Supplementary Material

Smiles rearrangement for the synthesis of diarylamines

Xiao Tian,a Ren-Min Wu,a Gang Liu,a Zhu-Bo Li,a He-Lin Wei,a Hao Yang,b Dong-Soo Shin,c Li-Ying Wang,a Hua Zuo*a,*

aCollege of Pharmaceutical Sciences, Southwest University, Chongqing, 400715, China
bCollege of Horticulture and Landscape Architecture, Southwest University, Chongqing, 400715, China
cDepartment of Chemistry, Changwon National University, Changwon, 641-773, South Korea
E-mail: zuohua@swu.edu.cn

Table of Contents

1. General remarks S1
2. General procedure of Ligand-free Smiles Rearrangement for the Synthesis of Diarylamines 3 S2
3. Synthesis and analytical data of 3a-u S2
4. References S9
5. Copies of NMR and MS spectra for compounds S10

1. General remarks

1H NMR and 13C NMR spectra were recorded in CDCl3 (300 MHz for 1H NMR and 75 MHz for 13C NMR, respectively) with tetramethylsilane as the internal reference on Bruker Advance 300 FT spectrometer. Chemical shifts were reported in parts per million. Mass spectra (MS) were measured by ESI. CDCl3 were used as delivered from Sigma-Aldrich. Silica gel (70-230 mesh) was used for flash column chromatography. All the reactions were monitored by TLC using 0.25 mm silica gel plates (Merck 60F254) with UV indicator. The microwave-assisted reaction time is the hold time at the final temperature. Unless otherwise noted, other reagents were obtained from commercial suppliers and used without further purification.
2. General Procedure for the Smiles Rearrangement for the Synthesis of Diarylamines (3)

To a magnetically stirred solution of the appropriate aryl amine 2 (1.0 mmol) and Cs₂CO₃ (3.2 mmol) in dry DMF cooled by ice bath were added chloroacetyl chloride (1.2 mmol) and substituted phenol 1 (1.0 mmol). The reaction mixture was then stirred for 30 min at room temperature and placed into microwave oven (600W, 150 °C) and irradiated for 30-80 min. The solvent was removed under vacuum and water (20 mL) was added into the residue. The mixture was then extracted by ethyl acetate (4 x 30 mL). The combined organic layers were dried over anhydrous MgSO₄ and evaporated under vacuum to give the crude product. Pure product was obtained by column chromatography on silica gel.

3. Synthesis and analytical data of (3a-u)

Scheme S1. N-(4-Methoxyphenyl)-3-methylbenzenamine 3a.¹

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a gray solid. Mp 72-75 °C (lit.¹ 75-76 °C). ¹H NMR (300 MHz, CDCl₃): δ 2.28 (s, 3H; CH₃), 3.80 (s, 3H; OCH₃), 5.45 (s, br, 1H; NH), 6.64-7.24 (m, 8H; ArH) ppm. ¹³C NMR (75 MHz, CDCl₃): δ 21.5 (CH₃), 55.6 (OCH₃), 112.8 (CH), 114.2 (CH), 114.6 (CH), 116.3 (CH), 120.5 (CH), 122.2 (CH), 129.1 (CH), 135.9 (C), 139.1 (C), 145.1 (C), 155.2 (C) ppm.

Scheme S2. 3-Methyl-N-phenylbenzenamine 3b.²

Following the general procedure, the crude product was purified over a silica gel
column using petroleum ether to give a yellow liquid. $^1$H NMR (300 MHz, CDCl$_3$): δ 2.29 (s, 3H; CH$_3$), 5.58 (s, 1H; NH), 6.85-7.28 (m, 9H; ArH) ppm. $^{13}$C NMR (75 MHz, CDCl$_3$): δ 20.7 (CH$_3$), 116.8 (CH), 117.8 (CH), 118.9 (CH), 120.2 (CH), 120.9 (CH), 129.3 (CH), 129.8 (CH), 130.9 (CH), 140.2 (C), 143.9 (C) ppm.

