylene (5.0 cm³) was carried out in the presence of TFSA (1.0 cm³) and TFA (5.0 cm³) at room temperature for 1 h. The decomposition of **6** at 10 °C was not accelerated in a benzene (5.0 cm³)–TFSA (1.0 cm³)–TFA (5.0 cm³) system as compared with that using CH₂Cl₂ instead of benzene; both decompositions went to completion within 15 min. The reaction with benzene gave *N*-butylaniline **7a** (5%) and butanal **8** (80%), and that with mesitylene also yielded *N*-butyl-2,4,6-trimethylaniline **7l** (21%) and **8** (30%). The reaction in the absence of aromatic compound produced aldehyde **8** in 85% yield. The yields were determined by GLC analysis using column A. The structure of **7l** was confirmed from the following spectroscopic results.

N-Butyl-2,4,6-trimethylaniline **7l**.¹⁹ Liquid: ν_{\max} (Nujol)/cm⁻¹ 3330, 1475, 1300, 1230, 1145, 1030, 850, 730, 560 and 500; δ_{H} (CDCl₃–CCl₄) 0.7–1.8 (7 H, br, MeCH₂CH₂ of butyl), 2.3 (9 H, s, Me of mesityl), 2.5–3.2 (3 H, br, NCH₂ and NH) and 6.9 (2 H, s, phenyl H); δ_{C} (CDCl₃–CCl₄) 13.9 (Me of butyl), 18.1 (2- and 6-Me of phenyl), 20.3 (MeCH₂), 20.4 (4-Me of phenyl), 33.2 (MeCH₂CH₂), 48.4 (NCH₂) and 126.7, 129.1, 130.5 and 143.5 (C-2, -3, -4 and -1 of phenyl).

The aromatic amination of benzene was carried out by using *tert*-butyl azide instead of butyl azide, but *N*-*tert*-butylaniline was not found by the GLC analysis of the reaction mixture. Acetone was detected by the GLC Mass spectroscopic analysis.

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