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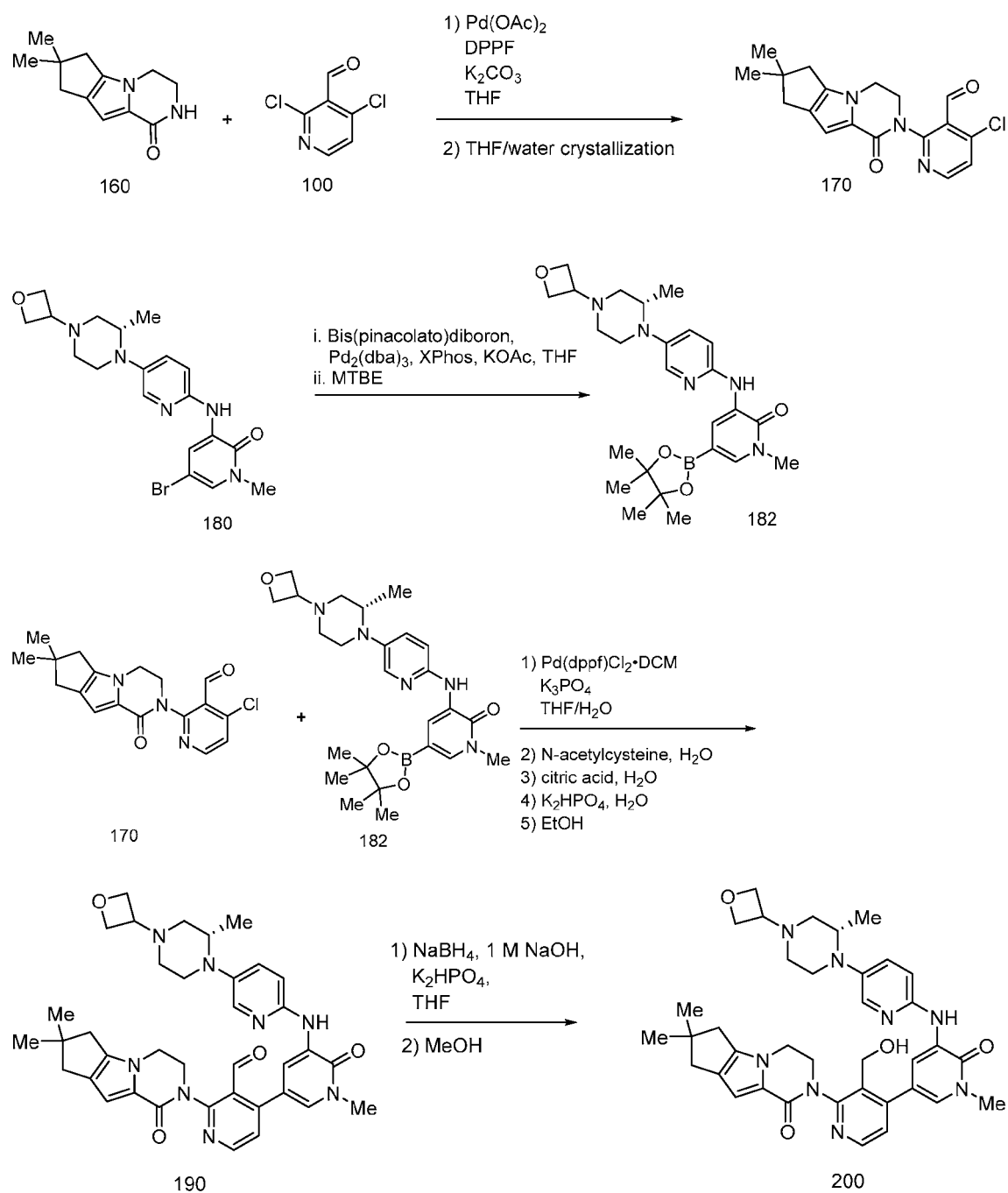


