Supporting materials

Microwave-Promoted Pd-Catalyzed Cyanation of Aryl Triflates: A Fast and Versatile Access to 3-Cyano-3-desoxy-10-ketomorphinans

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Experimental Section

General: ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, on a Bruker AC300 spectrometer. Chemical shifts are given as δ value (ppm) downfield from tetramethylsilane as an internal reference. Melting points were determined on a Thomas-Hoover capillary tube apparatus and are reported uncorrected. Element analyses, performed by Atlantic Microlabs, Atlanta, GA, were within $\pm 0.4\%$ of theoretical values. Analytical thin-layer chromatography (TLC) was carried out on 0.2-mm Kieselgel 60F 254 silica gel plastic sheets (EM Science, Newark). Flash chromatography was used for the routine purification of reaction products. The column output was monitored with TLC.

Microwave heating was performed in a SmithSynthesizerTM single mode cavity, producing continuous irradiation at 2450 MHz. Reaction temperature and pressure were determined using the built-in, on-line IR- and pressure sensors.

General Procedure¹ for Synthesis of Aryl triflates:

3-Hydroxy-N-alkyl-10-ketomorphinan² (1.53 mmol), which was prepared from levorphanol, was dissolved in anhydrous CH_2Cl_2 (10 mL) and Et_3N (4 mL). The mixture was cooled to 0°C , and then PhNTf_2 (1.0 g, 2.80 mmol) was added. The reaction mixture was allowed to warm to

room temperature overnight. The solution was diluted with CH_2Cl_2 , washed with 1N NaOH followed by brine, and then dried over anhydrous sodium sulfate. The solvent was removed *in vacuo* to afford a crude product, which was purified by column chromatography on silica gel (Hexane:ethyl acetate) to give the corresponding triflate.

(-)-3-Trifluoromethanesulfonyloxy-10-keto-N-

cyclobutylmethylmorphinan (**1a**) was obtained as a semi-solid in 85.8% yield. ^1H NMR (CDCl_3 , 300 MHz) δ : 8.07 (d, $J = 8.4$ Hz, 1H), 7.50 (m, 2H), 6.83 (s, 1H), 3.00 (m, 1H), 2.57 (m, 4H), 2.23 (m, 3H), 1.96 (m, 6H), 1.67 (m, 9 H); Anal. Calcd for $\text{C}_{22}\text{H}_{26}\text{F}_3\text{NO}_4\text{S}$: C 57.76, H 5.73, N 3.06. Found: C 57.99, H 5.72, N 3.10.

(-)-3-Trifluoromethanesulfonyloxy-10-keto-N-

methylmorphinan (**1b**) was obtained as yellow solid in 70.0% yield. M.p.: 123-124 $^\circ\text{C}$; ^1H NMR (CDCl_3 , 300 MHz) δ : 8.17 (d, $J = 7.8$ Hz, 1H), 7.26 (d, $J = 7.5$ Hz, 1H), 7.23 (s, 1H), 3.03 (m, 1H), 2.63 (m, 1H), 2.38 (m, 1H), 2.34 (s, 3H), 2.12 (m, 1H), 1.98 (m, 2H), 1.52 (m, 6H), 1.07 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 194.2, 153.8, 148.5, 134.8, 128.5, 119.5, 119.4, 68.2, 47.2, 46.8, 43.1, 40.9, 38.5, 36.3, 26.0, 25.7, 21.6.

(-)-3-Trifluoromethanesulfonyloxy-10-keto-N-

cyclopropylmethylmorphinan (**1c**) was obtained as yellow solid in 72.8% yield. M.p.: 86-88 $^\circ\text{C}$; ^1H NMR (CDCl_3 , 300 MHz) δ : 8.10 (d, $J = 9.0$ Hz, 1H), 7.20 (m,

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(2) Neumeyer, J. L.; Bidlack, J. M.; Zong, R. S.; Bakthavachalam, V.; Gao, P.; Cohen, D. J.; Negus, S. S.; Mello, N. K. *J. Med. Chem.* **2000**, *43*, 114-122.

