

Ethyl lactate as a tunable solvent for greener synthesis of aryl aldimines

Jacqueline S. Bennett,* Kaitlyn L. Charles, Matthew R. Miner, Caitlin F. Heuberger, Elijah J. Spina, Michael F. Bartels, and Taylor Foreman

Web Supplement

All reagents were used as received. Melting points were acquired on a BarlowWorld Scientific Limited SMP10 digital melting point apparatus. NMR spectra were acquired on a JEOL ECX-300 MHz spectrometer. EI-MS spectra were acquired on a Varian Saturn 2100T GC/MS/MS. IR spectra were acquired on a Varian 1000 Series FT-IR equipped with an ATR assembly.

Some starting materials are slow to dissolve. In these cases we heated these compounds in the presence of 1.5-4.5 mL of the solvent and then allowed the solution to cool to room temperature. All reactions, with the exception of **a**, were performed at room temperature.

- a. *N*-(4-nitrobenzylidene)-4-methoxyaniline (**a**): Yield: 94%, 133-134°C, orange plates. ¹H NMR (CDCl₃): δ 8.6 (s, 1H, N=CH), 8.3 (d, J=8.2 Hz, 2H, Ar), 8.1 (d, J=8.6 Hz, 2H, Ar), 7.3 (d, J= 8.6 Hz, 2H, Ar), 7.0 (d, J= 8.2 Hz, 2H, Ar), 3.9 (s, 3H, CH₃). ¹³C NMR (CDCl₃): δ 159.3, 154.9 (N=C), 143.8, 142.0, 129.2, 124.1, 122.7, 114.6, 55.6. MS (m/z, %): 257 (M⁺, 100), 258 (M+1, 18), 242 (74), 210 (21), 195 (24), 77 (23), 63 (21). IR: 1600, 1587, 1577, 1511, 1338, 1245, 1037, 844 cm⁻¹
- b. *N*-(4-chlorobenzylidene)-4-methoxyaniline (**b**): Yield: 93%, 127-129°C, beige plates. ¹H NMR (CDCl₃): δ 8.4 (s, 1H, N=CH), 7.8 (d, J= 8.6 Hz, 2H, Ar), 7.4 (d, J=8.6 Hz, 2H, Ar), 7.2 (d, J=8.6 Hz, 2H, Ar), 6.9 (d, J=8.6 Hz, 2H, Ar), 3.8 (s, 3H, OCH₃); ¹³C NMR (CDCl₃): δ 158.6, 156.8, 144.5, 137.0, 134.8, 129.8, 129.1, 122.4, 114.5, 55.6. MS (m/z, %) 245 (M⁺, 100), 246 (M+1, 22), 247 (M+2, 36), 233 (28), 232 (19), 231 (70), 167 (16), 78 (17), 63 (31), 50 (16). IR: 1621, 1600, 1576, 1506, 1253, 839 cm⁻¹
- c. *N*-cinnamylidene-4-methoxyaniline (**c**): Yield: 96%, 119-120°C, yellow plates. ¹H NMR (CDCl₃): δ 8.3 (dd, J=5.2,3.1 Hz, 1H, N=CH), 7.5 (dd, J=8.0, 1.5 Hz, 2H, Ar), 7.2 (d, J=9.1 Hz, 3H, Ar), 7.1 (m, 4H, Ar & CH=CH), 6.9 (d, J=9 Hz, 2H, Ar), 3.8 (s, 3H, OCH₃). ¹³C NMR (CDCl₃): δ 159.7 (N=C), 158.5, 144.5, 143.2, 135.8, 129.0, 128.9, 127.5, 122.3, 114.5, 55.6. MS (m/z, %): 237 (M⁺, 100), 238 (M+1, 51), 239 (M+2, 10), 222(17), 194 (13), 115 (44), 77 (25), 63 (24). IR: 1627, 1606, 1578, 1504, 1468, 1448, 1245, 829, 745, 692 cm⁻¹
- d. *N*-(4-methoxybenzylidene)-4-methoxyaniline (**d**): Yield: 93%, 144°C, gray plates. ¹H NMR (CDCl₃): 8.4 (s, 1H, N=CH), 7.8 (d, J=8.6, 2H, Ar), 7.2 (d, J=9.1 Hz, 2H, Ar), 7.0 (d, J=8.6 Hz, 2H, Ar), 6.9 (d, J=9.1 Hz, 2H, Ar), 3.9 (s, 3H, OCH₃), 3.8 (s, 3H, OCH₃). ¹³C NMR (CDCl₃): 161.9, 158.0 (N=C), 145.4, 130.3, 129.6, 122.2, 114.4, 114.2, 55.6, 55.5). MS (m/z, %): 242 (M⁺, 100), 243 (M+1, 21), 227 (83), 77 (15), 63 (17). IR 1620, 1606, 1576, 1509, 1470, 1240, 1169, 1028, 840 cm⁻¹
- e. *N*-(4-chlorobenzylidene)-4-toluidine (**e**): Yield: 96%, 124-125°C, cream plates. ¹H NMR (CDCl₃): δ 8.4 (s, 1H, N=CH), 7.8 (d, J=8.7 Hz, 2H, Ar), 7.4 (d, J=8.2 Hz, 2H, Ar), 7.2 (d, J=8.3 Hz, 2H, Ar), 7.1 (d, J=8.7 Hz, 2H, Ar), 2.4 (s, 3H, CH₃). ¹³C NMR (CDCl₃): δ : 158.1 (N=C), 149.1, 137.3, 136.2, 134.8, 129.95, 129.92, 129.2, 120.9, 21.1 MS (m/z, %): 230 (M⁺, 100), 231

