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Synthesis of Aminomethyl Arylsulfides *via* Novel Synthetic Auxiliary Benzotriazole Promoted by Samarium Diiodide

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Abstract: Aminomethyl arylsulfides are synthesized through nucleophilic substitution of a benzotriazolate anion by thiolates promoted by samarium diiodide.

Keywords: Aminomethyl arylsulfides, benzotriazole, samarium diiodide, disulfides.

Benzotriazole methodology has already come a long way, but in the last decade benzotriazole is an excellent synthetic auxiliary in many useful synthetic transformations[1-5]. Because benzotriazolate anion is a good leaving group, it may be used in place of a halogen in many reactions. The use of benzotriazole as a synthetic auxiliary has a number of significant advantages. For example, it is readily available and quite cheap; it is acidic with a pKa of about 8, which enables easy separation and recovery. Many types of compounds have been synthesized *via* benzotriazole auxiliary[5].

Samarium diiodide has been extensively applied to organic synthesis[6-9]. It has recently been found that thiolates ($RSSmI_2$) obtained from reductive cleavage of diorganyl disulfides with samarium diiodide are nucleophilic reagents, and some interesting reactions have taken place with them[10-11].

Although α-amino sulfides (N, S-acetals) in five or six membered rings are very common in hetereocyclic chemistry and are easily available[12], open chain hemithioaminals are relatively little explored. Aminomethyl phenyl sulfides are useful percursors in the preparation of (aminomethyl)-trialkyl-stannanes[13-14]. Some methods have been reported for preparation of hemithioaminals, for example, condensation of thiophenols with secondary amines and formaldehyde[15], reactions of N-[1-(benzotriazol-1-yl)alkyl]amine with sodium salts of thiols[16], *etc*. However, these methods suffered from using metallic sodium, alkaline medium and thiophenols. Here we wish to report that aminomethyl arylsulfides are synthesized through nucleophilic substitution of a benzotriazolate anion by thiolate promoted by SmI_2.

Scheme 1

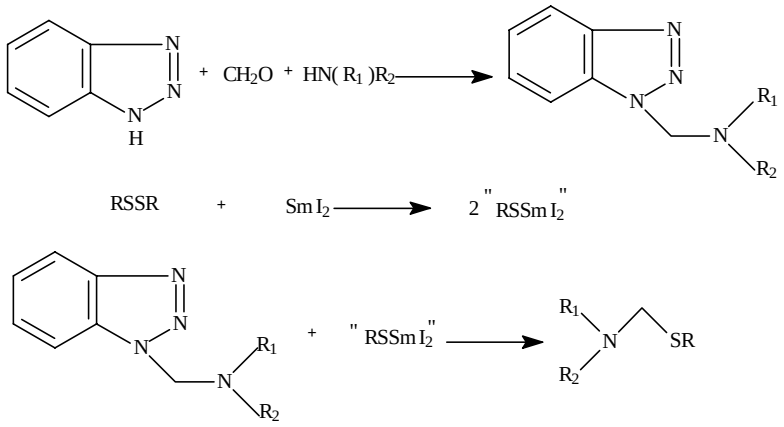

Table 1 Synthesis of aminomethyl sulfides.

Entry	R_1	R_2	R	Reaction times(h)	Yield*(%)
1	Ph	H	p-$CH_3C_6H_4$	12	82
2	Ph	H	p-ClC_6H_4	12	79
3	Ph	H	Ph	12	80
4	m-ClC_6H_4	H	Ph	14	75
5	o-$CH_3C_6H_4$	H	p-ClC_6H_4	12	78
6	o-$CH_3C_6H_4$	H	Ph	12	84
7	p-$CH_3C_6H_4$	H	p-ClC_6H_4	12	82
8	m-BrC_6H_4	H	p-$CH_3C_6H_4$	14	70
9	Ph	CH_3	Ph	12	80

*Yield of isolated product

The reactions were conducted at room temperaures. 1-(α-Aminoalkyl)-benzotriazoles are very easy to be prepared[17]. In view of the easily available starting material, good yield, mild and neutral reaction conditions as well as the simple operation, we think that the present procedure provides a useful method for synthesis of aminomethyl arylsulfides.