2H), 3.28 (s, 1H), 2.93 (d, $J = 7.8$ Hz, 1H), 2.62 (dd, $J = 5.4, 12.3$ Hz, 1H), 2.36 (d, $J = 13.5$ Hz, 1H), 2.17 (d, $J = 12.6$ Hz, 1H), 1.96 (m, 3H), 1.59 (m, 6H), 1.13 (m, 2H), 0.87 (m, 1H), 0.48 (d, $J = 7.2$ Hz, 2H), 0.25 (m, 1H), 0.06 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 195.1, 153.8, 148.7, 134.8, 128.4, 119.4, 119.3, 66.5, 60.2, 57.2, 46.8, 45.4, 40.9, 39.0, 36.3, 26.0, 25.8, 21.6, 9.0, 4.3, 3.3.

(-)-3-Trifluoromethanesulfonyloxy-10-keto-N-(2-phenylethyl)morphinan (1d) was obtained as yellow oil in 67.3% yield. ^1H NMR (CDCl_3 , 300 MHz) δ : 8.18 (d, $J = 7.8$ Hz, 1H), 7.18 (m, 7H), 3.25 (m, 1H), 2.94 (m, 1H), 2.77 (m, 2H), 2.53 (m, 1H), 2.34 (m, 1H), 2.01 (m, 3H), 1.50 (m, 6H), 1.18 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 194.8, 153.8, 148.6, 140.1, 134.8, 128.7, 128.5, 128.2, 125.9, 119.5, 119.4, 65.8, 56.9, 46.7, 45.8, 40.9, 39.0, 36.3, 33.8, 26.0, 25.8, 21.6.

(-)-3-Trifluoromethanesulfonyloxy-10-keto-N-(2-naphthylmethyl)morphinan (1e) was obtained as oil in 86.7% yield. ^1H NMR (CDCl_3 , 300 MHz) δ : 8.22 (dd, $J = 2.4, 8.4$ Hz, 1H), 7.80 (m, 3H), 7.53 (dd, $J = 1.8, 8.7$ Hz, 1H), 7.44 (m, 2H), 7.27 (m, 1H), 7.24 (m, 2H), 3.92 (d, $J = 13.5$ Hz, 1H), 3.51 (d, $J = 13.5$ Hz, 1H), 3.16 (d, $J = 3.0$ Hz, 1H), 2.69 (m, 1H), 2.35 (d, $J = 14.1$ Hz, 1H), 2.06 (m, 5H), 1.36 (m, 8H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 194.8, 153.8, 148.7, 135.8, 134.8, 133.2, 132.7, 128.5, 127.8, 127.7, 127.5, 127.1, 125.8, 125.5, 119.5, 119.4, 65.9, 59.4, 46.8, 45.3, 41.0, 39.0, 36.2, 26.0, 25.7, 21.6.

(-)-3-Trifluoromethanesulfonyloxy-10-keto-N-(3-methyl-2-butenyl)morphinan (1f) was obtained as yellow oil in 88.3% yield. ^1H NMR (CDCl_3 , 300 MHz) δ : 8.08 (d, $J = 8.1$ Hz, 1H), 7.16 (m, 2H), 5.14 (m, 1H), 3.08 (m, 2H), 2.82 (m, 1H), 2.69 (m, 1H), 2.28 (d, $J = 13.5$ Hz, 1H), 2.06 (d, $J = 12.6$ Hz, 1H), 1.87 (m, 2H), 1.64 (s, 3H), 1.55 (s, 3H), 1.36 (m, 4H), 1.10 (m, 4H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 195.1, 153.8, 148.6, 135.9, 134.8, 129.4, 128.4, 119.4, 119.3, 66.3, 52.9, 46.8, 45.0, 40.8, 39.0, 36.2, 26.0, 25.9, 25.7, 21.5, 18.0.

(-)-3-Trifluoromethanesulfonyloxy-10-keto-N-(2-methoxyethyl)morphinan (1g) was obtained as a yellow solid in 96.8% yield. M.p.: 76–78 °C; ^1H NMR (CDCl_3 , 300 MHz) δ : 8.18 (d, $J = 8.1$ Hz, 1H), 7.23 (m, 2H), 3.61 (m, 1H), 3.51 (m, 1H), 3.37 (s, 3H), 3.17 (s, 1H), 2.80 (m, 2H), 2.53 (m, 1H), 2.36 (d, $J = 13.5$ Hz, 1H), 2.19 (m, 1H), 2.02 (m, 2H), 1.50 (m, 6H), 1.30 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 195.0, 153.8, 148.6, 134.7, 128.4, 119.4, 119.3,

118.6 (q, $J = 318.7$ Hz), 69.5, 66.0, 58.8, 57.2, 54.4, 46.3, 45.9, 40.7, 38.8, 36.2, 25.9, 25.7, 21.5.

