A one-pot parallel reductive amination of aldehydes with heteroaromatic amines

Andrey V. Bogolubsky, † Yurii S. Moroz, *,†,‡ Pavel K. Mykhailiuk, $^{*,\dagger,\$}$ Dmitriy M. Panov, † Sergey E. Pipko, ‡ Anzhelika I. Konovets, $^{\dagger,\parallel}$ and Andrey Tolmachev †,‡

[†]Enamine Ltd., 23 Matrosova Street, Kyiv, 01103, Ukraine

[‡]ChemBioCenter, Kyiv National Taras Shevchenko University, 61 Chervonotkatska Street, Kyiv, 02094, Ukraine

§Department of Chemistry, Kyiv National Taras Shevchenko University, 64 Volodymyrska

Street, Kyiv, 01601, Ukraine

The Institute of High Technologies, Kyiv National Taras Shevchenko University, 4 Glushkov Street, Building 5, Kyiv, 03187, Ukraine

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Analytical data for the selected compounds

N-(4-fluorobenzyl)-5-methylisoxazol-3-amine (Entry 1, in Table 1)

Yield: 143 mg, 69%; yellowish solid, mp 78-80°C. **IR** (KBr): v (cm⁻¹) 3270, 3110, 3086, 3049, 2928, 2862, 1632, 1573, 1506, 1217, 1155; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 2.20 (s, 3H, CH₃), 4.20 (d, J = 6.1 Hz, 2H, CH₂), 5.65 (d, J = 0.6 Hz, 1H, Het), 6.53 (t, J = 5.2 Hz, 1H, NH), 7.13 (t, J = 8.8 Hz, 2H, Ar), 7.35 (m, 2H, Ar); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 12.1, 45.9, 93.7, 114.9 (d, J = 21 Hz), 129.4 (d, J = 8 Hz), 136.2 (d, J = 3 Hz), 161.0 (d, J = 245 Hz), 164.4, 167.6; **MS** (APCI) m/z [M+H]⁺ calculated for C₁₁H₁₂FN₂O: 207.1; found: 207.0; **Anal. Calcd.**: C, 64.07; H, 5.38; N, 13.58; found C, 63.80; H, 5.10; N, 13.70.

N-(2-chlorobenzyl)-5-methylisoxazol-3-amine (Entry 2, in Table 1)

Yield: 51 mg, 23%; yellow solid, mp 105-107°C; **IR** (KBr): v (cm⁻¹) 3255, 3187, 3072, 2929, 2871, 1627, 1560, 1520, 1356, 1050; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 2.21 (s, 3H, CH₃), 4.30 (d, J = 6.1 Hz, 2H, CH₂), 5.69 (s, 1H, Het), 6.59 (t, J = 6.1 Hz, 1H, NH), 7.29 (m, 2H, Ar), 7.42 (m, 2H, Ar); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 12.1, 44.3, 93.6, 127.1, 128.6, 129.0, 129.2, 132.3, 136.9, 164.2, 167.8; **MS** (APCI) m/z [M+H]⁺ calculated for C₁₁H₁₂ClN₂O: 223.1; found: 222.8; **Anal. Calcd.**: C, 59.33; H, 4.98; N, 12.58; found C, 59.10; H, 5.15; N, 12.45.

N-(2,3-dimethoxybenzyl)benzo[d]oxazol-2-amine (Entry 3, in Table 1)

$$-0 \longrightarrow HN \longrightarrow N$$

Yield: 241 mg, 84%; yellow solid, mp 79-81°C; **IR** (KBr): v (cm⁻¹) 3170, 3053, 3000, 2961, 2905, 2832, 1680, 1586, 1480, 1457, 1266, 1243, 1063; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 3.78(s, 3H, CH₃), 3.80 (s, 3H, CH₃), 4.53 (d, J = 5.9 Hz, 2H, CH₂), 6.92 – 6.99 (m, 3H, Ar), 7.02 (t, J = 7.9 Hz, 1H, Ar), 7.1 (t, J = 7.3 Hz, 1H, Ar), 7.23 (d, J = 7.7 Hz, 1H, Ar), 7.33 (d, J = 7.8 Hz, 1H, Ar), 8.34 (t, J = 5.5 Hz, 1H, NH); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 40.7, 55.8, 60.2, 108.6, 112.0, 115.6, 120.0, 120.2, 123.7, 123.9, 132.3, 143.3, 146.4, 148.2, 152.4, 162.5; **MS** (APCI) m/z [M+H]⁺ calculated for C₁₆H₁₇N₂O₃: 285.1; found: 285.0; **Anal. Calcd.**: C, 67.59; H, 5.67; N, 9.85; found C, 67.20; H, 5.90; N, 9.55.

N-(3,4,5-trimethoxybenzyl)benzo[*d*]oxazol-2-amine (Entry 4, in Table 1)

Yield: 100 mg, 32%; whitish solid, mp 112-114°C; **IR** (KBr): ν (cm⁻¹) 3335, 3250, 3178, 3063, 2954, 2937, 1677, 1648, 1586, 1457, 1415, 1247, 1128; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 3.63 (s, 3H, CH₃), 3.75 (s, 6H, 2CH₃), 4.46 (d, J = 6.0 Hz, 2H, CH₂), 6.72 (s, 2H, Ar), 6.98 (t, J = 7.7 Hz, 1H, Ar), 7.10 (t, J = 7.7 Hz, 1H, Ar), 7.24 (d, J = 7.7 Hz, 1H, Ar), 7.34 (d, J = 7.7 Hz, 1H, Ar), 7.41 (t, J = 5.7 Hz, 1H, NH); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 46.1, 55.9, 60.1, 104.7, 108.7, 115.6, 120.3, 123.7, 134.7, 136.6, 143.2, 148.2, 152.9, 162.5; **MS** (APCI) m/z [M+H]⁺ calculated for C₁₇H₁₉N₂O₄: 315.2; found: 315.0; **Anal. Calcd.**: C, 64.96; H, 5.77; N, 8.91; found C, 65.05; H, 5.90; N, 8.80.

N-benzyl-3-methyl-1,2,4-oxadiazol-5-amine (Entry 5, in Table 1)

Yield: 113 mg, 60%; yellowish solid, mp 108-110°C; **IR** (KBr): ν (cm⁻¹) 3293, 3178, 3069, 2930, 2882, 1661, 1414, 1355, 1302, 1010; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 2.08 (s, 3H, CH₃), 4.44 (d, J = 6.0 Hz, 2H, CH₂), 7.22 – 7.28 (m, 1H, Ar), 7.29 – 7.38 (m, 4H, Ar), 8.75 (t, J = 5.7 Hz, 1H, NH); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 11.5, 46.4, 127.2, 127.3, 128.5, 138.7, 167.0, 171.4; **MS** (APCI) m/z [M+H]⁺ calculated for C₁₀H₁₂N₃O: 190.1; found: 190.0; **Anal. Calcd.**: C, 63.48; H, 5.86; N, 22.21; found C, 63.20; H, 6.05; N, 22.10.

N-(4-fluorobenzyl)-3-methyl-1,2,4-oxadiazol-5-amine (Entry 6, in Table 1)

$$\mathsf{F} \overset{\mathsf{H}\mathsf{N}}{\longrightarrow} \overset{\mathsf{N}}{\longrightarrow} \mathsf{N}$$

Yield: 89 mg, 43%; yellowish solid, mp 82-84°C; **IR** (KBr): v (cm⁻¹) 3299, 3201, 3161, 3072, 2964, 2868, 1661, 1507, 1415, 1326, 1210, 1007; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 2.08 (s, 3H, CH₃), 4.40 (d, J = 6.0 Hz, 2H, CH₂), 7.16 (t, J = 8.8 H, 2H, Ar), 7.35 (m, 2H, Ar), 8.70 (m, 1H, NH); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 11.5, 45.7, 115.2 (d, J = 21 Hz), 129.3 (d, J = 8 Hz), 134.8 (d, J = 3 Hz), 161.0 (d, J = 244 Hz), 166.9, 171.3; **MS** (APCI) m/z [M+H]⁺ calculated for C₁₀H₁₁FN₃O: 208.1; found: 207.8; **Anal. Calcd.**: C, 57.97; H, 4.86; N, 20.28; found C, 57.80; H, 5.00; N, 20.44.

N-(2,3-dimethoxybenzyl)-[1,2,4]triazolo[4,3-a]pyridin-3-amine (Entry 11, in Table 1)

Yield: 57 mg, 20%; white solid, mp 182-184°C; **IR** (KBr): ν (cm⁻¹) 3431, 3181, 3053, 3003, 2954, 2924, 2832, 1635, 1598, 1592, 1486, 1230, 1088, 1003; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 3.79 (s, 3H, OCH₃), 3.81 (s, 3H, OCH₃), 4.60 (d, J = 5.6 Hz, 2H, CH₂), 6.73 (t, J = 6.5 Hz, 1H, NH), 7.02 (m, 5H, Ar), 7.43 (d, J = 9.3 Hz, 1H, Ar), 8.16 (d, J = 7.0 Hz, 1H, Ar); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 41.3, 55.8, 60.2, 111.4, 111.9, 115.5, 120.5, 122.4, 123.8, 125.5, 132.9, 146.2, 146.6, 148.7, 152.4; **MS** (APCI) m/z [M+H]⁺ calculated for C₁₅H₁₇N₄O₂: 285.1; found: 285.1; **Anal. Calcd.**: C, 63.37; H, 5.67; N, 19.71; found C, 63.44; H, 5.83; N, 19.83.

N-benzyl-5-methylthiazol-2-amine (Entry 13, in Table 1)

Yield: 161 mg, 79%; yellow solid, mp 98-100°C; **IR** (KBr): v (cm⁻¹) 3165, 3063, 2967, 2915, 2855, 1569, 1536, 1510, 1467, 1283, 1145; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 2.18 (s, 3H, CH₃), 4.38 (d, J = 4.8 Hz, 2H, CH₂), 6.65 (s, 1H, CH), 7.23 (m, 1H, Ar), 7.31 (m, 4H, Ar), 7.81 (m, 1H, NH); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 11.7, 47.5, 119.5, 126.9, 127.4, 128.3, 135.5, 139.6, 167.6; **MS** (APCI) m/z [M+H]⁺ calculated for C₁₁H₁₃N₂S: 205.1; found: 205.0; **Anal. Calcd.**: C, 64.67; H, 5.92; N, 13.71; found C, 64.55; H, 6.06; N, 13.85.

N-((2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-6-(methylsulfonyl)benzo[d]thiazol-2-amine (Entry 15, in Table 1)

Yield: 177 mg, 47%; white solid, mp 282-284°C; **IR** (KBr): v (cm⁻¹) 3217, 3194, 3082, 3030, 2941, 2895, 1612, 1572, 1510, 1303, 1280, 1141; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 3.17 (s, 3H, CH₃), 4.20 (s, 4H, 2CH₂O), 4.50 (d, J = 4.6 Hz, 2H, CH₂), 6.82 (s, 2H, Ar), 6.87 (s, 1H, Ar), 7.53 (d, J = 8.6 Hz, 1H, Ar), 7.72 (d, J = 8.6 Hz, 1H, Ar), 8.28 (s, 1H, Ar), 8.90 (m, 1H, NH); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 44.3, 46.9, 64.1, 64.2, 116.3, 117.1, 117.8, 120.5, 120.9, 125.0, 131.1, 131.4, 132.6, 142.7, 143.3, 156.5, 169.6; **MS** (APCI) m/z [M+H]⁺ calculated for C₁₇H₁₇N₂O₄S₂: 377.1; found: 377.0; **Anal. Calcd.**: C, 54.24; H, 4.28; N, 7.44; found C, 54.10; H, 4.40; N, 7.60.

N-(2-chlorobenzyl)-1,3,4-thiadiazol-2-amine (Entry 17, in Table 1)

Yield: 153 mg, 68%; yellow solid, Mp 87-89°C; **IR** (KBr): v (cm⁻¹) 3188, 3065, 2987, 2790, 1556, 1497, 1437, 1040; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 4.61 (m, 2H, CH₂), 7.30 (m, 2H, Ar), 7.44 (m, 2H, Ar), 8.32 (br. s, 1H, NH), 8.66 (s, 1H, Het); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 46.1, 127.3, 129.0, 129.3, 129.4, 132.6, 135.8, 142.9, 168.2; **MS** (APCI) m/z [M+H]⁺ calculated for C₉H₉ClN₃S: 226.0; found: 225.8; **Anal. Calcd.**: C, 47.90; H, 3.57; N, 18.62; found C, 47.83; H, 3.65; N, 18.70.

N-((2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-1,3,4-thiadiazol-2-amine (Entry 18, in Table 1)

Yield: 114 mg, 46%; white solid, mp 117-119°C; **IR** (KBr): v (cm⁻¹) 3204, 3086, 2997, 2947, 2924, 2882, 1590, 1566, 1506, 1441, 1319, 1283, 1260, 1072, 1050; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 4.20 (s, 4H, 2CH₂O), 4.35 (d, J = 5.6 Hz, 2H, CH₂), 6.80 (s, 2H, Ar), 6.84 (s, 1H, Ar), 8.19 (t, J = 4.8 Hz, 1H, NH), 8.61 (s, 1H, Het); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 47.9, 64.1, 64.2, 116.4, 116.9, 120.6, 131.7, 142.5, 142.6, 143.2, 168.5; **MS** (APCI) m/z

 $[M+H]^+$ calculated for $C_{11}H_{12}N_3O_2S$: 250.1; found: 249.8; **Anal. Calcd.**: C, 53.00; H, 4.45; N, 16.86; found C, 52.85; H, 4.65; N, 16.74.

N-(2,3-dimethoxybenzyl)-3-methylpyridin-2-amine (Entry 19, in Table 1)

Yield: 83 mg, 32%; white solid, mp 84-86°C; **IR** (KBr): v (cm⁻¹) 3417, 3008, 2963, 2936, 2899, 2836, 1598, 1507, 1480, 1275, 1060; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 2.11 (s, 3H, CH₃), 3.79 (s, 6H, 2OCH₃), 4.60 (d, J = 5.8 Hz, 2H, CH₂), 6.24 (t, J = 5.6 Hz, 1H, NH), 6.43 (m, 1H, Py), 6.81 (d, J = 7.4 Hz, 1H, Ar), 6.88 (d, J = 7.3 Hz, 1H, Ar), 6.94 (t, J = 7.9 Hz, 1H, Ar), 7.22 (d, J = 6.4 Hz, Py), 7.80 (d, J = 3.8 Hz, 1H, Py); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 17.0, 38.9, 55.7, 59.9, 111.1, 111.8, 116.6, 119.7, 123.6, 134.6, 136.4, 144.9, 146.3, 152.2, 156.8; **MS** (APCI) m/z [M+H]⁺ calculated for C₁₅H₁₉N₂O₂: 259.1; found: 259.0; **Anal. Calcd.**: C, 69.74; H, 7.02; N, 10.84; found C, 69.53; H, 7.13; N, 10.67.