Scheme S3. 3-Methyl-N-o-tolylbenzamine 3c.$^3$

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a yellow liquid. $^1$H NMR (300 MHz, CDCl$_3$): δ 2.22 (s, 3H; CH$_3$), 2.28 (s, 3H; CH$_3$), 5.29 (s, br, 1H; NH), 6.69-7.23 (m, 9H; ArH) ppm. $^{13}$C NMR (75 MHz, CDCl$_3$): δ 17.8 (CH$_3$), 21.45 (CH$_3$), 114.5 (CH), 118.1 (CH), 118.8 (CH), 121.3 (CH), 121.8 (CH), 126.7 (CH), 128.1 (C), 129.1 (CH), 130.8 (CH), 139.1 (C), 141.2 (C), 143.8 (C) ppm.

Scheme S4. di-m-Tolylamine 3d.$^4$

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a colorless liquid. $^1$H NMR (300 MHz, CDCl$_3$): δ 2.25 (s, 6H; CH$_3$), 5.46 (s, br, 1H; NH), 6.69 (d, $J$ = 7.2 Hz, 2H; ArH), 6.79-6.83 (m, 4H; ArH), 7.07-7.12 (m, 2H; ArH) ppm. $^{13}$C NMR (75 MHz, CDCl$_3$): δ 21.4 (CH$_3$), 114.8 (CH), 118.5 (CH), 121.6 (CH), 129.0 (CH), 139.0 (C), 143.1 (C) ppm.

Scheme S5. 3-Methyl-N-(4-nitrophenyl)benzamine 3e.

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a brown solid. Mp 130-133 °C. $^1$H NMR (300
MHz, CDCl\textsubscript{3}): \( \delta \) 2.37 (s, 3H; CH\textsubscript{3}), 6.29 (s, br, 1H; NH), 6.92 (d, \( J = 8.7 \) Hz, 2H; ArH), 6.97-7.02 (m, 3H; ArH), 7.25-7.27 (m, 1H, ArH), 8.11 (d, \( J = 8.5 \) Hz, 2H; ArH) ppm. \(^{13}\text{C} \) NMR (75 MHz, CDCl\textsubscript{3}): \( \delta \) 21.4 (CH\textsubscript{3}), 113.6 (CH), 119.0 (CH), 122.6 (CH), 125.5 (CH), 126.2 (CH), 129.5 (C), 139.4 (C), 139.6 (C), 139.7 (C), 150.3 (C) ppm.

MS (ESI, m/z)%: 229 (8) [M+1], 212 (57), 182 (74), 167 (100).

Scheme S6. \( N \)-(4-Methoxyphenyl)-4-methylbenzenamine 3f.\(^5\)

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a gray solid. Mp 80-82 \(^\circ\)C (lit.\(^5\) 82 \(^\circ\)C). \(^1\)H NMR (300 MHz, CDCl\textsubscript{3}): \( \delta \) 2.27 (s, 3H; CH\textsubscript{3}), 3.78 (s, 3H; OCH\textsubscript{3}), 5.38 (s, br, 1H; NH), 6.83-6.85 (m, 4H; ArH), 7.00-7.04 (m, 4H; ArH) ppm. \(^{13}\text{C} \) NMR (75 MHz, CDCl\textsubscript{3}): \( \delta \) 20.5 (CH\textsubscript{3}), 55.6 (OCH\textsubscript{3}), 114.6 (CH), 116.5 (CH), 121.1 (CH), 129.3 (C), 129.8 (CH), 136.6 (C), 142.4 (C), 154.7 (C) ppm.

Scheme S7. 4-Methyl-\( N \)-phenylbenzenamine 3g.\(^6\)

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a white solid. Mp 85-87 \(^\circ\)C (lit.\(^6\) 87 \(^\circ\)C). \(^1\)H NMR (300 MHz, CDCl\textsubscript{3}): \( \delta \) 2.24 (s, 3H; CH\textsubscript{3}), 5.49 (s, br, 1H; NH), 6.54-7.22 (m, 9H; ArH) ppm.