Figure 1

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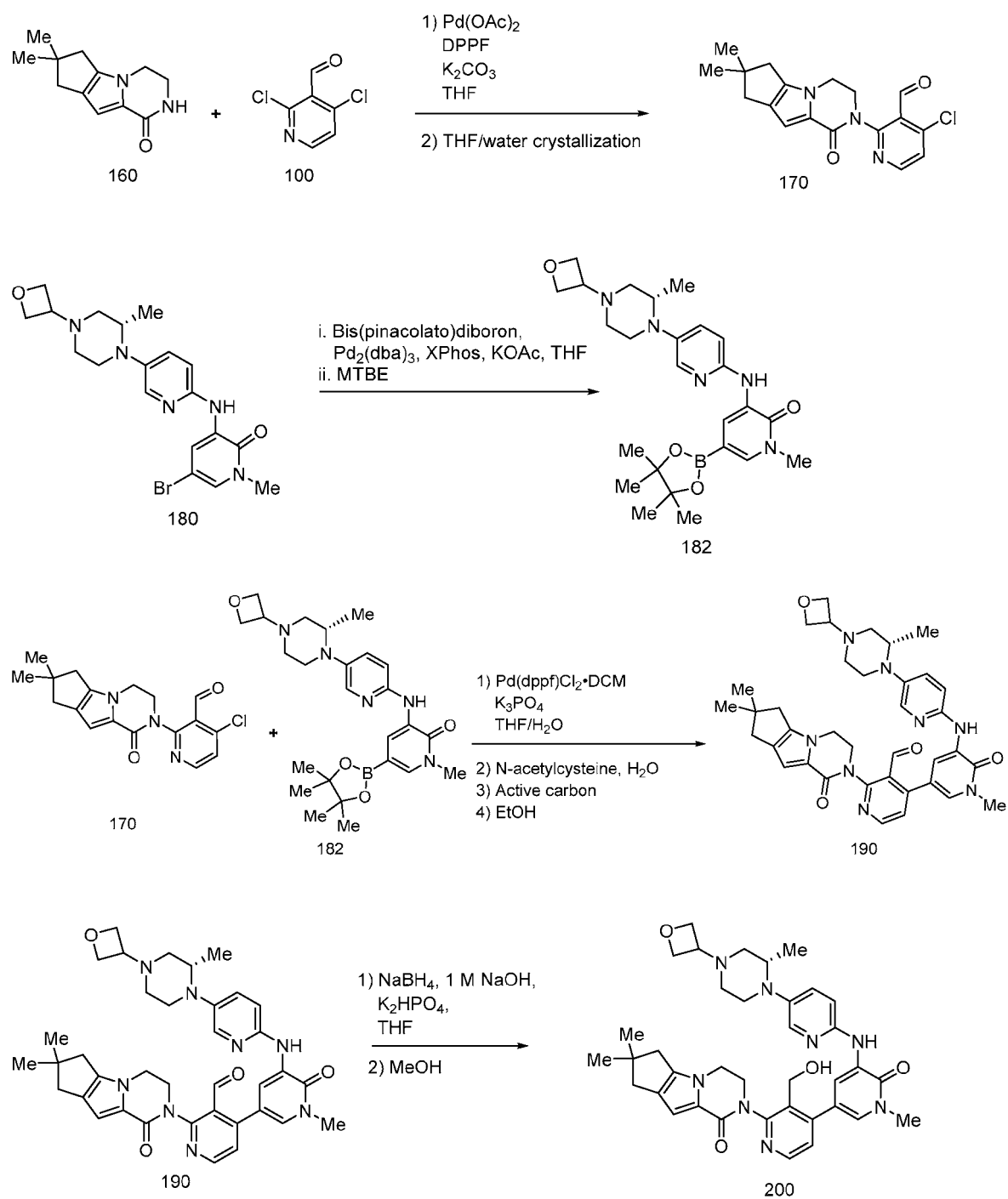


Figure 2

Oc1ccncc1 (60) + NBS $\xrightarrow[\text{69 ~ 74\% yield}]{\text{ACN, 25~55 } ^\circ\text{C, 2h}}$ O=C1NC(Br)C(Br)C=C1 (70) $\xrightarrow[\text{75 ~ 80\% yield}]{\text{Methyl p-tosylate, K}_2\text{CO}_3, \text{DMF}}$ CN1C(Br)C(Br)C=C1C=O (90)

