Observation of O→N Type Smiles Rearrangement in Certain Alkyl Aryl Nitro Compounds[1]

Natesan Selvakumar,* Deekonda Srinivas, Azagarsamy Malar Azhagan

Department of Discovery Chemistry, Discovery Research, Dr. Reddy's Laboratories Ltd., Miyapur, Hyderabad 500 050, India
Fax +91(40)3045438; E-mail: selvakumarn@drreddys.com

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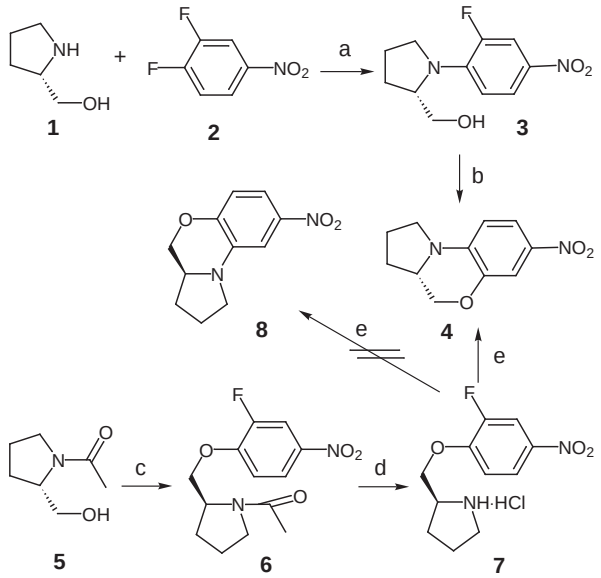
Abstract: Smiles rearrangements on some alkyl aryl nitro compounds having NH_2 group as the nucleophile and oxygen as the leaving group are reported.

Key words: rearrangement, nucleophilic addition, cyclization, isomerization, nitro compound

Smiles rearrangement falls under a broad category of intramolecular aromatic nucleophilic substitution of an appropriately placed nucleophile (YH) onto aromatic rings possessing a strong electron withdrawing group and a leaving group (X) properly positioned as shown in the Figure 1.[2] While the rearrangement is well studied on compounds having the two carbon atoms joining groups X and Y being part of an aromatic ring, it has not been well documented for compounds having aliphatic carbons in between X and Y groups although there have been reports of amides being used as nucleophiles while converting a phenolic hydroxyl group to an anilinic amine functionality.[3] Chromium tricarbonyl catalyzed Smiles rearrangements on certain unactivated aromatic systems have also been reported.[4] There was a recent report outlining the use of Smiles rearrangement in the preparation of certain heterocyclic pyridine derivatives.[5] As this type of rearrangement is not adequately explored, often products resulting out of this rearrangement are discarded as side products in literature.[6] In this report, we record our observations on Smiles rearrangements on some hitherto unknown substrates that possess two or three alkyl carbons in between X and Y groups.

Figure 1

In an ongoing program in our laboratory on the preparation of a variety of aromatic tricyclic compounds, we wished to make the angular tricyclic compound **8** (Scheme 1). Addition of prolinol **1** to 3,4-difluoronitrobenzene (**2**) afforded the linear tricycle **4** under basic conditions via the intermediate **3**. In an attempt to prepare the target tricyclic compound **8**, the N-protected prolinol **5**[7] was added to the 3,4-difluronitrobenzene (**2**) to yield the compound **6**, which upon deacetylation resulted in the nitro-amine **7** as its hydrochloride salt. However, the attempted cyclization of compound **7** under identical conditions employed for the cyclization of **3** resulted only in the linear tricycle **4** instead of the expected angular tricycle **8**. The overall transformation of the conversion of amine **7** to the tricyclic compound **4** involves a smooth Smiles rearrangement of amine **7** presumably leading to the rearranged alcohol **3** that in turn underwent further cyclization, as before, resulting in compound **4**.



Scheme 1 Reagents and conditions: (a) Et_3N, CH_3CN, r.t., 5 h (b) KOH, DMSO, H_2O, r.t., 4 h (c) **2**, NaH, THF, 0 °C to r.t., 9 h (d) conc HCl, reflux, 8 h (e) KOH, H_2O, 3:1 THF–DMSO, r.t., 8 h.