4-((dimethylamino)methyl)-N-(3,4,5-trimethoxybenzyl)pyridin-2-amine (Entry 21, in Table 1)

Yield: 315 mg, 95%; yellowish solid, mp $102\text{-}104^{\circ}\text{C}$; **IR** (KBr): v (cm⁻¹) 3411, 3217, 3076, 2997, 2963, 2944, 2855, 2813, 2776, 1599, 1576, 1503, 1454, 1250, 1158; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 2.11 (s, 6H, 2NCH₃), 3.63 (s, 3H, CH₃), 3073 (s, 6H, 2CH₃), 4.42 (d, J = 5.5 Hz, 2H, CH₂), 6.43 (d, J = 5.0 Hz, 1H, Py), 6.50 (s, 1H, Py), 6.67 (s, 2H, Ar), 6.90 (t, J = 4.8 Hz, 1H, NH), 7.90 (d, J = 5.2 Hz, 1H, Py); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 44.7, 45.1, 55.8, 60.0, 62.7, 104.6, 107.7, 112.4, 136.2, 136.4, 147.4, 148.4, 152.8, 159.1; **MS** (APCI) m/z [M+H]⁺ calculated for C₁₈H₂₆N₃O₃: 332.2; found: 332.0; **Anal. Calcd.**: C, 65.23; H, 7.60; N, 12.68; found C, 65.11; H, 7.75; N, 12.60.

N-benzyl-4-(4-methyl-4*H*-1,2,4-triazol-3-yl)pyridin-2-amine (Entry 23, in Table 1)

Yield: 111 mg, 42%; yellowish solid, mp 146-148°C; **IR** (KBr): ν (cm⁻¹) 3273, 3181, 3131, 3105, 3065, 3036, 2977, 2918, 1615, 1549, 1497, 1194; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 3.72 (s, 3H, NCH₃), 4.53 (d, J = 5.8 Hz, 2H, CH₂), 6.84 (d, J = 5.2 Hz, 1H, Py), 6.88 (s, 1H, Py), 7.22 (t, J = 7.1 Hz, 1H, Ar), 7.31 (m, 2H, Ar), 7.35 (m, 3H, NH + Ar), 8.11 (d, J = 5.2 Hz, 1H, Py), 8.58 (s, 1H, Het); ¹³C **NMR** (125 MHz, DMSO-d₆): δ (ppm) 32.2, 44.3, 106.9, 110.3, 126.7, 127.3, 128.3, 135.0, 140.4, 146.7, 148.5, 151.9, 159.1; **MS** (APCI) m/z [M+H]⁺ calculated for C₁₅H₁₆N₅: 266.1; found: 266.1; **Anal. Calcd.**: C, 67.90; H, 5.70; N, 26.40; found C, 67.75; H, 5.85; N, 26.30.

N-(2-chlorobenzyl)-4-(4-methyl-4H-1,2,4-triazol-3-yl)pyridin-2-amine (Entry 24, in Table 1)

Yield: 75 mg, 25%; yellowish solid, mp 186-188°C; **IR** (KBr): v (cm⁻¹) 3293, 3250, 3095, 3046, 2941, 2915, 1618, 1553, 1500, 1286, 1197, 1040; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 3.75 (s, 3H, NCH₃), 4.60 (d, J = 5.8 Hz, 2H, CH₂), 6.87 (d, J = 5.2 Hz, 1H, Py), 6.96 (s, 1H, Py), 7.28 (m, 2H, Ar), 7.39 (m, 2H, Ar), 7.44 (d, J = 7.7 Hz, 1H, Py), 8.09 (d, J = 5.2 Hz, 1H, NH), 8.59 (s, 1H, Het); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 32.3, 42.1, 107.2, 110.6, 127.2, 128.5, 128.8, 129.2, 132.3, 135.1, 137.4, 146.8, 148.4, 151.8, 158.8; **MS** (APCI) m/z [M+H]⁺ calculated for C₁₅H₁₅ClN₅: 300.1; found: 300.0; **Anal. Calcd.**: C, 60.10; H, 4.71; N, 23.36; found C, 60.05; H, 4.85; N, 23.23.

(3-chloro-6-(4-fluorobenzylamino)pyridin-2-yl)methanol (Entry 27, in Table 1)

Yield: 198 mg, 74%; yellow solid, mp 58-60°C; **IR** (KBr): v (cm⁻¹) 3332, 3046, 2918, 2866, 1595, 1507, 1408, 1220, 1076; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 4.43 (s, 2H, CH₂), 4.48 (d, J = 5.6, 2H, CH₂), 4.77 (br. s, 1H, OH), 6.44 (d, J = 8.6 Hz, 1H, Ar), 7.12 (t, J = 8.8 Hz, 2H, Ar), 7.30 (t, J = 5.3 Hz, 1H, NH), 7.38 (m, 3H, Ar); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 43.7, 61.7, 108.3, 115.0 (d, J = 20 Hz), 115.2, 129.3 (d, J = 9 Hz), 136.5 (d, J = 2.5 Hz), 137.9, 138.1, 153.4, 156.6, 161.2 (d, J = 243 Hz); **MS** (APCI) m/z [M+H]⁺ calculated for C₁₃H₁₃ClFN₂O: 267.1; found: 267.2; **Anal. Calcd.**: C, 58.55; H, 4.54; N, 10.50; found C, 58.45; H, 4.66; N, 10.34.

N-(3,4,5-trimethoxybenzyl)pyridin-3-amine (Entry 30, in Table 1)

Yield: 230 mg, 84%; brownish solid, mp 91-93°C; **IR** (KBr): ν (cm⁻¹) 3257, 3112, 3056, 3000, 2931, 2832, 2826, 1595, 1540, 1507, 1467, 1418, 1422, 1337, 1233, 1130, 1010; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 3.65 (s, 3H, CH₃), 3.74 (s, 6H, 2CH₃), 4.23 (d, J = 5.5 Hz, 2H, CH₂), 6.46 (t, J = 5.2 Hz, 1H, NH), 6.72 (s, 2H, Ar), 6.93 (m, 1H, Py), 7.04 (m, 1H, Py), 7.78 (s, 1H, Py), 8.06 (s, 1H, Py); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 46.6, 55.8, 60.0, 104.6, 117.9, 123.6, 135.4, 135.7, 136.4, 137.2, 144.8, 153.0; **MS** (APCI) m/z [M+H]⁺ calculated for C₁₅H₁₉N₂O₃: 275.1; found: 275.0; **Anal. Calcd.**: C, 65.68; H, 6.61; N, 10.21; found C, 65.55; H, 6.75; N, 10.14.

N-((2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-methylpyridin-3-amine (Entry 31, in Table 1)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & & \\ & \\ & & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ &$$

Yield: 92 mg, 36%; yellowish solid, mp 103-105°C; **IR** (KBr): v (cm⁻¹) 3434, 3030, 2993, 2938, 2871, 1579, 1506, 1467, 1302, 1277, 1060; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 2.35 (s, 3H, CH₃), 4.18 (s, 4H, 2CH₂), 4.22 (d, J = 5.9 Hz, 2H, CH₂), 5.85 (d, J = 5.7 Hz, 1H, NH), 6.64 (d, J = 8.1 Hz, 1H, Py), 6.80 (m, 3H, Ar), 6.88 (m, 1H, Py), 7.63 (d, J = 4.6 Hz, 1H, Py); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 21.0, 45.3, 64.0, 64.1, 115.3, 115.6, 116.9, 119.8, 121.7, 132.8, 135.6, 142.0, 142.2, 143.3, 143.7; **MS** (APCI) m/z [M+H]⁺ calculated for C₁₅H₁₇N₂O₂: 257.1; found: 257.0; **Anal. Calcd.**: C, 70.29; H, 6.29; N, 10.93; found C, 70.12; H, 6.45; N, 10.86.

Methyl 5-(benzylamino)nicotinate (Entry 33, in Table 1)

Yield: 177 mg, 73%; whitish solid, mp 128-130°C; **IR** (KBr): ν (cm⁻¹) 3253, 3049, 3007, 2951, 2860, 1717, 1597, 1418, 1315, 1224, 1099; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 3.80 (s, 3H, CH₃), 4.35 (d, J = 5.2 Hz, 2H, CH₂), 6.89 (t, J = 5.2 Hz, 1H, NH), 7.23 (t, J = 7.1 Hz, 1H, Ar), 7.26 – 7.40 (m, 5H, 4Ar + 1Py), 8.22 (s, 1H, Py), 8.30 (s, 1H, Py); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 46.0, 52.2, 117.6, 125.6, 127.0, 127.3, 128.5, 137.3, 139.1, 139.3, 144.6, 165.9; **MS** (APCI) m/z [M+H]⁺ calculated for $C_{14}H_{15}N_2O_2$: 242.1; found: 243.0; **Anal. Calcd.**: C, 69.41; H, 5.82; N, 11.56; found C, 69.33; H, 5.96; N, 11.50.

N-(2,3-dimethoxybenzyl)-6-(methylsulfonyl)pyridin-3-amine (Entry 35, in Table 1)

$$-0 \longrightarrow HN \longrightarrow S \longrightarrow S$$

Yield: 161 mg, 50%; white solid, mp 142-144°C; **IR** (KBr): v (cm⁻¹) 3243, 3078, 3003, 2934, 2835, 1579, 1477, 1302, 1161, 1125; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 3.09 (s, 3H, SO₂CH₃), 3.78 (s, 3H, OCH₃), 3.80 (s, 3H, OCH₃), 4.36 (d, J = 5.6 Hz, 2H, CH₂), 6.86 (d, J = 6.9 Hz, 1H, Py), 7.01 (m, 3H, Ar), 7.35 (t, J = 5.4, 1H, NH), 7.69 (d, J = 8.6 Hz, Py), 8.09 (d, J = 2.2 Hz, 1H, Py); ¹³C **NMR** (125 MHz, DMSO-d₆): δ (ppm) 40.7, 40.9, 55.8, 60.4, 112.2, 116.5, 120.2, 122.6, 124.1, 131.5, 135.2, 143.6, 146.7, 147.6, 152.5; **MS** (APCI) m/z [M+H]⁺ calculated for C₁₅H₁₉N₂O₄S: 323.1; found: 323.1; **Anal. Calcd.**: C, 55.89; H, 5.63; N, 8.69; found C, 55.80; H, 5.70; N, 8.59.

N-(4-fluorobenzyl)-1,3-dimethyl-1H-pyrazolo[3,4-b]pyridin-5-amine (Entry 40, in Table 1)

Yield: 59 mg, 22%; white solid, mp 96-98°C; **IR** (KBr): ν (cm⁻¹) 3290, 3046, 2928, 2839, 1602, 1507, 1477, 1224, 1151; ¹**H NMR** (500 MHz, DMSO-d₆): δ (ppm) 2.64 (s, 3H, CH₃), 3.86 (3H, NCH₃), 4.29 (d, J = 5.9 Hz, 2H, CH₂), 6.25 (t, J = 5.8 Hz, 1H, NH), 7.04 (d, J = 2.2 Hz, 1H, Het), 7.15 (t, J = 8.9 Hz, 2H, Ar), 7.44 (m, 2H, Ar), 8.16 (d, J = 2.4 Hz, 1H, Het); ¹³**C NMR** (125 MHz, DMSO-d₆): δ (ppm) 12.1, 33.2, 46.5, 106.3, 114.4, 115.1 (d, J = 21 Hz), 129.4 (d, J = 7.5 Hz), 135.9 (d, J = 3.8 Hz), 137.2, 139.7, 140.3, 144.3, 145.8, 161.3 (d, J = 239 Hz); **MS** (APCI) m/z [M+H]⁺ calculated for C₁₅H₁₆FN₄: 271.1; found: 271.0; **Anal. Calcd.**: C, 66.65; H, 5.59; N, 20.73; found C, 66.60; H, 5.73; N, 20.55.

LC-MS spectra of the crude mixtures.

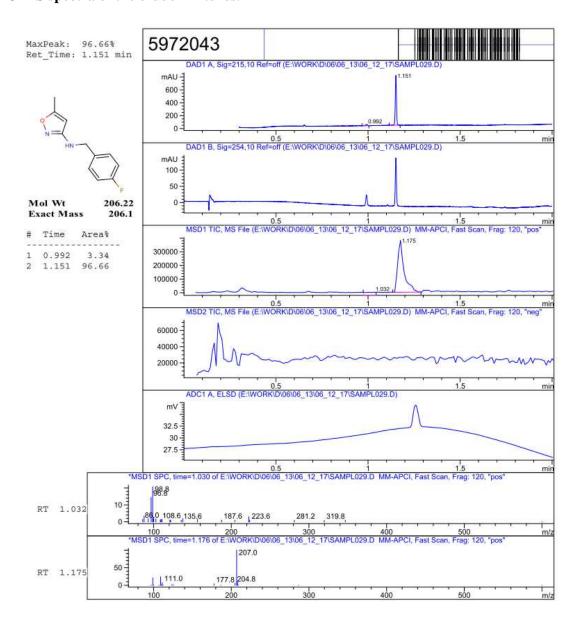


Figure S1. Entry 1, in Table 1: peak was assigned to the product (rt 1.15 min).