3-Trifluoromethanesulfonyloxy-morphine (3): To a slurry of Morphine- H_2O (10 g, 32.8 mmol) in CH_2Cl_2 (500 mL) at 0°C was added a solution of Et_3N (7 mL). The mixture was stirred for 1h at ambient temperature, and then N-phenyltrifluoromethanesulfonimide (14 g, 39.4 mmol) was added. After being stirred for 24 h, the reaction mixture was extracted with 10% aqueous KHCO_3 (100 mL). The organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo. The solid was dissolved in ether (100 mL), and extracted with 1N HCl (4 x 120 mL). The pH of the acidic layer was adjusted to 9 by adding ammonium hydroxide. The aqueous layer was then extracted with CH_2Cl_2 and the extracts were washed with brine, dried with Na_2SO_4 , filtered and evaporated to get solid. The solid residue was further washed by anhydrous ether to give the triflate **3**³ as a white solid, 9.4 g (68.6%). m.p.: 121–123°C; ^1H NMR (CDCl_3 , 300 MHz) δ : 6.89 (d, $J = 8.4$ Hz 1H), 6.64 (d, $J = 8.4$ Hz 1H), 5.70 (d, $J = 10.2$ Hz, 1H), 5.29 (d, $J = 9.6$ Hz 1H), 5.02 (d, $J = 6.3$ Hz, 1H), 4.20 (m, 1H), 3.38 (m, 1H), 3.05 (m, 1H), 2.90 (brs, 1H), 2.61 (m, 2H), 2.36 (m, 5H), 2.09 (m, 1H), 1.90 (d, $J = 11.4$ Hz, 1H).

(-)-3-Trifluoromethanesulfonyloxy-N-cyclopropyl methylmorphinan (5) was prepared according to the same procedure as described for the preparation of triflate **1** in 76% yield. ^1H NMR (CDCl_3 , 300 MHz) δ : 7.16 (s, 1H), 7.12 (m, 1H), 6.99 (dd, $J = 2.1, 8.7$ Hz, 1H), 3.1 (m, 1H), 2.96 (d, $J = 18.9$ Hz, 1H), 2.66 (m, 2H), 2.46 (m, 1H), 2.31 (m, 2H), 1.85 (m, 3H), 1.66 (d, $J = 11.7$ Hz, 1H), 1.56 (d, $J = 12.3$ Hz, 1H), 1.37 (m, 6H), 0.85 (m, 1H), 0.50 (m, 2H), 0.11 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 144.7, 140.0, 134.9, 125.6, 122.8 (q, $J = 318.7$ Hz), 114.5, 114.4, 56.3, 51.8, 41.7, 41.0, 38.1, 34.6, 32.9, 23.1, 22.8, 20.7, 18.2, 5.8.

3-Methyl-4-acetylphenyl triflate (7) was obtained as pale yellow oil in 98% yield. ^1H NMR (CDCl_3 , 300 MHz) δ : 7.9 (m, 1H), 7.84 (m, 1H), 7.33 (dd, $J = 4.5, 8.1$ Hz, 1H), 2.60 (s, 3H), 2.43 (s, 3H).

4-Propionylphenyl triflate (9) was obtained as colorless oil in 97.4% yield. ^1H NMR (CDCl_3 , 300 MHz) δ : 8.07 (d, $J = 7.2$ Hz, 2H), 7.37 (d, $J = 7.2$ Hz, 2H), 3.02 (q, $J = 7.2$

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Hz, 2H), 1.23 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 198.7, 152.2, 136.6, 121.5, 118.6 (q, $J = 318.7$ Hz), 31.8, 7.8.

General Procedure for Microwave-Promoted cyanation.

