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Novel applications of 2-cyanoethylanilines in the synthesis of conjugated primary and secondary anilines

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Abstract—2-Cyanoethyl anilines were controllably cleaved by 1 equiv of potassium *t*-butoxide in dry THF with a reaction that can be used in situ with the Wittig reaction to synthesize conjugated primary and secondary anilines.

Conjugated aromatic amines are of great interest because of their potential applications as nonlinear optical materials,[1] as hole transporting materials for electrophotography, and as electroluminescent materials.[2] Preparation of conjugated tertiary anilines is straightforward and well documented.[3] Commonly, conjugated systems consist of aromatic rings and carbon–carbon double bonds. Such structures are generally synthesized by either a Wittig (or Wittig–Horner) reaction or Heck reaction. The alkene reactant in the Heck reaction is also usually prepared by a Wittig reaction. Primary and secondary anilines are important materials. They are also intermediate materials as precursors for complicated tertiary anilines. However, preparation of primary and secondary conjugated anilines is not straightforward. Direct use of primary and secondary anilines in a Wittig reaction is impossible because of the side reaction with aldehyde. So they must be protected before the reaction. In fact, synthesizing and protecting amino-aryl-aldehyde is also difficult. For example, although 4-aminobenzaldehyde can be synthesized in its monomer form, it polymerizes quickly in organic solvents.[4] Thus, protected amino-aryl-phosphonium salts or phosphates have to be used as one of the reactants in a Wittig reaction. Such compounds are usually not commercially available and require multi-step reactions to prepare.

We discovered that when 2-cyanoethyl anilines were treated with 1 equiv of potassium *t*-butoxide in dry THF at room temperature, the 2-cyanoethyl group was cleaved nearly quantitatively. To our surprise, this reaction, though very efficient, does not significantly interfere with Wittig (or Wittig–Horner) reaction. Thus, when primary or secondary conjugated anilines are synthesized by a Wittig reaction, the 2-cyanoethyl group can be either kept on the product for future cleavage or cleaved in situ. The 2-cyanoethyl group has been used to protect carboxylic acid[5] and thiouridine,[6] but it has never been reported as a protecting group of aromatic amines. Plakidin et al. observed the cleavage of a 2-cyanoethyl aniline by diethyl amine at 130 °C.[7] Babayan et al. reported thermal and alkaline cleavage of quaternary ammonium salts containing the 2-cyanoethyl group.[8] They prepared MeNHR [R = allyl, benzyl, $CH_2CHCClCH_3$, $CH_2CHC(CH_3)_2$] by reacting KOH with the corresponding $RNMeCH_2CH_2CN$ at 140–250 °C. Our method of using potassium *t*-butoxide in dry THF is more efficient and very convenient for synthesizing conjugated primary and secondary anilines. 2-Cyanoethyl aniline can be prepared easily by reacting the corresponding aniline with acrylonitrile.[9] However, a more practical way is using commercially available 2-cyanoethyl anilines. More than 1000 commercially available compounds can be found in the Scifinder database.

As a demonstration of this reaction, a solution of 4-[(2-cyanoethyl)methylamino]benzaldehyde and diethyl (2-thienylmethyl)phosphonate in THF was treated with 1 equiv of 1 N potassium *t*-butoxide solution in THF, **1** formed (76% yield) together with a small amount of **2** (12% yield). When 2 equiv of potassium *t*-butoxide were

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Keywords: Cleavage; 2-Cyanoethyl aniline; Primary anilines; Secondary anilines.

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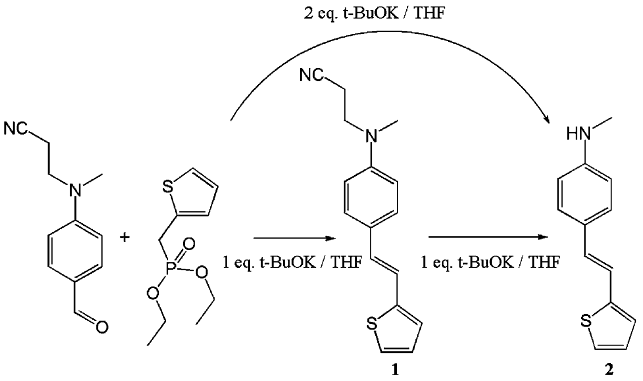
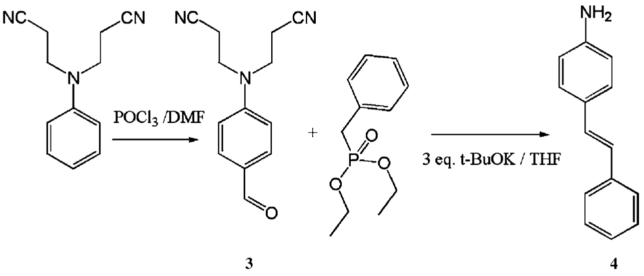


Scheme 1.



