Pergamon

Tetrahedron Letters, Vol. 35, No. 41, pp. 7613-7616, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)01592-9

Hydrogenation of 1-Benzyl-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-aziridine-2-carboxylic acid ethyl ester[1]

Horst-Dieter Ambrosi[a], Wolfram Duczek[a], Matthias Ramm[b], and Klaus Jähnisch[c]*

Institut für Angewandte Chemie[c], Rudower Chaussee 5, D-12484 Berlin-Adlershof, Germany

Technische Fachhochschule Berlin[a], Luxemburger Straße 10, D-13353 Berlin

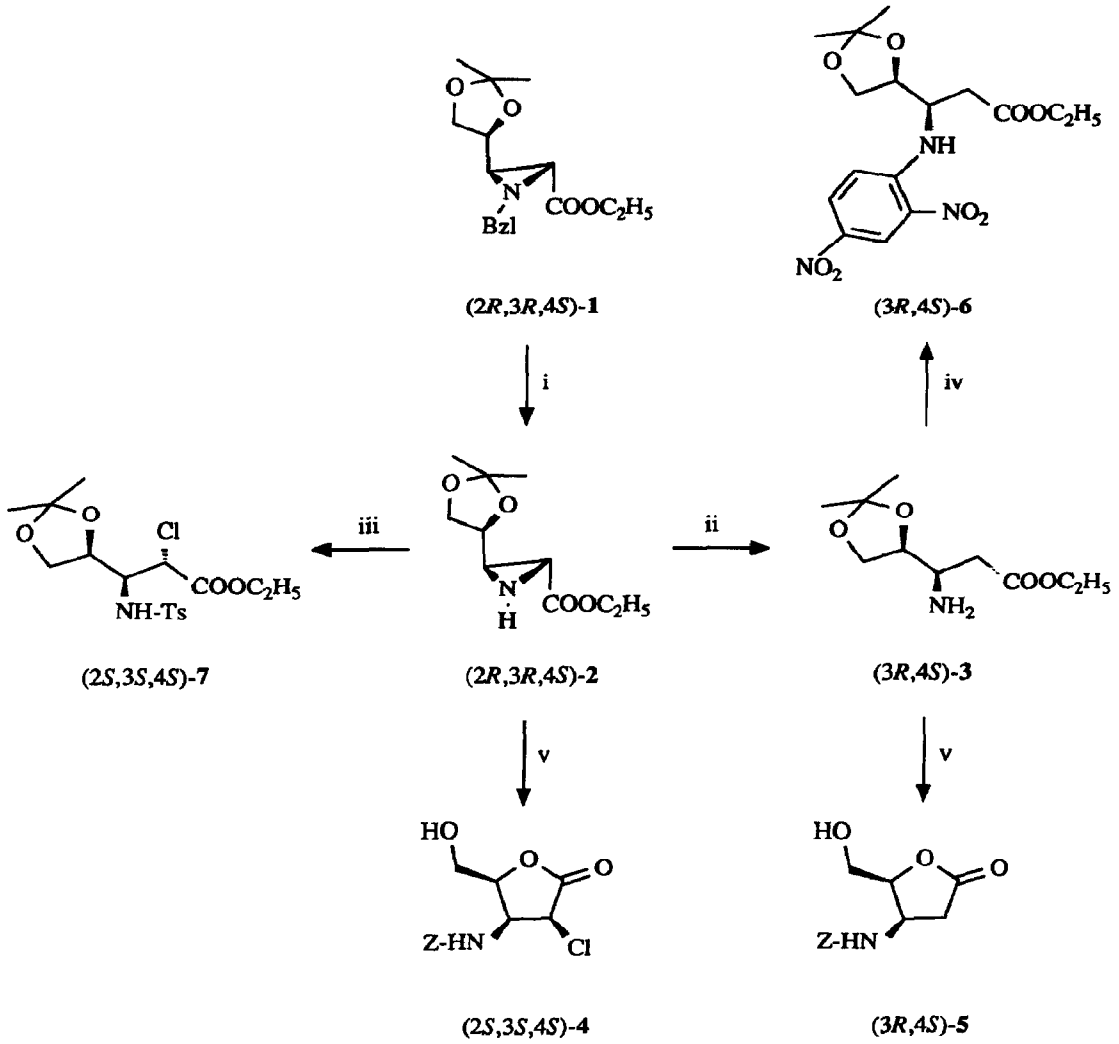
Freie Universität Berlin, Institut für Kristallographie[b], Takustraße 6, D-14195 Berlin

