Free-Radical Version of the Strecker Synthesis to α -Aminoamides Promoted by Aqueous $\text{H}_2\text{O}_2/\text{TiCl}_3/\text{HCONH}_2$ System

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Supporting Information

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Experimental Section

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General. All materials were purchased from commercial suppliers and used without further purification. All reactions were performed at room temperature (20 °C). NMR spectra were recorded at 500 or 400 MHz for ^1H and 125 or 100 MHz for ^{13}C , measured in DMSO. Chemical shifts (δ) were presented in ppm using the DMSO peak (2.50 ppm for ^1H and 39.43 ppm for ^{13}C) as an internal standard. Melting points were measured on Köppfler apparatus and are uncorrected. ESI-MS were performed on Esquire 3000 plus ion-trap mass spectrometer equipped with an ESI source. Tandem mass spectra were obtained by CID with helium collision gas after isolation of the precursor ion. The following aqueous solutions were used: 35 % solution of H_2O_2 , a 15 % solution of TiCl_3 (C. Erba). Flash column chromatography (FCC) was performed by using 40-63 μm silica gel packing.

General procedure for formamide addition to in situ formed aldimines. Hydrogen peroxide (5 mmol, ca. 0.5 mL), diluted in 4.5 mL of formamide, was added dropwise in 15-20 min to a stirred homogeneous solution containing the amine **1** (4 mmol), the aldehyde **2** (2 mmol) and TiCl_3 (8 mmol, ca. 8 mL of a 15% aqueous acidic solution) in 10 mL of formamide. The end of the reaction was showed by a sharp change of color from blu to orange. At this point, the reaction was quenched with 5 mL of H_2O and added with a 30% aqueous NH_3 solution until basic pH and extracted with EtOAc (3x50 mL). The combined organic layers were concentrated in vacuo and the residue left was dissolved in CHCl_3 (20 mL). The solution was then washed twice with 5 mL of H_2O in order to remove the formamide leftover, which is insoluble in CHCl_3 but very soluble in H_2O . The organic layers were then dried and concentrated in vacuo. Purification by FCC of the crude residue afforded the α -aminoamides **3** as the last eluted products (elution order: unreacted aldehyde **2**, unreacted amine **1**, formanilide and α -aminoamide **3**). Most α -aminoamides **3** have been directly obtained in a pure crystalline form by dissolving the crude residue in a suitable solvent.

Spectroscopic data.

2-(4-Methoxyphenylamino)-propionamide (3a). The crude residue was dissolved in hot CHCl_3 ; on standing, 233 mg (60 %) of **3a** crystallized out in pure form: mp 173-6 °C; ^1H NMR (500 MHz, DMSO) δ 1.28 (3H, CH_3 , d, J = 7.0 Hz), 3.63 (3H, OCH_3 , s), 3.66 (1H, CH, qd, J = 7.0, 7.3 Hz, q after D_2O exch., J = 7.0 Hz), 5.25 (1H, NH, d, J = 7.3 Hz, D_2O exch), 6.51 (2H, Ar H, d, J = 9.0 Hz), 6.71 (2H, Ar H, d, J = 9.0 Hz), 6.89 (1H, NH_2 , s, D_2O exch.), 7.22 (1H, NH_2 , s, D_2O exch.) ppm. ^{13}C NMR (DMSO) δ 18.9 (CH_3), 53.2 (OCH_3), 55.2 (CH), 113.7 (2CH), 114.4 (2CH), 141.8 (C-N), 151.0 (C-O), 173.6 (C=O) ppm. EI-MS m/z 194 (M^+ , 20), 150 (M- CONH_2 , 100), 136 (20).

2-(4-Methoxyphenylamino)-4-methylpentanoic acid amide (3b). Purification by FCC ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 98:2) of the crude residue gave **3b** (354 mg, 75 %): mp 98-101 °C; ^1H NMR (400 MHz, DMSO) δ 0.86 (3H, CH_3 , d, J = 6.6 Hz), 0.93 (3H, CH_3 , d, J = 6.6 Hz), 1.46-1.56 (2H, CH_2 , ddd, J = 5.9, 8.5, 13.6 Hz), 1.76 (1H, CH, m), 3.60 (1H, CH-N, ddd, J = 5.9, 8.1, 8.5 Hz, dd after D_2O exch., J = 5.9, 8.5 Hz), 3.63 (3H, OCH_3 , s), 5.15 (1H, NH, d, J = 8.1 Hz, s, D_2O exch.), 6.54 (2H, Ar H, d, J = 8.8 Hz), 6.70 (2H, Ar H, d, J = 8.8 Hz), 6.89 (1H, NH_2 , s, D_2O exch.), 7.25 (1H, NH_2 , s, D_2O exch.) ppm. ^{13}C NMR (DMSO) δ 21.8 (CH_3), 22.7 (CH_3), 24.2 (CH), 42.0 (CH_2), 55.2 (CH), 56.3 (OCH_3), 113.6 (2CH), 114.4 (2CH), 142.1 (C-N), 150.9 (C-O), 176.2 (C=O) ppm. EI-MS m/z 236 (M^+ , 15), 192 (M- CONH_2 , 100), 136 (30).