It is believed that the amine nitrogen in compound **7**, being more nucleophilic than oxygen, undergoes an intramolecular aromatic nucleophilic addition resulting in an intermediate of type **9** as shown in Scheme 2. The intermediate **9** further opens up as shown leading eventually to the alcohol **3**, which in turn cyclizes under the basic reaction conditions yielding the tricycle **4**. The occurrence of Smiles rearrangement was confirmed by isolating the intermediate **3** in high yields under controlled conditions of exposing compound **7** to aqueous potassium hydroxide in THF–DMSO, 3:1 for a lesser period of time (ca. 2 hours) at room temperature.

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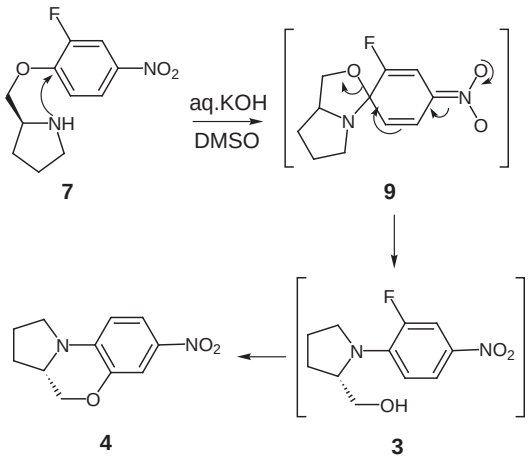
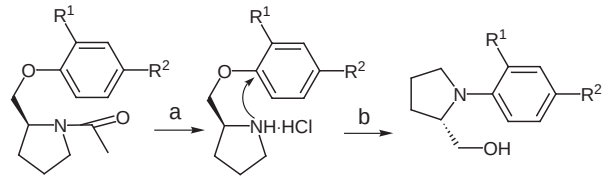


Scheme 2

In order to assess the feasibility of the Smiles rearrangement in these substrates, experiments were carried out on compounds having different aromatic rings. Thus, the amines **11**, **14** and **17**, prepared respectively from 4-fluoronitrobenzene, 2-fluoronitrobenzene and 1-fluoro-2,4-dinitrobenzene as their hydrochlorides by a route analogous to the preparation of compound **7** (Scheme 3), were exposed to basic conditions to result in rearranged compounds as expected.



10: R^1=H, R^2=NO_2 **11:** R^1=H, R^2=NO_2 **12:** R^1=H, R^2=NO_2

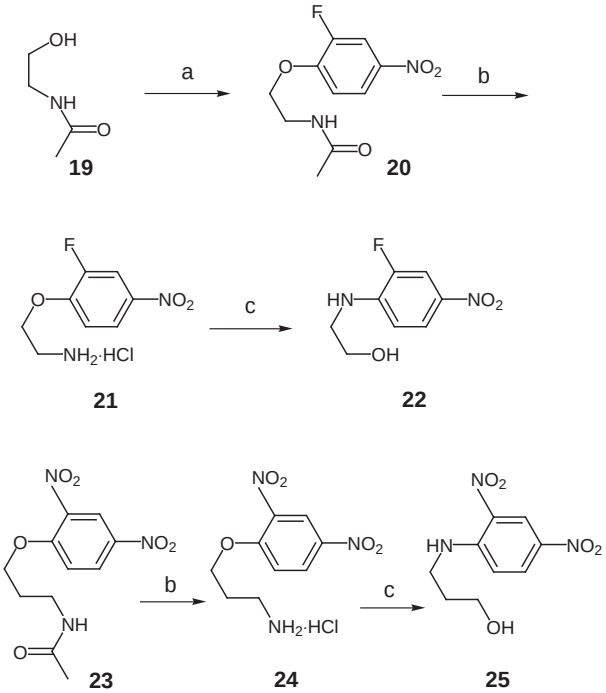
13: R^1=NO_2, R^2=H **14:** R^1=NO_2, R^2=H **15:** R^1=NO_2, R^2=H

16: R^1, R^2=NO_2 **17:** R^1, R^2=NO_2 **18:** R^1,R^2=NO_2

Scheme 3 Reagents and conditions: (a) concd HCl, reflux (b) KOH, DMSO, H_2O, 60 °C.

