Pergamon

Tetrahedron Letters, Vol. 38, No. 38, pp. 6779-6780, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)01551-7

Efficient Conversion of (*S*)-Methionine into (*R*)-Garner Aldehyde

Jalluri S. Ravi Kumar and Apurba Datta*

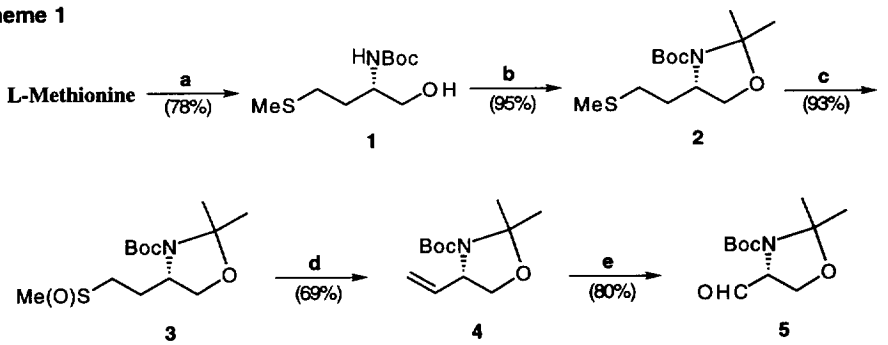
Organic III, Indian Institute of Chemical Technology, Hyderabad - 500 007, India

Abstract : An efficient method has been developed for the conversion of L-methionine into N,O-protected D-serinal (Garner aldehyde) in good overall yield. © 1997 Elsevier Science Ltd.

N-(*tert*-Butoxycarbonyl)-N,O-isopropylidene serinal, the so called Garner aldehyde, is one of the most widely used chiral building blocks in contemporary organic synthesis.[1] In the original procedure [2] and its subsequent modifications [3], both the (*S*)- and (*R*)- form of this aldehyde has been synthesized starting from L- and D-serine respectively. In continuation of our work on the synthesis of novel amino acids [4], we needed considerable quantities of the (*R*)-Garner aldehyde (D-serine derived) and contemplated an alternative synthesis using a cheaper starting material. Interestingly, in their approach towards Aspergillomarasmine A, Ohfune *et al* have reported [5] the conversion of L-methionine to a masked serine equivalent *via* sequential sulfoxide formation, dehydrosulfenylation and ozonolysis of the resulting alkene. Encouraged by this approach we planned on a synthesis of (*R*)-Garner aldehyde following a similar strategy. The results of the studies thus undertaken are reported herein.

In a one-pot reaction, L-methionine was converted to the corresponding N-Boc-amino alcohol **1** (scheme 1) in good yield and high optical purity {$[\alpha]_D$ = -12.9 (c=2.6, $CHCl_3$); *ent*-**1** $[\alpha]_D$ = +13.7 (c=2.5, $CHCl_3$)[5]}. N,O-Acetonide protection of amino alcohol **1** followed by $NaIO_4$ oxidation of the sulfide to the

Scheme 1



a. $LiAlH_4$, THF, Δ, then $(Boc)_2O$, CH_2Cl_2, Δ. **b.** $Me_2C(OMe)_2$, $BF_3.Et_2O$ (cat), acetone, rt. **c.** $NaIO_4$, $NaHCO_3$, MeOH, H_2O, 0°C. **d.** 1,2-Dichlorobenzene, 175-180°C, 5-6 h. **e.** i) OsO_4 (cat), NMO, acetone, rt. ii) $NaIO_4$-SiO_2, CH_2Cl_2, rt.

corresponding sulfoxide **3** was performed in high yield under standard reaction conditions. Thermal *syn* elimination of the sulfoxide functionality resulted in the vinyl oxazolidine derivative **4** {$[\alpha]_D$ =-14.3 (c=1.2, $CHCl_3$); *ent*-**4** $[\alpha]_D$ = +15.6 (c=2.5, $CHCl_3$)[3a]} in 69% yield. Finally, oxidative degradation of the alkene to aldehyde completed the proposed synthesis of Garner aldehyde **5** [6], similar in all respect to the reported compound[2] {$[\alpha]_D$ = 88.2 (c=1, $CHCl_3$); Lit.[2] $[\alpha]_D$ = 95 (c=1.84, $CHCl_3$). It is worth mentioning that ozonolysis of the alkene **4** (O_3, CH_2Cl_2, -78°C, then Ph_3P or Me_2S) also affords the aldehyde **5** in good yield (84%) but with lower enantiomeric purity (82% ee).

