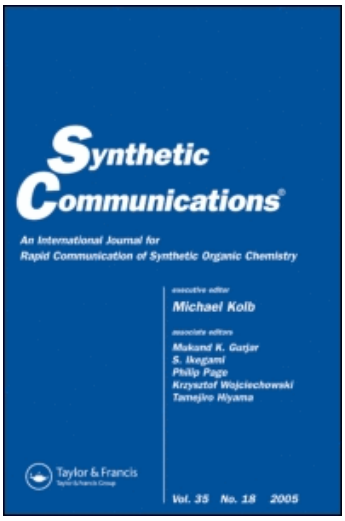


Synthetic Communications
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597304

A New Synthesis of O-Benzyl-L-Threonine

Shui-Tein Chen [a]; Shih-Hsiung Wu [a]; Kung-Tsung Wang [a]
[a] Institute of Biological Chemistry, Academia Sinica and Institute of Biochemical Sciences, National Taiwan University, Taipei, Taiwan ROC

Online Publication Date: 01 December 1989

To cite this Article Chen, Shui-Tein, Wu, Shih-Hsiung and Wang, Kung-Tsung(1989)'A New Synthesis of O-Benzyl-L-Threonine',Synthetic Communications,19:20,3589 — 3593
To link to this Article: DOI: 10.1080/00397918908052769
URL: http://dx.doi.org/10.1080/00397918908052769

SYNTHETIC COMMUNICATIONS, 19(20), 3589-3593 (1989)

A NEW SYNTHESIS OF O-BENZYL-L-THREONINE

Shui-Tein Chen, Shih-Hsiung Wu* and Kung-Tsung Wang

Institute of Biological Chemistry, Academia Sinica
and
Institute of Biochemical Sciences,
National Taiwan University
P. O. Box 23 -106, Taipei 10098 Taiwan R O C

Abstract

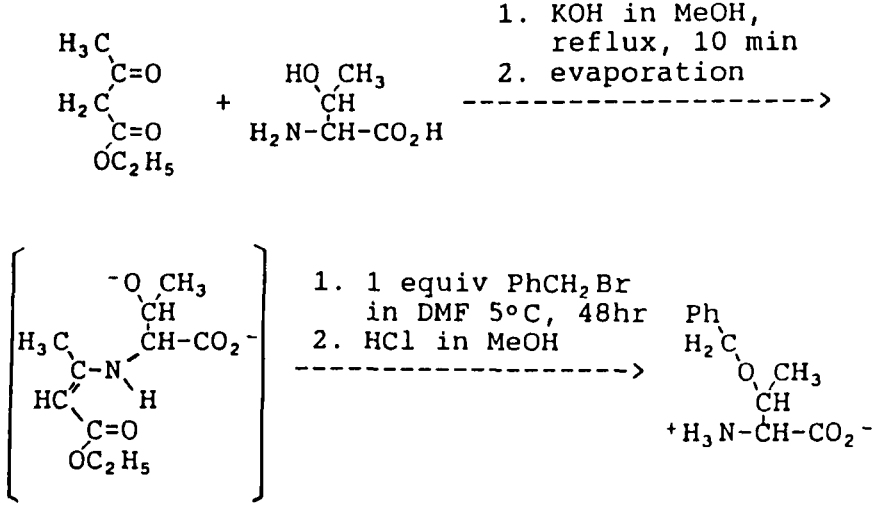
O-Benzyl-L-threonine can be prepared in a one-pot synthesis in 80% yield by using ethyl acetoacetate to protect the α-amino group, followed by treatment with benzyl bromide and removal of the N-protecting group under acidic conditions.