O=C1NC(Br)C(Br)C=C1 (70) $\xrightarrow[\text{69 ~ 77\% yield}]{\text{Boc}_2\text{O, 25 } ^\circ\text{C, 18 h}}$ CN1C(Br)C(Br)C=C1C(=O)OC(C)(C)C (40)

halogen-c1cc(C(=O)O)ccn1 (50, halogen = Br or Cl) + CN1C(Br)C(Br)C=C1C(=O)OC(C)(C)C (40) $\xrightarrow[\text{78.8\% Yield}]{\text{K}_3\text{PO}_4 (2.0 \text{ eq}), \text{Pd}(\text{OAc})_2 (1.2\%), \text{BINAP} (1.2\%), \text{dioxane} (10 \text{ w/w}), 95\text{--}105^\circ\text{C, 15h}}$ CN1C(Br)C(Br)C=C1C(=O)OC(C)(C)C (40) + O=[N+]([O-])c1ccc(N2CC[C@H](C)CC2)cc1 (153) $\xrightarrow[\text{90.0\% Yield}]{\text{1) 7 ~ 8\% HCl, 2) NaOH}}$ O=[N+]([O-])c1ccc(N2CC[C@H](C)CC2)cc1 (153)

O=C1OC(=O)C1 (20) (1.6 eq) $\xrightarrow[\text{85.7\% Yield}]{\text{NaBH}(\text{OAc})_3 (3.0 \text{ eq}), \text{HOAc} (1.5\text{--}1.7 \text{ eq}), \text{DCM} (20 \text{ w/w}), 38\text{--}42^\circ\text{C, 3 h}}$ CN1C(Br)C(Br)C=C1C(=O)OC(C)(C)C (40) + O=[N+]([O-])c1ccc(N2CC[C@H](C)CC2)cc1 (153) $\xrightarrow[\text{96.6\% Yield}]{\text{H}_2, 10\% \text{ Pd/C} (5\% \text{ w/w}), \text{MeOH} (5 \text{ v/w}), 45\text{--}55^\circ\text{C}}$ CN1C(Br)C(Br)C=C1C(=O)OC(C)(C)C (40) + O=[N+]([O-])c1ccc(N2CC[C@H](C)CC2)cc1 (153)

O=C1NC(Br)C(Br)C=C1 (70) $\xrightarrow[\text{70.6\% Yield}]{\text{Pd}_2(\text{dba})_3, \text{Xantphos}, \text{K}_3\text{PO}_4, \text{dioxane}, 100^\circ\text{C, 15 h}}$ O=C1NC(Br)C(Br)C=C1 (70)