In a 10-mL glass tube were placed triflate (0.2 mmol), $\text{Zn}(\text{CN})_2$ (47 mg, 0.4 mmol), $\text{Pd}(\text{Ph}_3\text{P})_4$ (19 mg, 0.016 mmol), 5 mL of DMF, and a magnetic stir bar. The vessel was sealed with a septum and placed into the microwave cavity. Microwave irradiation was used and the temperature was rapidly increased from room temperature to 200°C. Once 200°C was reached, the reaction mixture was held at this temperature for 15 min and then cooled rapidly to room temperature. The reaction vessel was opened and the contents were poured into a separating funnel. Saturated sodium carbonate and water were added, and the mixture was extracted with ethyl acetate (50 mL x 3). The extracts were combined, washed with brine and dried over anhydrous sodium sulfate. After evaporation of the solvent, the residue was subjected to silica gel column chromatography to yield the corresponding nitrile compounds.

(-)-3-Cyano-3-desoxy-10-keto-N-cyclobutylmethyl

morphinan (2a) was obtained as a yellow viscous solid.

^1H NMR (CDCl_3 , 300 MHz) δ : 8.11 (d, $J = 7.8$ Hz, 1H), 7.64 (s, 1H), 7.62 (d, $J = 7.8$ Hz, 1H), 3.08 (m, 1H), 2.61 (m, 3H), 2.41 (d, $J = 13.8$ Hz, 1H), 2.28 (m, 1H), 1.96 (m, 6H), 1.69 (m, 4 H), 1.48 (m, 5H), 1.13 (m, 1H), 1.00 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 195.6, 146.3, 137.7, 130.7, 129.6, 126.1, 118.2, 117.5, 66.7, 61.3, 46.4, 45.3, 40.9, 38.5, 36.0, 33.7, 27.3, 26.7, 26.0, 25.7, 21.7, 18.6; Anal. Calcd for $\text{C}_{22}\text{H}_{26}\text{N}_2\text{O}$: C 79.00, H 7.84, N 8.38. Found: C 78.83, H 8.12, N 8.36.

(-)-3-Cyano-3-desoxy-10-keto-N-methylmorphinan (2b)

was obtained as a yellow solid. M.p.: 188-190 °C; ^1H NMR (CDCl_3 , 300 MHz) δ : 8.13 (d, $J = 8.4$ Hz, 1H), 7.67 (s, 1H), 7.63 (d, $J = 8.4$ Hz, 1H), 3.05 (d, $J = 2.7$ Hz, 1H), 2.65 (m, 1H), 2.43 (d, $J = 14.1$ Hz, 1H), 2.33 (s, 3H), 2.12 (dt, $J = 3.0, 13.2$ Hz, 1H), 1.97 (m, 2H), 1.52 (m, 5H), 1.16 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 194.8, 146.2, 137.7, 130.8, 129.8, 126.3, 118.2, 117.7, 68.1, 47.1, 46.6, 43.1, 40.9, 38.1, 36.0, 26.0, 25.6, 21.7; Anal. Calcd for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O} \cdot 0.2\text{H}_2\text{O}$: C 76.13, H 7.24, N 9.87. Found: C 76.45, H 7.16, N 9.86.

(-)-3-Cyano-3-desoxy-10-keto-N-cyclopropylmethyl

morphinan (2c) was obtained as a yellow solid. M.p.: 114-

116 °C; ^1H NMR (CDCl_3 , 300 MHz) δ : 8.07 (d, $J = 7.8$ Hz, 1H), 7.64 (s, 1H), 7.58 (d, $J = 7.8$ Hz, 1H), 3.28 (d, $J = 3.0$ Hz, 1H), 2.90 (m, 1H), 2.58 (dd, $J = 5.7, 12.9$ Hz, 1H), 2.40 (d, $J = 13.8$ Hz, 1H), 2.15 (dt, $J = 3.3, 13.2$ Hz, 1H), 1.94 (m, 3H), 1.50 (m, 6H), 1.10 (m, 3H), 0.48 (m, 2H), 0.22 (m, 2H), 0.05 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 195.7, 146.4, 137.7, 130.7, 129.7, 126.2, 118.3, 117.6, 66.4, 60.1, 46.5, 45.3, 40.9, 38.7, 36.0, 26.0, 25.7, 21.7, 8.9, 4.2, 3.3; Anal. Calcd for $\text{C}_{21}\text{H}_{24}\text{N}_2\text{O}$: C 78.71, H 7.55, N 8.74. Found: C 78.62, H 7.57, N 8.61.