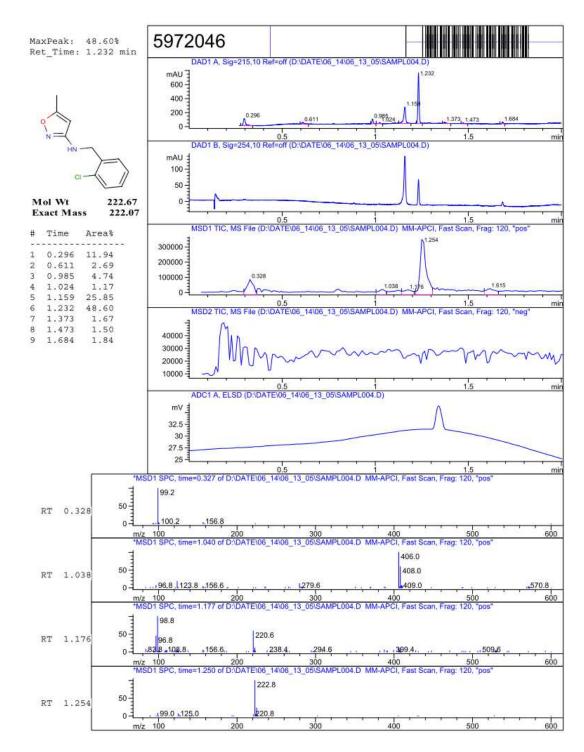


Figure S2. Entry 2, in Table 1: peaks were assigned to the starting amine (rt 0.3 min), the aldehyde (rt 0.99 min), the tertiary amine (rt1.02 min), the intermediate imine (rt 1.16 min), and the product (rt 1.23 min).

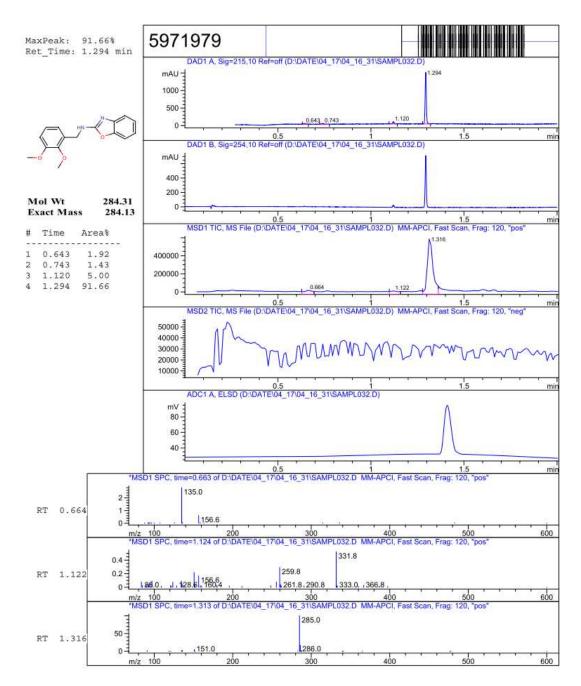


Figure S3. Entry 3, in Table 1: peaks were assigned to the starting amine (rt 0.64 min) and the product (rt 1.29 min).

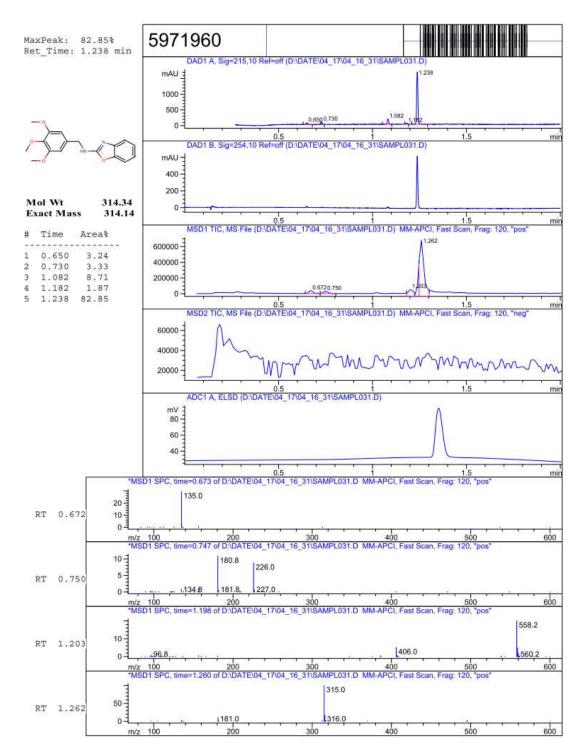


Figure S4. Entry 4, in Table 1: peaks were assigned to the starting amine (rt 0.65 min), the aldehyde (rt 1.08 min) and the product (rt 1.23 min).

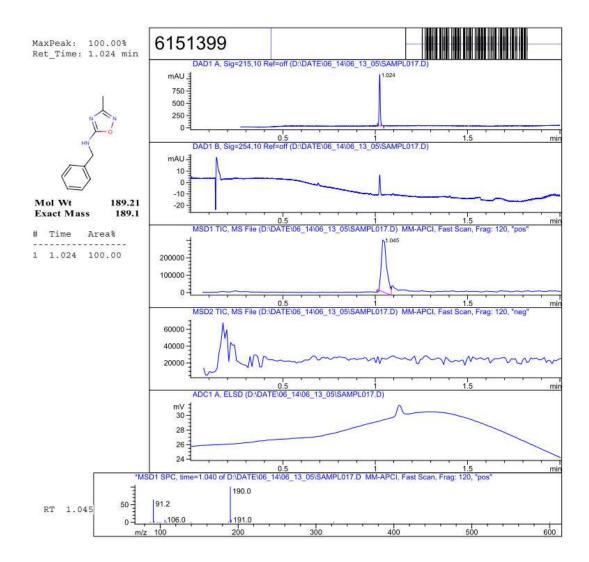


Figure S5. Entry 5, in Table 1: peak was assigned to the product (rt 1.02 min).

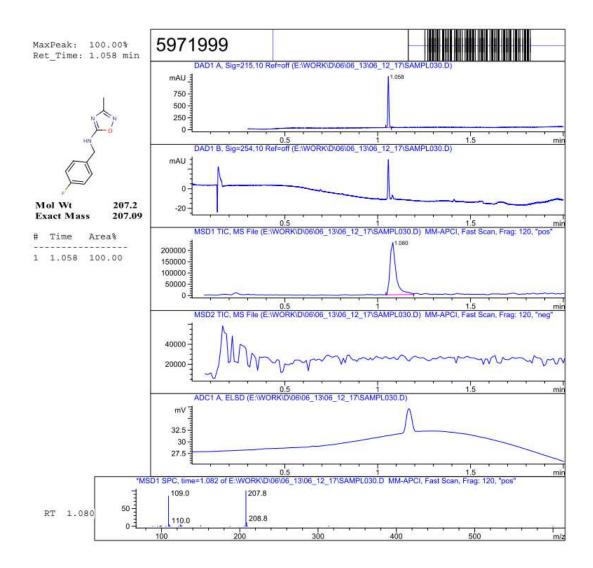


Figure S6. Entry 6, in Table 1: peak was assigned to the product (rt 1.06 min).

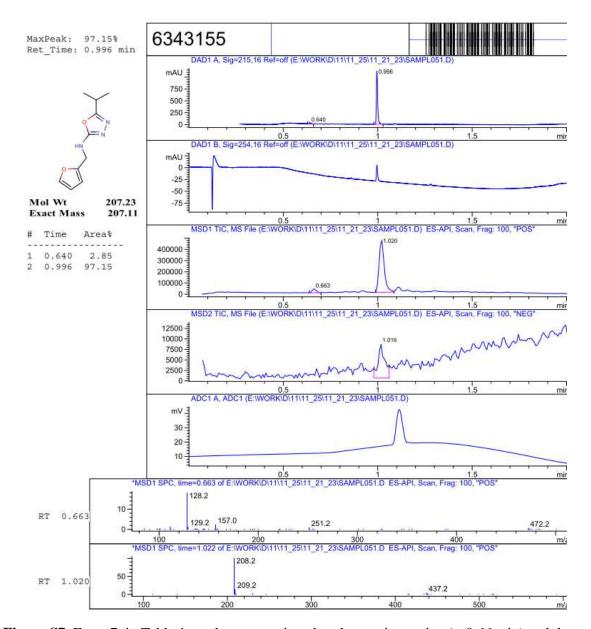


Figure S7. Entry 7, in Table 1: peaks were assigned to the starting amine (rt 0.66 min) and the product (rt 1.00 min).

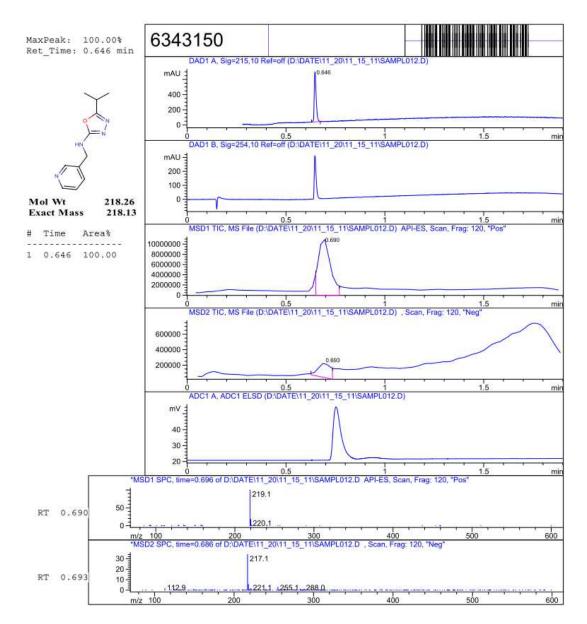


Figure S8. Entry 8, in Table 1: peak was assigned to the product (rt 0.65 min).

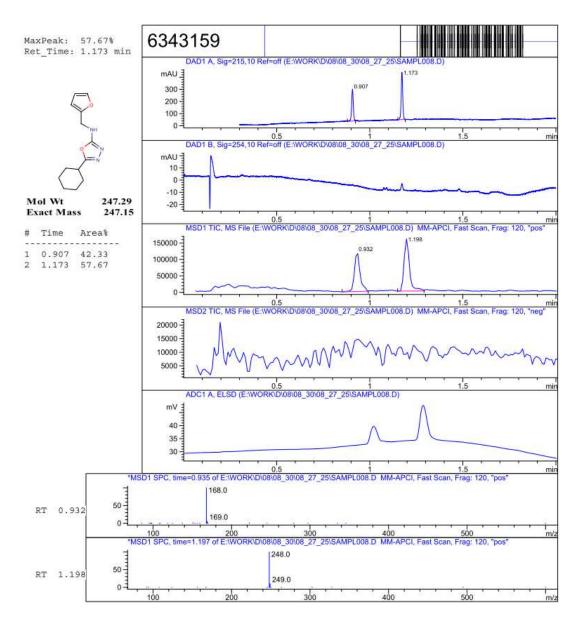


Figure S9. Entry 9, in Table 1: peaks were assigned to the starting amine (rt 0.91 min) and the product (rt 1.17 min).

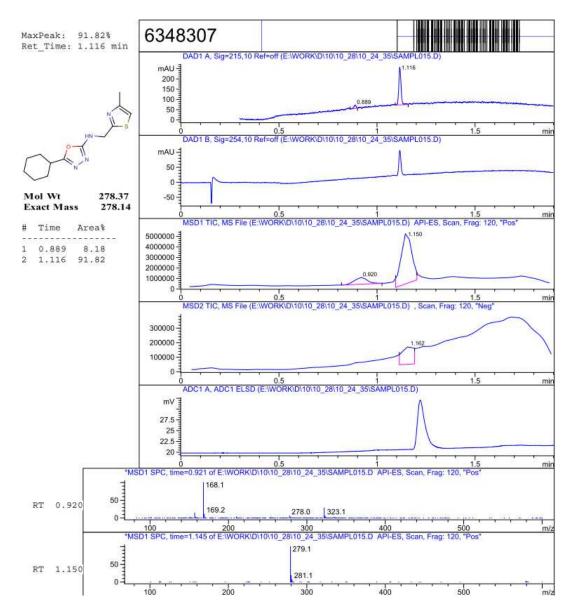


Figure S10. Entry 10, in Table 1: peaks were assigned to the starting amine (rt 0.89 min) and the product (rt 1.12 min).

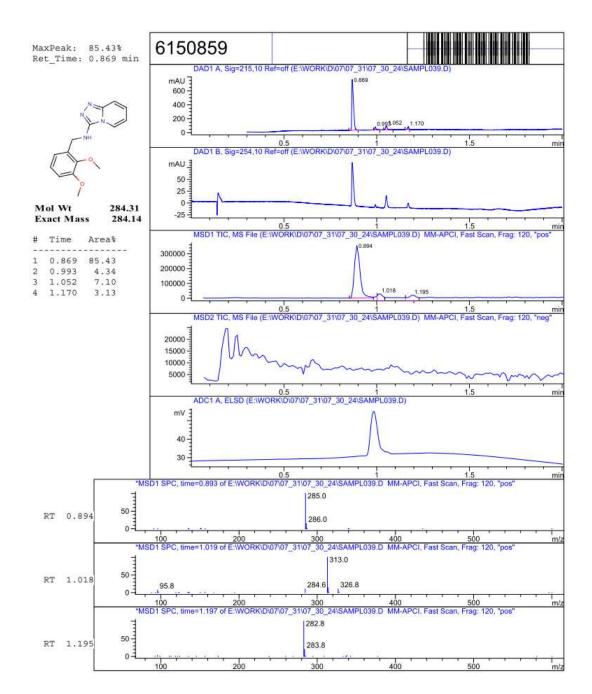


Figure S11. Entry 11, in Table 1: peak was assigned to the product (rt 0.87 min).

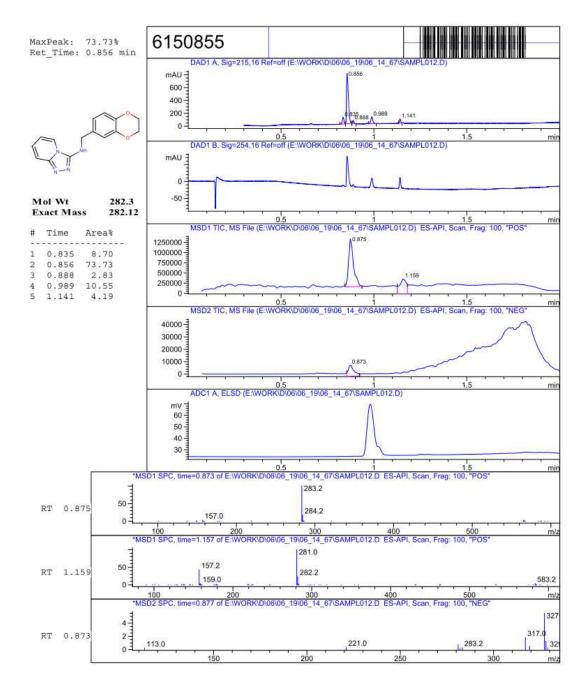


Figure S12. Entry 12, in Table 1: peaks were assigned to the product (rt 0.86 min), the aldehyde (rt 0.99 min), and the intermediate imine (rt 1.14 min).