Overall yield: 41.4%

Figure 3

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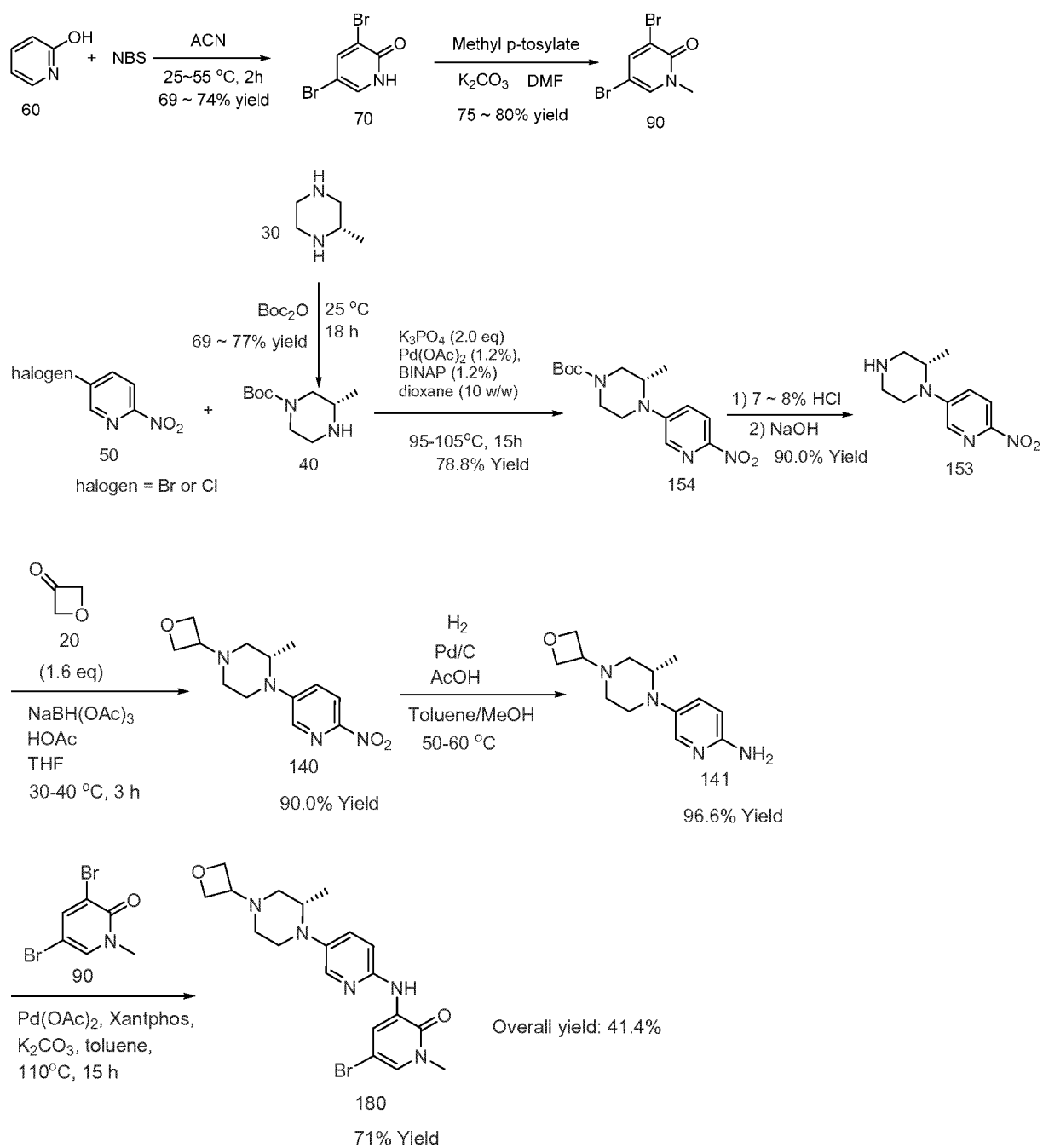