(-)-3-Cyano-3-desoxy-10-keto-N-(2-phenylethyl)

morphinan (2d) was obtained as yellow solid. ^1H NMR (CDCl_3 , 300 MHz) δ : 8.11 (d, $J = 7.8$ Hz, 1H), 7.66 (d, $J = 1.2$ Hz, 1H), 7.60 (dd, $J = 1.5, 7.8$ Hz, 1H), 7.23 (m, 5H), 3.26 (m, 1H), 2.92 (m, 1H), 2.74 (m, 2H), 2.50 (m, 1H), 2.44 (d, $J = 6.9$ Hz, 1H), 2.12 (m, 1H), 1.97 (m, 1H), 1.49 (m, 6H), 1.10 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 195.5, 146.3, 140.0, 137.7, 130.8, 129.8, 128.7, 128.2, 126.3, 126.0, 118.3, 117.7, 65.8, 56.9, 46.4, 45.7, 40.9, 38.6, 36.0, 33.8, 26.0, 25.8, 21.7; Anal. Calcd for $\text{C}_{25}\text{H}_{26}\text{N}_2\text{O} \cdot 1/4\text{H}_2\text{O}$: C 80.07, H 7.12, N 7.47. Found: C 80.32, H 8.15, N 7.41.

(-)-3-Cyano-3-desoxy-10-keto-N-(2-naphthylmethyl)

morphinan (2e) was obtained as yellow solid. ^1H NMR (CDCl_3 , 300 MHz) δ : 8.18 (d, $J = 7.8$ Hz, 1H), 7.79 (m, 4H), 7.65 (m, 2H), 7.53 (d, $J = 8.1$ Hz, 1H), 7.45 (m, 2H), 3.90 (d, $J = 13.5$ Hz, 1H), 3.52 (d, $J = 13.5$ Hz, 1H), 3.18 (s, 1H), 2.68 (d, $J = 8.7$ Hz, 1H), 2.42 (d, $J = 14.1$ Hz, 1H), 2.18 (d, $J = 12.9$ Hz, 1H), 1.99 (m, 2H), 1.45 (m, 8H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 195.5, 146.4, 137.7, 135.7, 133.2, 132.7, 130.8, 129.8, 127.9, 127.7, 127.5, 127.1, 126.3, 125.9, 125.6, 118.3, 117.7, 65.9, 59.4, 46.5, 45.2, 41.0, 38.6, 36.0, 26.0, 25.6, 21.7; Anal. Calcd for $\text{C}_{28}\text{H}_{26}\text{N}_2\text{O}$: C 82.73, H 6.45, N 6.89. Found: C 82.45, H 6.47, N 6.88.

(-)-3-Cyano-3-desoxy-10-keto-N-(3-methyl-2-butenyl)

morphinan (2f) was obtained as yellow oil. ^1H NMR (CDCl_3 , 300 MHz) δ : 8.05 (dd, $J = 2.0, 7.8$ Hz, 1H), 7.58 (m, 2H), 5.12 (t, $J = 6.9$ Hz, 1H), 3.10 (m, 2H), 2.80 (m, 1H), 2.68 (m, 1H), 2.34 (d, $J = 14.1$ Hz, 1H), 2.05 (m, 1H), 1.86 (m, 2H), 1.64 (s, 3H), 1.57 (s, 3H), 1.40 (m, 5H), 1.16 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 195.8, 146.4, 137.7, 135.9, 130.7, 129.7, 126.2, 120.7, 118.3, 117.6, 66.3, 52.9, 46.6, 44.9, 40.9, 38.7, 36.0, 26.0, 25.9, 25.7, 21.7, 18.0; Anal. Calcd for $\text{C}_{22}\text{H}_{26}\text{N}_2\text{O} \cdot 0.5\text{H}_2\text{O}$: C 76.93, H 7.92, N 8.16. Found: C 76.54, H 7.82, N 7.88.