2-(4-Methoxyphenylamino)-3-methylbutyramide (3c). Purification by FCC ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 98:2) of the crude residue gave **3c** (275 mg, 62 %): mp 99-101 °C; ^1H NMR (400 MHz, CDCl_3) δ 1.04 (3H, CH_3 , d, J = 7.0 Hz), 1.06 (3H, CH_3 , d, J = 7.0 Hz), 2.32 (1H, CH, qqd, J = 7.0, 7.0, 2.3 Hz), 3.48 (1H, CH, br, d after D_2O exch., J = 2.3 Hz), 3.74 (3H, OCH_3 , s), 3.75 (1H, NH, br, D_2O exch.), 5.87 (1H, NH_2 , s, D_2O exch.), 6.60 (2H, Ar H, d, J = 8.8 Hz), 6.71 (1H, NH_2 , s, D_2O exch.), 6.78 (2H, Ar H, d, J = 8.8 Hz) ppm. ^{13}C NMR (CDCl_3) δ 17.7 (CH_3), 19.6 (CH_3), 31.1 (CH), 55.7 (OCH_3), 65.5 (CH-N), 114.9 (2CH), 114.8 (2CH), 141.4 (C-N), 153.0 (C-O), 176.2 (C=O) ppm. EI-MS m/z 222 (M^+ , 20), 178 (M- CONH_2 , 100), 134 (30), 122 (40).

2-(4-Methoxyphenylamino)-3-methylpentanoic acid amide (3d).). Purification by FCC (EtOAc/hexane, 6:4) of the crude residue gave **3d** (307 mg, 65 %) as a 7:3 inseparable mixture of diastereoisomers: mp 100-105 °C; ¹H NMR (500 MHz, DMSO): more abundant isomer, δ 0.86 (3H, CH₃, t, J = 7.5 Hz), 0.91 (3H, CH₃, d, J = 7.0 Hz), 1.18-1.27 (1H, CH₂, m), 1.57-1.65 (1H, CH₂, m), 1.67-1.75 (1H, CH, m), 3.43 (1H, CH-N, dd, J = 7.1, 8.5 Hz, d after D₂O exch., J = 7.1 Hz), 3.63 (3H, OCH₃, s), 5.04 (1H, NH, d, J = 8.5 Hz, D₂O exch.), 6.57 (2H, Ar H, d, J = 8.9 Hz), 6.69 (2H, Ar H, d, J = 8.9 Hz), 6.95 (1H, NH₂, s, D₂O exch.), 7.26 (1H, NH₂, s, D₂O exch.) ppm; less abundant isomer, δ 0.86 (3H, CH₃, t, J = 7.5 Hz), 0.93 (3H, CH₃, d, J = 7.1 Hz), 1.17-1.27 (1H, CH₂, m), 1.44-1.52 (1H, CH₂, m), 1.76-1.83 (1H, CH, m), 3.50 (1H, CH-N, dd, J = 5.6, 8.5 Hz, d after D₂O exch., J = 5.6 Hz), 3.63 (3H, OCH₃, s), 4.99 (1H, NH, d, J = 8.5 Hz, D₂O exch.), 6.58 (2H, Ar H, d, J = 8.9 Hz), 6.70 (2H, Ar H, d, J = 8.9 Hz), 6.97 (1H, NH₂, s, D₂O exch.), 7.23 (1H, NH₂, s, D₂O exch.) ppm. ¹³C NMR (DMSO): more abundant isomer, δ 11.0 (CH₃), 15.5 (CH₃), 24.9 (CH₂), 36.9 (CH), 55.2 (OCH₃), 61.9 (CH), 113.8 (2CH), 114.4 (2CH), 142.5 (C-N), 150.9 (C-O), 175.0 (C=O) ppm; less abundant isomer: δ 11.5 (CH₃), 14.9 (CH₃), 25.7 (CH₂), 37.1 (CH), 55.2 (OCH₃), 62.4 (CH), 113.8 (2CH), 114.4 (2CH), 142.53 (C-N), 151.0 (C-O), 175.2 (C=O) ppm. EI-MS *m/z* 236 (M⁺, 15), 192 (M-CONH₂, 100), 134 (40).