Scheme S8. 4-Methyl-\( N \)-\( o \)-tolylbenzenamine 3h.\(^7\)

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a yellow viscous oil. \(^1\)H NMR (300 MHz, CDCl\textsubscript{3}): \( \delta \) 2.25 (s, 3H; CH\textsubscript{3}), 2.30 (s, 3H; CH\textsubscript{3}), 5.29 (s, br, 1H; NH), 6.85-6.95 (m, 3H; ArH), 7.06-7.24 (m, 5H; ArH) ppm. \(^{13}\text{C} \) NMR (75 MHz, CDCl\textsubscript{3}): \( \delta \) 17.8 (CH\textsubscript{3}),
20.6 (CH₃), 117.2 (CH), 118.6 (CH), 121.0 (CH), 126.7 (CH), 126.9 (C), 129.8 (CH), 130.4 (C), 130.8 (CH), 141.0 (C), 142.0 (C) ppm.

Scheme S8. 4-Methyl-N-\textit{m}-tolylbenzenamine 3i.⁸

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a yellow viscous oil. \(^1\)H NMR (300 MHz, CDCl₃): \(\delta 2.27 \) (d, 6H; CH₃), 5.49 (s, br, 1H; NH), 6.68 (d, \(J = 7.2\) Hz, 1H; ArH), 6.80 -7.21 (m, 7H; ArH) ppm. \(^{13}\)C NMR (75 MHz, CDCl₃): \(\delta 20.6 \) (CH₃), 21.5 (CH₃), 113.9 (CH), 117.5 (CH), 118.8 (CH), 121.1 (CH), 129.1 (CH), 129.8 (CH), 130.7 (C), 139.1 (C), 140.3 (C), 143.8 (C) ppm.

Scheme S9. 4-Methyl-N-(4-nitrophenyl)benzenamine 3j.⁹

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a brown solid. \(\text{Mp} 132-135\degree\text{C (lit.} 137\degree\text{C).} \) \(^1\)H NMR (300 MHz, CDCl₃): \(\delta 2.36 \) (s, 6H; CH₃), 5.49 (s, br, 1H; NH), 6.86 (d, \(J = 9.0\) Hz, 2H; ArH), 7.11 (d, \(J = 8.1\) Hz, 2H; ArH), 7.19 (d, \(J = 8.0\) Hz, 2H; ArH), 8.08 (d, \(J = 9.0\) Hz, 2H; ArH) ppm. \(^{13}\)C NMR (75 MHz, CDCl₃): \(\delta 20.9 \) (CH₃), 113.1 (CH), 122.6 (CH), 126.2 (CH), 130.2 (CH), 134.8 (C), 136.6 (C), 139.2 (C), 150.8 (C) ppm.

Scheme S10. \textit{dip}-Tolylamine 3k.¹⁰

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a light yellow solid. \(\text{Mp 74-77}\degree\text{C (lit.} 73-75\degree\text{C).} \) \(^1\)H NMR (300 MHz, CDCl₃): \(\delta 2.28 \) (s, 6H; CH₃), 5.49 (s, br, 1H; NH), 6.93 (d, \(J = 8.0\) Hz, 4H; ArH), 7.05 (d, \(J = 8.0\) Hz, 4H; ArH) ppm. \(^{13}\)C NMR (75 MHz, CDCl₃):
δ 20.6 (CH₃), 117.9 (CH), 129.8 (CH), 130.1 (C), 141.1 (C) ppm.

Scheme S11. N-(4-Methoxyphenyl)-4-nitrobenzenamine 3l.¹¹

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a brown solid. Mp 149-152 °C (lit.¹¹ 152-153 °C). ¹H NMR (300 MHz, CDCl₃): δ 3.84 (s, 3H; OCH₃), 6.16 (s, 1H; NH), 6.76 (d, J = 8.8 Hz, 2H; ArH), 6.94 (d, J = 8.4 Hz, 2H; ArH), 7.16 (d, J = 8.4 Hz, 2H; ArH), 8.08 (d, J = 8.8 Hz, 2H; ArH) ppm. ¹³C NMR (75 MHz, CDCl₃): δ 55.5 (OCH₃), 112.6 (CH), 114.9 (CH), 125.5 (CH), 126.3 (CH), 131.9 (C), 139.0 (C), 151.7 (C), 157.4 (C) ppm.