(M+1, 56), 232 (M+2, 38), 229 (85), 91 (64), 77 (12), 65 (40). 1625, 1567, 1545, 1506, 1085, 1013, 829, 670 cm⁻¹

- f. MeOH *N*-(4-hydroxybenzylidene)-4-toluidine (**f**): Yield: 90%, 217-220°C, white plates. ¹H NMR (DMSO-d₆): δ 10.1 (s, 1H, OH), 8.4 (s, 1H, N=CH), 7.7 (d, J=8.7 Hz, 2H, Ar), 7.2 (d, J=8.7 Hz, 2H, Ar), 7.1 (d, J=8.7 Hz, 2H, Ar), 6.9 (d, J=8.7 Hz, 2H, Ar), 2.3 (s, 3H, CH₃). ¹³C NMR (DMSO-d₆): δ 161.0, 160.0 (N=C), 149.9, 135.1, 131.1, 130.1, 128.2, 121.3, 116.2, 21.1. MS (m/z, %): 211 (M⁺, 100), 212 (M+1, 13), 91 (33), 77 (19), 65 (37), 63 (13). IR: 1606, 1601, 1577, 1514, 1510, 1444, 1287, 1164, 839, 649 cm⁻¹
- g. *N*-(2-hydroxybenzylidene)-4-toluidine (**g**): Yield: 97%, 94°C, yellow needles (strongly fluorescent under UV light). ¹H NMR (CDCl₃): δ 13.4 (s, 1H, OH), 8.6 (s, 1H, N=CH), 7.4 (m, 1H, Ar), 7.2 (m, 4H, Ph), 7.0 (d, J=8 Hz, 1H, Ar), 6.9 (dt, J=7, 1.2 Hz, 2H, Ar), 2.4 (s, 3H, CH₃). ¹³C NMR (CDCl₃): δ 161.8, 161.2 (N=C), 145.8, 137.0, 133.0, 132.2, 130.1, 121.1, 119.1, 117.3, 21.2. MS (m/z, %): 211 (M⁺, 100), 212 (M+1, 19), 210 (89), 92 (42), 78 (18), 65 (38). IR: 1619, 1599, 1571, 1540, 1511, 1284, 817, 762, 642 cm⁻¹
- h. *N*-(4-chlorobenzylidene)aniline (**h**): Yield: 95%, 63-64°C, very pale yellow plates. ¹H NMR (CDCl₃): δ 8.4 (s, 1H, N=CH), 7.9 (d, J=8.7 Hz, 2H, Ar), 7.4 (m, 4H, Ar), 7.2 (m, 3H, Ar). ¹³C NMR (CDCl₃): δ 159.0 (N=C), 151.7, 137.5, 134.8, 130.1, 129.3, 129.2, 126.3, 121.0. MS (m/z, %): 215 (M⁺, 100), 217 (M+2, 34), 104 (16), 77 (87), 63 (12). IR: 1624, 1589, 1567, 1488, 1088, 829, 760, 696 cm⁻¹