2-(4-Methoxyphenylamino)-3-phenylbutyramide (3e). Purification by FCC (EtOAc/hexane, 6:4) of the crude residue gave **3e** (228 mg, 40 %) as a 2:1 mixture of diastereoisomers. Recrystallization from ether gave the more abundant isomer in pure form: mp 126-8 °C; ¹H NMR (400 MHz, DMSO) δ 1.31 (3H, CH₃, d, J = 7.0 Hz), 3.16 (1H, CH, quintet, J = 7.0 Hz), 3.62 (3H, OCH₃, s), 3.85 (1H, CH, dd, J = 7.0, 9.2 Hz, d, after D₂O exch., J = 7.0 Hz), 5.11 (1H, NH, d, J = 9.2 Hz, D₂O exch.), 6.55 (2H, Ar H, d, J = 8.8 Hz), 6.66 (2H, Ar H, d, J = 8.8 Hz), 6.84 (1H, NH₂, s, D₂O exch.), 7.17 (1H, Ph H, t, J = 7.3 Hz), 7.22 (1H, NH₂, s, D₂O exch.), 7.27 (2H, Ph H, t, J = 7.3 Hz), 7.32 (2H, Ph H, d, J = 7.3 Hz) ppm. ¹³C NMR (CDCl₃) δ 17.0 (CH₃), 42.0 (CH), 55.2 (OCH₃), 63.3

(CH), 114.1 (2CH), 114.3 (2CH), 126.0 (CH), 127.4 (2CH), 128.0 (2CH), 141.9(C), 144.4 (C-N), 151.0 (C-O), 174.8 (C=O) ppm. EI-MS m/z 284 (M^+ , 10), 240 (M-CONH₂, 20), 179 (M-PhCHCH₃, 90), 134 (100). The less abundant isomer was not obtained in pure form, but always contaminated with the more abundant one and its spectroscopic data were deduced by difference (the ¹H and ¹³C NMR spectra reported refer to a 9:1 mixture of the more/less abundant isomer). Less abundant isomer: ¹H NMR (400 MHz, DMSO) δ 1.24 (3H, CH₃, d, J = 7.0 Hz), 3.00 (1H, CH, qd, J = 7.0, 9.3 Hz), 3.60 (3H, OCH₃, s), 3.86 (1H, CH, dd, J = 9.3, 9.6 Hz, d, after D₂O exch., J = 9.3 Hz), 4.84 (1H, NH, d, J = 9.6 Hz, D₂O exch.), 6.50 (2H, Ar H, d, J = 8.8 Hz), 6.64 (2H, Ar H, d, J = 8.8 Hz), 7.05 (1H, NH₂, s, D₂O exch.), 7.15-7.3 (5H, Ph H, m), 7.5 (1H, NH₂, s, D₂O exch.) ppm. ¹³C NMR (CDCl₃) δ 19.2 (CH₃), 42.0 (CH), 55.1 (OCH₃), 63.2 (CH), 113.86 (2CH), 113.92 (2CH), 126.0 (CH), 127.4 (2CH), 128.0 (2CH), 141.9 (C), 144.4 (C-N), 151.0 (C-O), 174.8 (C=O) ppm. EI-MS m/z 284 (M^+ , 10), 240 (M-CONH₂, 20), 179 (M-PhCHCH₃, 90), 134 (100).

2-(Cyclohexyl)-2-(4-methoxyphenylamino)-acetamide (3f). Purification by FCC (CH₂Cl₂/MeOH, 98:2) of the crude residue afforded **3f** (262 mg, 50 %), mp 101-105 °C; ¹H NMR (400 MHz, CDCl₃) δ 1.13-1.34 (6H, 3CH₂, m), 1.67-1.80 (4H, 2CH₂, m), 1.94 (1H, CH, m), 3.48 (1H, CH-N, d, J = 4.4 Hz), 3.73 (3H, OCH₃, s), 6.02 (1H, NH₂, s, D₂O exch), 6.59 (2H, Ar H, d, J = 8.8 Hz), 6.73 (1H, NH₂, s, D₂O exch), 6.77 (2H, Ar H, d, J = 8.8 Hz) ppm. ¹³C NMR (CDCl₃) δ 26.0 (CH₂), 26.1 (CH₂), 26.2 (CH₂), 28.3 (CH₂), 30.1 (CH₂), 41.0 (CH), 55.7 (OCH₃), 65.3 (CH-N), 114.7 (2CH), 114.9 (2CH), 141.3 (C-N), 152.9 (C-O), 176.3 (C=O) ppm. EI-MS m/z 262 (M^+ , 10), 218 (M-CONH₂, 100), 136(50).

