Erratum

An Improved Synthesis of 1,4,7-Triazacyclononanes (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-1,4,7triazacyclononane (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 ¹H NMR spectrum was similar but not identical to that of 9, a known compound which could be obtained by an alternate route and independently synthesized according to Scheme 2.1 More significantly, the ¹³C NMR spectrum of the obtained product has four aromatic and five aliphatic carbon signals and is distinctly different from that of 1-tosyl-1,4,7-triazacyclononane (9) which has eight carbon signals. The product is assigned to have the structure 1-(2'aminoethyl)-4-tosylpiperazine (23) (revised Scheme 4). The formation of a six-membered ring is consistent with the reaction of 7 with *N*,*N*-dimethylethylenediamine (10) in giving 1-methyl-4-tosylpiperazine (11) as we had reported in Scheme 3.

Revised Scheme 4: Reaction of 7 with 13

We also re-examined the coupling of **7** with 1,4,7-triazaheptane (**19**) using potassium carbonate in refluxing acetonitrile (Scheme 7). The product obtained was found not to be 1-tosyl-1,4,7,10-tetraazacyclododecane (**20**), a known compound independently synthesized by an alter-

nate route.² While the product was isomeric with **20** according to its mass spectrum, its ¹H and ¹³C 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 ¹³C NMR spectrum (revised Scheme 7).

Revised Scheme 7: Reaction of 7 with 19

In conclusion, ethylenediamine (13) and 1,4,7-triazaheptane (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_2CO_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 (SiO₂, CH₂Cl₂–MeOH–Et₃N = 2:1:0.05 as eluent) to give 23 as a pale yellow oil (2.0 g, 78%).

 1 H NMR (400 MHz, CDCl₃): δ = 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, CDCl₃): δ = 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): calcd for $C_{13}H_{22}N_3O_2S$ (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), K_2CO_3 (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 N_2 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%).

¹H NMR (400 MHz, CDCl₃): δ = 7.58 (d, J = 8.0 Hz, 2 H), 7.27 (d, J = 8.0 Hz, 2H), 2.95 (br, 4 H), 2.70 (t, J = 6.0 Hz, 2 H), 2.59 (p, J = 6.0 Hz, 2 H), 2.47 (br t, 4 H), 2.43 (t, J = 6.0 Hz, 2H), 2.37 (s, 3 H).

 ^{13}C NMR (100 MHz, CDCl₃): δ = 143.7, 132.4, 129.6, 127.8, 57.4, 52.3, 52.2, 46.1, 46.0, 41.4, 21.5.

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

HRMS (ESI): calcd for $C_{15}H_{27}N_4O_2S$ [M $^+$ + H]: 327.1855; found: 327.1856.

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ADDENDA AND ERRATA

References

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- (2) Compound **20** could be obtained by mono-tosylation of commercially available **2**. See: (a) Ohashi, M.; Konkol, M.; Del Rosal, I.; Poteau, R.; Maron, L.; Okuda, J. *J. Am. Chem. Soc.*, **2008**, *130*, 6920. (b) Leivers, M.; Breslow, R. *Bioorg. Chem.*, **2001**, *29*, 345.