Synthetic Application of Aminosilanes: Selective Bromination of Anilines via Reaction of Anilinosilanes with *N*-Bromosuccinimide

Wataru ANDO*, Hidetoshi TSUMAKI

Department of Chemistry, University of Tsukuba, Sakura-mura, Niihari-gun, Ibaraki, 305, Japan

Although electrophilic substitution of aromatic amines by bromine is a well-known reaction, no reliable and mild method exists for the selective monobromination of reactive aromatic amines[1]. The effects of mild brominating agents such as dioxan perbromide[2], alkyl bromides in dimethyl sulfoxide[3], or 2,4,4,6-tetrabromocyclohexa-2,5-dienone[4] cannot be generalized for all aromatic amines. Recently, it has been reported that indirect bromination of aniline can be achieved by reaction of the aniline hydrobromide salt with dimethyl sulfoxide to afford *p*- and *o*-bromoaniline in a 12:1 ratio[5]. *N*-bromosuccinimide-dimethylformamide (NBS-DMF) has also been reported to be a mild and selective nuclear monobromination reagent for reactive aromatic compounds[6].

In this paper we report a selective monobromination of aromatic amines via reaction of the anilinosilanes (**1**) with *N*-bromosuccinimide. Various anilinosilanes (**1**) were found to react readily with *N*-bromosuccinimide in carbon tetrachloride to afford bromoanilinosilane derivatives (**2**); subsequent addition of methanol yielded bromoanilines (**3**) in good yield without products of further bromination being obtained.

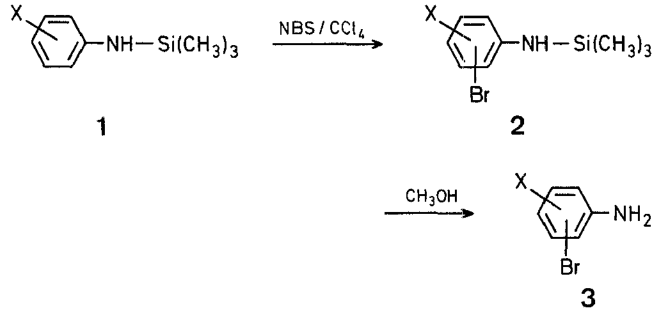
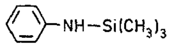
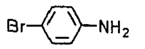
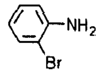
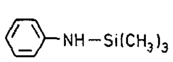
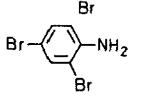
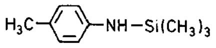
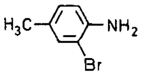
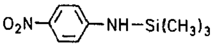
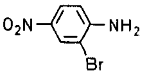
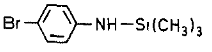
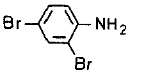
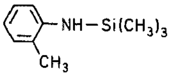
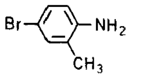
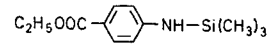
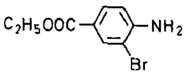
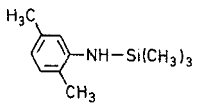
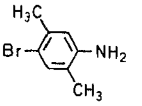


Table. Selective Bromination of Anilines via Reaction of the *N*-Trimethylsilyl Derivatives (**1**) with *N*-Bromosuccinimide

Anilinosilanes **1**		Reaction conditions	Products **3**	Yield[a,b] [%]	m.p. or b.p./torr [°C]	Lit. m.p. or b.p./torr [°C]
a		−20°, 24 h (1.0 equiv NBS)		92	m.p. 66°	m.p. 66.5°[7]
(a′)			+ 	5	b.p. 126°/29	b.p. 229°/760[7]
(a″)		−15°, 15 h (2.0 equiv NBS)		93	m.p. 80.5°	m.p. 80.5°[7]
b		r.t., 24 h		77	b.p. 133°/26	b.p. 240°/760[7]
c		80°, 3 h		67	m.p. 104°	m.p. 104.5°[7]
d		r.t., 24 h		84	m.p. 80°	m.p. 80.5°[7]
e		r.t., 12 h		91	m.p. 55°	m.p. 56°[7]
f		80°, 5 h		74	m.p. 91.5°	m.p. 91°[8]
g		r.t., 12 h		95	m.p. 255°[c] (dec)	m.p. 255° (dec)[9]

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[a] Yield of isolated product of ≥99% purity as determined by T.L.C., I.R., and ^{1}H-N.M.R. spectrometry.