2-(4-Methoxyphenylamino)-3,3-dimethylbutyro amide (3g). In entry 8 of Table 1, an excess of aldehyde has been used: by increasing the molar ratio of trimethylacetaldehyde/PMP-NH₂ from 1:2 to 4:1 the yield of **3g** increased from 20 to 45 %. Purification by FCC (CH₂Cl₂/MeOH, 98:2) of the crude residue afforded **3g** (213 mg, 45 %), mp 120-123 °C; ¹H NMR (400 MHz, DMSO) δ 1.01 (9H, 3CH₃, s), 3.42 (1H, CH, d, J = 9.6 Hz, s after D₂O exch), 3.63 (3H, OCH₃, s), 4.82 (1H, NH, d, J = 9.6 Hz, D₂O exch.), 6.63 (2H, Ar H, d, J = 9.2 Hz), 6.70 (2H, Ar H, d, J = 9.2 Hz), 6.91 (1H,

NH₂, D₂O exch.), 7.25 (1H, NH₂, s, D₂O exch.) ppm. ¹³C NMR (DMSO) δ 26.8 (3CH₃), 33.3 (C), 55.2 (OCH₃), 65.9 (CH), 114.2 (2CH), 114.3 (2CH), 142.6 (C-N), 151.0 (C-O), 174.0 (C=O) ppm.

(E)-2-(4-Methoxyphenylamino)-4-phenyl-butyl-3-enoic acid amide (3h). Product **3h** crystallized out in a pure form (311 mg, 55 %) from the crude residue dissolved in EtOAc/Et₂O, mp 164-166 °C; ¹H NMR (500 MHz, DMSO) δ 3.63 (3H, OCH₃, s), 4.44 (1H, CH-N, dd, J = 6.6, 7.5 Hz, d after D₂O exch., J = 6.6 Hz), 5.47 (1H, NH, d, J = 7.5 Hz), 6.34 (1H, CH, dd, J = 6.6, 16.0 Hz), 6.62 (2H, Ar H, d, J = 8.9 Hz), 6.71 (1H, CH, d, J = 16.0 Hz), 6.73 (2H, Ar H, d, J = 8.9 Hz), 7.17 (1H, NH₂, s, D₂O exch.), 7.24 (1H, Ph H, t, J = 7.5 Hz), 7.33 (2H, Ph H, t, J = 7.5 Hz), 7.40 (2H, Ph H, d, J = 7.5 Hz), 7.51 (1H, NH₂, s, D₂O exch.) ppm. ¹³C NMR (DMSO) δ 55.2 (OCH₃), 59.9 (CH), 114.1 (2CH), 114.4 (2CH), 126.1 (2CH), 127.5 (CH), 127.6 (CH), 128.6 (CH), 130.8 (CH), 136.2 (C), 141.3 (C-N), 151.2 (C-O), 173.0 (C=O) ppm. EI-MS *m/z* 282 (M⁺), 238 (M-CONH₂, 100).

2-(4-Methoxyphenylamino)-2-phenylacetamide (3i). Purification by FCC (EtOAc/hexane, 1.1) of the crude residue afforded **3i** (405 mg, 79 %), mp 110-113 °C (Lit.^a 114-116 °C); ¹H NMR (400 MHz, DMSO) δ 3.61 (3H, OCH₃, s), 4.84 (1H, CH-N, d, J = 7.2 Hz, s after D₂O exch.), 5.66 (1H, NH, d, J = 7.2 Hz, D₂O exch.), 6.59 (2H, Ar H, d, J = 8.8 Hz), 6.68 (2H, Ar H, d, J = 8.8 Hz), 7.11 (1H, NH₂, s, D₂O exch.), 7.25 (1H, Ph H, m), 7.32 (2H, Ph H, t, J = 7.0 Hz), 7.50 (2H, Ph H, d, J = 7.3 Hz), 7.61 (1H, NH₂, s, D₂O exch.) ppm. ¹³C NMR (DMSO) δ 55.1 (OCH₃), 61.2 (CH), 114.1 (2CH), 114.3 (2CH), 127.1 (2CH), 127.2 (2CH), 128.1 (2CH), 139.7 (C), 141.1 (C-N), 151.1 (C-O), 172.9 (C=O) ppm. EI-MS *m/z* 256 (M⁺, 20), 212 (M-CONH₂, 100).