Abstract: Hydrogenation of 1-benzyl-aziridine-2-carboxylic acid ethyl ester **1** yielded the enantiomerically pure 1H-aziridine **2** or the ß-amino acid ester **3** as main products depending on the reaction time. The Z-protected derivatives of **2** and **3** were transformed into the γ-lactones **4** and **5**, respectively.

Stereochemically defined aziridine-2-carboxylates are useful intermediates for the synthesis of modified optically active amino acids. Either substituted α-amino acids[2,3,4] or ß-amino acids[5,6] can be prepared by nucleophilic attack of the aziridine ring at C-3 or C-2, respectively.

We have recently reported on an asymmetric synthesis of aziridine-2-carboxylic acid derivatives by addition of benzylamine to chiral α-bromoacrylates.[7] Our further investigation is aimed at using these new chiral building blocks in the synthesis of new amino acid derivatives.

In this paper we report on the hydrogenation of optically pure 1-benzyl-aziridine-2-carboxylic acid ethyl ester **1** in the presence of Pd-C. When the hydrogenation was interrupted after 20 min, the 1H-aziridine **2** was isolated in 71% yield besides 22% of the ß-amino acid ester **3** which upon treatment with 2,4-dinitro-fluorobenzene afforded the crystalline derivative **6**. On the other hand, when the hydrogenation was stopped after 3 days, the ß-amino acid ester **3** was isolated exclusively.[8] Scheme 1 shows the hydrogenation of (*2R,3R,4S*)-**1**. Acylation of **2** with Z-Cl in pyridine and subsequent treatment with HCL in dioxane yielded the γ-lactone **4**.[9] The formation of **4** can be explained by an opening of the aziridine ring followed by a subsequent ring closure to give the α-chloro-γ-lactone **4**. The absolute configuration of (*2S,3S,4S*)-**4** was determined by X-ray analysis[10] (Figure 1). In a similar way the ß-amino acid ester **3** was transformed into the γ-lactone **5**. In an attempt to tosylate **2** with p-toluenesulfonyl chloride in pyridine an unexpected regio- and stereoselective ring opening of the aziridine was found to give the crystalline α-chloro-ß-tosylamino propionic



i: Pd-C (10%), H_2 (1.01 bar), EtOH, rt., 20 min; ii: Pd-C (10%), H_2 (1.01 bar), EtOH, rt., 3d; iii: Ts-Cl, pyridine, 0°C → rt., 12h; iv: $C_6H_3F(NO_3)_2$, $NaHCO_3$, EtOH, rt., 12h; v: 1. Z-Cl, pyridine, 0°C → rt., 12h; 2. HCl, dioxane, rt., 3h.

Scheme 1

acid ethyl ester 7 in 81% yield.[11]

All the compounds were fully characterized by conventional spectroscopic and analytical methods.

Further applications of optically active aziridine carboxylic acid derivatives, e.g. in peptide synthesis or further nucleophilic ring-opening reactions, are currently being investigated.

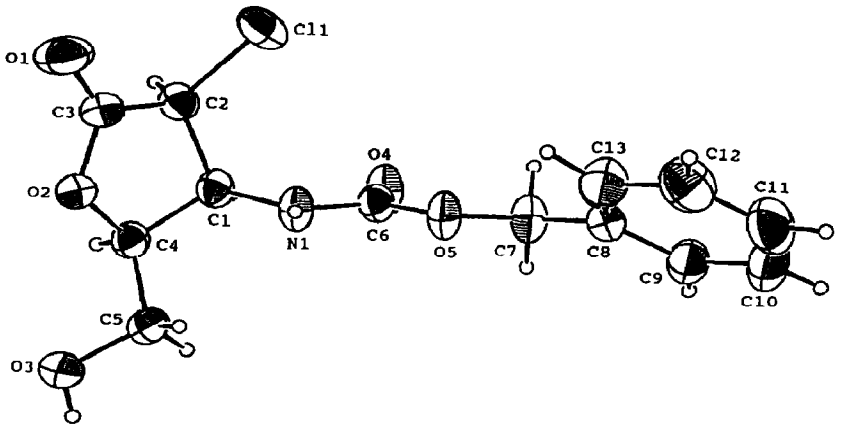


Figure 1: Crystal structure (ORTEP)[10] of γ-lactone (*2S,3S,4S*)-4

Acknowledgements: This work was supported by the Fonds der Chemischen Industrie.

