Erratum

An Improved Synthesis of 1,4,7-Triazacyclonanones (tacns) and 1,4,7,10-Tetraazacyclododecanes (cyclens)

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In the reaction of compound 7 with ethylenediamine (13) according to Scheme 4, it was reported that 1-tosyl-1,4,7-triazacyclononane (9) was obtained in 78% isolated yield. However, after being alerted by other laboratories, we repeated the same reaction under identical experimental conditions and did not obtain compound 9 as the product of the reaction. While the compound obtained was isomeric with 9 according to its mass spectrum, its $^1$H NMR spectrum was similar but not identical to that of 9, a known compound which could be obtained by an alternate route. While the product was isomeric with 9 according to its mass spectrum, its $^1$H and $^{13}$C NMR spectra were different from those of 20. The product is consistent with a piperazine structure 24, with four aromatic and six aliphatic carbon signals in its $^{13}$C NMR spectrum (revised Scheme 7).

1-(2'-Aminoethyl)-4-tosylpiperazine (23)

In conclusion, ethylenediamine (13) and 1,4,7-triazahexane (19) did react with 7 but did not give the corresponding tacn 9 or cyclen 20.

1-(2'-Aminoethyl)-4-tosylpiperazine (23)

Compound 7 (5.83 g, 10.0 mmol), K$_2$CO$_3$ (8.00 g, 58.0 mmol), ethylenediamine (0.60 g, 10.0 mmol) and anhydrous MeCN (50 mL) were added to a round-bottom flask. The mixture was heated to reflux under an N$_2$ atmosphere for 12 h. The mixture was cooled to r.t. and filtered. The filtrate was concentrated and the residue was purified by flash chromatography (SiO$_2$, CH$_2$Cl$_2$–MeOH–Et$_3$N= 2:1:0.05 as eluent) to give 23 as a pale yellow oil (2.0 g, 78%).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.63 (d, $J$ = 7.4 Hz, 2 H), 7.32 (d, $J$ = 7.4 Hz, 2 H), 3.01 (br, 4 H), 2.73 (t, $J$ = 6.0 Hz, 2 H), 2.52 (br t, 4 H), 2.43-2.40 (m, 5 H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 143.7, 132.4, 129.6, 127.8, 60.2, 52.2, 46.0, 38.4, 21.5.

LRMS (ESI): $m/z$ = 284 ([M$^+$ + H], 100).

HRMS (ESI): calcld for C$_{13}$H$_{22}$N$_3$O$_2$S (M$^+$ + H): 284.1433; found: 284.1423.
1-(1',4'-Diazahexyl)-4-tosylpiperazine (24)

1,4,7-Triazaheptane (19, 0.40 g, 4.00 mmol), compound 7 (2.30 g, 4.00 mmol), K₂CO₃ (6.00 g, 40.0 mmol) and anhydrous MeCN (20 mL) were added to a round-bottom flask. The mixture was heated to reflux under an N₂ atmosphere for 18 h. The mixture was cooled to r.t. and filtered. The filtrate was concentrated and the residue was purified by chromatography (SiO₂, CH₂Cl₂–MeOH = 2:1 as eluent) to give a light yellow oil (1.2 g, 83%).

\[ 1^1\text{H NMR (400 MHz, CDCl}_3\):}\ \delta = 7.58 (d, \ J = 8.0 \text{ Hz, 2 H}), 7.27 (d, \ J = 8.0 \text{ Hz, 2 H}), 2.95 (br, 4 \text{ H}), 2.70 (t, \ J = 6.0 \text{ Hz, 2 H}), 2.59 (p, \ J = 6.0 \text{ Hz, 2 H}), 2.47 (br t, 4 \text{ H}), 2.43 (t, \ J = 6.0 \text{ Hz, 2 H}), 2.37 (s, 3 \text{ H}). \]

\[ 1^3\text{C NMR (100 MHz, CDCl}_3\):}\ \delta = 143.7, 132.4, 129.6, 127.8, 57.4, 52.3, 52.2, 46.1, 46.0, 41.4, 21.5. \]

\[ 1^3\text{C NMR (100 MHz, DMSO-d}_6\):}\ \delta = 143.7, 132.4, 129.6, 127.8, 57.4, 52.3, 52.2, 46.1, 46.0, 41.4, 21.5. \]

\[ \text{LRMS (ESI): m/z = 327 ([M^+ + H], 100), 349 ([M^+ + Na], 29).} \]

\[ \text{HRMS (ESI): calcd for C}_{15}\text{H}_{27}\text{N}_4\text{O}_2\text{S} [M^+ + H]: 327.1855; found: 327.1856.} \]

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References
