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$SnCl_4$ and $SbCl_5$ promoted aromatization of enamines

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Abstract—Aromatic amines have been synthesized efficiently from enamines using $SnCl_4$ and $SbCl_5$ in CH_2Cl_2 at room temperature.

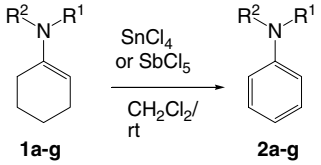
1. Introduction

Aromatic amines are an important family of intermediates in organic synthesis. They also play a central role in applied chemistry.[1] Numerous methods for the synthesis of amino-aromatic compounds have been reported. These include electrophilic aromatic nitration followed by reduction,[2] nucleophilic aromatic substitution,[3] direct amination,[4] reduction of aromatic imines,[5] electro reductive aromatization of imines and diimines,[6] transition metal catalyzed synthesis of aryl amines from aryl halides and triflates,[7] Diels–Alder reactions[8] and the reaction of cyclohexanone enolates with nitro arenes.[9] Recently, Bräse and Meijere reported a novel reaction for the synthesis of aromatic amines from enamines upon treatment with $Pd(OAc)_2$ in the presence of iodobenzene, Et_3N and Ph_3P in DMF.[10] This reaction is further reported in the literature using various other catalysts such as $TiCl_4/Et_3N$,[11] Pd(II) complexes[12] and Pd/C in the presence of 4 Å molecular sieves.[13] Many of the synthetic protocols for aromatic amines reported so far suffer from one or more disadvantages such as harsh reaction conditions, poor yields, prolonged reaction times and the use of hazardous and often expensive acid catalysts. These processes also generate waste-containing catalysts and solvents, which have to be recovered, treated and disposed.

Stannic chloride, tin tetrachloride and antimony pentachloride are used extensively in organic synthesis as Lewis acids enhancing a variety of organic reactions. For example, $SnCl_4$ is used to promote electrophilic aromatic substitutions such as Friedel–Crafts alkylation,[14a] nucleophilic additions such as Evans aldol[14b] reactions, the Mukaiyama–Michael[14c] reaction, pericyclic reactions such as the Diels–Alder[14d] and ene reactions.[14e] $SnCl_4$ is classified as a hard Lewis acid according to hard and soft acids and bases (HSAB) theory and therefore interacts preferentially with hard oxygen (*O*-donor) and nitrogen bases (*N*-donor). Since it is known that $SnCl_4$ (an inorganic acceptor) forms s-type[15] or p-type[16] electron donor–acceptor (EDA) complexes with aryl donors (naphthol, etc.), charge transfer (CT) interactions might play a role in these electron-transfer reactions. Many studies on thermal and photochemical reactions via EDA complexes have been reported.[17] $SbCl_5$ is also used to promote electrophilic aromatic substitutions including Friedel–Crafts alkylation,[11] electrophilic additions to alkenes and 1,3-dienes.[14b]

Pursuing the course of our studies on imine, oxime and enamine reactions,[18] herein we report an efficient procedure for the synthesis of aromatic amines from enamines in the presence of $SnCl_4$ and $SbCl_5$ (Scheme 1).

We synthesized morpholine, piperazine and pyrrolidine enamines in the presence of catalytic amounts of *p*-toluenesulfonic acid in toluene. Diethylamine enamines were



Scheme 1.

Keywords: Aromatization; Enamines; $SnCl_4$; $SbCl_5$.
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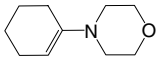
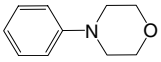
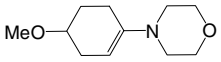
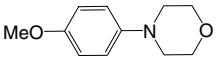
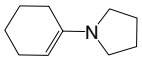
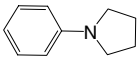
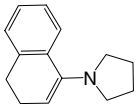
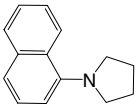
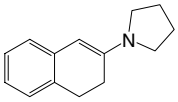
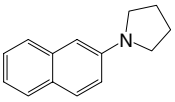
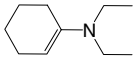
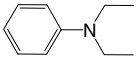
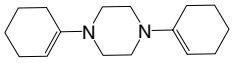
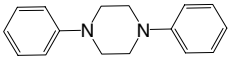
Table 1. Synthesis of aromatic amines from enamines in the presence of $SnCl_4$ or $SbCl_5$ Lewis acids in CH_2Cl_2 at room temperature