2-(4-Hydroxyphenyl)-2-(4-methoxyphenylamino)-acetamide (3j). Product **3j** crystallized out in a pure form (360 mg, 66 %) by dissolving the crude residue in MeOH/H₂O, mp 192-196 °C; ¹H NMR (500 MHz, DMSO) δ 3.61 (3H, OCH₃, s), 4.69 (1H, CH, d, J = 7.1 Hz, s after D₂O exch.), 5.52 (1H, NH, d, J = 7.1 Hz, D₂O exch.), 6.57 (2H, Ar H, d, J = 8.9 Hz), 6.68 (2H, Ar H, d, J = 8.9 Hz), 6.71 (2H, Ar H, d, J = 8.5 Hz), 7.04 (1H, NH₂, s, D₂O exch.), 7.29 (2H, Ar H, d, J = 8.5 Hz),

7.51 (1H, NH₂, s, D₂O exch.), 9.32 (1H, OH, s, D₂O exch.) ppm. ¹³C NMR (DMSO) δ 55.6 (OCH₃), 61.1 (CH), 114.6 (2CH), 114.7 (2CH), 115.2 (2CH), 128.6 (2CH), 130.1 (C), 141.5 (C-N), 151.5 (C-O), 156.8 (C-O), 174.2 (C=O) ppm. ESI-MS *m/z* 273 [(M+H)⁺, 100], 256 (50).

2-Benzo[1,3]-dioxol-5-yl-2-(4-methoxyphenylamino)-acetamide (3k). Product **3k** crystallized out in pure form (420 mg, 70 %) by dissolving the crude residue in CHCl₃/Et₂O, mp 127-130 °C; ¹H NMR (500 MHz, DMSO) δ 3.61 (3H, OCH₃, s), 4.75 (1H, CH, d, J = 7.6 Hz, s after D₂O exch.), 5.61 (1H, NH, d, J = 7.6 Hz, D₂O exch.), 5.96 (2H, CH₂, AB system, J = 1.16 Hz), 6.57 (2H, Ar H, d, J = 9.0 Hz), 6.67 (2H, Ar H, d, J = 9.0 Hz), 6.84 (1H, Ar' H, d, J = 8.1 Hz), 6.97 (1H, Ar' H, dd, J = 1.7, 8.1 Hz), 7.05 (1H, Ar' H, d, J = 1.7 Hz), 7.06 (1H, NH₂, s, D₂O exch.), 7.53 (1H, NH₂, s, D₂O exch.) ppm. ¹³C NMR (DMSO) δ 55.1 (OCH₃), 60.7 (CH), 100.7 (CH₂), 107.3 (CH), 107.7 (CH), 114.1 (2CH), 114.3 (2CH), 114.8 (CH), 120.5 (CH), 133.7 (C), 141.0 (C-N), 146.3 (C-O), 147.0 (C-O), 151.0 (C-O), 172.8 (C=O) ppm. ESI-MS *m/z* 301 [(M+H)⁺, 100], 284 (25).

2-(2-Hdroxyphenyl)-2-(4-methoxyphenylamino)-acetamide (3l). Purification of the crude residue by FCC (EtOAc/hexane, 1.1) afforded **3l** (164 mg, 30 %), mp 171-174 °C; ¹H NMR (500 MHz, DMSO) δ 3.61 (3H, OCH₃, s), 5.12 (1H, CH, d, J = 7.0 Hz, s after D₂O exch.), 5.54 (1H, NH, d, J = 7.0 Hz, D₂O exch.), 6.57 (1H, Ar H, td, J = 1.1, 7.6 Hz), 6.86 (1H, Ar H, dd, J = 1.1, 8.1 Hz), 7.08 (1H, Ar H, td, J = 1.6, 7.6 Hz), 7.17 (1H, NH₂, s, D₂O exch.), 7.22 (1H, NH₂, s, D₂O exch.), 7.29 (1H, Ar H, dd, J = 1.6, 7.6 Hz), 9.83 (1H, OH, s, D₂O exch.) ppm. ¹³C NMR (DMSO) δ 55.6 (OCH₃), 55.7 (CH), 114.5 (2CH), 114.8 (2CH), 115.6 (CH), 119.6 (CH), 125.7 (C), 128.0 (CH), 128.8 (CH), 141.5 (C-N), 151.6 (C-O), 155.0 (C-O), 173.9 (C=O) ppm. ESI-MS *m/z* 373 [(M+H)⁺, 100], 256 (30), 150 (40).