While the mononitro compounds **11** and **14** needed several hours to complete the rearrangement leading to nitro compounds **12** and **15** respectively, the highly electron deficient dinitro compound **17** rearranged in 15 minutes to give rise to the isomerized dinitro compound **18**. Further confirmation for the feasibility of Smiles rearrangement was derived from a NMR experiment that was conducted on compound **11**. Addition of 5 equivalents of potassium carbonate to an NMR tube containing a sample of **11** in DMSO-d_6 resulted in appreciable isomerization to compound **12** within 30 minutes. This was confirmed by the appearance of a new set of doublets corresponding to aromatic protons of **12**. The conversion of the angular compound **11** to the rearranged compound **12** was completed up to 50% upon leaving **11** in the NMR tube for 15 hours and the conversion was nearly complete after 6 days. This experiment clearly demonstrates the vulnerability of the above compounds to undergo Smiles rearrangement.

To explore the occurrence of Smiles rearrangement on a primary acyclic amine,[8] compound **21** was synthesized as shown in Scheme 4. The compound **19**, prepared as per the literature procedure for compound **5**,[7] afforded the nitro-acetamide **20** under standard conditions that underwent deacetylation resulting in the nitro-amine **21** as its hydrochloride salt. Subjecting the salt **21** to the usual basic conditions lead to the rearranged product **22** in 82% yield as the sole product.[9]



Scheme 4 Reagents and conditions: (a) **2**, NaH, THF, r.t. (b) concd HCl, reflux (c) KOH, DMSO, H_2O, 60 °C, 4 h.

In order to understand the reactivity of substrates with three aliphatic carbons in between X and YH groups, compound **23** was prepared as usual from *N*-acetyl-3-hydroxypropylamine and 1-chloro-2,4-dinitrobenzene. It was deacetylated to yield the amine **24**. The compound **24** underwent smooth Smiles rearrangement to give the rearranged compound **25**.

The above experiments have clearly established the feasibility of Smiles rearrangement in substrates having two or three aliphatic carbon atoms in between groups X and Y wherein NH_2 group plays the role of YH and oxygen atom plays the role of group X. We believe that this account would caution those who are attempting to prepare compounds of this nature.

Melting points are uncorrected. Unless otherwise mentioned, all ^{1}H NMR spectra were recorded in $CDCl_3$ at 200 MHz. All ^{13}C NMR spectra were done at 50 MHz in DMSO-d_6. Chemical shifts are reported in δ units with respect to TMS and DMSO-d_6 as internal standard respectively for ^{1}H NMR and ^{13}C NMR. Unless otherwise

mentioned, all the solvents used were of LR grade. Flash chromatography was performed using silica gel (100–200 mesh). All the organic extracts were dried over Na_2SO_4 after work up. Petroleum ether (PE) with a bp range of 60–80 °Cwas used.

(2*S*)-1-(2-Fluoro-4-nitrophenyl)azolan-2-ylmethanol (3)

To a soln of L-prolinol (**1**) (76 mg, 0.75 mmol) in anhyd CH_3CN (5 mL) was added dropwise Et_3N (159 mg, 1.57 mmol) followed by 3,4-difluoronitrobenzene (**2**) (100 mg, 0.63 mmol) at r.t. under Ar. After stirring for 5 h at the same temperature, the reaction mixture was worked up by addition of H_2O and extraction with EtOAc (3 × 25 mL). The combined organic extracts were washed with H_2O, brine and dried. The evaporation of solvent afforded the nitro-alcohol **3** as a yellow solid (120 mg, 80%) that was suitable for the next step. An analytical sample was obtained by further purification on a column of silica gel; mp 92–94 °C.

IR (KBr): 1609, 1522, 1309 cm^{-1}.

^1H NMR: δ = 7.80–8.00 (m, 2 H), 6.67 (t, *J* = 9.4 Hz, 1 H), 4.27 (br s, 1 H), 3.40–3.74 (m, 4 H), 1.90–2.20 (m, 4 H).