In conclusion, the present synthesis of (*R*)-Garner aldehyde compares well with the known methods in terms of optical purity and overall yield of the product while offering the advantage of replacing the more expensive starting material D-serine with L-methionine, a substantially cheaper and more readily available natural amino acid.

Acknowledgments : We thank Dr. M. K. Gurjar for his support and encouragement. JSRK also thanks UGC, New Delhi for a research fellowship.

References and Notes

IICT communication No. 3854

1. For some recent applications, see : (a) Kozikowski, A. P.; Ding, Q.; Spiegel, S. *Tetrahedron Lett.* **1996**, *37*, 3279-3282. (b) Marshall, J. A.; Beaudoin, S. *J. Org. Chem.* **1996**, *61*, 581-586. (c) Doi, Y.; Ishibashi, M,; Kobayashi, J. *Tetrahedron*, **1996**, *52*, 4573-4580. (d) Sibi, M. P.; Deshpande, P. K.; La Loggia, A. J.; Christensen, J. W. *Tetrahedron Lett.* **1995**, *36*, 8961-8964. (e) Moore, W. J.; Luzzio, F. A. *Tetrahedron Lett.* **1995**, *36*, 6599-6602. (f) Koskinen, A. M. P.; Hassila, H.; Myllymaki, V. T.; Rissanen, K. *Tetrahedron Lett.* **1995**, *36*, 5619-5622.
2. Garner, P.; Park, J. M. *J. Org. Chem.* **1987**, *52*, 2361-2364.
3. (a) McKillop, A.; Taylor, R. J. K.; Watson, R. J.; Lewis, N. *Synthesis*, **1994**, 31-33. (b) Williams, L.; Zhang, Z.; Shao, F.; Carroll, P. J.; Joullié, M. M. *Tetrahedron*, **1996**, *52*, 11673-11694. (c) Dondoni, A.; Perrone, D. *Synthesis*, **1997**, 527-529.
4. Ravi Kumar, J. S.; Datta, A. *Tetrahedron Lett.* **1997**, *38*, 473-476.
5. Ohfune, Y.; Kurokawa, N. *Tetrahedron Lett.* **1984**, *25*, 1071-1074. For a similar approach for the synthesis of vinylglycine, see : Ardakani, A. A.; Rapoport, H. *J. Org. Chem.* **1980**, *45*, 4817-4820.
6. All the compounds synthesized were fully characterized by IR, ^1H and ^{13}C NMR and mass spectroscopy and by comparison with known compounds, wherever applicable. Some characteristic data for compounds **2** and **3** are as follows: **2**: light yellow liquid; $[\alpha]_D$ = 39.5 (c=1.3, $CHCl_3$); IR (neat) 1695 cm^{-1}; ^{1}HNMR (200 MHz, $CDCl_3$) δ 1.48(br s, 12H), 1.56(br s, 3H), 1.84(m, 2H), 2.09(s, 3H), 2.48(m, 2H), 3.72(d, J=7.7 Hz, 1H), 3.92(m, 2H).

   3: light yellow liquid; $[\alpha]_D$ = 44 (c=1.1, $CHCl_3$); IR (neat) 1691, 1045 cm^{-1}; ^{1}HNMR (200 MHz, $CDCl_3$) δ 1.49(br s, 12H), 1.57(br s, 3H), 2.08(m, 2H), 2.58(s, 3H), 2.70(m, 2H), 3.77(br d, J=8.9 Hz, 1H), 3.98(m, 2H); ^{13}CNMR (50 MHz, $CDCl_3$) δ 152.4, 93.6, 80.2, 66.9, 55.9, 51.3, 38.5, 28.3, 27.8, 27.5, 26.8, 26.6, 24.2; EIMS: 274 (M^+ -OH).

(*Received in UK* 14 *July* 1997; *accepted* 25 *July* 1997)