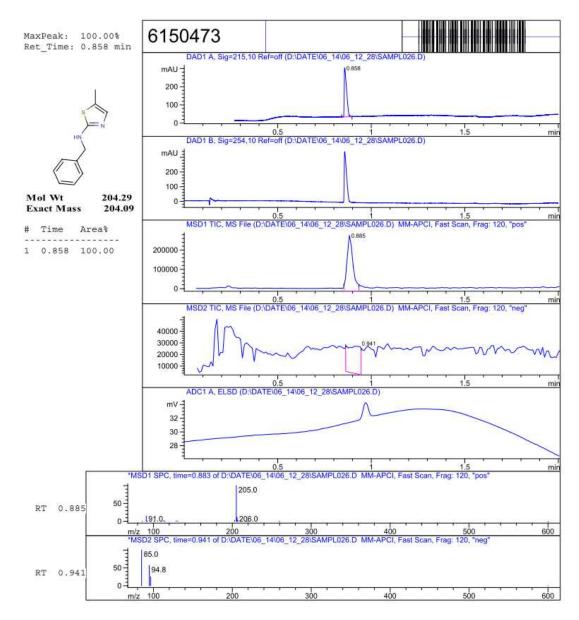


Figure S13. Entry 13, in Table 1: peak was assigned to the product (rt 0.86 min).

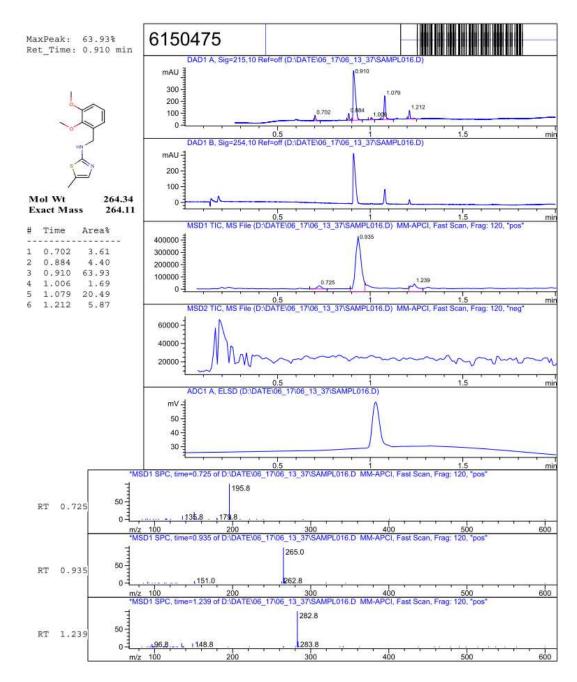


Figure S14. Entry 14, in Table 1: peaks were assigned to the product (rt 0.91 min) and the aldehyde (rt 1.08 min).

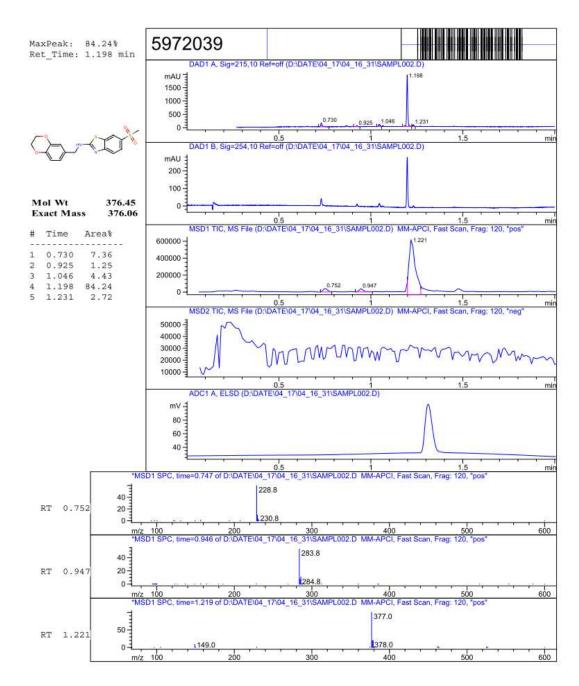


Figure S15. Entry 15, in Table 1: peaks were assigned to the starting amine (rt 0.73 min), the aldehyde (1.05 min), and the product (rt 1.2 min).

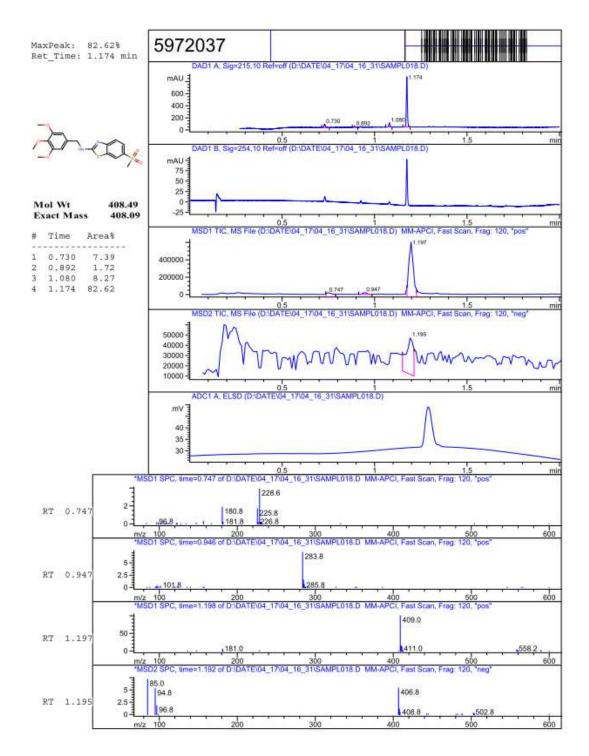


Figure S 16. Entry 16, in Table 1: peaks were assigned to the starting amine (rt 0.73 min), the aldehyde (1.08 min), and the product (rt 1.17 min).

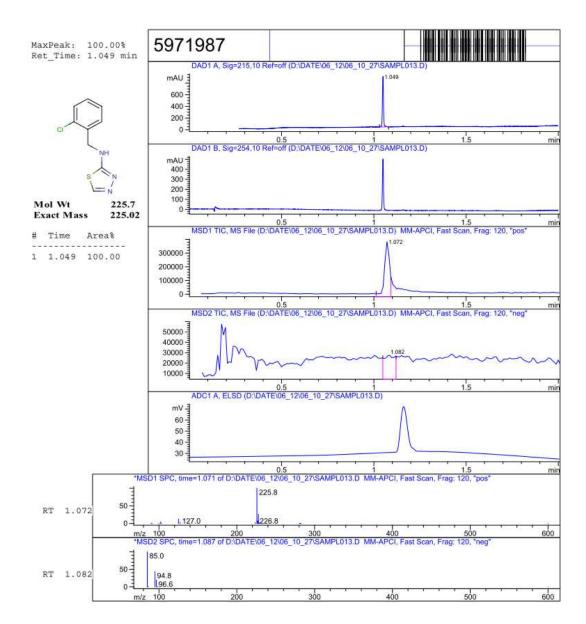


Figure S17. Entry 17, in Table 1: peak was assigned to the product (rt 1.05 min).

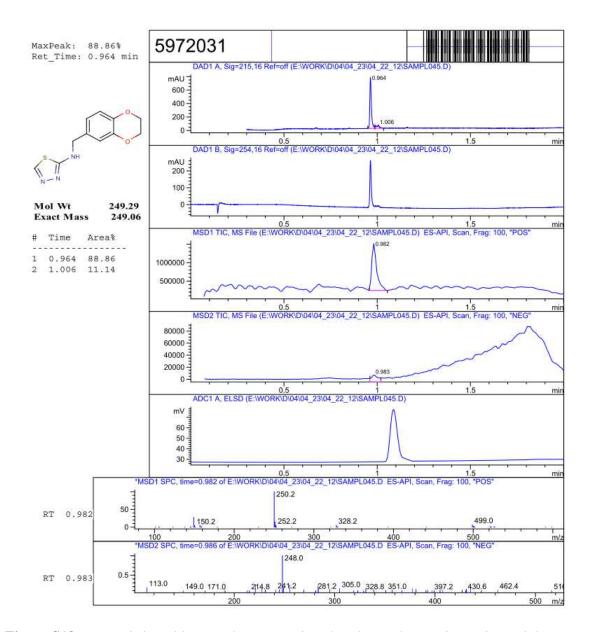


Figure S18. Entry 18, in Table 1: peaks were assigned to the product (rt 0.96 min) and the aldehyde (rt 1.01 min).

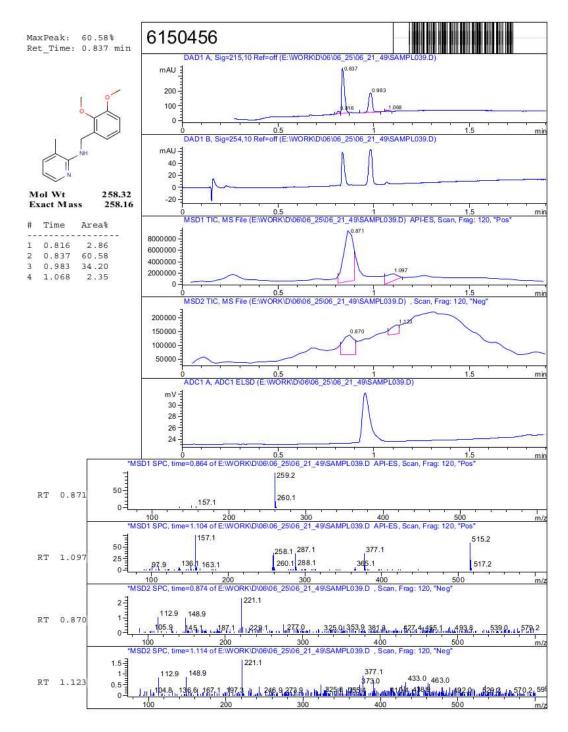


Figure S19. Entry 19, in Table 1: peaks were assigned to the product (rt 0.87 min), the aldehyde (rt 0.98 min), and the intermediate imine (rt 1.07 min).

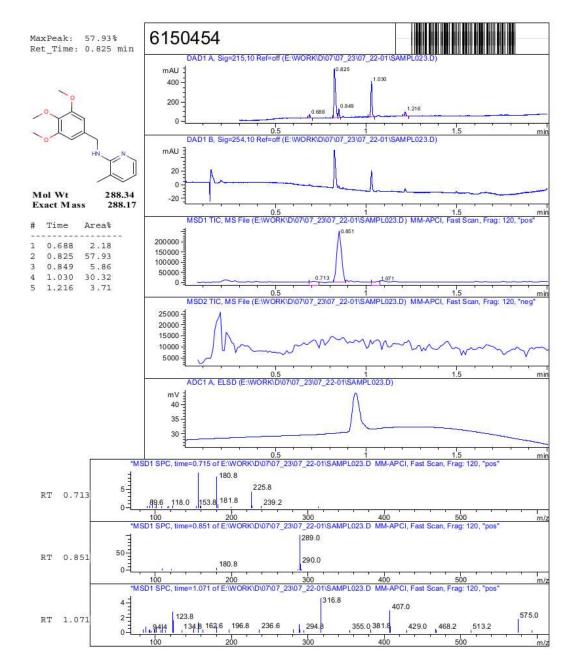


Figure S20. Entry 20, in Table 1: peaks were assigned to the product (rt 0.83 min) and the aldehyde (rt 1.03 min).

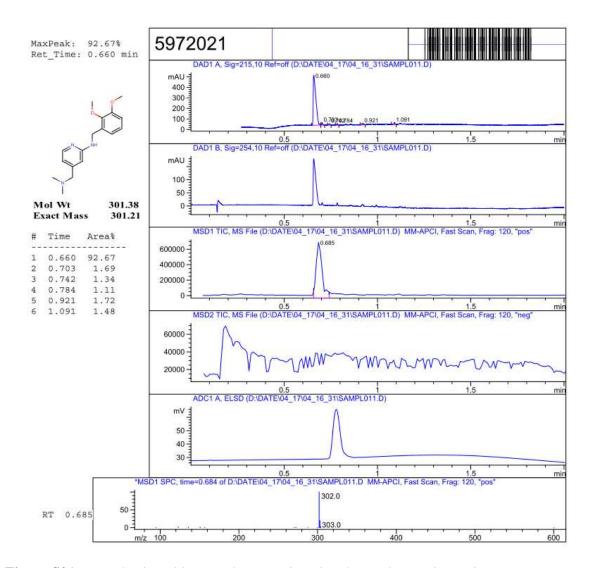


Figure S21. Entry 21, in Table 1: peak was assigned to the product (rt 0.66 min).

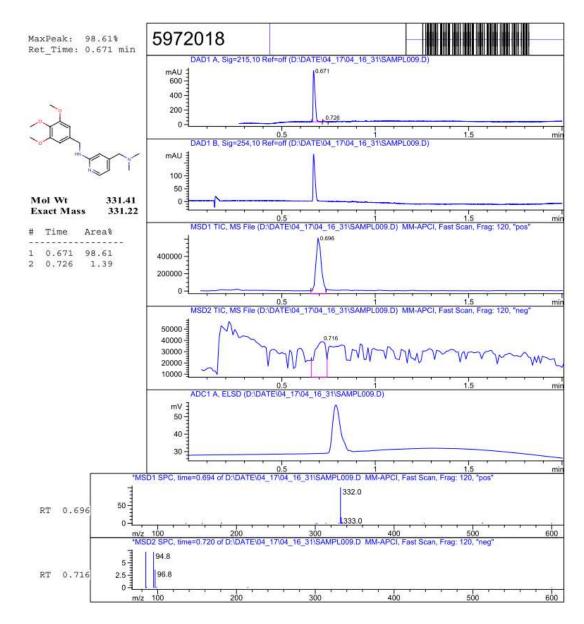


Figure S22. Entry 22, in Table 1: peak was assigned to the product (rt 0.67 min).