^{13}C NMR: δ = 150.0 (d, *J* = 241.7 Hz, 1 C), 141.6 (d, *J* = 8.2 Hz, 1 C), 134.9 (d, *J* = 8.2 Hz, 1 C), 121.7, 114.3 (d, *J* = 6.3 Hz, 2 C), 112.2 (d, *J* = 26.4 Hz, 1 C), 61.51, 61.39, 50.4 (d, *J* = 5.7 Hz, 1 C), 27.6, 22.4.

MS-EI: *m*/*z* (%) = 240 [M^+], 209, 163.

Anal. Calcd for $C_{11}H_{13}N_2O_3F$: C, 55.00; H, 5.45; N, 11.66. Found: C, 55.00; H, 5.40; N, 11.58.

(6a*S*)-3-Nitro-6a,7,8,9-tetrahydro-6*H*-azolo[1,2-*d*]benzo[*b*]-[1,4]oxazine (4)

To a soln of the nitro-alcohol **3** (100 mg, 0.42 mmol) in DMSO (8 mL) at r.t. was added powdered KOH (70 mg, 1.24 mmol) followed by few drops of H_2O. After stirring for 4 h at the same temperature, the reaction mixture was worked up by addition of H_2O and extraction with EtOAc (3 × 25 mL). The combined organic extracts were washed with H_2O, brine and dried. The evaporation of solvent afforded product **4** as a yellow solid (70 mg, 77%). An analytical sample was obtained by recrystallization in EtOH.

Mp 158–160 °C.

IR (KBr): 1600, 1487, 1292 cm^{-1}.

^1H NMR: δ = 7.85 (dd, *J* = 8.8, 2.4 Hz, 1 H), 7.72 (d, *J* = 2.4 Hz, 1 H), 6.42 (d, *J* = 9.3 Hz, 1 H), 4.55 (dd, *J* = 10.3, 3.4 Hz, 1 H), 3.28–3.72 (m, 4 H), 2.22–1.94 (m, 3 H), 1.53–1.39 (m, 1 H).

^{13}C NMR: δ = 141.0, 140.7, 135.1, 119.9, 110.3, 109.6, 67.6, 55.4, 47.1, 27.8, 23.0.

MS-EI: *m*/*z* (%) = 220 [M^+], 190, 174.

Anal. Calcd for $C_{11}H_{12}N_2O_3$: C, 59.98; H, 5.50; N, 12.73. Found: C, 59.86; H, 5.35; N, 12.55.

1-[(2*S*)-2-(2-Fluoro-4-nitrophenoxymethyl)azolan-1-yl]-1-ethanone (6)

To a soln of *N*-acetyl-L-prolinol (**5**) (200 mg, 1.39 mmol) in anhyd THF (15 mL) at 0 °C under Ar was added NaH (60% in oil, 40 mg, 1.67 mmol) followed by 3,4-difluoronitrobenzene (**2**) (222 mg, 1.39 mmol). The reaction mixture was stirred while warming to r.t. over 9 h and then worked up by addition of H_2O followed by extraction with EtOAc (3 × 40 mL). The combined organic extracts were washed with H_2O, brine and dried. The residue obtained upon evaporation of the solvents was chromatographed over silica gel. The nitro-amide **6** was obtained upon elution with PE–EtOAc, 1:1 as a yellowish gum (210 mg, 53%) that exists as rotamers.

IR (neat): 1640, 1525, 1347 cm^{-1}.

^1H NMR: δ = 8.07–7.94 (m, 2 H), 7.28–7.20 (m, 1 H), 4.50–4.20 (m, 3 H), 3.60–3.40 (m, 2 H), 2.30–2.00 (m, 7 H).

^{13}C NMR: δ = 168.9 and 168.6 (1 C), 152.3 and 152.1 (1 C), 150.2 (d, *J* = 246.8 Hz, 1 C), 140.0 (d, *J* = 7.3 Hz, 1 C), 121.2 (d, *J* = 2.7 Hz, 1 C), 113.9, 111.8 (d, *J* = 22.8 Hz, 2 C), 70.6 and 68.8 (2 C), 56.2 and 54.8 (1 C), 47.4 and 45.2 (1 C), 28.2 and 27.3 (1 C), 23.6 and 22.0 (1 C), 22.5 and 21.7 (1 C).

