Electronic supplementary information

Improved Modular Synthesis of H₄octapa and H₂dedpa, and Yttrium Coordination Chemistry Towards δ⁶/δ⁹Y Radiopharmaceuticals.

Eric W. Price†§, Jacqueline F. Cawthray†§, Michael J. Adam§, and Chris Orvig*†

†Medicinal Inorganic Chemistry Group, Department of Chemistry, University of British Columbia, 2036 Main Mall, Vancouver, British Columbia, Canada, V6T 1Z1;

§TRIUMF, 4004 Wesbrook Mall, Vancouver, British Columbia, Canada, V6T 2A3;
Supplementary Figure S1. $^1$H NMR spectrum (400 MHz, CDCl₃, RT) of tert-Butyl 6-(methyl)picolinate (1).

Supplementary Figure S2. $^{13}$C NMR spectrum (100 MHz, CDCl₃, RT) of tert-Butyl 6-(methyl)picolinate (1).
Supplementary Figure S3. $^1$H NMR spectrum (300 MHz, CDCl$_3$, RT) of tert-Butyl 6-(bromomethyl)picolinate (2).

Supplementary Figure S4. $^{13}$C NMR spectrum (75 MHz, CDCl$_3$, RT) of tert-Butyl 6-(bromomethyl)picolinate (2).
Supplementary Figure S5. $^1$H NMR spectrum (400 MHz, CDCl$_3$, RT) of
$N,N'$-(2-Nitrobenzenesulfonamide)-$N,N'$-[6-(tert-butoxycarbonyl)pyridin-2-yl]methyl]-1,2-diaminoethane (4).

Supplementary Figure S6. $^{13}$C NMR spectrum (100 MHz, CDCl$_3$, RT) of
$N,N'$-(2-Nitrobenzenesulfonamide)-$N,N'$-[6-(tert-butoxycarbonyl)pyridin-2-yl]methyl]-1,2-diaminoethane (4).
Supplementary Figure S7. $^1$H NMR spectrum (400 MHz, CDCl$_3$, RT) of $N,N'$-[6-(tert-Butoxycarbonyl)pyridin-2-yl]methyl-1,2-diaminoethane (5).

Supplementary Figure S8. $^{13}$C NMR spectrum (100 MHz, CDCl$_3$, RT) of $N,N'$-[6-(tert-Butoxycarbonyl)pyridin-2-yl]methyl-1,2-diaminoethane (5).

Supplementary Figure S9. $^1$H NMR spectrum (300 MHz, MeOD, RT) of H$_2$dedpa, $N,N'$-[(6-carboxylato)pyridin-2-yl]methyl]-1,2-diaminoethane (6).
Supplementary Figure S10. $^{13}$C NMR spectrum (75 MHz, MeOD, RT) of H$_2$dedpa, $N,N'$-[(6-carboxylato)pyridin-2-yl)methyl]-1,2-diaminoethane (6).

Supplementary Figure S11. ATR-IR spectrum (neat) of H$_2$dedpa, $N,N'$-[(6-carboxylato)pyridin-2-yl)methyl]-1,2-diaminoethane (6).
Supplementary Figure S12. 1H NMR spectrum (400 MHz, CDCl₃, RT) of \( N,N'\)-[(tert-Butoxycarbonyl)methyl]-\( N,N'\)-[6-(tert-butoxycarbonyl)pyridin-2-yl]methyl]-1,2-diaminoethane (7).

Supplementary Figure S13. 13C NMR spectrum (100 MHz, CDCl₃, RT) of \( N,N'\)-[(tert-Butoxycarbonyl)methyl]-\( N,N'\)-[6-(tert-butoxycarbonyl)pyridin-2-yl]methyl]-1,2-diaminoethane (7).
Supplementary Figure S14. $^1$H NMR spectrum (300 MHz, MeOD, RT) of H$_2$octapa, $N,N'$-[(6-carboxylato)pyridin-2-yl)methyl]-$N,N'$-diacetic acid-1,2-diaminoethane (8).

Supplementary Figure S15. $^{13}$C NMR spectrum (100 MHz, MeOD, RT) of H$_2$octapa, $N,N'$-[(6-carboxylato)pyridin-2-yl)methyl]-$N,N'$-diacetic acid-1,2-diaminoethane (8).
Supplementary Figure S16. ATR-IR spectrum (neat) of H₄octapa, N,N'([(6-carboxylato)pyridin-2-yl)methyl]-N,N'-diacetic acid-1,2-diaminoethane (8).

Supplementary Figure S17. ¹H NMR spectrum (300 MHz, DMSO-d₆, RT) of [Y(octapa)]⁺ (9).
Supplementary Figure S18. $^1$H NMR spectrum (400 MHz, D$_2$O, RT) of [Y(octapa)]; (9).

