Category

Peptide Chemistry

Key words

lithiation

amino acids

carboxylation

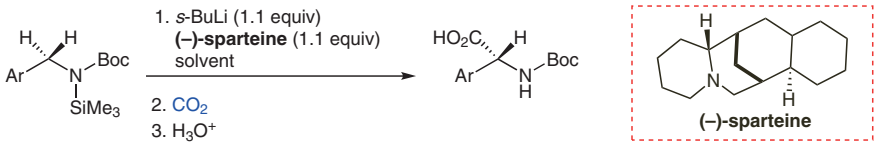
N-Boc *N*-trimethylsilylbenzylamines

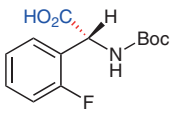
C. BARBERIS, N. VOYER*, J. ROBY, S. CHÉNARD, M. TREMBLAY, P. LABRIE (UNIVERSITÉ LAVAL, STE FOY, CANADA)

Rapid Access to N-Boc Phenylglycine Derivatives via Benzylic Lithiation Reaction

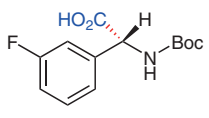
Tetrahedron **2001**, *57*, 2965–2972, DOI: 10.1016/S0040-4020(01)00159-4.

Benzylic Lithiation Reaction for the Synthesis of Unnatural Amino Acids

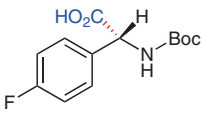




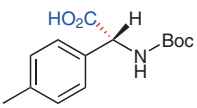
Et_2O, 87% yield, er = 57:43
hexane, 79% yield, er = 72:28
PhMe, 95% yield, er = 74:26



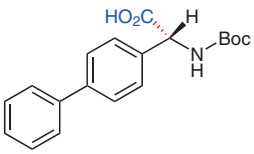
Et_2O, 95% yield, er = 60:40
hexane, 84% yield, er = 75:25
PhMe, 80% yield, er = 85:15



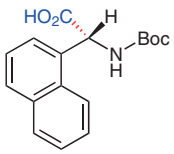
Et_2O, 52% yield, er = 64:36
hexane, 44% yield, er = 79:21
PhMe, 84% yield, er = 84:16



Et_2O, 14% yield, er = 58:42
hexane, 80% yield, er = 82:18
PhMe, 92% yield, er = 80:20



Et_2O, 28% yield, er = 87:13
hexane, 41% yield, er = 98:2
PhMe, 95% yield, er = 90:10



Et_2O, 26% yield, er = 62:38
hexane, 87% yield, er = 81:19
PhMe, 94% yield, er = 82:18

Significance: Unnatural amino acids play a pivotal role in the peptide chemistry. Hence, peptide development chemists are highly attracted towards the development of new methods for the synthesis of unnatural amino acids. In 2001, Voyer and co-workers developed a new method for the synthesis of amino acids using carboxylation of lithiated *N*-Boc *N*-trimethylsilylbenzylamine derivatives.

Comment: A series of unnatural amino acids were synthesized by carboxylation of lithiated *N*-Boc *N*-trimethylsilylbenzylamine derivatives. The reaction could produce *N*-Boc phenylglycine derivatives with moderate optical purity in good yields. Yields and optical purities depend on the solvent, substrate, and chiral complex used in the reaction.

SYNFACTS Contributors: Hisashi Yamamoto, Isai Ramakrishna
Synfacts 2023, 19(12), 1278 Published online: 15.11.2023
DOI: 10.1055/s-0043-1763561; **Reg-No.:** H10023SF