MS-CI: 283 [M^+ + 1], 126, 112.

(2*S*)-2-(2-Fluoro-4-nitrophenoxymethyl)azolane Hydrochloride (7)

A soln of the nitro-amide **6** (200 mg, 0.71 mmol) in concd HCl (10 mL) was refluxed for 8 h and then the volatiles were evaporated. The resultant solid was suspended in toluene and the volatiles were removed under reduced pressure. This process was repeated once again to remove traces of HCl to afford the nitro-amine **7** as its hydrochloride salt (150 mg, 76%).

IR (KBr): 2880, 2721, 1523, 1345, 1295 cm^{-1}.

^1H NMR: δ = 9.94 (br s, 1 H), 9.60 (br s, 1 H), 8.30–8.10 (m, 2 H), 7.55–7.35 (m, 1 H), 4.49 (b, *J* = 4.9 Hz, 2 H), 3.99 (br s, 1 H), 3.21 (br s, 2 H), 2.15–1.65 (m, 4 H).

MS-CI: *m*/*z* (%) = 241 [M^+ + 1], 170, 91.

Rearrangement of (7)

To a stirred suspension of the nitro-amine **7** (150 mg, 0.54 mmol) in a mixture of THF (10 mL) and DMSO (3.5 mL) at r.t. was added powdered KOH (91 mg, 1.63 mmol) followed by few drops of H_2O. The progress of the reaction was monitored by TLC that revealed the completion of reaction after 8 h of stirring. The reaction mixture was diluted with H_2O and extracted with EtOAc (3 × 30 mL). The combined organic extracts were washed with H_2O, brine and dried. The evaporation of solvent afforded a yellow solid (90 mg, 69%). The TLC and the spectral data obtained for this compound was identical to the rearranged product **4** as prepared earlier.

10

Yellowish gum, exists as rotamers.

IR (neat): 1640, 1341, 1265 cm^{-1}.

^1H NMR: δ = 8.19 (d, *J* = 9.3 Hz, 2 H), 7.04 (d, *J* = 9.3 Hz, 2 H), 4.50–3.90 (m, 3 H), 3.60–3.40 (m, 2 H), 2.20–1.95 (m, 7 H).

^{13}C NMR: δ = 169.0 and 168.5 (2 C), 163.8 and 163.5 (2 C), 141.0 and 140.8 (2 C), 125.8 (2 C), 114.9 (2 C), 69.7 and 67.9 (2 C), 56.4 and 55.0 (2 C), 47.4 and 45.2 (2 C), 28.2 and 27.3 (2 C), 23.5 and 22.1 (2 C), 22.5 and 21.7 (2 C).

MS-CI: *m*/*z* (%) = 265 [M^+ + 1], 126, 112.

11

Hygroscopic solid.

IR (KBr): 2907, 2746, 1594, 1345 cm^{-1}.

^1H NMR: (DMSO-d_6): δ = 9.92 (br s, 1 H), 9.40 (br s, 1 H), 8.25 (d, *J* = 9.3 Hz, 2 H), 7.20 (d, *J* = 9.3 Hz, 2 H), 4.50–3.80 (m, 3 H), 3.30–3.10 (m, 2 H), 2.30–1.60 (m, 4 H).

MS-CI: *m*/*z* (%) = 223 [M^+ + 1].

12

Yellow solid; mp 107–109 °C.

IR (neat): 3457, 1600, 1307 cm^{-1}.

^1H NMR: (DMSO-d_6): δ = 8.05 (d, *J* = 9.1 Hz, 2 H), 6.69 (d, *J* = 9.1 Hz, 2 H), 4.91 (t, *J* = 5.4 Hz, 1 H), 3.92 (br s, 1 H), 3.60–3.20 (m, 4 H), 2.20–1.80 (m, 4 H).

^{13}C NMR: δ = 151.6, 135.4, 125.7 (2 C), 111.0 (2 C), 60.5, 60.3, 48.3, 27.7, 22.5.

