One-Pot Preparation of *o*-Xylylene Diamine and its Related Amines

Shun-ichi Kawahara and Tadafumi Uchimaru*

Department of Physical Chemistry, National Institute of Materials and Chemical Research, Agency of Industrial Science and Technology, MITI, Tsukuba Science City 305–8565, Japan

Reprint request to Dr. T. Uchimaru.
Fax: +81-298-61-4487.
E-mail: t_uchimaru@home.nimc.go.jp

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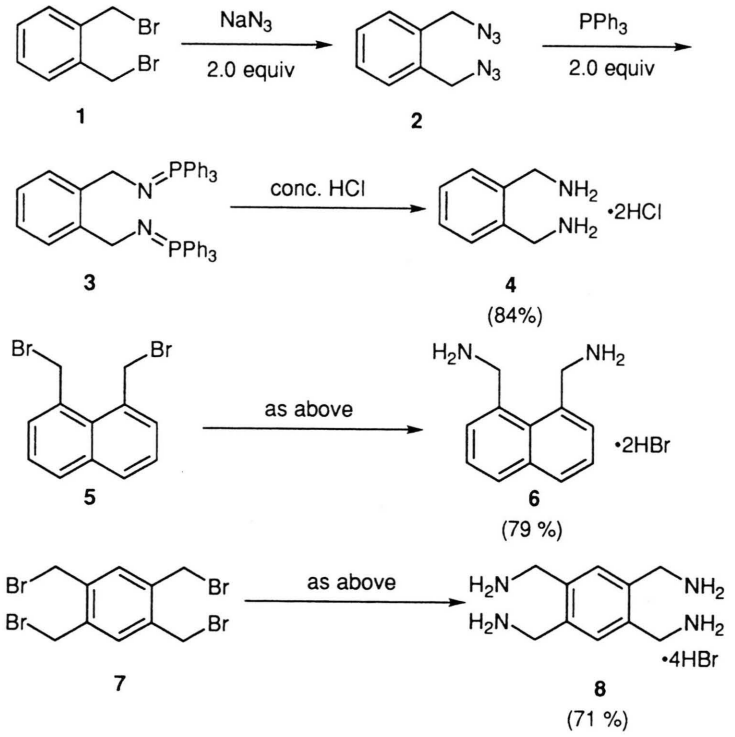
A method for one-pot preparation of *o*-xylylene diamine, 1,8-diaminomethylnaphthalene, and 1,2,4,5-tetrakis(aminomethyl)benzene has been developed. The procedure is simpler and the yield of the reaction is higher than by the conventional method.

o-Xylylene diamine is an important compound as a ligand and the starting material of ligands [1]. On the other hand, Saady *et al.* used it as two benzyl protected amino groups in characteristic nucleotide analogue synthesis [2]. The Gabriel reaction is frequently used for the preparation of *o*-xylylene diamine. While it is an effective method, the operation is complex; for example, diphthalimidate, which is an intermediate of *o*-xylylene diamine, is heated in refluxed aqueous hydrazine in a sealed tube [1, 3].

There are some other methods for preparation of *o*-xylylene diamine: hydrogenolysis [4] or electrolysis [5] of phthalazine, hydrogenolysis of phthalonitrile [6], acidic cleavage of *tert*-butoxycarbonyl derivatives [7], and alkylation of urea followed by hydrolysis [8]. However, each method described above has inherent shortcomings, in terms of yield, complex operation, generality for the preparation of similar compounds, availability of the starting materials, and so on. Not only *o*-xylylene diamine, but also in general, aromatic compounds having two or more closely located aminomethyl groups would be important and useful as a starting material of ligand. Thus, a new method for easy and efficient preparation of such aromatic amines has been highly demanded.



Scheme 1.

0932–0776/2000/1000–0985 $06.00

Here, we report a method for one-pot preparation of *o*-xylylene diamine, 1,8-diaminomethylnaphthalene, and 1,2,4,5-tetrakis(aminomethyl)benzene using the Staudinger reaction (Scheme 1) [9, 10], starting from the corresponding bromomethyl compounds. An analytically pure compound as dihydrohalide was obtained after recrystallization. Thus, this method is convenient for preparation of aromatic compounds, having closely located aminomethyl groups, on a laboratory scale.