In peptide synthesis, the hydroxyl group of threonine should be protected to avoid side reactions which may arise from inter- or intramolecular O-acylation[1]. Usually the hydroxyl group is blocked in the form of benzyl ether. This protecting group is indeed satisfactory as it

---

* To whom correspondence should be addressed.

is stable during chain-elongation and can be removed by catalytic hydrogenation or treatment with HF after the coupling steps[2]. Some methods which are used to synthesize N-tert-butyloxycarbonyl-O-benzylserine in moderate yield have been applied to prepare N-tert-butyloxycarbonyl-O-benzylthreonine in quite low yield[3,4]. In order to solve this synthetic problem, we developed a facile method to prepare O-benzyl-L-threonine in high yield.



Scheme I.

As shown in Scheme I, the α-amino group of threonine is first temporarily protected by ethyl acetoacetate[5], then carefully reacted with one equivalent of benzyl bromide and the N-protecting group is finally deprotected under acidic treatment.

Experimental section :

L-Threonine is purchased from Kyowa Fermentation Co., Tokyo, Japan. Solvents for synthesis are from ALPS Chemicals Inc. Taipei, Taiwan. Thin-layer chromatography is performed on silica gel G. 60 (E. Merck. FRG) precoated on a glass plate. Polygosil 60-4063 C_8 (pore size : 60 A°, pore volume : 0.75 ml/g) is purchased from Macherey-Nagel (FRG). The melting point is taken on a Buchi 510 melting apparatus and uncorrected. Optical rotation is measured on polartronic universal polarimeter (Schmidt & Haensch). The ^{1}H-NMR spectrum is recorded with a 300 MHz Bruker instrument.

One-pot Synthesis of O-benzyl-L-threonine :

L-Threonine (11.9 g, 0.1 mol) is dissolved in 0.5 N methanolic potassium hydroxide (200 ml) with

gentle heating. Ethyl acetoacetate (16 ml, 0.12 mol) is then added, and the mixture is refluxed for 10 min and the solvent is removed under reduced pressure. The residue is dissolved in dimethylformamide (100 ml), and then benzyl bromide (13.5 ml, 0.11 mol) is added. The resulting mixture is stirred at 5°C for 48 h and 1 N methanolic hydrogen chloride (200 ml) added. After stirring for 10 min, the solution is evaporated in vacuo. The residue is dissolved in water (240 ml). The solution is divided into three portions and purified by a preparative RP-C_8 column (60 x300 mm) eluted with water containing 20% methanol. The desired fractions are collected, evaporated and the residue recrystallized from water (75 ml) to give pure O-benzyl-L-threonine; yield : 15.2 g (80%); mp 213-215°C; $[\alpha]_D^{25}$ -25.5°, (C=2, 1 N HCl); $[\alpha]_D^{25}$ -30.9°,(C=1.1, AcOH)[lit[6] : $[\alpha]_D^{25}$ -30.4°, (C= 1.1, AcOH)]; ^{1}H-NMR (D_2O) δ 1.16 - 1.19 (d, 3H,-CH_3), 3.50 (d, 1H, α-CH), 4.01 (m, 1H, β-CH), 4.37-4.52 (q, 2H, -CH_2- adjacent to benzyl group), 7.21 (m, 5H, -C_6H_5).

References:

1. Bodanszky, M., Martinez, J. In " The Peptides : Analysis, Synthesis, Biology " Vol. 5, Gross, E., Meienhofer, J. (Eds.), Academic Press, Inc. New York, 1983, p.139.
2. Bodanszky, M., In " Principles of Peptide Synthesis " Springer-Verlag, Berlin, Heidelberg, New York, Tokyo, 1984, p.126.
3. Hruby, V. J., Ehler, K. W., J. Org. Chem. 1970, 35, 1690.
4. Sugano, H., Miyoshi, M., J. Org. Chem. 1976, 41, 2352.
5. Maclaren, J. A., Aust. J. Chem. 1972, 25, 1293.
6. Mizoguchi, T.; Levin, G.; Woolley, D. W.; Stewart, J. M., J. Org. Chem. 1968, 33, 903.

(Received in The Netherlands 21 July 1989)