MS-CI: *m*/*z* (%) = 223 [M^+ + 1], 191, 145.

Anal. Calcd for $C_{11}H_{14}N_2O_3$: C, 59.45; H, 6.35; N, 12.61. Found: C, 59.51; H, 6.35; N, 12.52.

13

Light yellow solid, exists as rotamers; mp 91–93 °C.

IR (neat): 1641, 1526, 1417 cm^{-1}.

^1H NMR: (400 MHz): δ = 7.81 (dd, *J* = 8.3, 2.0 Hz, 1 H), 7.53–7.49 (m, 1 H), 7.19 (d, *J* = 8.3 Hz, 1 H), 7.00 (t, *J* = 7.8 Hz, 1 H), 4.43–4.21 (m, 3 H), 3.62–3.43 (m, 2 H), 2.07 (s, 3 H), 2.23–1.92 (m, 4 H).

^{13}C NMR: δ = 168.9 and 168.6 (2 C), 151.2 and 149.9 (2 C), 139.5, 134.4 and 134.3 (1 C), 124.9 and 124.8 (1 C), 120.8 and 120.6 (1 C), 115.1 and 114.9 (1 C), 70.2 and 68.4 (1 C), 56.3 and 55.0 (1 C), 47.5 and 45.2 (1 C), 28.2 and 27.3 (1 C), 23.5 and 22.0 (1 C), 22.5 and 21.6 (1 C).

MS-CI: *m*/*z* (%) = 265 [M^+ + 1], 142, 112, 100.

Anal. Calcd for $C_{13}H_{16}N_2O_4$: C, 59.08; H, 6.10; N, 10.60. Found: C, 59.04; H, 6.19; N, 10.53.

14

Hygroscopic solid.

IR (KBr): 3424, 2883, 1522, 1282 cm^{-1}.

^1H NMR: (DMSO-d_6): δ = 9.80 (br s, 1 H), 9.22 (br s, 1 H), 7.95 (d, *J* = 7.8 Hz, 1 H), 7.71 (t, *J* = 7.8 Hz, 1 H), 7.40 (d, *J* = 8.3 Hz, 1 H), 7.18 (t, *J* = 7.3 Hz, 1 H), 4.55–3.90 (m, 3 H), 3.30–3.00 (m, 2 H), 2.20–1.70 (m, 4 H).

MS-CI: *m*/*z* (%) = 223 [M^+ + 1], 91.

15

Orange solid; mp 82–84 °C.

IR (neat): 3398, 1604, 1511, 1276 cm^{-1}.

^1H NMR: (400 MHz): δ = 7.78 (dd, *J* = 8.3, 1.5 Hz, 1 H), 7.41–7.37 (m, 1 H), 7.11 (d, *J* = 8.8 Hz, 1 H), 6.84–6.80 (m, 1 H), 4.17–4.11 (m, 1 H), 3.84 (dd, *J* = 11.2, 3.4 Hz, 1 H), 3.59–3.49 (m, 2 H), 2.75–2.71 (m, 1 H), 2.19–1.97 (m, 3 H), 1.84–1.74 (m, 2 H).

^{13}C NMR: δ = 142.0, 137.5, 132.9, 126.1, 117.2, 115.9, 62.0, 60.1, 52.3, 28.9, 24.3.

MS-CI: *m*/*z* (%) = 223 [M^+ + 1], 191, 175.

Anal. Calcd for $C_{11}H_{14}N_2O_3$: C, 59.45; H, 6.35; N, 12.61. Found: C, 59.42; H, 6.50; N, 12.54.

16

Light yellow solid, exists as rotamers; mp 97–99 °C.

IR (neat): 1638, 1608, 1532, 1345 cm^{-1}.

^1H NMR: (400 MHz): δ = 8.73 (d, *J* = 2.4 Hz, 1 H), 7.42 (dd, *J* = 9.3, 2.9 Hz, 1 H), 7.44 (d, *J* = 9.3 Hz, 1 H), 4.48–4.39 (m, 3 H), 3.60–3.46 (m, 2 H), 2.09 (s, 3 H), 2.18–1.97 (m, 4 H).