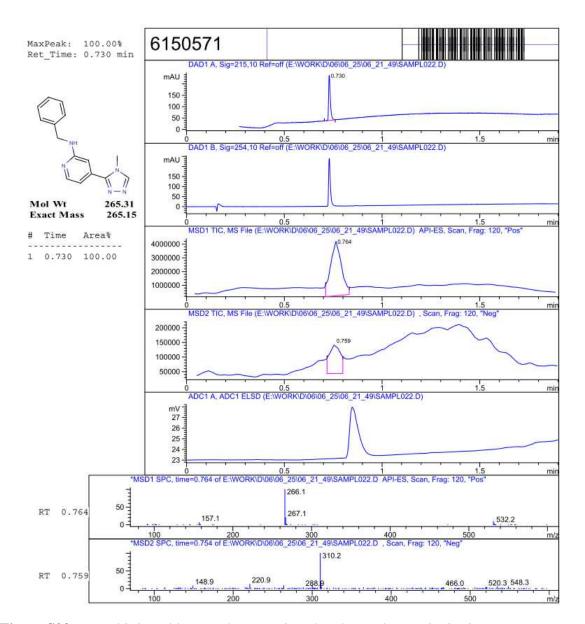


Figure S23. Entry 23, in Table 1: peak was assigned to the product (rt 0.73 min).

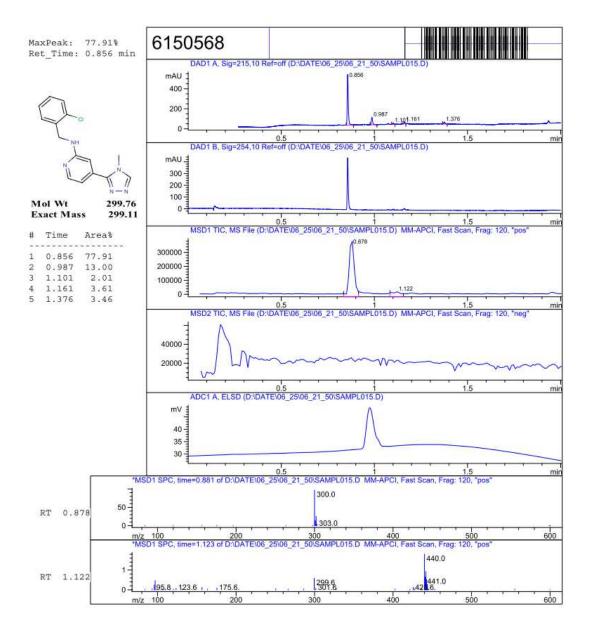


Figure S24. Entry 24, in Table 1: peaks were assigned to the product (rt 0.86 min), the aldehyde (0.99 min), and the tertiary amine (1.1 min).

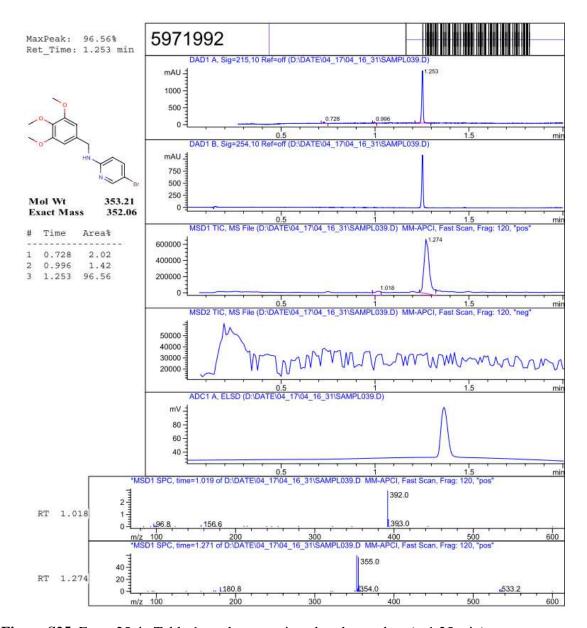


Figure S25. Entry 25, in Table 1: peak was assigned to the product (rt 1.25 min).

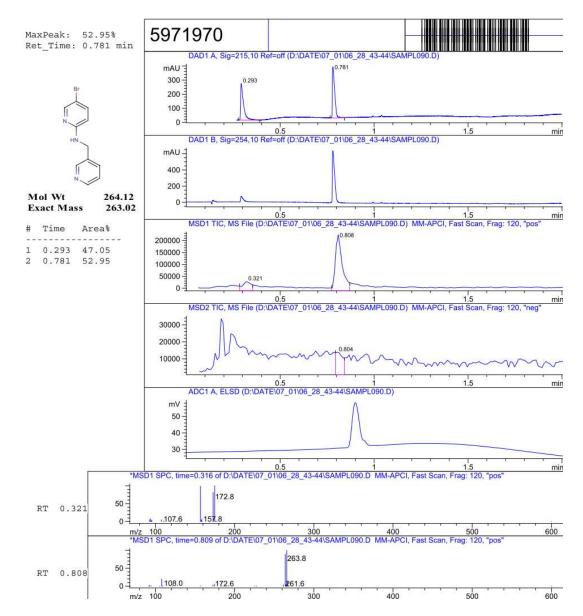


Figure S26. Entry 26, in Table 1: peaks were assigned to the starting amine (rt 0.29 min) and the product (rt 0.78 min).

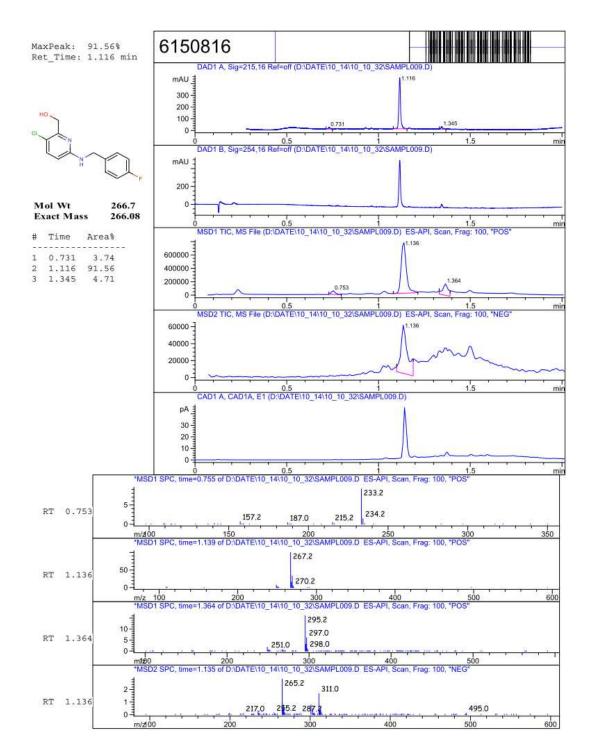


Figure S27. Entry 27, in Table 1: peak was assigned to the product (rt 1.12 min).

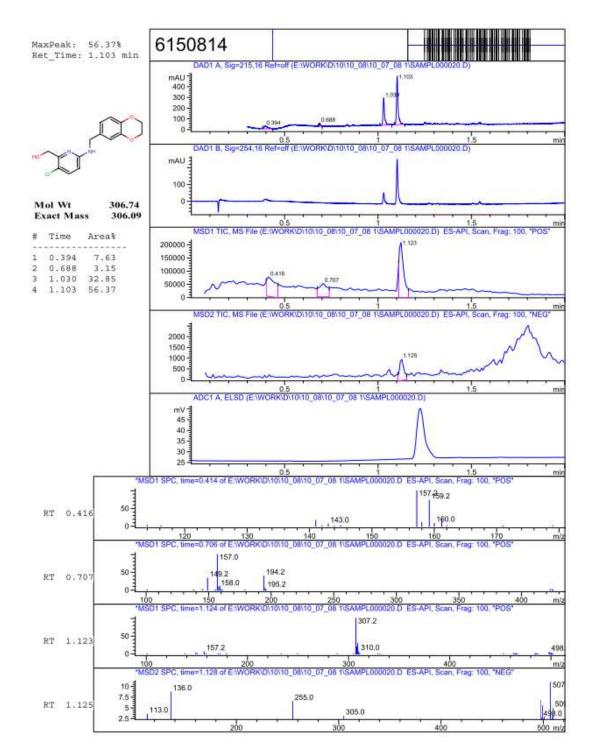


Figure S28. Entry 28, in Table 1: peaks were assigned to the aldehyde (rt 1.03 min) and the product (rt 1.1 min).

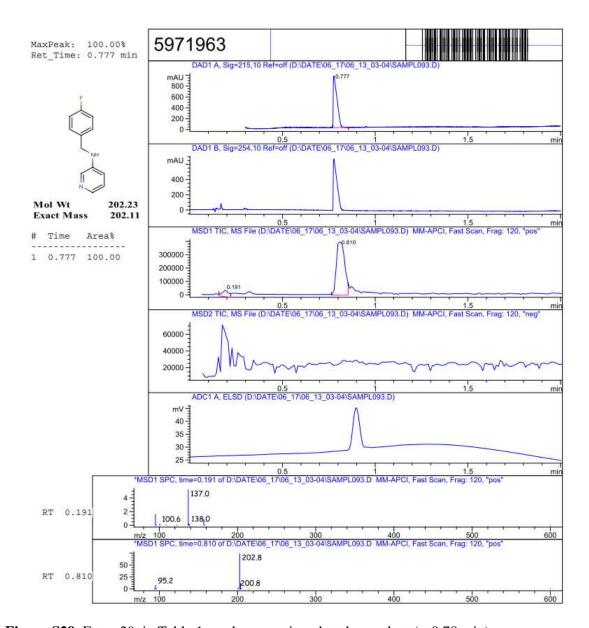


Figure S29. Entry 29, in Table 1: peak was assigned to the product (rt 0.78 min).

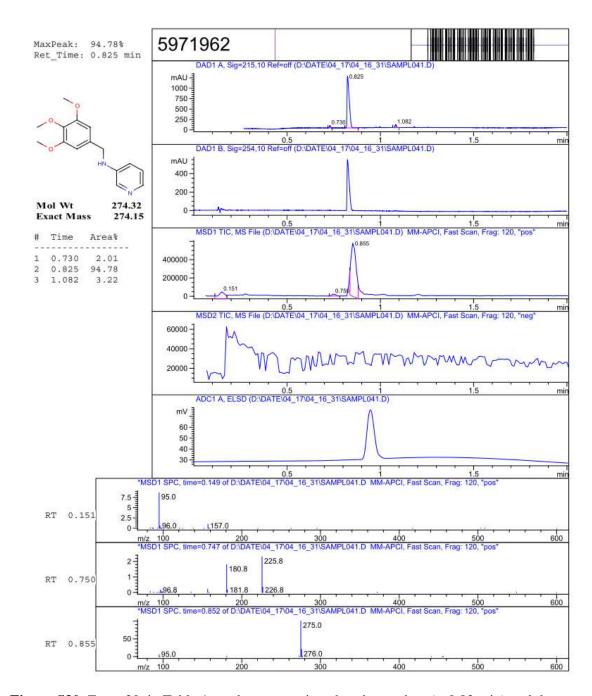


Figure S30. Entry 30, in Table 1: peaks were assigned to the product (rt 0.83 min) and the aldehyde (rt 1.08 min).

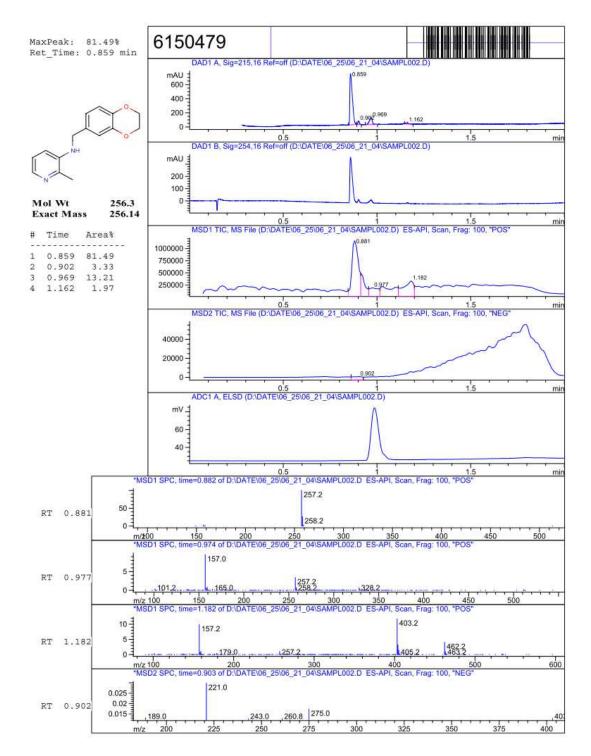


Figure S31. Entry 31, in Table 1: peaks were assigned to the product (rt 0.86 min), the aldehyde (rt 0.97 min), and the tertiary amine (rt 1.16 min).

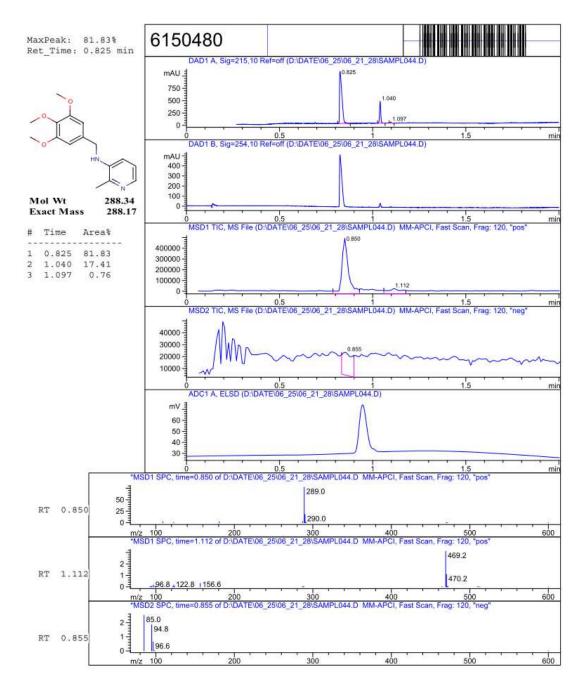


Figure S32. Entry 32, in Table 1: peaks were assigned to the product (rt 0.83 min), the aldehyde (rt 1.04 min), and the tertiary amine (rt 1.1 min).