(-)-3-Cyano-3-desoxy-10-keto-N-(2-methoxyethyl)

morphinan (2g) was obtained as a yellow viscous solid. ^1H NMR (CDCl_3 , 300 MHz) δ : 8.11 (m, 1H), 7.65 (m, 2H), 3.53 (m, 2H), 3.36 (s, 3H), 3.18 (s, 1H), 2.78 (m, 2H), 2.47 (m, 2H), 2.19 (m, 1H), 2.01 (m, 2H), 1.57 (m, 5H), 1.08 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 195.7, 146.4, 137.6, 130.8, 129.8, 126.2, 118.3, 117.7, 69.6, 66.0, 58.9, 54.5, 46.2, 45.8, 40.7, 38.5, 36.0, 26.0, 25.7, 21.7; Anal. Calcd for $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_2$: C 74.04, H 7.46, N 8.64. Found: C 74.00, H 7.53, N 8.41.

3-Cyano-3-desoxy-morphine (4) was obtained as a pale yellow solid. M.p.: 191-192 $^\circ\text{C}$; ^1H NMR (CDCl_3 , 300 MHz) δ : 7.20 (d, $J = 8.1$ Hz 1H), 6.68 (d, $J = 8.1$ Hz 1H), 5.71 (d, $J = 9.0$ Hz, 1H), 5.30 (d, $J = 8.1$ Hz 1H), 5.02 (d, $J = 5.7$ Hz, 1H), 4.23 (s, 1H), 3.37 (m, 1H), 3.12 (m, 1H), 2.64 (m, 1H), 2.35 (m, 10H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 144.7, 141.3, 133.4, 131.3, 130.7, 128.4, 123.5, 119.8, 115.8, 66.8, 58.1, 45.8, 43.0, 42.6, 41.3, 40.6, 35.3, 21.6; Anal. Calcd for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_2 \cdot 1.0\text{H}_2\text{O}$: C 69.21, H 6.45, N 8.97. Found: C 69.22, H 6.12, N 8.53.

(-)-3-Cyano-3-desoxy-N-cyclopropyl methylmorphinan

(6) was obtained as pale yellow oil. ^1H NMR (CDCl_3 , 300 MHz) δ : 7.53 (d, $J = 1.5$, 1H), 7.38 (dd, $J = 1.8$, 8.1, 1H), 7.20 (d, $J = 8.1$ Hz, 1H), 3.0 (m, 1H), 2.97 (m, 1H), 2.66 (m, 2H), 2.40 (m, 1H), 2.29 (m, 2H), 1.83 (m, 3H), 1.60 (d, $J = 12.0$ Hz, 1H), 1.56 (m, 1H), 1.33 (m, 6H), 0.87 (m, 1H), 0.55 (m, 2H), 0.10 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 144.3, 142.6, 129.8, 128.8, 128.7, 119.7, 110.1, 61.6, 55.7, 44.9, 42.0, 38.0, 36.4, 34.9, 27.8, 26.9, 26.6, 25.6, 19.0, 7.2; GC-MS: 306 ($\text{M}^+ + 1$); Anal. Calcd for $\text{C}_{21}\text{H}_{26}\text{N}_2 \cdot 0.5\text{H}_2\text{O}$: C 79.96, H 8.63, N 8.88. Found: C 79.53, H 8.70, N 8.93.

3-Methyl-4-acetylbenzonitrile (8)

was obtained as white solid. M.p.: 76-78 $^\circ\text{C}$; ^1H NMR (CDCl_3 , 300 MHz) δ : 7.89 (s, 1H), 7.84 (d, $J = 5.1$ Hz, 1H), 7.72 (d, $J = 5.1$ Hz, 1H), 2.63 (s, 6H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 196.9, 142.5, 139.7, 132.8, 129.6, 125.8, 117.2, 116.7, 26.7, 20.5; Anal. Calcd for $\text{C}_{10}\text{H}_9\text{NO}$: C 75.45, H 5.70, N 8.80. Found: C 75.15, H 5.66, N 8.77.

4-Propionylbenzonitrile (10)⁴

was obtained as a white solid. ^1H NMR (CDCl_3 , 300 MHz) δ : 8.06 (d, $J = 7.8$ Hz,

2H), 7.78 (d, $J = 7.8$ Hz, 2H), 3.03 (q, $J = 6.9$ Hz, 2H), 1.24 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ : 199.2, 139.7, 132.4, 128.3, 117.9, 116.1, 32.1, 7.8.

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