Figure 4

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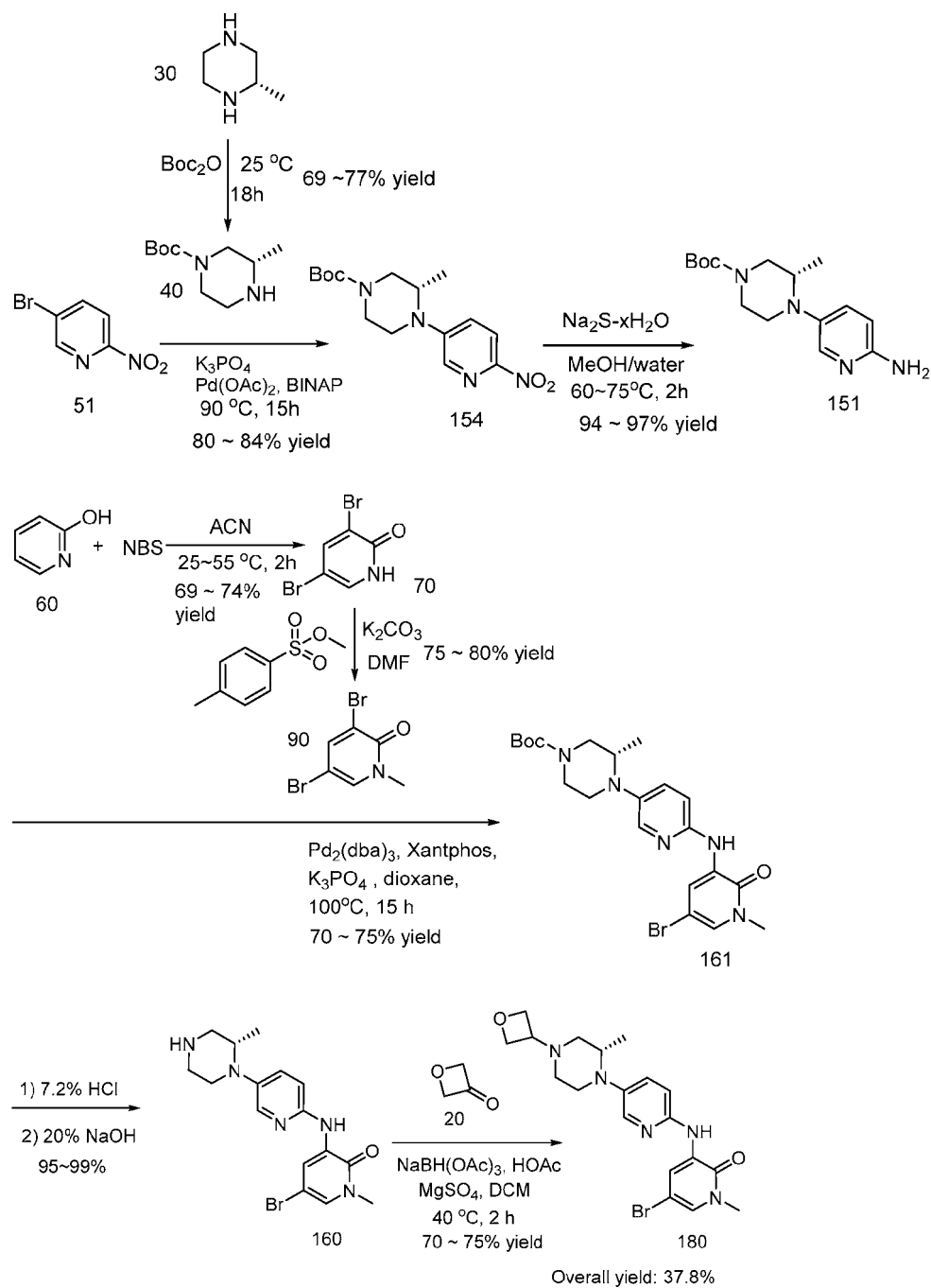