Experimental Section

o-Xylylene diamine (**4**): *o*-Xylylene dibromide (**1**, 2.63 g, 10 mmol) was dissolved in THF-EtOH-water (40 + 30 + 10 ml). Sodium azide (1.39 g, 20 mmol) in water (20 ml) was added, then the solution was refluxed for 1 h [11]. It was not necessary to carry out the reaction in the dark on this time scale. After cooling the solution to r. t., triphenylphosphine (5.25 g, 20 mmol) was gradually added to the solution. Exothermic nitrogen evolution started instantly. After the nitrogen evolution finished, the solution was heated to reflux for 0.5 h. Then 35% aq. hydrochloric acid (20 ml) was added, then heated to reflux for 2 h. The reaction mixture was concentrated to about 20 ml in *vacuo*. The precipitate of triphenylphosphine oxide was removed by filtration. The filtrate was washed with $CHCl_3$ (20 ml) three times to remove the remaining phosphine oxide. Then, the aqueous layer was concentrated to about 5 ml *in vacuo*, with a hot-water bath (about 50–60 °C). Cooling to r. t. gave colorless needles of **4**. Recrystallization from hot water gave colorless prisms of **4** (1.89 g, 84%). Free *o*-xylylene diamine was prepared as follows: **4** (1.05 g, 5 mmol) was dissolved in aq. sodium hydoxide (5 mol/l, 5 ml). The residue was extracted with ether (5 × 10 ml). The organic layer was dried over sodium sulfate, then evaporation *in vacuo* gave a colorless oil of **4** (0.84 g, 62%). Spectral data for *o*-xylylene diamine in this procedure was in good agreement with the literature [2].

o-Xylylene diamine dihydrochloride hemihydrate (**4**·2 HCl·0.5 H_2O): M. p. 261–267 °C (dec.). – IR (KBr): ν = 3100–2000, 1935, 1641, 1585, 1495 cm^{-1}. – ^1H NMR (300 MHz, D_2O): δ = 4.35 (s, 4H, $CH_2NH_3^+$), 4.82 (s, 6H, $CH_2NH_3^+$), 7.50–7.60 (m, 4H, Ar). – ^{13}C NMR (75 MHz, D_2O): δ = 39.4 (CH_2), 130.2, 130.3 (Ar, 3, 4, 5 and 6), 131.4 (Ar, 1 and 2). – $C_8H_{15}Cl_2N_2O_{0.5}$ (218.13): calcd. C 44.05, H 6.93, N 12.84; found C 44.24, H 6.91, N 12.57.

o-Xylylene diamine (**4**, *free form*): ^1H NMR (300 MHz, $CDCl_3$): δ = 1.65 (s, 4H, CH_2NH_2), 3.91 (s, 4H, CH_2NH_2), 7.23–7.33 (m, 4H, Ar). – ^{13}C NMR (75 MHz, D_2O): δ = 44.0 (CH_2), 127.4 (Ar, 3 and 6), 128.6 (Ar, 4 and 5), 141.1 (Ar, 1 and 2). The ^1H NMR chemical shifts of NH_2 protons are highly dependent on the conditions, *i. e.*, temperature, concentration, trace amount of water in solution, and so on.

1,8-Diaminomethylnaphthalene dihydrobromide (**6**) was prepared from 1,8-dibromomethylnaphthalene (**5**) by the same procedure, except that 47% aq. hydrobromic acid was used instead of hydrochloric acid, because the resulting dihydrobromide was much easier to crystallize, compared with the corresponding dihydrochloride. Starting from 500 mg of **5** (1.6 mmol), 440 mg (79%) colorless needles of **6** were obtained.

1,8-Diaminomethylnaphthalene dihydrobromide (**6**): IR (KBr): ν = 3100–2000, 1579, 1477, 1375 cm^{-1}. – ^1H NMR (300 MHz, D_2O): δ = 4.72 (s, 4H, $CH_2NH_3^+$), 4.75 (s, 6H, $CH_2NH_3^+$), 7.56–7.65, 8.02–8.05 (m, 6H, Ar). – ^{13}C NMR (75 MHz, D_2O): δ = 43.8 (CH_2), 126.0 (Ar, 3 and 6), 127.8 (Ar, 2 and 7), 130.5 (Ar, 4 and 5), 131.9 (Ar, 1 and 8), 133.6 (Ar, 10), 135.7 (Ar, 9). – $C_{12}H_{16}Br_2N_2$ (348.08): calcd. C 41.41, H 4.63, N 8.05; found C 41.22, H 4.60, N 7.94.