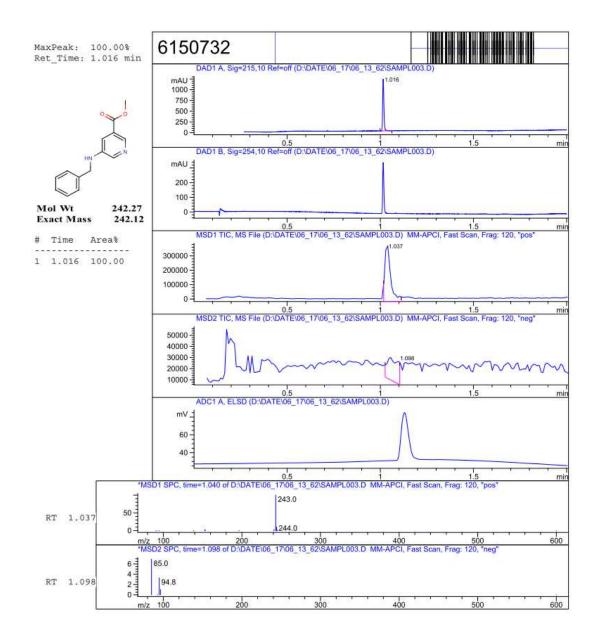


Figure S33. Entry 33, in Table 1: peak was assigned to the product (rt 1.02 min).

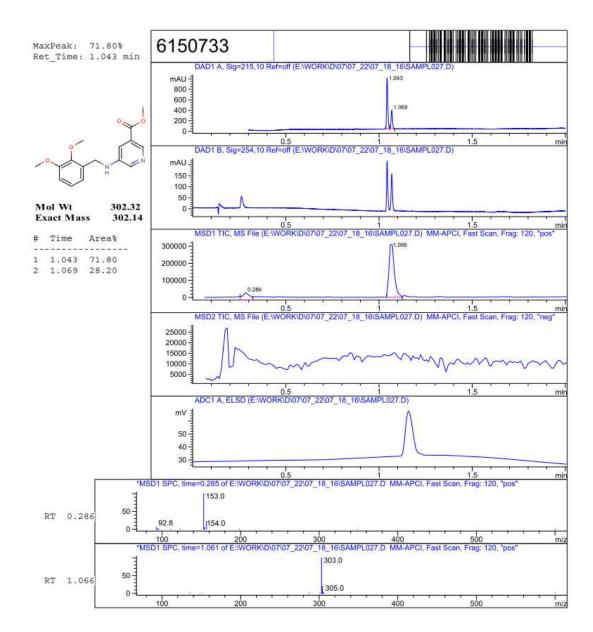


Figure S34. Entry 34, in Table 1: peaks were assigned to the starting amine (rt 0.26 min), the product (rt 1.04 min), and the aldehyde (rt 1.07 min).

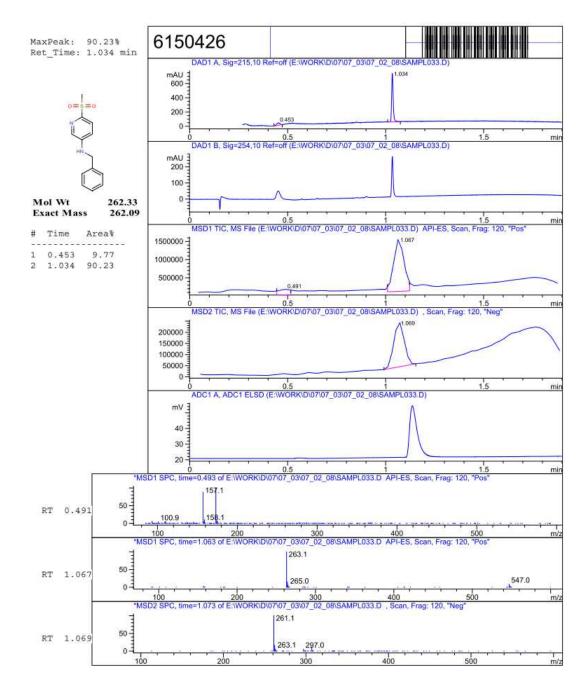


Figure S35. Entry 35, in Table 1: peaks were assigned to the starting amine (rt 0.45 min) and the product (rt 1.03 min).

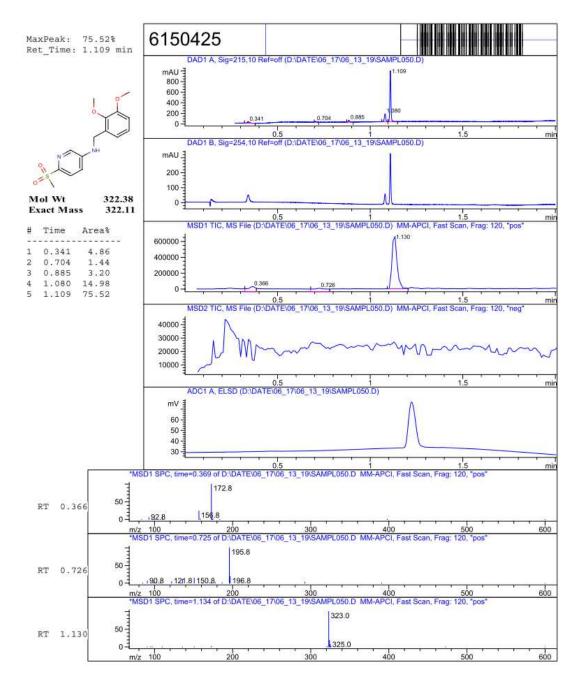


Figure S36. Entry 36, in Table 1: peaks were assigned to the starting amine (rt 0.34 min), the aldehyde (rt 1.08 min), and the product (rt 1.11 min).

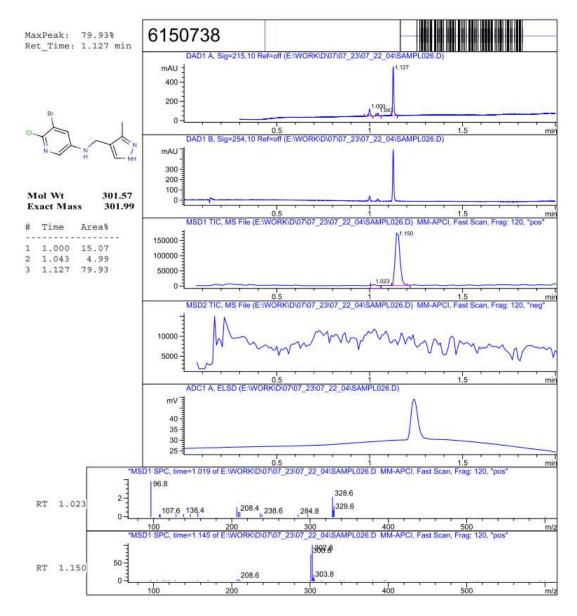


Figure S37. Entry 37, in Table 1: peaks were assigned to the side product (rt 1.00 min) and the product (rt 1.13 min).

Possible structure of the side product

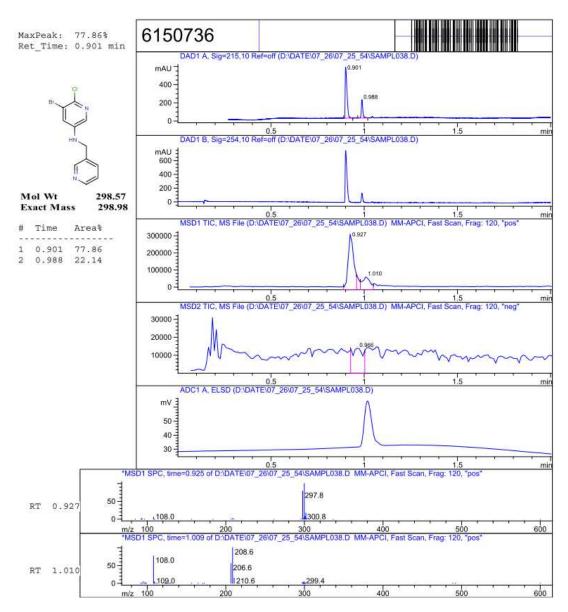


Figure S38. Entry 38, in Table 1: peaks were assigned to the product (rt 0.90 min) and the starting amine (rt 0.99 min).

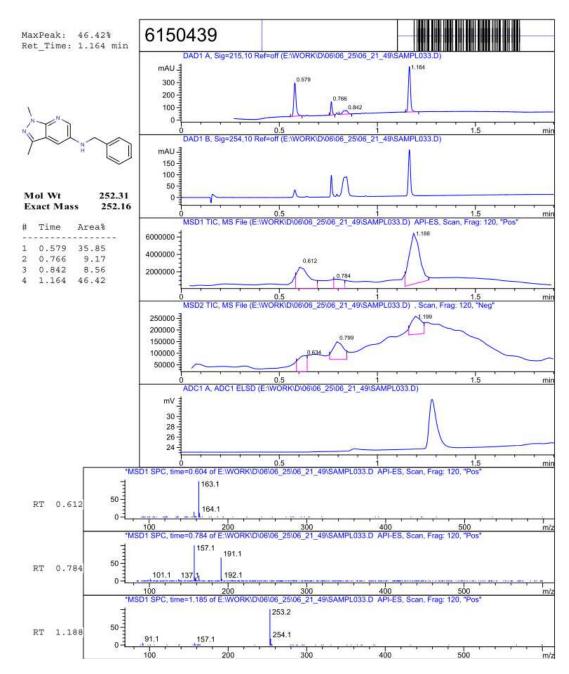


Figure S39. Entry 39, in Table 1: peaks were assigned to the starting amine (rt 0.61 min), the acylated starting amine (rt 0.77 min), the aldehyde (rt 0.84 min), and the product (rt 1.16 min).

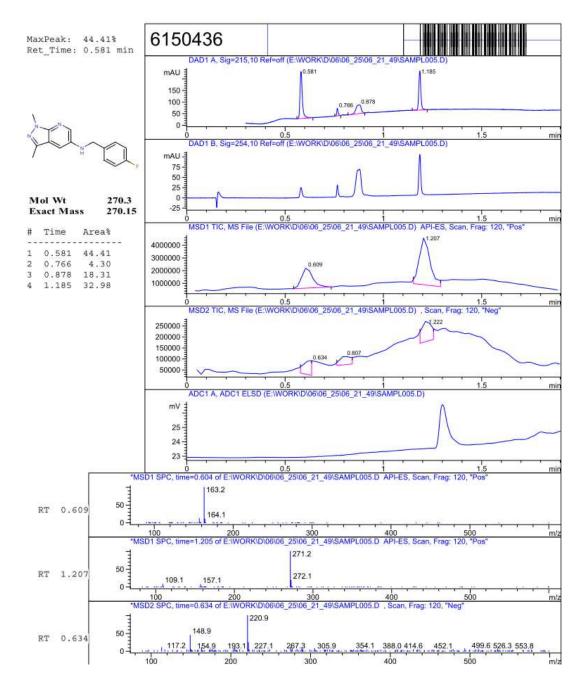
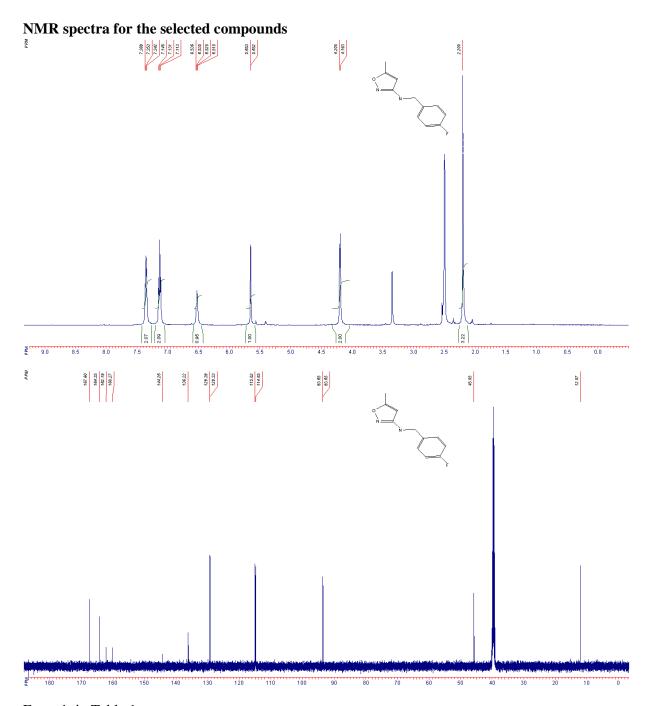
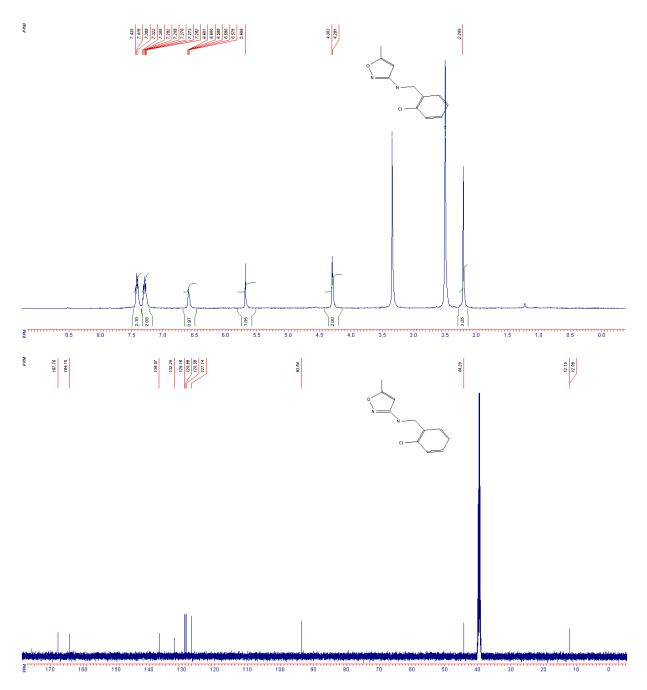


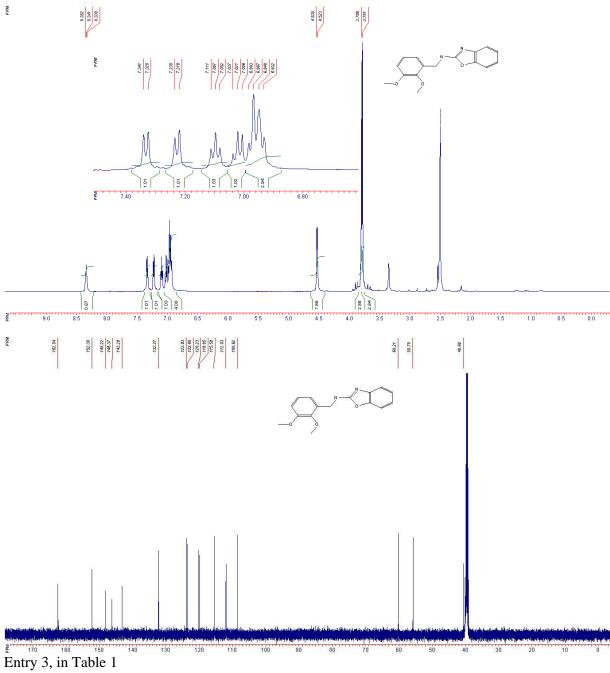
Figure S40. Entry 40, in Table 1: peaks were assigned to the starting amine (rt 0.58 min), the aldehyde (rt 0.88 min), and the product (rt 1.19g min).