Figure 5

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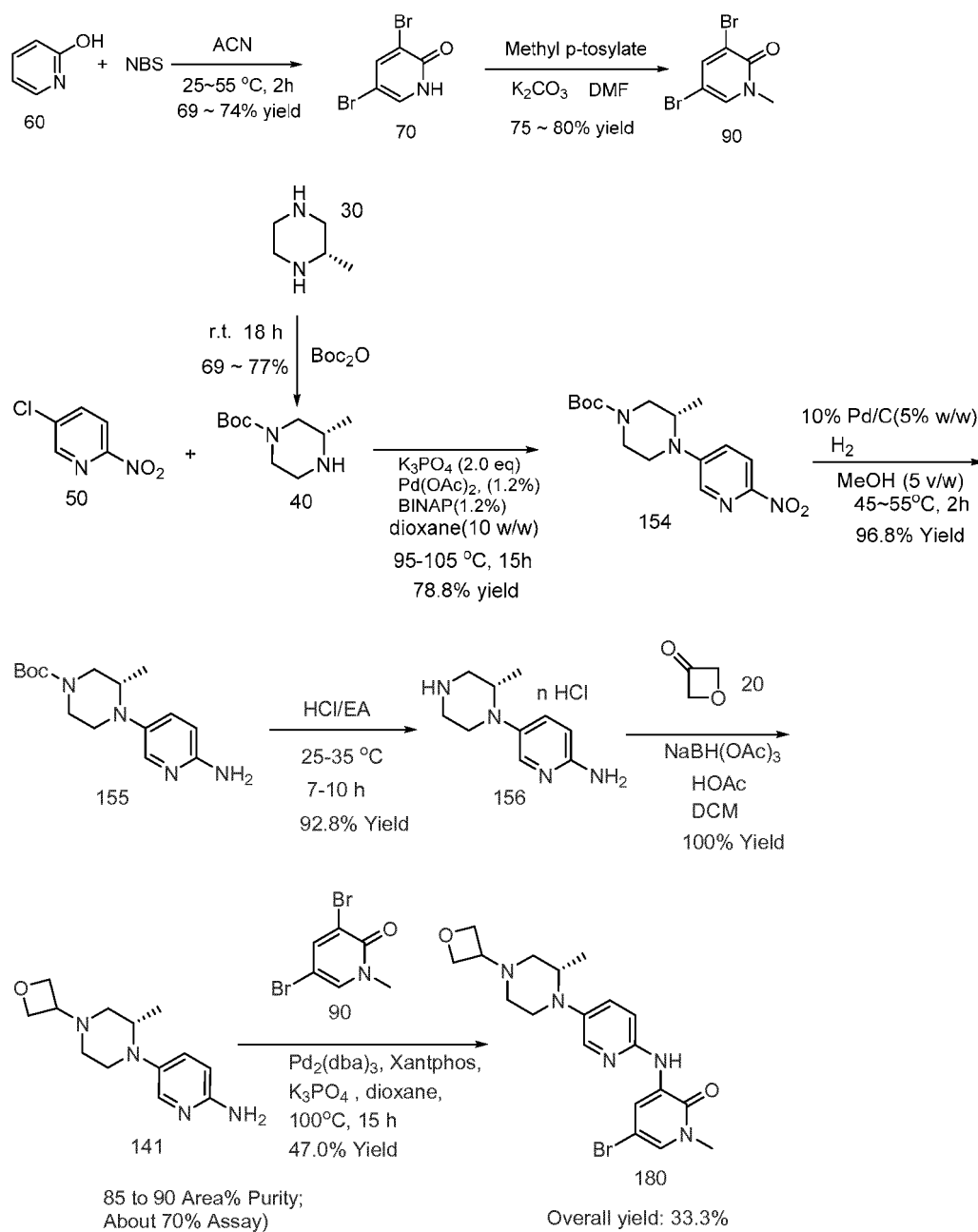