2-(2-Methoxyphenyl)-2-(4-methoxyphenylamino)-acetamide (3m). By dissolving the crude residue in Et₂O, **3m** crystallized out in pure form (343 mg, 60 %), mp 203-205 °C. ¹H NMR (500 MHz, DMSO) δ 3.61 (3H, OCH₃, s), 3.86 (3H, OCH₃, s), 5.16 (1H, CH, d, J = 7.5 Hz, s after D₂O exch.), 5.57 (1H, NH, d, J = 7.5 Hz, D₂O exch.), 6.56 (2H, Ar H, d, J = 8.9 Hz), 6.68 (2H, Ar H, d, J

= 8.9 Hz), 6.90 (1H, Ar H, td, J = 0.9, 7.5 Hz), 7.02 (1H, Ar H, dd, J = 0.9, 7.5 Hz), 7.15 (1H, NH₂, s, D₂O exch.), 7.21 (1H, NH₂, s, D₂O exch.), 7.25 (1H, Ar H, td, J = 1.9, 7.5 Hz), 7.37 (1H, Ar H, dd, J = 1.9, 7.5 Hz) ppm. ¹³C NMR (DMSO) δ 54.8 (CH), 55.2 (OCH₃), 55.5 (OCH₃), 111.0 (CH), 113.9 (2CH), 114.3 (2CH), 120.3 (CH), 127.4 (CH), 127.5 (CH), 128.5 (C), 141.3 (C-N), 151.1 (C-O), 156.7 (C-O), 172.8 (C=O) ppm. EI-MS *m/z* 286 (M⁺, 10), 242 (M-CONH₂), 227 (20), 212 (25).

2-(3-Methoxyphenyl)-2-(4-methoxyphenylamino)acetamide (3n). By dissolving the crude residue in CHCl₃/Et₂O, product **3n** crystallized out in a pure form (338 mg, 59 %), mp 131-134 °C. ¹H NMR (500 MHz, DMSO) δ 3.61 (3H, OCH₃, s), 3.74 (3H, OCH₃, s), 4.81 (1H, CH, d, J = 7.8 Hz, s after D₂O exch.), 5.65 (1H, NH, d, J = 7.8 Hz, D₂O exch.), 6.58 (2H, Ar H, d, J = 9.0 Hz), 6.82 (1H, Ar' H, dd, J = 2.3, 7.8 Hz), 7.06 (1H, NH₂, s, D₂O exch.), 7.08 (2H, Ar' H, m), 7.23 (1H, Ar' H, t, J = 7.8 Hz), 7.57 (1H, NH₂, s, D₂O exch.) ppm. ¹³C NMR (DMSO) δ 54.9 (OCH₃), 55.1 (OCH₃), 61.1 (CH), 112.4 (CH), 113.0 (CH), 114.1 (2CH), 114.3 (2CH), 119.3 (CH), 129.0 (CH), 141.1 (C), 141.3 (C), 151.1 (C-N), 159.1 (C-O), 172.7 (C=O) ppm. ESI-MS *m/z* 287 [(M+H⁺), 100], 270 (10).

2-(4-Methoxyphenyl)-2-(4-methoxyphenylamino)acetamide (3p). By dissolving the crude residue in CHCl₃/Et₂O, product **3p** crystallized out in a pure form (377 mg, 66 %), mp 145-150 °C. ¹H NMR (500 MHz, DMSO) δ 3.61 (3H, OCH₃, s), 3.73 (3H, OCH₃, s), 4.77 (1H, CH, d, J = 7.5 Hz, s after D₂O exch.), 5.60 (1H, NH, d, J = 7.5 Hz, D₂O exch.), 6.58 (2H, Ar H, d, J = 8.9 Hz), 6.68 (2H, Ar H, d, J = 8.9 Hz), 6.89 (2H, Ar' H, d, J = 8.5 Hz), 7.07 (1H, NH₂, s, D₂O exch.), 7.41 (2H, Ar' H, d, J = 8.5 Hz), 7.55 (1H, NH₂, s, D₂O exch.) ppm. ¹³C NMR (DMSO) δ 54.9 (OCH₃), 55.1 (OCH₃), 60.6 (CH), 113.5 (2CH), 114.1 (2CH), 114.3 (2CH), 128.2 (2CH), 131.7 (C), 141.2 (C-N), 151.0 (C-O), 158.5 (C-O), 173.2 (C=O) ppm. ESI-MS *m/z* 287 [(M+H⁺), 100], 270 (20).

2-(4-Bromophenyl)-2-(4-methoxyphenylamino)acetamide (3q). Purification of the crude residue by FCC (EtOAc/hexane, 1:1) afforded **3q** (428 mg, 64 %), mp 108-110 °C. ¹H NMR (400 MHz, DMSO) δ 3.61 (3H, OCH₃, s), 4.86 (1H, CH, d, J = 7.9 Hz, s after D₂O exch.), 5.71 (1H, NH, d, J

= 7.9 Hz, D₂O exch.), 6.56 (2H, Ar H, d, J = 8.9 Hz), 6.67 (2H, Ar H, d, J = 8.9 Hz), 7.15 (1H, NH₂, s, D₂O exch.), 7.45 (2H, Ar' H, d, J = 8.4 Hz), 7.52 (2H Ar' H, d, J = 8.4 Hz), 7.63 (1H, NH₂, s, D₂O exch.) ppm. ¹³C NMR (DMSO) δ 55.1 (OCH₃), 60.4 (CH), 114.2 (2CH), 114.3 (2CH), 120.3 (C-Br), 129.2 (2CH), 130.9 (2CH), 139.3 (C), 140.8 (C-N), 151.2 (C-O), 173.3 (C=O) ppm. EI-MS *m/z* 336-334 (M⁺, 15), 292-290 (M-CONH₂, 100).