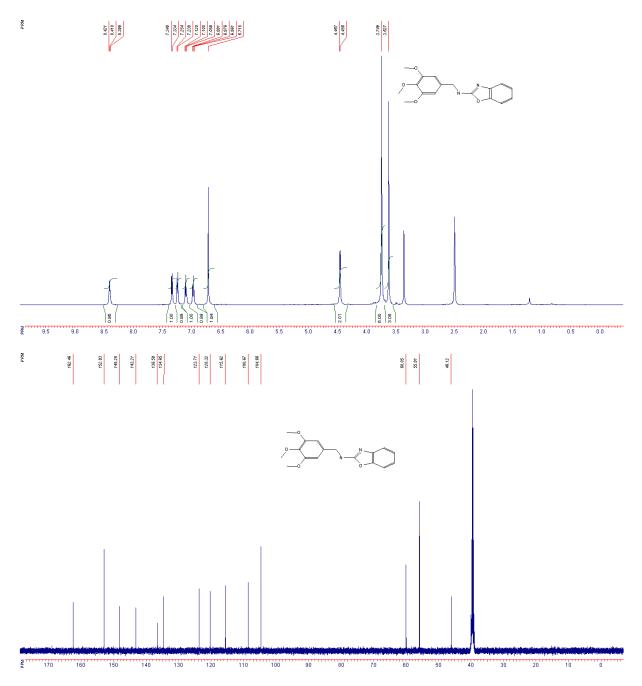


Entry 1, in Table 1

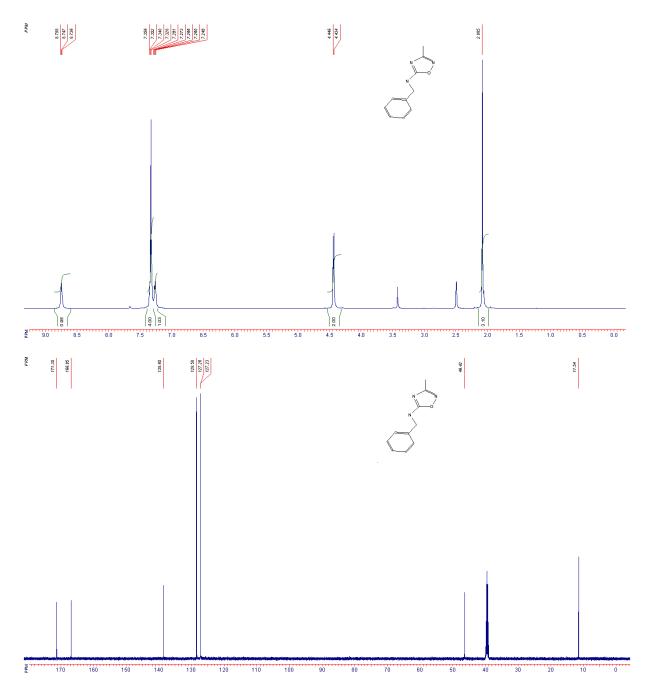


Entry 2, in Table 1

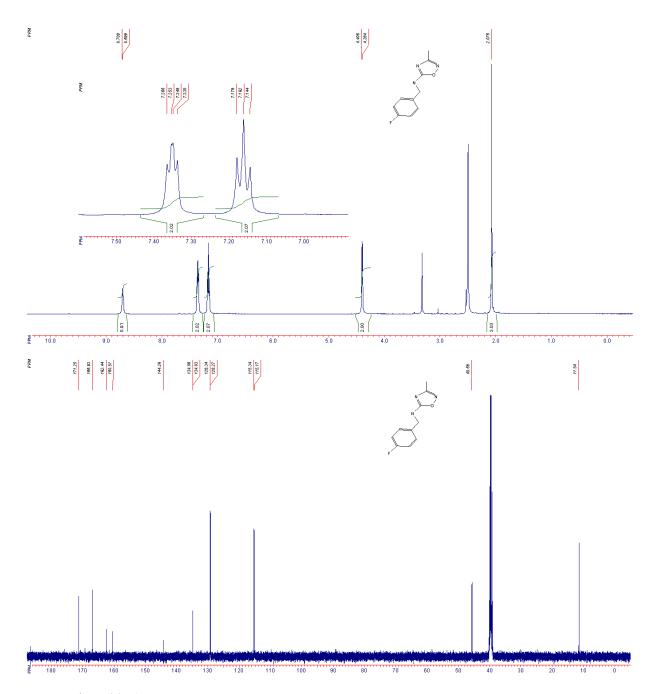




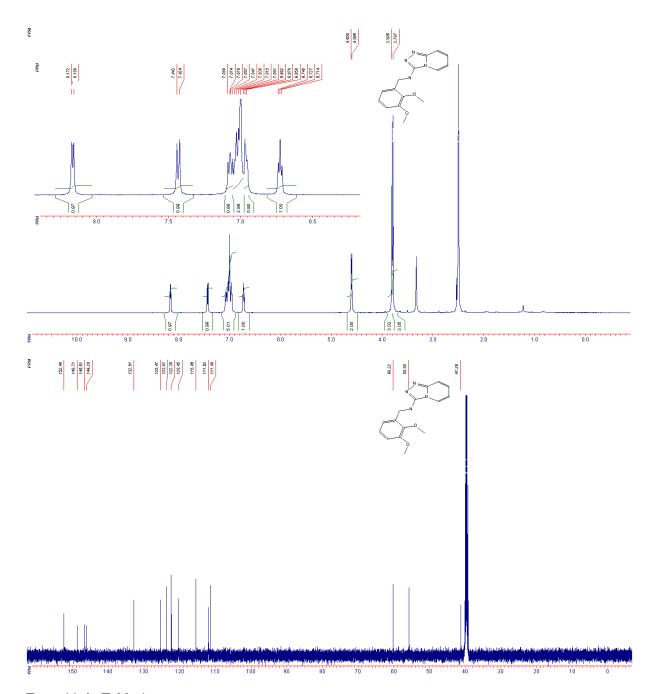
Entry 4, in Table 1



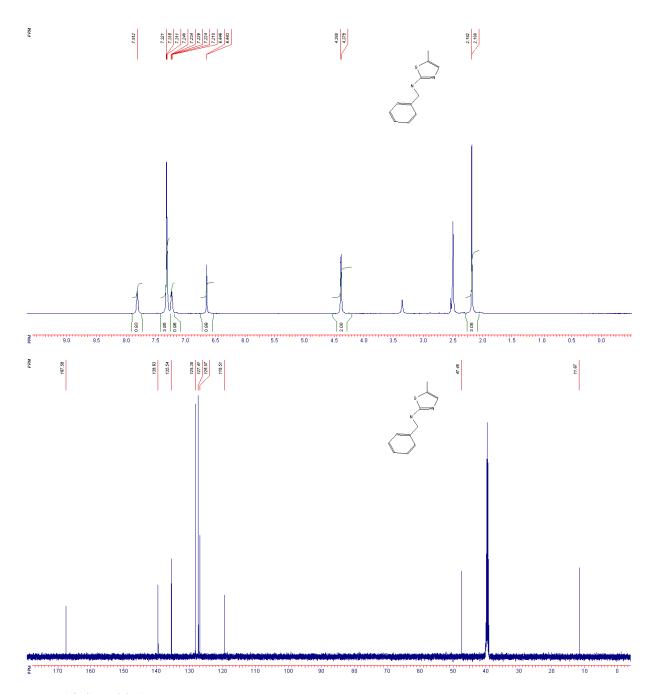
Entry 5, in Table 1



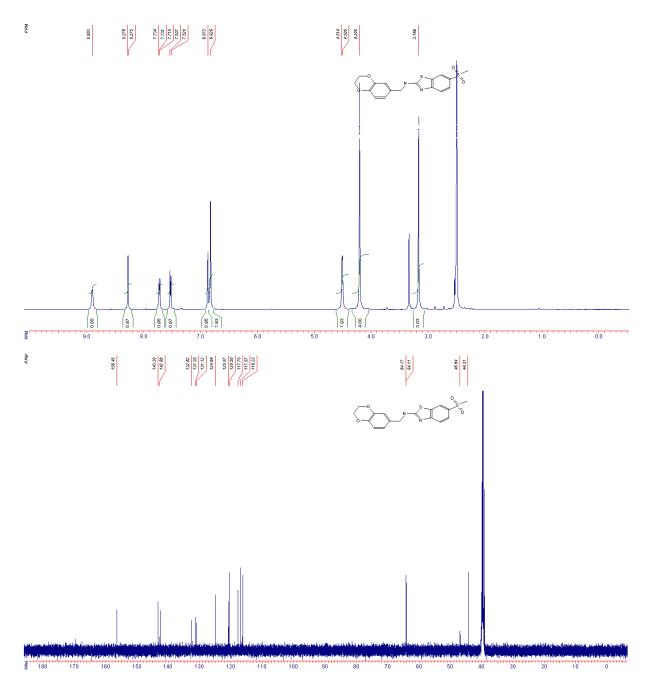
Entry 6, in Table 1



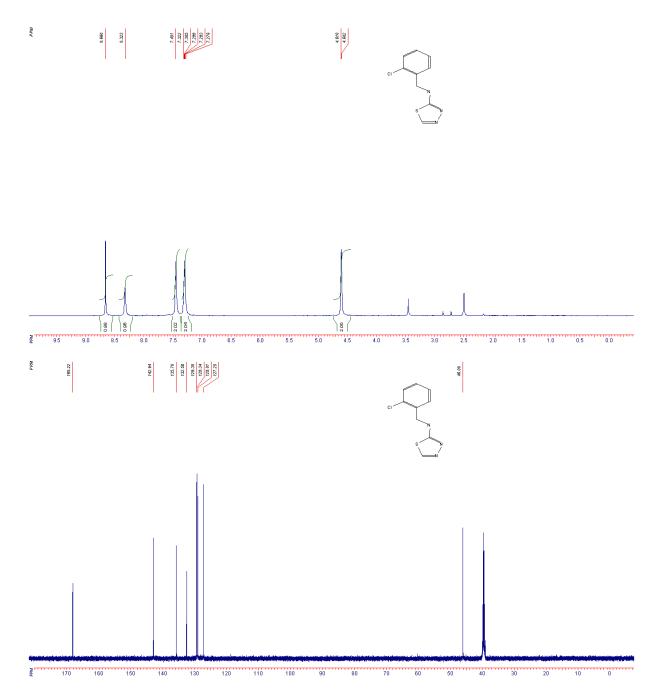
Entry 11, in Table 1



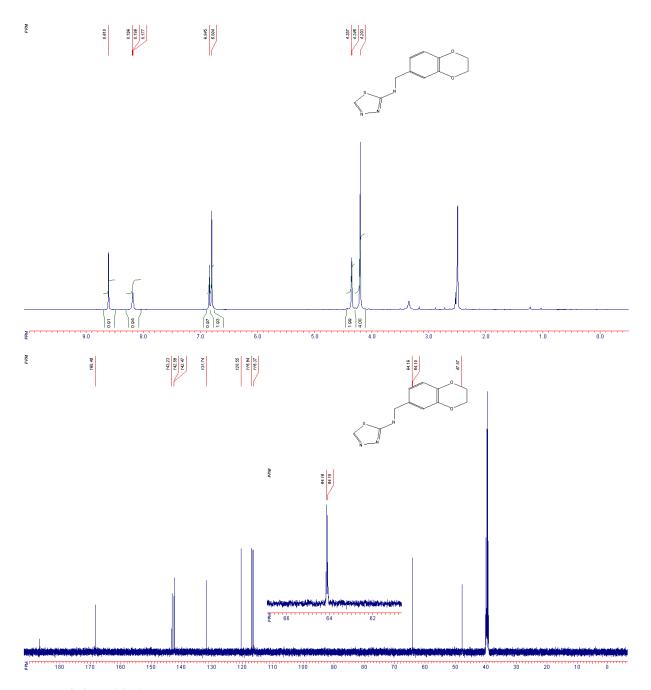
Entry 13, in Table 1



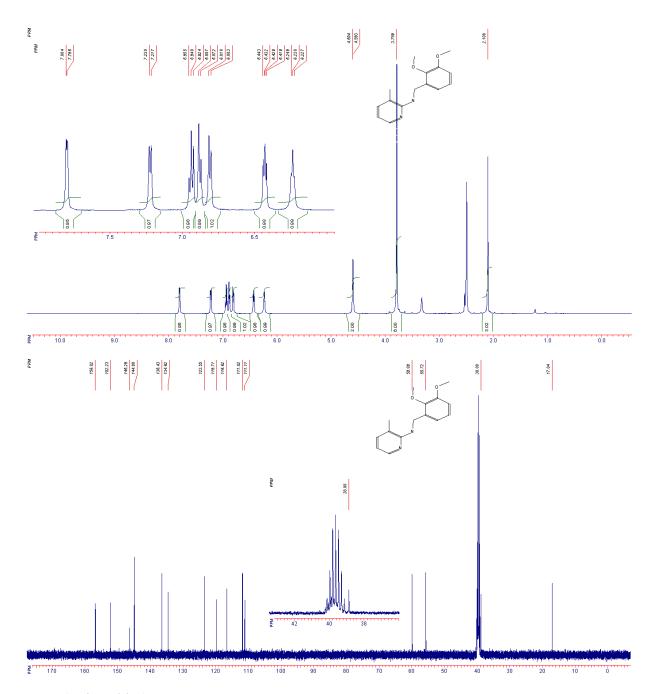
Entry 15, in Table 1



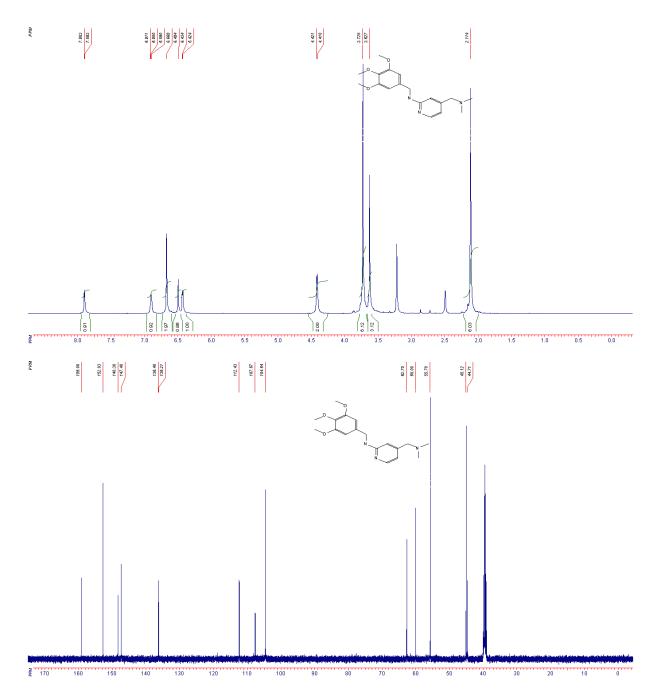