Scheme S12. 4-Nitro-N-phenylbenzenamine 3m.¹²

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a brown solid. Mp 131-133 °C (lit.¹² 131 °C). ¹H NMR (300 MHz, CDCl₃): δ 6.40 (s, 1H; NH), 6.94 (d, J = 9.0 Hz, 2H; ArH), 7.14-7.42 (m, 5H; ArH), 8.11 (d, J = 9.0 Hz, 2H; ArH) ppm. ¹³C NMR (75 MHz, CDCl₃): δ 113.6 (CH), 121.9 (CH), 124.6 (C), 126.2 (CH), 139.4 (C), 139.6 (C), 150.2 (C) ppm.

Scheme S13. 4-Nitro-N-o-tolybenzenamine 3n.

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a brown solid. Mp 130-133 °C. ¹H NMR (300 MHz, CDCl₃): δ 2.25 (s, 3H; CH₃), 6.10 (s, 1H; NH), 6.72 (d, J = 8.9 Hz, 2H; ArH), 7.18-7.31 (m, 4H; ArH), 8.08 (d, J = 8.9 Hz, 2H; ArH) ppm. ¹³C NMR (75 MHz, CDCl₃): δ 17.8 (CH₃), 113.0 (CH), 124.7 (CH), 126.1 (CH), 126.2 (CH), 127.1 (CH),
131.4 (CH), 133.2 (C), 137.5 (C), 139.1 (C), 151.3 (C) ppm. MS (ESI, m/z)(%): 229 (9) [M+1], 212 (100), 182 (77), 168 (94).

Scheme S14. 3-methyl-N-(3-nitrophenyl)benzenamine 3o.\textsuperscript{13}

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a yellow solid. Mp 145-147 °C (lit.\textsuperscript{13} 146 °C); \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 4.36 (s, br, 1H; NH), 6.63 (d, J = 8.9 Hz, 2H; Ar\textsubscript{H}), 7.21-7.26 (m, 3H; Ar\textsubscript{H}), 8.1 (d, J = 8.8 Hz, 1H; Ar\textsubscript{H}), 8.2 (d, J=8.9 Hz, 2H; Ar\textsubscript{H}) ppm. \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): δ 113.2 (CH), 117.2 (CH), 125.9 (CH), 126.2 (C) ppm.

Scheme S15. 4-(4-methoxyphenylamino)benzaldehyde 3p.\textsuperscript{14}

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a brown solid. Mp 108-111 °C (lit.\textsuperscript{14} 113 °C). \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 3.83 (s, 3H; OCH\textsubscript{3}), 6.08 (s, 1H; NH), 6.85 (d, J = 8.4 Hz, 2H; Ar\textsubscript{H}), 6.92 (d, J = 8.7 Hz, 2H; Ar\textsubscript{H}), 7.16 (d, J = 8.7 Hz, 2H; Ar\textsubscript{H}), 7.70 (d, J = 8.4 Hz, 2H; Ar\textsubscript{H}), 9.75 (s, 1H; CHO) ppm. \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): δ 55.5 (OCH\textsubscript{3}), 113.4 (CH), 114.8 (CH), 125.1 (CH), 127.8 (C), 132.2 (CH), 132.6 (C), 151.4 (C), 157.0 (C), 190.2 (CHO) ppm.

Scheme S16. 4-(phenylamino)benzaldehyde 3q.\textsuperscript{15}

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a brown solid. Mp 94-97 °C (lit.\textsuperscript{15} 95-97 °C). \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 6.38 (s, 1H; NH), 7.02 (d, J = 8.2 Hz, 2H; Ar\textsubscript{H}), 7.09-7.39 (m, 5H; Ar\textsubscript{H}), 7.74 (d, J = 8.2 Hz, 2H; Ar\textsubscript{H}), 9.78 (s, 1H; CHO) ppm. \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): δ 114.4 (CH), 121.3 (CH), 123.8 (CH), 128.4 (C), 129.5
Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a brown solid. Mp 85-87 °C. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 2.25 (s, 3H; CH$_3$), 6.00 (s, 1H; NH), 6.82 (d, $J$ = 8.4 Hz, 2H; ArH), 7.13-7.27 (m, 4H; ArH), 7.71 (d, $J$ = 8.4 Hz, 2H; ArH), 9.76 (s, 1H; CHO) ppm. $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 17.9 (CH$_3$), 113.8 (CH), 124.1 (CH), 125.4 (CH), 127.0 (CH), 127.9 (C), 131.3 (CH), 132.1 (CH), 132.6 (C), 138.0 (C), 151.0 (C), 190.3 (CHO) ppm. MS (ESI, $m/z$)(%): 212 (28) [M+1], 184 (12), 183 (9), 182 (14), 169 (52), 168 (24), 103 (48), 88 (100), 75 (11), 60 (10).