Supplementary Figure S19. $^{13}$C NMR spectrum (75 MHz, D$_2$O, RT) of [Y(octapa)]; (9).
**Supplementary Figure S20.** $^1$H NMR spectrum (300 MHz, CDCl$_3$, RT) of $N,N'$-(2-Nitrobenzenesulfonamide)·$N,N'$-[6-(methoxycarbonyl)pyridin-2-yl]methyl]-1-(p-nitrobenzyl)-1,2-diaminoethane (12).

**Supplementary Figure S21.** $^{13}$C NMR spectrum (75 MHz, CDCl$_3$, RT) of $N,N'$-(2-Nitrobenzenesulfonamide)·$N,N'$-[6-(methoxycarbonyl)pyridin-2-yl]methyl]-1-(p-nitrobenzyl)-1,2-diaminoethane (12).
Supplementary Figure S22. $^1$H NMR spectrum (400 MHz, CDCl$_3$, RT) of $N,N'$-[6-(Methoxycarbonyl)pyridin-2-yl]methyl]-1-(p-nitrobenzyl)-1,2-diaminoethane (13).

Supplementary Figure S23. $^{13}$C NMR spectrum (100 MHz, CDCl$_3$, RT) of $N,N'$-[6-(Methoxycarbonyl)pyridin-2-yl]methyl]-1-(p-nitrobenzyl)-1,2-diaminoethane (13).
Supplementary Figure S24. $^1$H NMR spectrum (400 MHz, MeOD, RT) of $p$-SCN-Bn-H$_2$dedpa, $N,N'$-{$([6$-carboxylato]pyridin-2-yl)methyl}-1-$(p$-benzylisothiocyanato)-1,2-diaminoethane (14).

Supplementary Figure S25. $^{13}$C NMR spectrum (100 MHz, MeOD, RT) of $p$-SCN-Bn-H$_2$dedpa, $N,N'$-{$([6$-carboxylato]pyridin-2-yl)methyl}-1-$(p$-benzylisothiocyanato)-1,2-diaminoethane (14).
**Supplementary Figure S26.** ATR-IR spectrum (neat) of $p$-SCN-Bn-H$_2$dedpa, $N,N'$-[[6-carboxylato]pyridin-2-yl]methyl]-1-(p-benzylisothiocyanato)-1,2-diaminoethane (14).

**Supplementary Figure S27.** $^1$H NMR spectrum (400 MHz, CDCl$_3$, RT) of $N,N'$-[[tert-Butoxycarbonyl)methyl]-$N,N'$-[[6- tert-butoxycarbonyl]pyridin-2-yl]methyl]-1-(p-nitrobenzyl)-1,2-diaminoethane (15).
Supplementary Figure S28. $^{13}$C NMR spectrum (100 MHz, CDCl$_3$, RT) of $N,N'-$[(tert-Butoxycarbonyl)methyl]-$N,N'-$-[(6-tert-butoxycarbonyl)pyridin-2-yl]methyl}-1-(p-nitrobenzyl)-1,2-diaminoethane (15).

Supplementary Figure S29. $^1$H NMR spectrum (400 MHz, MeOD, RT) of $p$-SCN-Bn-H$_4$octapa, $N,N'$-[(Carboxylato)methyl]-$N,N'$-[(6-carboxylato)pyridin-2-yl]methyl}-1-(p-benzylisothiocyanato)-1,2-diaminoethane (16).
Supplementary Figure S30. $^{13}$C NMR spectrum (150 MHz, MeOD, RT) of $p$-SCN-Bn-H$_4$octapa, $N,N'$-[(Carboxylato)methyl]-$N,N'-$\{[(6-carboxylato)pyridin-$2$-$yl]$methyl\}-1-(p$-benzylisothiocyanato)-1,2$-$diaminoethane (16).

Supplementary Figure S31. ATR-IR spectrum (neat) of $p$-SCN-Bn-H$_4$octapa, $N,N'$-[(Carboxylato)methyl]-$N,N'-$\{[(6-carboxylato)pyridin-$2$-$yl]$methyl\}-1-(p$-benzylisothiocyanato)-1,2$-$diaminoethane (16).
Supplementary Figure S32. $^1$H-$^1$H COSY NMR full spectrum of [Y(octapa)]$^-$ (600 MHz, D$_2$O, RT).
Supplementary Figure S33. $^1$H-$^{13}$C HSQC NMR full spectrum of [Y(octapa)]$^-$ (400 MHz, 100 MHz, D$_2$O, RT).
Supplementary Figure S34. RP-HPLC chromatograph of [Y(octapa)], mobile phase A: deionized H$_2$O, B: acetonitrile, gradient 10% to 100% B over 30 minutes, product $t_R = 9.5$ min.