^{13}C NMR: δ = 169.0 and 168.6 (1 C), 155.9 and 155.6 (1 C), 139.7 and 139.6 (1 C), 138.5, 129.3 and 129.1 (1 C), 121.1 and 121.0 (1 C), 115.9 and 115.6 (1 C), 71.4 and 69.8 (1 C), 56.1and 54.8 (1 C), 47.5 and 45.3 (1 C), 28.2 and 27.2 (1 C), 23.5 and 22.0 (1 C), 22.5 and 21.6 (1 C).

MS-EI: *m*/*z* (%) = 310 [M^+], 126, 112, 100.

Anal. Calcd for $C_{13}H_{15}N_3O_6$: C, 50.49; H, 4.89; N, 13.59. Found: C, 50.45; H, 4.89; N, 13.48.

17

Hygroscopic solid.

IR (KBr): 3423, 2873, 1611, 1345 cm^{-1}.

^1H NMR: (DMSO-d_6): δ = 9.89 (br s, 1 H), 9.45 (br s, 1 H), 8.79 (d, *J* = 2.4 Hz, 1 H), 8.56 (dd, *J* = 9.3, 2.9 Hz, 1 H), 7.62 (d, *J* = 9.3 Hz, 1 H), 4.70–3.90 (m, 3 H), 3.30–3.00 (m, 2 H), 2.30–1.70 (m, 4 H).

MS-CI: *m*/*z* (%) = 268 [M^+ + 1], 102.

18

Thick gum.

IR (neat): 3419, 1605, 1524, 1325 cm^{-1}.

^1H NMR: (400 MHz): δ = 8.70 (d, *J* = 2.4 Hz, 1 H), 8.20 (dd, *J* = 9.8, 2.4 Hz, 1 H), 7.15 (d, *J* = 9.8 Hz, 1 H), 4.28–4.23 (m, 1 H), 3.85 (dd, *J* = 11.7, 4.4 Hz, 1 H), 3.70 (dd, *J* = 11.7, 3.4 Hz, 1 H), 3.59–3.53 (m, 1 H), 2.90–2.85 (m, 1 H), 2.32–2.25 (m, 1 H), 2.15–2.05 (m, 2 H), 1.88–1.80 (m, 1 H).

^{13}C NMR: δ = 145.7, 134.7, 134.5, 127.0, 123.4, 117.5, 61.6, 61.3, 52.8, 27.8, 24.3.

MS-CI: *m*/*z* (%) = 268 [M^+ + 1], 236, 220.

20

Light yellow solid; mp 109–111 °C.

IR (neat): 1658, 1525, 1348, 756 cm^{-1}.

^1H NMR: δ = 8.15–7.95 (m, 2 H), 7.10–6.95 (m, 1 H), 6.29 (br s, 1 H), 4.23 (t, *J* = 5.1 Hz, 1 H), 3.74 (q, *J* = 5.4 Hz, 1 H), 2.04 (s, 3 H).

^{13}C NMR: δ = 169.8, 152.3 and 152.1 (1 C), 150.3 (d, *J* = 247.2 Hz, 1 C), 140.0 (d, *J* = 7.7 Hz, 1 C), 121.2 (d, *J* = 2.7 Hz, 1 C), 113.9, 111.8 (d, *J* = 22.8 Hz, 1 C), 68.3, 38.0, 22.4.

MS-CI: *m*/*z* (%) = 243 [M^+ + 1].

21

Hygroscopic solid.

IR (KBr): 3426, 2910, 1345, 1285.

^1H NMR: (DMSO-d_6): δ = 8.41 (br s, 3 H), 8.25–8.15 (m, 2 H), 7.50–7.40 (m, 1 H), 4.46 (t, *J* = 4.9 Hz, 1 H), 3.26 (t, *J* = 4.9 Hz, 1 H).

MS-CI: *m*/*z* (%) = 201 [M^+ + 1].

22

Light yellow solid; mp 98–100 °C.

IR (KBr): 3526, 3296, 1615 cm^{-1}.

