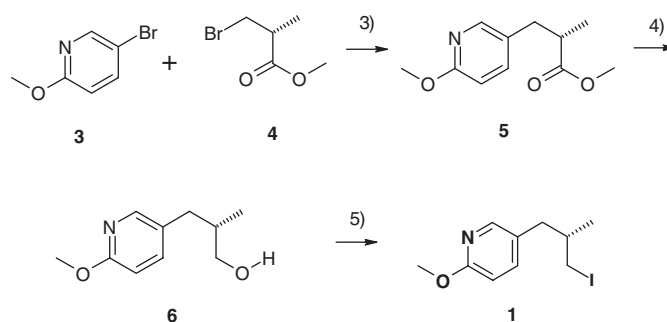
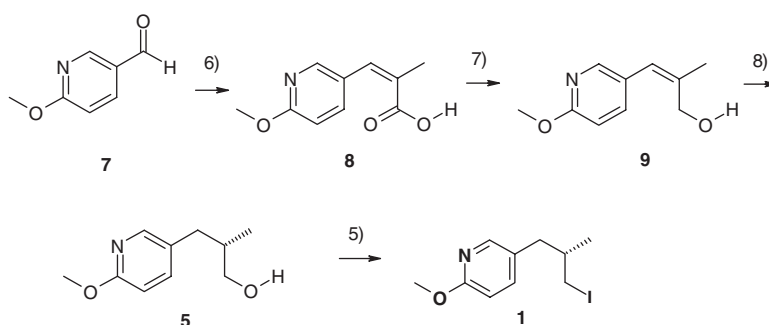
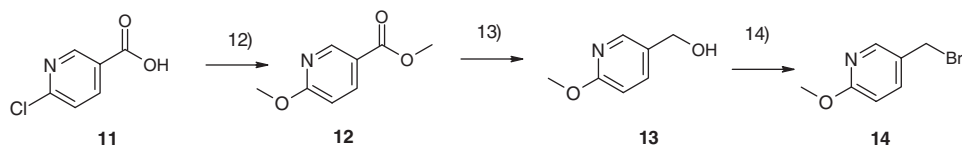




Scheme 2 Research synthesis. *Reaction conditions:* (3) methyl-3-bromo-2(S)-2-methyl propionate **4**, ZnEt_2 , MnBr_2 , CuCl , DMPU/THF, Pd(dppf)Cl_2 , CH_2Cl_2 , 43%; (4) LiAlH_4 , THF, 82%; (5) MeP(I)(OPh)_3 , DMF, 89%.



Scheme 3 Chemical development synthesis.³ *Reaction conditions:* (6) $(\text{EtO})_2\text{HPO}/\text{NaH}$, HOOCCHBrCH_3 , 79%; (7) LiAlH_4 , THF, 89%; (8) $\text{H}_2/[\text{Rh(nbd)Cl}_2]$, (R) -*p*-DMA-MeObiphep, $p(\text{H}_2) = 80$ bar, 60°C , 19 h, 92% ee, 97%.



Scheme 4 Synthesis of the intermediate **14**. *Reaction conditions:* (12) MeOH, H_2SO_4 , 65°C , 12 h, 58%; (13) LiAlH_4 , diethyl ether, 30°C , 1 h, 68%; (14) PBr_3 , CH_2Cl_2 , 61% (unstable).

this particular approach.⁴ The diastereoselective synthesis makes use of an α -alkylation of the propionyl derivative **10** with the corresponding nucleophile **14**.

Results

Labeling of NVP-ACQ090 **2** (overview)

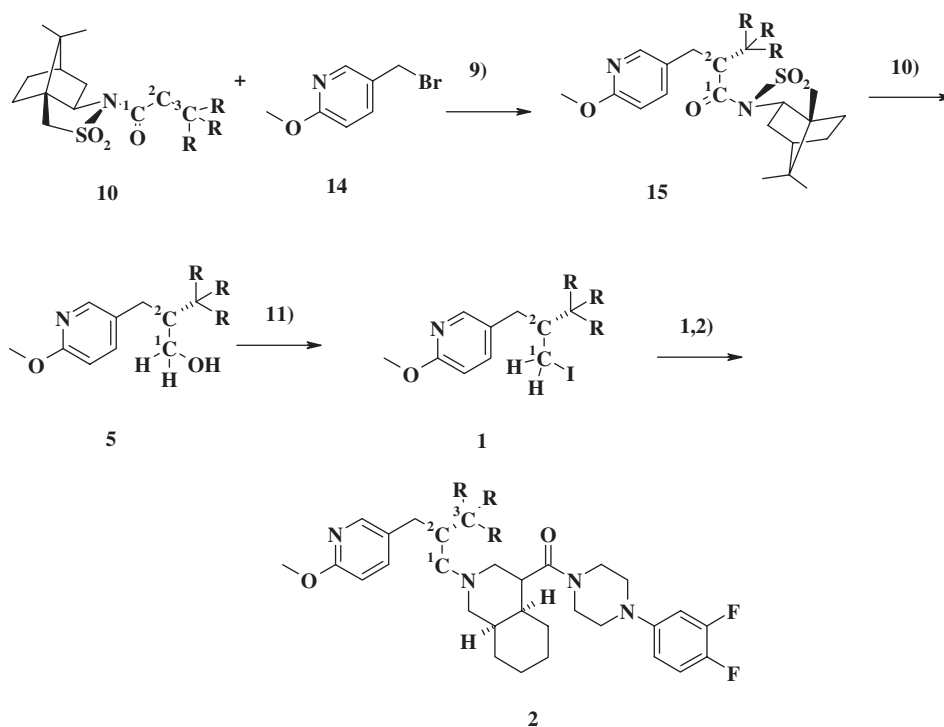
Since it readily polymerized the picolyl bromide **14** was immediately used (Schemes 4 and 5).⁵

Conclusion

The N - $[^{14}\text{C}]$ propionyl bornane-10,2-sultam **10** provided an excellent auxiliary for the diastereoselective synthesis of labeled 5-((*S*)-3-iodo-2-methyl-propyl)-2-methoxy-pyridine **1** – a suitable key intermediate of labeled ACQ090 **2**.

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Name	¹ C	² C	³ C	R
A	¹⁴ C	¹² C	¹² C	¹ H
B	¹³ C	¹³ C	¹³ C	² H

Scheme 5 Synthesis of NVP-ACQ090 **2**. Reaction conditions: (9) THF, -78°C , 1 M NaHMDS, HMPT, **14**, $\text{N}(\text{n-Bu})_4\text{I}$, -78°C , 5 min, 62%; (10) THF, Et_2O , 1 M LiAlH_4 in Et_2O , 0°C , 3 h, 64%; (11) DMF, methyltriphenoxyphosphonium iodide, 0°C , 1 h, 30%; (1) K_2CO_3 , DMF, 25°C , 24 h, 56%; (2) fumaric acid, 2-propanol/diethylether. Analytical characterization of 2A/B: (R)TLC, HPLC >98% (RS), >98%ee, MS 2.2 GBq/mmol, NMR.

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