2-(4-Fluorophenyl)-2-(4-methoxyphenylamino)-acetamide (3r). Purification of the crude residue by FCC (EtOAc/hexane, 6:4) afforded **3r** (329 mg, 60 %), mp 151-154 °C. ¹H NMR (500 MHz, DMSO) δ 3.61 (3H, OCH₃, s), 4.87 (1H, CH, d, J = 7.6 Hz, s after D₂O exch.), 5.69 (1H, NH, d, J = 7.6 Hz, D₂O exch.), 6.58 (2H, Ar H, d, J = 9.0 Hz), 6.68 (2H, Ar H, d, J = 9.0 Hz), 7.13 (1H, NH₂, s, D₂O exch.), 7.15 (2H, Ar H, t, J = 8.7 Hz), 7.53 (1H Ar H, d, J = 8.7 Hz), 7.54 (1H Ar H, d, J = 8.7 Hz), 7.62 (1H, NH₂, s, D₂O exch.) ppm. ¹³C NMR (DMSO) δ 55.1 (OCH₃), 60.4 (CH), 114.2 (2CH), 114.3 (2CH), 114.8 (2CH, d, ²J_{C-F} = 21.4 Hz), 128.95 (2CH, d, ³J_{C-F} = 7.6 Hz), 135.9 (C, d, ⁴J_{C-F} = 3.1 Hz), 141.0 (C-N), 151.1 (C-O), 161.4 (C-F, d, ¹J_{C-F} = 242.6 Hz), 172.7 (C=O) ppm. ESI-MS *m/z* 275 [(M+H)⁺, 100], 258 (25).

2-(4-Methoxyphenylamino)-2-naphthalen-1-yl-acetamide (3s). Purification of the crude residue by FCC (EtOAc/hexane, 4:6) afforded **3s** (226 mg, 37 %), mp 157-160 °C. The low yield of **3s** is mainly due to the low solubility of 1-naphthylaldehyde in the reaction medium. ¹H NMR (400 MHz, DMSO) δ 3.62 (3H, OCH₃, s), 5.55 (1H, CH, d, J = 7.4 Hz, s after D₂O exch.), 5.85 (1H, NH, d, J = 7.4 Hz, D₂O exch.), 6.68 (4H, Ar H, AB system, J = 9.2 Hz), 7.30 (1H, NH₂, s, D₂O exch.), 7.47-7.58 (3H, napht H, m), 7.64 (1H, NH₂, s, D₂O exch.), 7.68 (1H napht H, d, J = 7.0 Hz), 7.87 (1H napht H, d, J = 8.1 Hz), 7.95 (1H naphth H, d, J = 7.7 Hz), 8.29 (1H napht H, d, J = 8.1 Hz) ppm. ¹³C NMR (DMSO) δ 55.2 (OCH₃), 58.4 (CH), 113.9 (2CH), 114.4 (2CH), 123.7 (CH), 125.1 (CH), 125.3 (CH), 125.5 (CH), 126.1 (CH), 127.9 (CH), 128.5 (CH), 131.2 (C), 133.4 (C), 135.2 (C), 141.6 (C-N), 151.2 (C-O), 173.1 (C=O) ppm. EI-MS *m/z* 306 [(M⁺, 10), 262 (M-CONH₂, 100), 134 (40).

2-(4-Methoxyphenylamino)-2-naphthalen-2-yl-acetamide (3t). By dissolving the crude residue in Et₂O, **3t** crystallized out (367 mg, 60 %), mp 198-200 °C. ¹H NMR (400 MHz, DMSO) δ 3.60 (3H, OCH₃, s), 5.05 (1H, CH, d, J = 7.6 Hz, s after D₂O exch.), 5.81 (1H, NH, d, J = 7.6 Hz, D₂O exch.), 6.67 (4H, Ar H, AB system, J = 9.3 Hz), 7.18 (1H, NH₂, s, D₂O exch.), 7.46-7.53 (2H, naphth H, m), 7.68 (1H naphth H, dd, J = 1.7, 8.4 Hz), 7.69 (1H, NH₂, s, D₂O exch.), 7.88 (3H naphth H, m), 8.03 (1H naphth H, s) ppm. ¹³C NMR (DMSO) δ 51.1 (OCH₃), 61.3 (CH), 114.2 (2CH), 114.3 (2CH), 125.3 (CH), 125.7 (CH), 125.8 (CH), 126.0 (CH), 127.3 (CH), 127.5 (CH), 127.6 (CH), 132.3 (C), 132.6 (C), 137.4 (C), 141.1 (C-N), 151.1 (C-O), 172.7 (C=O) ppm. ESI-MS *m/z* 307 [(M+H)⁺, 100], 290 (20).