^1H NMR: δ = 8.01 (dd, *J* = 10.5, 1.3 Hz, 1 H), 7.89 (dd, *J* = 11.6, 2.4 Hz, 1 H), 6.73–6.64 (m, 1 H), 5.08 (br s, 1 H), 3.95 (t, *J* = 5.3 Hz, 1 H), 3.46 (t, *J* = 5.1 Hz, 1 H), 1.80 (br s, 1 H).

^{13}C NMR: δ = 148.3 (d, *J* = 240.5 Hz, 1 C), 143.6 (d, *J* = 12.0 Hz, 1 C), 134.5 (d, *J* = 7.5 Hz, 1 C), 122.4, 110.3 (d, *J* = 22.6 Hz, 1 C), 109.5 (d, *J* = 4.4 Hz, 1 C), 59.4, 45.0.

MS-EI: *m*/*z* (%) = 200 [M^+], 169, 123.

Anal. Calcd for $C_8H_9N_2O_3F$: C, 48.00; H, 4.53; N, 14.00. Found: C, 47.87; H, 4.56; N, 13.92.

23

Yellow solid; mp 114–115 °C.

IR (KBr): 3273, 1646, 1343 cm^{-1}.

^1H NMR: δ = 8.82 (d, *J* = 2.4 Hz, 1 H), 8.47 (dd, *J* = 9.1, 2.4 Hz, 1 H), 7.26 (d, *J* = 9.1 Hz, 1 H), 6.40 (br s, 1 H), 4.36 (t, *J* = 5.6 Hz, 2 H), 3.56–3.48 (m, 2 H), 2.15 (q, *J* = 5.9 Hz, 2 H), 2.03 (s, 3 H).

^{13}C NMR: δ = 169.1, 156.0, 139.3, 138.2, 129.2, 121.0, 115.5, 68.4, 35.2, 28.5, 22.5.

MS-CI: *m*/*z* (%) = 284 [M^+ + 1].

Anal. Calcd for $C_{11}H_{13}N_3O_6$: C, 46.65; H, 4.63; N, 14.84. Found: C, 46.66; H, 4.52; N, 14.78.

24
Hygroscopic solid.

IR (KBr): 3424, 2926, 1521, 1354 cm^{-1}.

^1H NMR: (DMSO-d_6): δ = 8.78 (d, *J* = 2.4 Hz, 1 H), 8.53 (dd, *J* = 9.3, 2.4 Hz, 1 H), 8.16 (br s, 3 H), (d, *J* = 9.3 Hz, 1 H), 4.44 (t, *J* = 5.4 Hz, 2 H), 3.00–2.90 (m, 2 H), 2.12 (t, *J* = 6.3 Hz, 2 H).

MS-CI: *m*/*z* (%) = 242 [M^+ + 1].

25
Yellow solid; mp 67–69 °C.

IR (KBr): 3374, 1623, 1339 cm^{-1}.

^1H NMR: δ = 9.15 (d, *J* = 2.4 Hz, 1 H), 8.90 (br s, 1 H), 8.29 (dd, *J* = 9.7, 2.7 Hz, 1 H), 6.99 (d, *J* = 9.7 Hz, 1 H), 3.91 (t, *J* = 5.4 Hz, 2 H), 3.61 (q, *J* = 6.5 Hz, 2 H), 2.05 (q, *J* = 6.2 Hz, 2 H), 1.68 (br s, 1 H).

^{13}C NMR: δ = 148.0, 134.5, 129.7, 129.4, 123.4, 114.9, 58.8, 41.1, 30.9.

MS-CI: *m*/*z* (%) = 242 [M^+ + 1].

Anal. Calcd for $C_9H_{11}N_3O_5$: C, 44.82; H, 4.60; N, 17.42. Found: C, 44.62; H, 4.68; N, 17.24.

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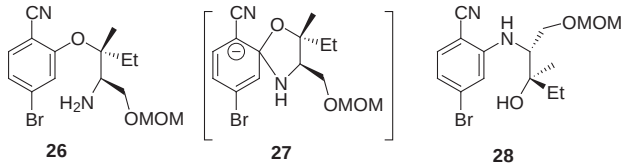

Figure 2

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