Erratum

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

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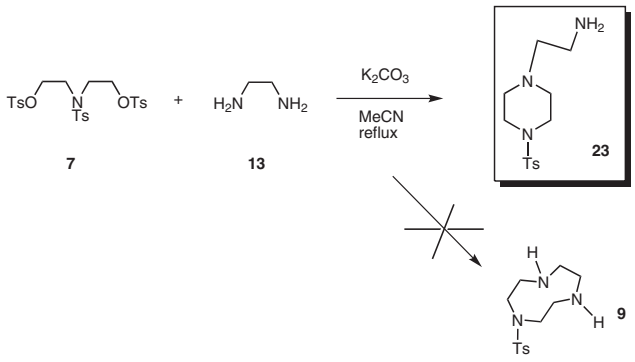
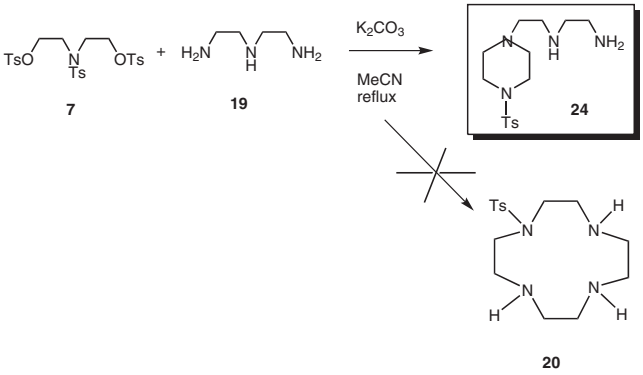
In the reaction of compound **7** with ethylenediamine (**13**) according to Scheme 4, it was reported that 1-tosyl-1,4,7-triazacyclononane (**9**) was obtained in 78% isolated yield. However, after being alerted by other laboratories, we repeated the same reaction under identical experimental conditions 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 and independently synthesized according to Scheme 2.[1] More significantly, the ^{13}C 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 alternate route.[2] While the product was isomeric with **20** 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).



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 (SiO_2, CH_2Cl_2–MeOH–Et_3N = 2:1:0.05 as eluent) to give 23 as a pale yellow oil (2.0 g, 78%).

^{1}H NMR (400 MHz, $CDCl_3$): 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, $CDCl_3$): 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 (SiO_2, CH_2Cl_2–MeOH = 2:1 as eluent) to give a light yellow oil (1.2 g, 83%).

^{1}H NMR (400 MHz, $CDCl_3$): 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, $CDCl_3$): 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.

Acknowledgment

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References

(1) (a) Flassbeck, C.; Wieghardt, K. *Z. Anorg. Allg. Chem.* **1992**, *608*, 60. (b) Romakh, V. B.; Therrien, B.; Labat, G.; Stoekli-Evans, H.; Shul'pin, G. B.; Suss-Fink, G. *Inorg. Chim. Acta* **2006**, *359*, 3297. (c) Romakh, V. B.; Therrien, B.; Karmazin-Brelot, L; Labat, G.; Stoekli-Evans, H.; Shul'pin, G. B.; Suss-Fink, G. *Inorg. Chim. Acta* **2006**, *359*, 1619. (d) Bambirra, S.; Leusen, D. V.; Cornelis G. J.; Tazelaar, A. M.; Hessen, B. *Organometallics* **2007**, *26*, 1014.

(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.