[b] All bromoanilines **3a-g** are known compounds and gave correct physical and spectral (I.R., N.M.R.) characteristics.

[c] m.p. (dec) of hydrobromide salt.

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When anilinotrimethylsilane (**1a**) was reacted with 1.0 equiv of *N*-bromosuccinimide (see Table) 4-bromoaniline (**3a**) was produced regioselectively in 92% yield along with only 5% isomeric 2-bromoaniline (**3a'**). Similar treatment of **1a** with 2.0 equiv of *N*-bromosuccinimide resulted in the formation of 2,4-dibromoaniline (**3a''**) in 93% yield. Treatment of 4-methylanilinotrimethylsilane (**1b**) with 1.0 equiv of *N*-bromosuccinimide gave 2-bromo-4-methylaniline (**3b**) in 77% yield; no benzyl bromide derivatives being obtained. In view of the importance of methoxylated natural products, we tried to apply the method to the synthesis of bromomethoxylated anilines. However, attempts to react 4-methoxyanilinotrimethylsilane with *N*-bromosuccinimide under various conditions were unsuccessful.

Although it is assumed that *N*-bromosuccinimide constantly produces traces of bromine in the reaction system, the direct treatment of anilinosilanes with bromine as a control experiment gave poor results. Probably, nucleophilic attack of bromine on a silicon atom cleaves the Si—N bond to afford a bromosilane and a highly reactive *N*-bromoaniline prior to generation of the intermediate *N*-bromoanilinosilane.

Major advantages of the present modification are the facts that the amount of *N*-bromosuccinimide used strictly determines the degree of bromination of the anilines and that, in contrast to the requirement of acid or alkali in the deacetylation of acetanilide, desilylation can be carried out by a very simple procedure under mild and neutral conditions. Since anilinosilanes can be prepared quantitatively from anilines and chlorotrimethylsilane[10] this approach provides a simple and highly selective bromination of anilines in two steps.

2,4-Dibromoaniline (3d) from 4-Bromoanilinotrimethylsilane (1d); Typical Procedure:

To a stirred suspension of *N*-bromosuccinimide (1.86 g, 10.45 mmol) in dry tetrachloromethane (20 ml) under nitrogen, 4-bromoanilinotrimethylsilane (**1d**; 2.55 g, 10.45 mmol) is added by syringe. Stirring is continued for 24 h at room temperature in the dark. G.L.C. analysis (1 m × 5 mm stainless-steel column, 1% Silicon SF-96 on Celite 545, 178 °C) then shows the formation of 2,4-dibromoanilinotrimethylsilane[a] (**2d**) as a major product. Succinimide is removed by suction filtration, methanol (10 ml) is added to the filtrate, the solution is evaporated after 1 minute in vacuo, and the black-red residual product is column-chromatographed on silica gel using benzene as eluent to give 2,4-dibromoaniline (**3d**); yield: 2.2 g (84%); m.p. 80 °C [m.p. as well as I.R.- and ^{1}H-N.M.R.-spectral characteristics of **3d** thus obtained were in agreement with those of an authentic sample].

[a] ^{1}H-N.M.R. (CCl_4/TMS): $\delta = 0.31$ [s, 9 H, Si(C$\underline{H}_3$)$_3$]; 4.01 (br s, 1 H, N$\underline{H}$); 6.46–7.73 ppm (m, 3 H$_{arom}$).

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[*] Address for correspondence.

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