Figure 6

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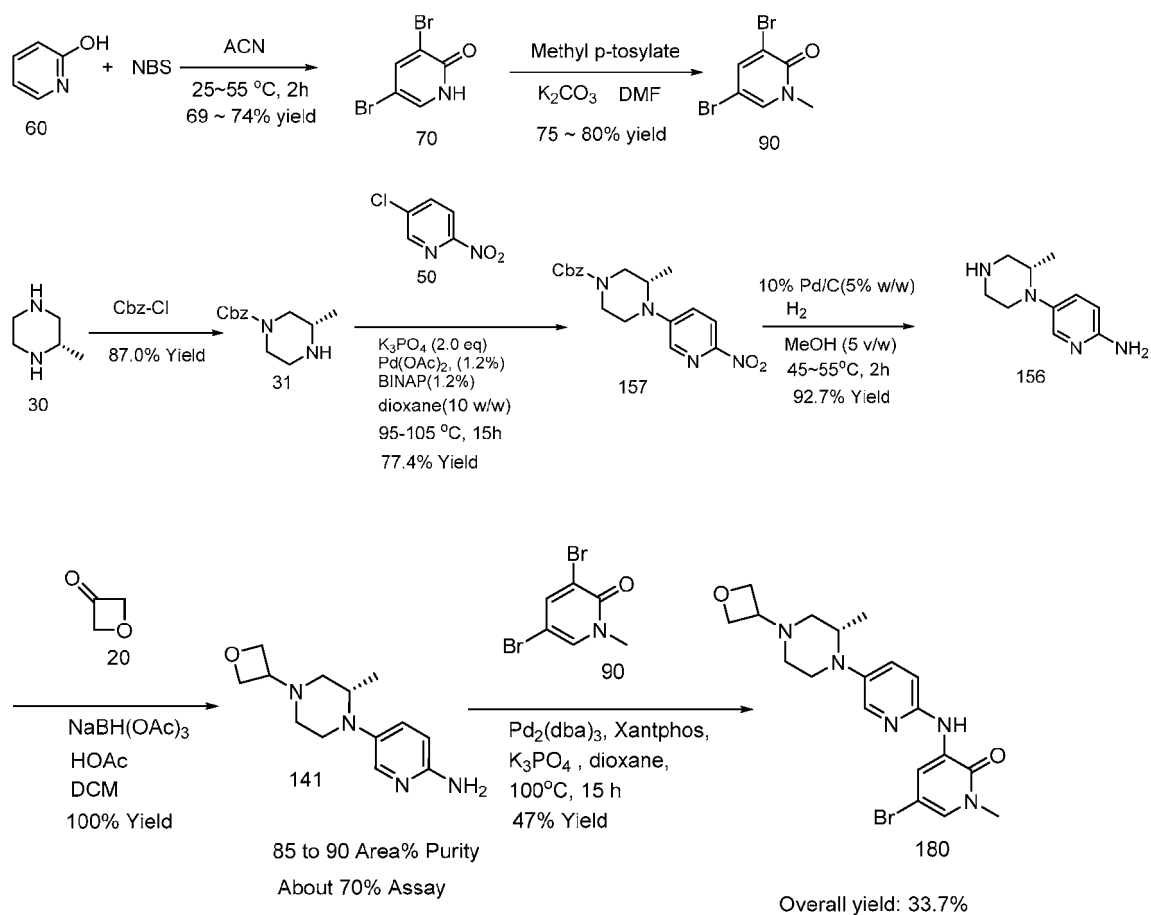


Figure 7

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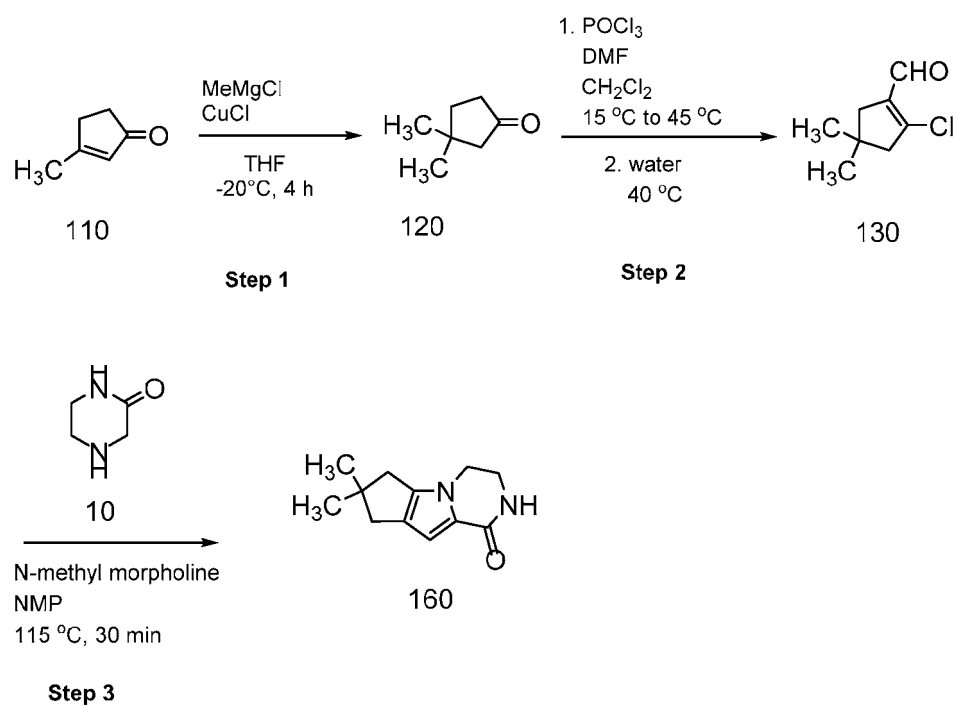