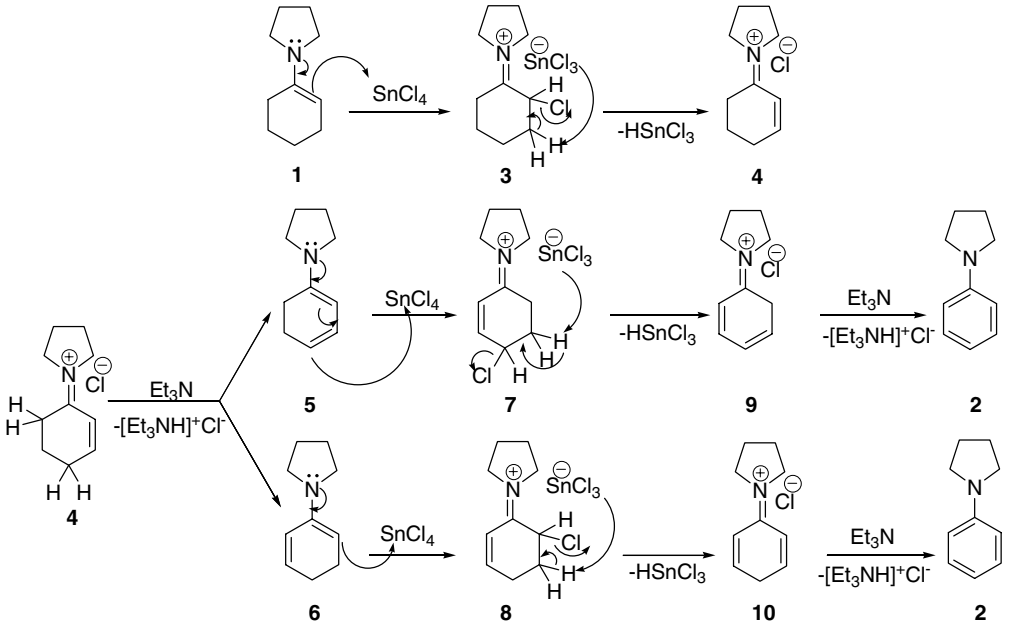
Entry	Substrate **1**	Product **2**	Yield % ($SnCl_4$)	Yield % ($SbCl_5$)
a			85	70
b			83	66
c			87	69
d			76	65
e			84	71
f			79	67
g			82	72

prepared in anhydrous diethyl ether in the presence of 4 Å molecular sieves.[19]

Our successful results on the $SnCl_4$ and $SbCl_5$ promoted synthesis of aromatic amines are given in Table 1. In a typical experimental procedure, a mixture of enamine (1 mmol) and $SnCl_4$ or $SbCl_5$ (2 mmol) was stirred for 12 h in anhydrous CH_2Cl_2 at room temperature. After completion of the reaction and evaporation of the solvent, pure products were obtained by distillation under vacuum or by column chromatography. The reactions proceeded smoothly and efficiently in all cases.

In attempts to optimize the reactions, we found that an excess molar ratio of Lewis acid (2 equiv for morpholine and pyrrolidine enamines and 4 equiv for piperazine enamines) and the use of anhydrous solvents and reagents were required. The reaction of enamines in the absence of $SnCl_4$ and $SbCl_5$ did not occur even after 24 h.

A possible mechanism for the formation of the aromatic amines is shown in (Scheme 2). $SnCl_4$ is expected to form complex **3** with the enamine. Elimination of $HSnCl_3$ results in formation of the iminium salt **4**.



Scheme 2.

Further elimination of HCl from **4** by Et_3N leads to the formation of isomeric enamines **5** and **6**. Either of the two isomers can aromatize to **2** following the same mechanistic path by which enamine **5** was formed.

All the products (except **2g**)[20] are known compounds, and were characterized by comparison of their melting points, IR and ^1H NMR spectral data with those reported in the literature.

In conclusion, we have developed an efficient synthesis of aromatic amines via aromatization of cyclic enamines using $SnCl_4$ or $SbCl_5$.

2. General procedure for the preparation of aromatic amines

Dichloromethane (20 mL), enamine (5 mmol) and Et_3N (17 mmol) were kept under N_2. $SnCl_4$ or $SbCl_5$ (12 mmol of a 1:1 solution of $SnCl_4$ or $SbCl_5/CH_2Cl_2$) in dichloromethane (10 mL) was added dropwise at 0 °C over 15 min. The reaction mixture was stirred for 0.5 h at 0 °C and then stirred further for 12 h at 25 °C. The reaction was quenched with saturated K_2CO_3 solution (15 mL), the organic layer separated and the aqueous layer extracted with dichloromethane (2×25 mL). The combined organics were dried over anhydrous K_2CO_3. The solvent was removed and the residue was chromatographed on a silica gel column using EtOAc/hexane (1:9) mixture as eluent.

Acknowledgement

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Heravi, M. M. *Ind. J. Heterocycl. Chem.* **2001**, *11*, 175–176; (e) Bigdeli, M. A.; Nikje, M. M. A.; Heravi, M. M. *Phosphorus Sulfur Silicon Relat. Elem.* **2002**, *177*, 15–18.

19. Westheimer, F. H.; Taguchi, K. *J. Org. Chem.* **1971**, *36*, 1570–1572.
20. Spectral data for **2g**: (isolated yield 82%, mp 162–164 °C) white crystals. IR (KBr, cm^{-1}): 2950, 3100, 3250. ^1H NMR ($CDCl_3$, 250 MHz): δ 3.35 (8H, s, $4CH_2$), 6.89 (4H, t, $^3J = 7.5$ Hz, 4CH), 6.98 (4H, d, $^3J = 7.5$ Hz, 4 CH), 7.30 (2H, d, $^3J = 7.5$ Hz, 2CH). ^{13}C NMR ($CDCl_3$, 62.9 MHz): 49.5, 116.4, 120.1, 129.2, 151.3. MS (*m*/*z*, 70 eV): 238 (M^+, 90), 132 (60), 105 (100), 77 (75), 51 (35). Calcd for $C_{16}H_{18}N_2$: C, 80.67; H, 7.56; N, 11.77. Found: C, 80.64; H, 7.66; N, 11.62.