1,2,4,5-Tetrakis(aminomethyl)benzene tetrahydrochloride (**8**) was prepared from 1,2,4,5-tetrakis-(bromomethyl)benzene (**7**) by the same procedure, except that i) equivalent amounts of sodium azide and triphenylphosphine (4.0 equiv) were applied, and ii) hydrobromic acid was used instead of hydrochloric acid. After acidic hydrolysis of the phosphazene, the reaction mixture was darkly colored. Thus, using the proper quantity of charcoal is recommended for decoloration. Starting from 900 mg of **7** (2.0 mmol) gave 735 mg (71%) colorless prisms of **8**. Free 1,2,4,5-tetrakis-(aminomethyl)benzene was not extracted from alkaline (pH >14) water by $CHCl_3$.

1,2,4,5-Tetrakis(aminomethyl)benzene tetrahydrobromide (**8**): IR (KBr): ν = 3100–2000, 1993, 1578, 1508, 1484 cm^{-1} – ^1H NMR (300 MHz, D_2O): δ = 4.39 (s, 8H, $CH_2NH_3^+$), 4.72 (s, 12H, $CH_2NH_3^+$), 7.68 (m, 2H). – ^{13}C NMR (75 MHz, D_2O): δ = 39.1 (CH_2), 132.0 (Ar, 3 and 6), 133.6 (Ar, 1, 2, 4 and 5). – $C_{10}H_{22}Br_4N_4$ (517.93): calcd. C 23.19, H 4.28, N 10.82; found C 23.49, H 4.35, N 11.06.

[1] R. C. Brasted, T. D. O'Brien, W. L. Heino, Inorg. Chem. **3**, 503 (1964).
[2] M. Saady, A. Valleix, L. Llbeau, C. Mioskowski, J. Org. Chem. **60**, 3685 (1995); M. Saady, L. Llbeau, C. Mioskowski, Tetrahedron Lett. **36**, 4237 (1995).
[3] H. Strassman, H. Ber. Dtsch. Chem. Ges. **21**, 576 (1888); S. Gabriel, G. Pinkus, H. Ber. Dtsch. Chem. Ges. **26**, 2210 (1893); H. Ing, H. Manske, J. Chem. Soc. 203 (1952); H. R. Rodriguez, B. Zitko, G. De Stevens, J. Org. Chem. **33**, 670 (1968).
[4] G. Lunn, J. Org. Chem. **52**, 1043 (1987).
[5] P. Knowles, K. R. H. Wooldridge, J. Chem. Soc. Perkin Trans. 1 975 (1972).
[6] H. Lund, E. T. Jensen, Acta. Chem. Scand. **24**, 1867 (1970).
[7] L. A. Carpino, J. Org. Chem. **29**, 2820 (1964).
[8] C. Dauth, H. G. O. Becker, J. Prakt. Chem. **313**, 686 (1971).
[9] Y. G. Gololobov, I. N. Zhmurova, L. F. Kasukhin, Tetrahedron **37**, 437 (1981); L. Horner, A. Gross, Liebigs Ann. Chem. **591**, 117 (1955); A. Deeb, H. Sterk, T. Kappe, Liebigs Ann. Chem. 1225 (1991).
[10] Catalytic hydrogenolysis of azides is an alternative method for preparation of the amines: J. H. Boyer, F. C. Canter, Chem. Rev. **54**, 1 (1954).
[11] *o*-Xylylene diazide (**2**) can be isolated, but it is better to treat the reaction mixture with phosphine without isolation and purification of *o*-xylylene diazide, considering the stability of azide compounds. *o*-Xylylene diazide (**2**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.23 (s, 4H, CH_2N_3), 7.25–7.35 (m, 4H, Ar). – ^{13} CNMR (75 MHz, $CDCl_3$): δ = 52.2 (CH_2N_3), 129.1, 130.2 (Ar, 3, 4, 5 and 6) 133.9 (Ar, 1 and 2).