2-Furan-2-yl-2-(4-methoxyphenylamino)-acetamide (3u). By dissolving the crude residue in Et₂O, **3u** crystallized out on standing at 0 °C overnight (418 mg, 85 %), mp 123-126 °C. ¹H NMR (500 MHz, DMSO) δ 3.64 (3H, OCH₃, s), 4.96 (1H, CH, d, J = 8.5 Hz, s after D₂O exch.), 5.57 (1H, NH, d, J = 8.5 Hz, D₂O exch.), 6.37 (1H, furan H, d, J = 3.3 Hz), 6.41 (1H, furan H, dd, J = 1.9, 3.3 Hz), 6.65 (2H, ar H, d, J = 8.9 Hz), 6.73 (2H, Ar H, d, J = 8.9 Hz), 7.25 (1H, NH₂, s, D₂O exch.), 7.57 (1H, NH₂, s, D₂O exch.), 7.58 (1H, furan H, d, J = 1.9 Hz) ppm. ¹³C NMR (500 Mz, DMSO) δ 55.2 (OCH₃), 55.9 (CH), 107.3 (CH, furan), 110.3 (CH, furan), 114.3 (2CH), 114.4 (2CH), 141.0 (C-N), 142.1 (CH, furan), 151.5 (C-O), 152.3 (C-O, furan), 171.0 (C=O) ppm. ESI-MS *m/z* 247 [(M+H)⁺, 100], 230 (70).

2-Phenyl-2-(*p*-tolylamino)-acetamide (3v). Purification by FCC (EtOAc/hexane, 4:6) of the crude residue afforded **3v** (375 mg, 78 %), mp 112-114 °C (Lit.^b 113-114 °C). ¹H NMR (400 MHz, DMSO) δ 2.12 (3H, CH₃, s), 4.89 (1H, CH, d, J = 7.6 Hz, s after D₂O exch.), 5.80 (1H, NH, d, J = 7.6 Hz, D₂O exch.), 6.54 (2H, Ar H, d, J = 8.4 Hz), 6.85 (2H, Ar H, d, J = 8.4 Hz), 7.11 (1H, NH₂, s, D₂O exch.), 7.25 (1H, Ph H, t, J = 7.3 Hz), 7.32 (2H, Ph H, t, J = 7.3 Hz), 7.50 (2H, Ph H, d, J = 7.3 Hz), 7.60 (1H, NH₂, s, D₂O exch.) ppm. ¹³C NMR (DMSO) δ 19.8 (CH₃), 60.6 (CH), 113.1

(2CH), 124.8 (C), 127.0 (2CH), 127.2 (CH), 128.0 (2CH), 129.0 (2CH), 139.6 (C-N), 144.7 (C-O), 172.7 (C=O) ppm. ESI-MS m/z 241 [(M+H)⁺, 100], 224 (10), 196 (15).

2-(4-Bromophenylamino)-2-phenylacetamide (3z). By dissolving the crude residue in CHCl₃/Et₂O, **3z** crystallized out in pure form (366 mg, 60 %), mp 173-176 °C (Lit.^c 174 °C). ¹H NMR (400 MHz, DMSO) δ 4.90 (1H, CH, d, J = 7.3 Hz, s after D₂O exch.), 6.31 (1H, NH, d, J = 7.3 Hz, D₂O exch.), 6.59 (2H, Ar H, d, J = 8.7 Hz), 7.15 (1H, NH₂, s, D₂O exch.), 7.17 (2H, Ar H, d, J = 8.7 Hz), 7.27 (1H, Ph H, t, J = 7.3 Hz), 7.34 (2H, Ph H, t, J = 7.3 Hz), 7.50 (2H, Ph H, d, J = 7.3 Hz), 7.64 (1H, NH₂, s, D₂O exch.) ppm. ¹³C NMR (DMSO) δ 60.1 (CH), 107.1 (C-Br), 114.9 (2CH), 127.0 (2CH), 127.3 (CH), 128.1 (2CH), 131.1 (2CH), 139.1 (C-N), 146.3 (C-O), 172.1 (C=O) ppm. ESI-MS m/z 307-306 [(M+H)⁺, 100], 290-288 (10), 262-260 (5).

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3c

3i

3m

3v