Figure 8

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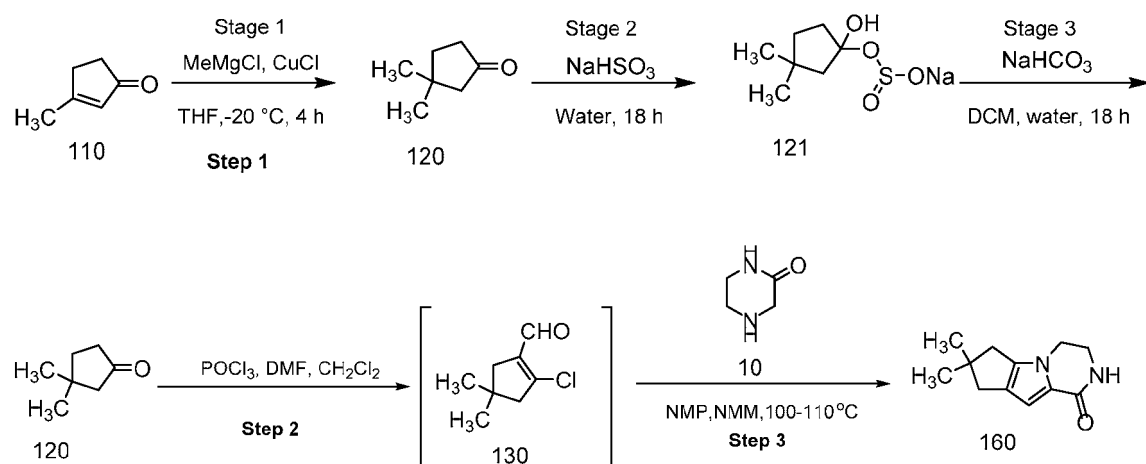


Figure 9

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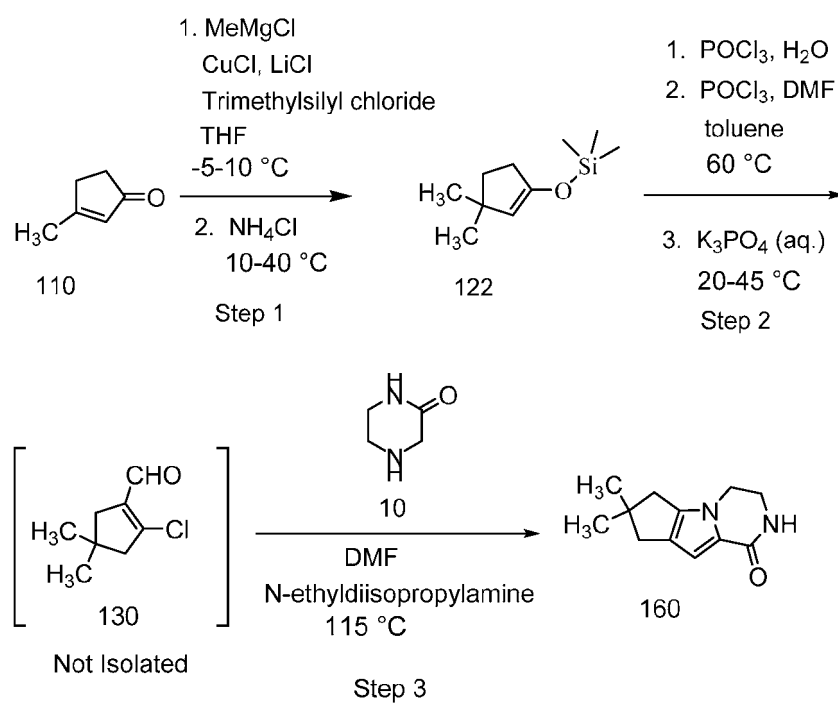


Figure 10