Experimental

Melting points were uncorrected. HMPA was dried by CaH_2 and was then distilled *in vacuo*. Tetrahydrofuran was distilled from sodium/benzophenone ketyl immediately before use. IR spectra were recorded on a PE-683 spectrometer. Mass spectra were recorded on a HP5989B spectrometer. ^{1}H NMR spectra were obtained with a JEOL PMX 60si spectrometer in CCl_4 solution using TMS as internal standard. The reactions were performed in a Schlenk type glass apparatus under a nitrogen atmosphere.

General Procedure

To a solution of SmI_2 (2.2mmol, in 22mL THF), 0.5mL HMPA and 1mmol disulfide are added. After stirring for 1 hr at 40°C, 2mmol of 1-(α-aminoalkyl)-benzotriazoles is added. After stirring for the given hours at room temperatures (see **Table 1**), the reaction mixture is treated with dilute hydrochloric acid (0.1M, 5mL) and extracted twice with ether. The combined organic layers are washed with saturated sodium thiosulfate solution (20 mL) and brine (20 mL). After the solution is dried over anhydrous $MgSO_4$, the solvents are removed under reduced pressure. The residue is purified by preparative TLC (silica gel) with cyclohexane and ethyl acetate (3:1) as eluent.

PhNHCH$_2$SC$_6$H$_4$CH$_3$-*p*: m.p. 38°C; ^{1}H NMR: 7.2-6.4 (9H, m), 4.40 (2H, s), 3.75 (1H, s, NH), 2.20 (3H, s). IR: 3440 cm^{-1}. m/z: 229.

PhNHCH$_2$SPhCl-*p*: m.p. 51°C; ^{1}H NMR: 7.4-6.3 (9H, m), 4.40 (2H, s), 3.93 (1H, s, NH). IR: 3440 cm^{-1}. m/z: 249.

PhNHCH$_2$SPh: oil; ^{1}H NMR: 7.2-6.4 (10H, m), 4.50 (2H, s), 3.90 (1H, s, NH). IR: 3450 cm^{-1}. m/z: 215.

***m*-ClPhNHCH$_2$SPh**: oil; ^{1}H NMR: 7.2-6.4 (9H, m), 4.50 (2H, s), 3.92 (1H, s, NH). IR: 3440 cm^{-1}. m/z: 249.

o*-CH$_3$C$_6$H$_4$NHCH$_2$SC$_6$H$_4$Cl-*p: m.p. 68°C; ^{1}H NMR: 7.2-6.4 (8H, m), 4.45 (2H, s), 3.83 (1H, s, NH), 1.93 (3H, s). IR: 3435 cm^{-1}. m/z: 263.

***o*-CH$_3$PhNHCH$_2$SPh**:oil; ^{1}H NMR: 7.1-6.3 (9H, m), 4.50 (2H, s), 3.70 (1H, s, NH), 1.90 (3H, s). IR: 3460 cm^{-1}. m/z: 229.

p*-CH$_3$PhNHCH$_2$SPhCl-*p: m.p. 65°C; ^{1}H NMR: 7.2-6.4 (8H, m), 4.40 (2H, s), 3.75 (1H, s, NH), 1.85 (3H, s). IR: 3440 cm^{-1}. m/z: 263.

m*-BrPhNHCH$_2$SPhCH$_3$-*p: oil; ^{1}H NMR: 7.2-6.4 (8H, m), 4.40 (2H, s), 3.95 (1H, s, NH), 2.18 (3H, s). IR: 3440 cm^{-1}. m/z: 307.

Ph(CH$_3$)NCH$_2$SPh: m.p. 36-38°C (Lit.[18] 36.4-38°C); ^{1}H NMR: 7.2-6.4 (10H, m), 4.80 (2H, s), 2.76 (3H, s).

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