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a brown solid. Mp 117-119 °C. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 2.34 (s, 3H; CH$_3$), 6.37 (s, 1H; NH), 6.92-7.24 (m, 6H; ArH), 7.71-7.74 (d, $J$ = 8.3 Hz, 2H; ArH), 9.77 (s, 1H; CHO) ppm. $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 21.4 (CH$_3$), 114.4 (CH), 118.3 (CH), 121.9 (CH), 124.7 (CH), 128.2 (C), 129.3 (CH), 132.1 (CH), 139.5 (C), 139.9 (C), 150.0 (C), 190.4 (CHO) ppm. MS (ESI, $m/z$)(%): 212 (33) [M+1], 183 (21), 169 (69), 103 (81), 88 (100), 75 (34), 73 (6), 60 (21).

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a brown solid. Mp 115-117 °C. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 2.38 (s, 3H; CH$_3$), 6.27 (s, 1H; NH), 6.90-7.25 (m, 7H; ArH), 7.71-7.74 (d, $J$ = 8.3 Hz, 2H; ArH), 9.76 (s, 1H; CHO) ppm. $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 17.9 (CH$_3$), 113.8 (CH), 124.1 (CH), 125.4 (CH), 127.0 (CH), 127.9 (C), 131.3 (CH), 132.1 (CH), 132.6 (C), 138.0 (C), 151.0 (C), 190.3 (CHO) ppm. MS (ESI, $m/z$)(%): 212 (28) [M+1], 184 (12), 183 (9), 182 (14), 169 (52), 168 (24), 103 (48), 88 (100), 75 (11), 60 (10).
column using petroleum ether to give a brown solid. Mp 85-88 °C. $^1$H NMR (300 MHz, CDCl$_3$): δ 2.35 (s, 3H; CH$_3$), 6.20 (s, 1H; NH), 6.95 (d, $J = 8.4$ Hz, 2H; ArH), 7.10 (d, $J = 8.1$ Hz, 2H; ArH), 7.18 (d, $J = 8.1$ Hz, 2H; ArH), 7.72 (d, $J = 8.4$ Hz, 2H; ArH), 9.77 (s, 1H; CHO) ppm. $^{13}$C NMR (75 MHz, CDCl$_3$): δ 20.8 (CH$_3$), 113.9 (CH), 122.1 (CH), 128.1 (C), 130.1 (CH), 132.1 (CH), 134.0 (C), 137.2 (C), 150.5 (C), 190.3 (CHO) ppm.

Scheme S20. 4-(3-nitrophenylamino)benzaldehyde 3u.

Following the general procedure, the crude product was purified over a silica gel column using petroleum ether to give a yellow solid. Mp 152-155 °C. $^1$H NMR (300 MHz, CDCl$_3$): δ 6.35 (s, 1H; NH), 7.13 (d, $J = 8.1$ Hz, 2H; ArH), 7.49-7.52 (m, 2H; ArH), 7.83 (d, $J = 8.1$ Hz, 2H; ArH), 7.87-8.04 (m, 2H; ArH), 9.87 (s, 1H; CHO) ppm. $^{13}$C NMR (75 MHz, CDCl$_3$): δ 114.1 (CH), 116.1 (CH), 117.6 (CH), 122.3 (C), 125.2 (C), 130.4 (C), 132.1 (CH), 142.1 (C), 147.6 (C), 148.5 (C), 190.3 (CHO) ppm. MS (ESI, m/z)(%): 243 (16) [M+1], 197 (42), 168 (80), 167 (100).

4. References

11. McNulty, James; Cheekoor, Sreedhar; Bender, Timothy P.; Coggan, Jennifer A. European J. Org. Chem. 2007, 9, 1423.

5. Copies of NMR and MS spectra for compounds