Entry 17, in Table 1



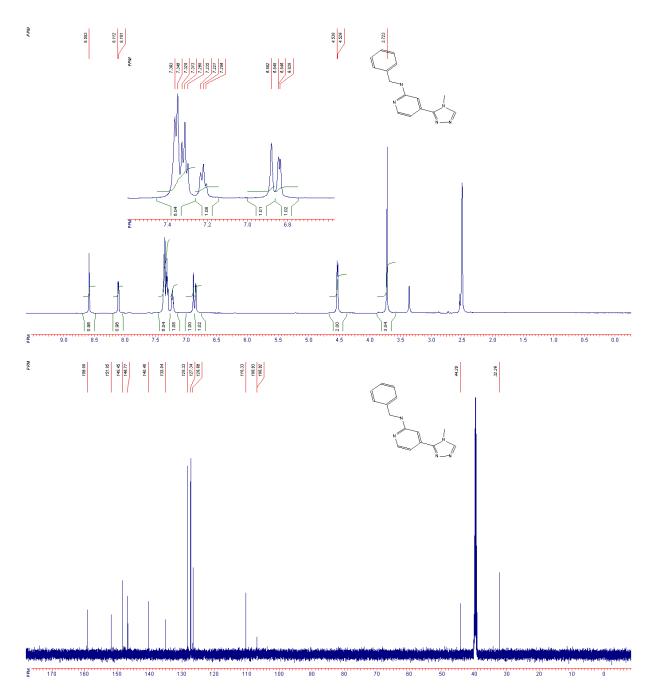
Entry 18, in Table 1



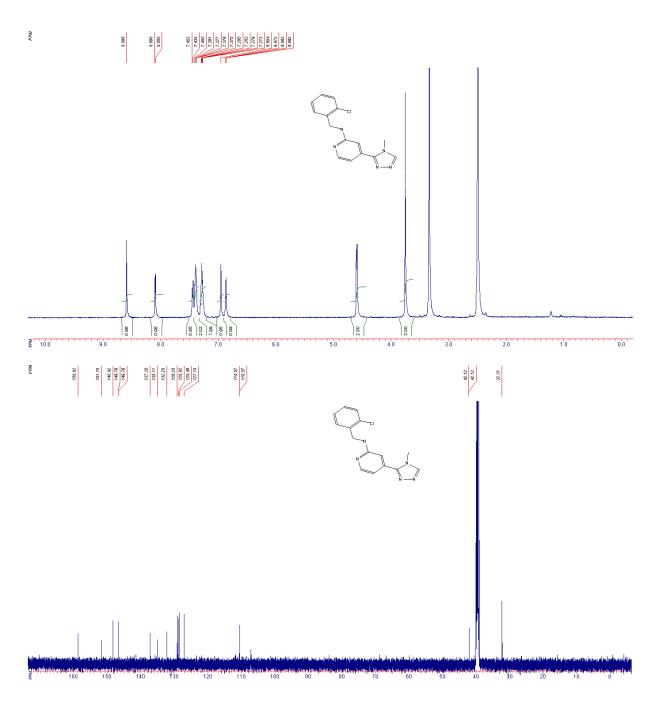
Entry 19, in Table 1



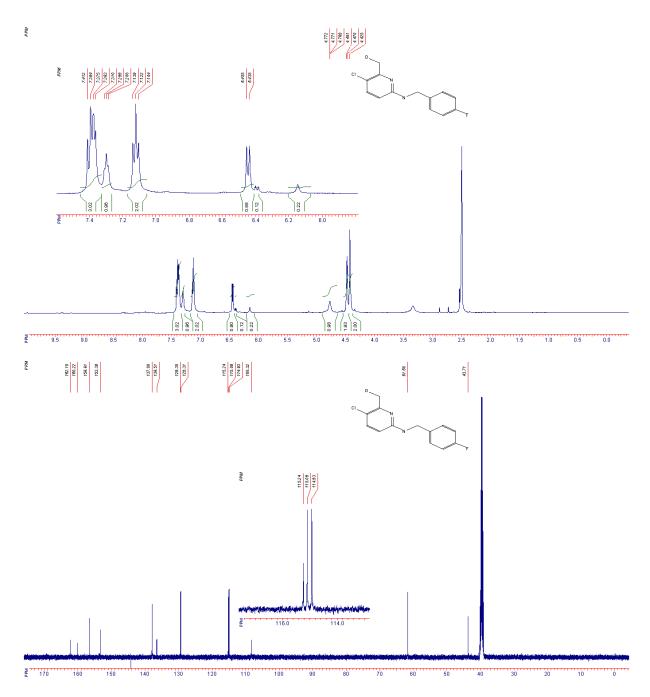
Entry 22, in Table 1



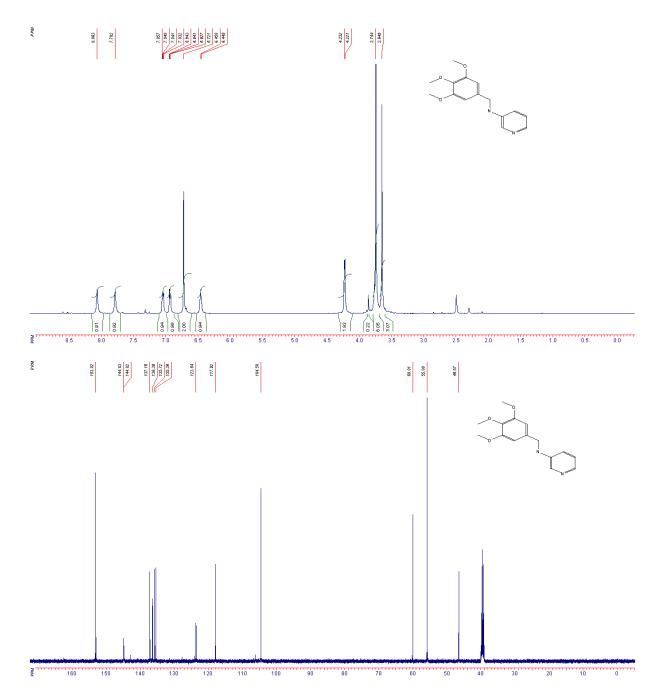
Entry 23, in Table 1



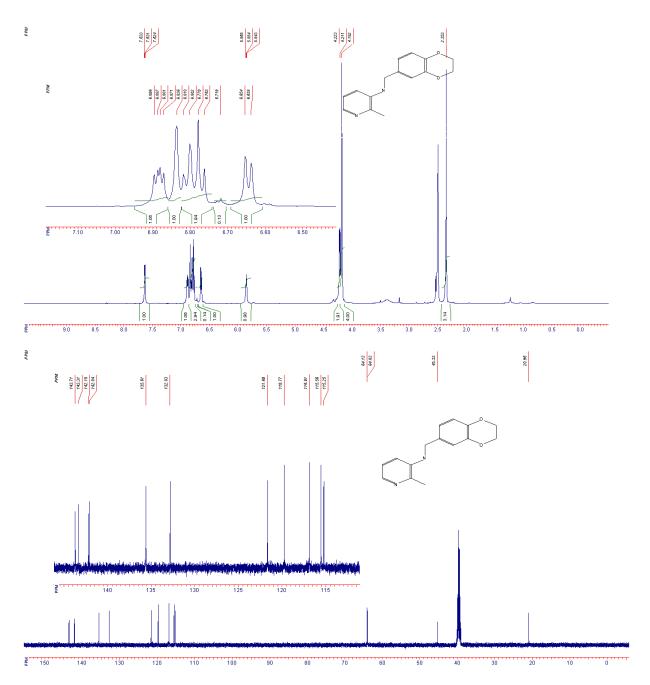
Entry 24, in Table 1



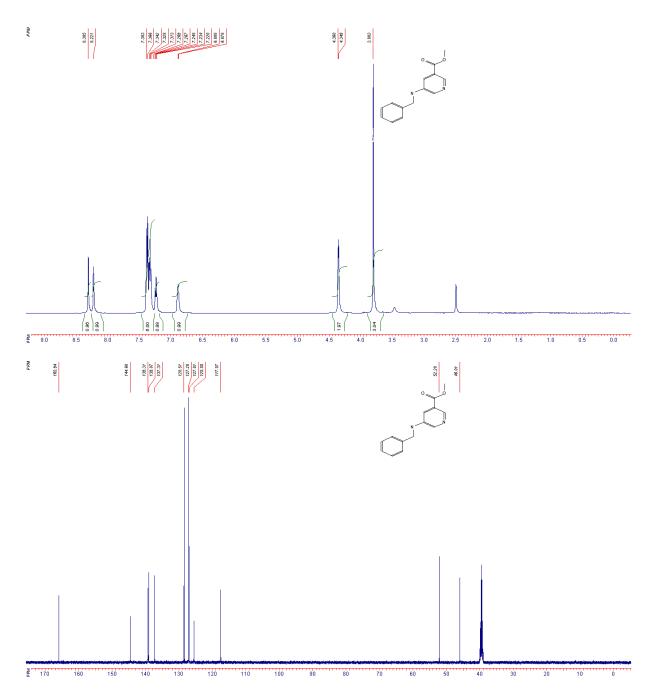
Entry 27, in Table 1



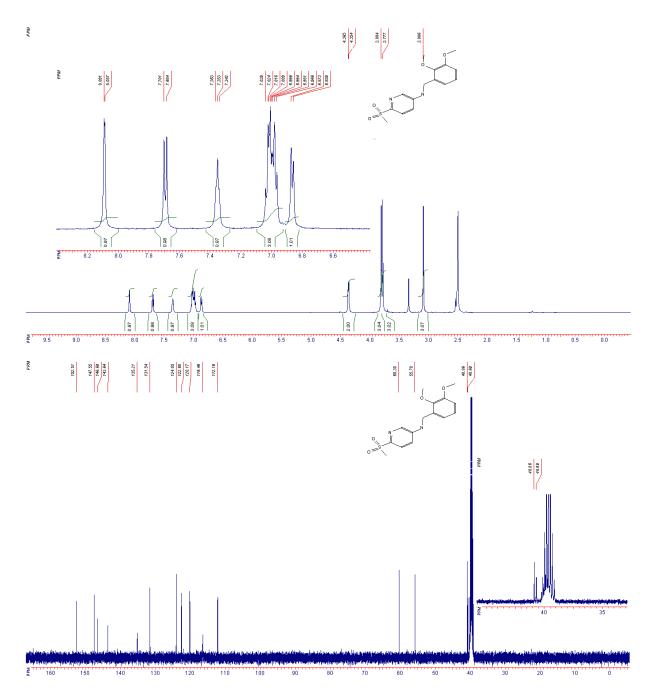
Entry 30, in Table 1



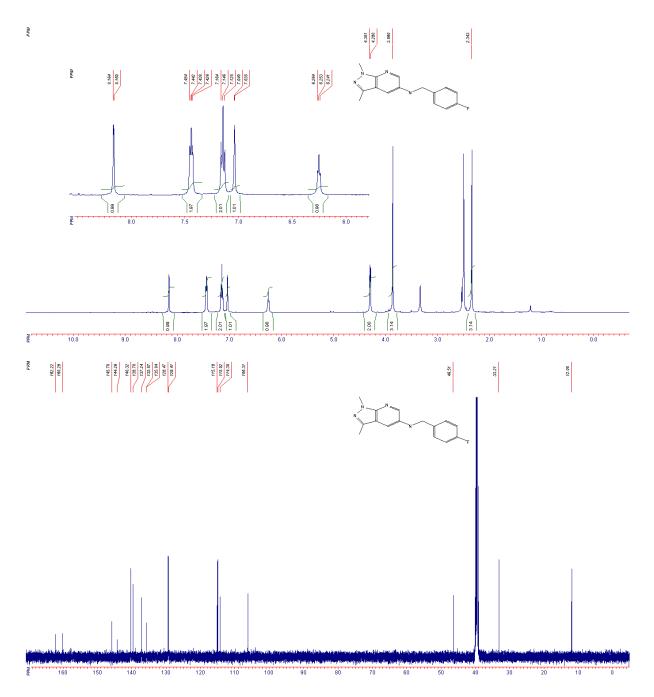
Entry 31, in Table 1



Entry 33, in Table 1



Entry 36, in Table 1



Entry 40, in Table 1