- i. *N*-(4-bromobenzylidene)aniline (**i**): Yield: 99%, 71-72°C, white plates. ¹H NMR (CDCl₃): δ 8.4 (s, 1H, N=CH), 7.8 (d, J=8.2 Hz, 2H, Ar), 7.43 (d, J=8.2 Hz, 2H, Ar), 7.41 (m, 2H, Ar), 7.2 (m, 3H, Ar). ¹³C NMR (CDCl₃): δ 159.0, 151.6, 135.1, 132.1, 130.2, 129.3, 126.3, 125.9, 120.9. MS (m/z, %): 259 (M⁺, 49), 260 (M+1, 62), 261 (M+2, 84), 261 (M+2, 73), 104 (16), 77 (100), 63 (14), 51 (46). IR: 1622, 1584, 1564, 1487, 1070, 1008, 880, 823, 764, 696 cm⁻¹
- j. *N*-cinnamylideneaniline (**j**): Yield: 98%, 108-109°C, yellow plates. ¹H NMR (CDCl₃): 8.3 (dd, J=6.6 Hz, 2.0 Hz, 1H, N=CH), 7.5 (m, 2H, Ar), 7.4 (m, 5H, Ar), 7.2 (m, 5H, Ar & CH=CH). ¹³C NMR (CDCl₃): 161.8, 151.8, 144.2, 135.7, 129.7, 129.3, 129.0, 128.7, 127.6, 126.2, 121.0. MS (m/z, %): 207 (M⁺, 100), 208 (M+1, 33), 128 (17), 77 (41), 51 (31). IR: 1625, 1600, 1575, 1484, 1447, 750, 688 cm⁻¹
- k. *N*-(4-hydroxybenzylidene)aniline (**k**): Yield: >99%, 193-194°C, pale yellow plates. ¹H NMR (acetone-d₆): δ 9.0 (s, 1H, OH), 8.4 (s, 1H, N=CH), 7.8 (d, J=8.7 Hz, 2H, Ar), 7.4 (m, 2H, Ar), 7.2 (m, 3H, Ar), 7.0 (d, J=8.7 Hz, 2H, Ar). ¹³C NMR (acetone-d₆): 160.6, 159.7 (N=C), 152.7, 130.7, 129.1, 128.7, 125.3, 120.9, 115.7. MS (m/z, %): 197 (M⁺, 100), 197 (M+, 73), 198 (M+1, 11), 84 (14), 77 (75), 76 (14), 65 (16), 63 (12), 51 (43), 50 (19). IR: 1613, 1603, 1580, 1516, 1445, 1286, 1191, 1166, 841, 759, 690 cm⁻¹
- l. *N*-(4-bromobenzylidene)-4-chloroaniline (**l**): Yield: 96%, 119-120°C, white plates. ¹H NMR (CDCl₃): δ 8.4 (s, 1H, N=CH), 7.8 (d, J=8.7 Hz, 2H, Ar), 7.51 (d, J=8.7 Hz, 2H, Ar), 7.45 (d, J=8.7 Hz, 2H, Ar), 7.1 (d, J=8.7 Hz, 2H, Ar). ¹³C NMR (CDCl₃): δ 159.3 (N=C), 150.6, 137.6, 134.3, 132.4, 130.1, 129.3, 122.7, 120.0, 116.8. MS (m/z, %): 293 (M⁺, 34), 294 (M+1, 65), 295 (M+2, 99), 295 (M+2, 100), 296 (m+3, 38), 297 (M+4, 27), 157 (21), 155 (22), 89 (19), 76 (48), 75 (57), 74 (20), 63 (25), 50 (43). IR: 1622, 1598, 1568, 1489, 1071, 833 cm⁻¹