Scheme 2.

used, **1** was cleaved in situ and only **2** formed in 85% yield. **2** can also be synthesized by treating **1** with 1 equiv of potassium *t*-butoxide (Scheme 1).

When bis-2-cyanoethyl aniline is used, primary conjugated anilines can be synthesized. Primary conjugated anilines can be synthesized by reducing the corresponding nitro compounds. For example, 4-aminostilbene was prepared by reducing 4-nitrostilbene.[10] Our method provides an alternative route. To demonstrate this, 4-[di-2-cyanoethyl-amino]benzaldehyde **3** was synthesized from commercially available *N*,*N*-bis(cyanoethyl)aniline by a Vilsmeier formylation. A mixture of **3**and diethyl benzylphosphonate in THF was treated with 3 equiv of 1 N potassium *t*-butoxide solution in THF to give 4-aminostilbene in 62% separated yield (Scheme 2).

The procedures of preparing **2** and **4**, and the characterizations of compounds **1**–**4** are attached in Ref. 11.

In conclusion, we reported an efficient method to cleave 2-cyanoethyl aniline. This method makes the 2-cyanoethyl group a potential protecting group for amines. More importantly, it can be used in situ with the Wittig reaction to synthesize secondary and primary conjugated anilines.

Acknowledgements

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11. Synthetic procedure of **2**: To a mixture of 1.88 g (10 mmol) of 4-[(2-cyanoethyl)methylamino]benzaldehyde and 2.53 g (11.5 mmol) of diethyl (2-thienylmethyl)phosphonate in 20 mL of dry THF was added 23 mL of 1 N potassium *t*-butoxide solution in THF at 0 °C. The mixture was stirred at room temperature for 24 h. The reaction was quenched and washed by 20 mL of water. The aqueous layer was extracted by 20 mL of CH_2Cl_2 twice. The organic layers were combined and concentrated under reduced pressure. The residue was purified by chromatograph on silica using 1:4 ethylacetate/hexane as the eluant to give 1.83 g of **2** (85% yield). Procedure of **4**: To a mixture of 0.684 g (3 mmol) of **3** and 1.37 g (6 mmol) of diethyl benzylphosphonate in 5 mL of dry THF was added 10 mL of 1 N potassium *t*-butoxide solution in THF at 0 °C. The mixture was stirred at room temperature for 24 h. The reaction was quenched and washed by 20 mL of water. The aqueous layer was extracted by 20 mL of CH_2Cl_2 twice. The organic layers were combined and concentrated under reduced pressure. The residue was purified by chromatograph on alumina using 7:3 CH_2Cl_2/hexane as the eluant to give 0.36 g of **4** (62% yield).
1, ^{1}H NMR, δ (ppm, $CDCl_3$): 7.39 (2H, d, $J = 8.9$ Hz), 7.15–6.95 (4H, m), 6.84 (1H, d, $J = 16.1$ Hz), 6.73 (2H, d, $J = 8.9$ Hz), 3.73 (2H, t, $J = 6.9$ Hz), 3.07 (3H, s), 2.61 (2H, t, $J = 6.9$ Hz); MS (Electron Spray): 269.1 (M+H$^+$). **2**, ^{1}H NMR, δ (ppm, $CDCl_3$): 7.32 (2H, d, $J = 8.6$ Hz), 7.13–6.94 (4H, m), 6.84 (1H, d, 16.1 Hz), 6.62 (2H, d, $J = 8.6$ Hz), 4.52 (1H, b, NH), 2.87 (3H, s); MS (Electron Spray): 216.1 (M+H$^+$). **3**, ^{1}H NMR, δ (ppm, $CDCl_3$): 9.81 (1H, s), 7.81

(2H, d, $J = 9.0$ Hz), 6.73 (2H, d, $J = 9.0$ Hz), 3.90 (4H, t, $J = 6.5$ Hz), 2.71 (4H, t, $J = 6.5$ Hz); MS (Electron Spray): 228.1 ($M+H^+$). **4**, ^1H NMR, δ (ppm, $CDCl_3$): 7.46 (2H, d, $J = 7.0$ Hz), 7.34–7.18 (5H, m), 7.02 (1H, d, $J = 15.0$ Hz), 6.90 (1H, d, $J = 15.0$ Hz), 6.66 (2H, d, $J = 8.4$ Hz), 3.73 (b, 2H, NH_2). MS (Electron Spray): 196.1 ($M+H^+$).