- m. *N*-benzylidene-4-bromoaniline (**m**): Yield: 93%, 66-68°C, yellow prisms. ¹H NMR (CDCl₃): δ 8.4 (s, 1H, N=CH), 7.9 (d, J=7.4, 2H, Ar), 7.5 (m, 5H, Ar), 7.3 (s, 1H, Ar), 7.1 (d, J=7.0 Hz, 2H, Ar). ¹³C NMR (CDCl₃): δ 160.9 (HC=NR), 151.1, 136.0, 132.3, 131.8, 129.0, 128.9, 122.7, 119.4. MS (m/z, %): 259 (M⁺, 55), 260 (M+1, 88), 261 (M+2, 92), 89 (12), 77 (26), 76 (26), 75 (22), 63 (18). IR: 1626, 1577, 1489, 1190, 1007, 820, 760, 692, 670 cm⁻¹
- n. *N*-(2-hydroxybenzylidene)-4-bromoaniline (**n**): Yield: 96%, 111°C, yellow needles. ¹H NMR (CDCl₃): δ 13.0 (s, 1H, OH), 8.6 (s, 1H, N=CH), 7.5 (d, J=8.7 Hz, 2H, Ar), 7.4 (d, J=7.4 Hz, 2H, Ar), 7.1 (d, J=8.7, 2H, Ar), 7.03 (d, J=8.3 Hz, 1H, Ar), 6.95 (dt, J=7.5, 0.8 Hz, 1H, Ar). ¹³C NMR (CDCl₃): δ 163.1, 161.2 (N=C), 147.6, 133.6, 132.6, 132.5, 122.9, 119.3, 119.1, 117.4. ¹³C NMR (CDCl₃): 163.1 (N=C), 161.2, 147.6, 133.6, 132.60, 132.56, 122.9, 119.3, 119.1, 117.4. MS (m/z, %): 275 (M⁺, 90), 276 (M+1, 82), 277 (M+2, 100), 278 (M+3, 13), 196 (19), 195 (19), 167 (19), 157 (19), 155 (21), 120 (24), 102 (15), 91 (17), 84 (21), 77 (39), 76 (47), 75 (43), 74 (19), 73 (16), 65 (23), 63 (31). IR: 1615, 1569, 1482, 1283, 1187, 1009, 829, 755 cm⁻¹
- o. *N*-(4-chlorobenzylidene)-4-chloroaniline (**o**): Yield: 97%, 110-111°C, green plates. ¹H NMR (CDCl₃): δ 8.4 (s, 1H, N=CH), 7.8 (d, J=8.7 Hz, 2H, Ar), 7.5 (d, J=8.2 Hz, 2H, Ar), 7.4 (d, J=8.7 Hz, 2H, Ar), 7.1 (d, J=8.2 Hz, 2H, Ar). ¹³C NMR (CDCl₃): δ 159.2 (N=C), 150.2, 137.7, 134.5, 131.8, 130.1, 129.4, 129.3, 122.3. MS (m/z, %): 249 (M⁺, 86), 250 (M+1, 100), 251 (M+2, 89), 252 (M+3, 67), 253 (M+4, 23), 149 (23), 138 (22), 113 (30), 111 (89), 77 (20), 75 (95), 63 (23). IR 1626, 1591, 1567, 1489, 1401, 1193, 1086, 1011, 886, 833 cm⁻¹
- p. *N*-cinnamylidene-4-chloroaniline (**p**): Yield: 97%, 105°C, yellow needles. ¹H NMR (CDCl₃): δ 8.2 (d, J=7.4 Hz, 1H, N=CH), 7.5 (m, 2H, Ar), 7.4 (m, 3H, Ar), 7.36 (m, 4H, Ar & C=C), 7.1 (m, 2H Ar). ¹³C NMR (CDCl₃): δ 162.1 (N=C), 150.2, 144.8, 135.5, 131.8, 129.9, 129.4, 129.1, 128.3, 127.7, 122.4. MS (m/z, %): 240 (M⁺, 100), 241 (M+1, 34), 242 (M+2, 39), 209 (15), 207 (19), 128 (40), 115 (18), 111 (28), 77 (29), 75 (38). IR: 1626, 1603, 1593, 1575, 1486, 1103, 833, 751, 691, 647 cm⁻¹
- q. *N*-(2-hydroxybenzylidene)-4-chloroaniline (**q**): Yield: 96%, 104°C, yellow needles. ¹H NMR (CDCl₃): δ 13.0 (s, 1H, OH), 8.6 (s, 1H, N=CH), 7.4 (m, 4H, Ar), 7.3 (m, 2H, Ar), 7.0 (d, 8.7 Hz, 1H, Ar), 6.9 (t, J=7.6 Hz, 1H, Ar). ¹³C NMR (CDCl₃): δ 163.1, 161.2 (N=X), 133.6, 132.5, 129.7, 122.6, 119.3, 117.4. MS (m/z, %): 231 (M⁺, 100), 232 (M+1, 42), 233 (M+2, 33), 113 (13), 111 (37), 84 (26), 77 (29), 75 (47), 65 (224), 63 (21). 3409, 1639, 1611, 1568, 1487, 1273, 1091, 838, 756, 699 cm⁻¹