References and Notes

1. Chemistry of Aziridine Carboxylic Acids, Part 6. Part 5.: Ref. 7.
2. Legters, L.; Thijs, L.; Zwanenburg, B. *Tetrahedron Lett.* **1989**, *30*, 4881.
3. Bodenau, J.; Chanet-Ray, J.; Vessiere, R. *Synthesis* **1992**, 288.
4. Baldwin, J.E.; Spivey, A.C.; Schofield, C.J.; Sweeney, J.B. *Tetrahedron* **1993**, *49*, 6309.
5. Dubois, L.; Metha, A.; Tourette, E.; Dodd, R.H. *J. Org. Chem.* **1994**, *59*, 434.
6. Tronchet, J.M.; Massoud, A.M. *Heterocycles* **1989**, *29*, 419.
7. Ambrosi, H.-D.; Duczek, W.; Gründemann, E.; Ramm, M.; Jähnisch, K. *Liebigs Ann. Chem.* **1994**, in press.
8. A solution of aziridine 1 (1g; 3.27 mmol) in ethanol (15 ml) containing Pd-C (0.1g; 10%) was hydro-

genated 20 min. at rt. The catalyst was filtered off (Celite) and the solvent evaporated in vacuo. Chromatography on silica gel using n-hexane/acetone (2.5:1) gave pure aziridine **2** (0.5g; 71%) and ß-amino acid ethyl ester **3** (0.16g; 22%) as colourless oils.

Selected data for (*2R,3R,4S*)-**2**: $[\alpha]^{20}_D$ = -65.7° (c = 1, $CHCl_3$); b.p. 60°C (3 10^{-3}mbar); ^{1}H NMR ($CDCl_3$, HMDS): δ 1.12 (3H,t); 1.23 (3H,s); 1.26 (3H,s); 2.42 (2H,m); 3.80 (3H,m); 3.98 (1H,m); 4.15 (2H,q); ^{13}C NMR ($CDCl_3$, HMDS): δ 14.1; 25.4; 26.7; 32.2; 39.8; 61.8; 66.4; 76.5; 109.8; 171.9; (*2S,3S,4R*)-**2**: $[\alpha]^{20}_D$ = +67.3° (c = 1, $CHCl_3$); Selected data for (*3R,4S*)-**3**: $[\alpha]^{20}_D$ = +20.5° (c = 1, $CHCl_3$); b.p. 60°C (3 10^{-3} mbar); ^{1}H NMR ($CDCl_3$, HMDS): 1.20 (3H,t), 1.29 (3H,s), 1.37 (3H,s), 1.49 (2H,s), 2.31 (2H,m), 3.16 (1H,m), 3.70 (1H,m), 3.95 (2H,m), 4.10 (2H,q); ^{13}C NMR ($CDCl_3$, HMDS); δ 14.2; 25.2; 26.5; 39.4; 50.6; 60.5; 66.4; 79.0; 109.3; 171.9; (*3S,4R*)-**3**: $[\alpha]^{20}_D$ = -18.4° (c = 1, $CHCl_3$).

9. γ-Lactone (*2S,3S,4S*)-**4**: m.p. 98 °C; $[\alpha]^{20}_D$ = +46.3° (c = 1, $CHCl_3$); (*2R,3R,4R*)-**4**: m.p. 98 °C; $[\alpha]^{20}_D$= -44.8° (c = 1, $CHCl_3$).

10. Johnson, C.K. *ORTEPII*, Report ORNL-3794, revised, Oak-Ridge National Laboratory, Tennessee, USA, 1971.

11. A solution of p-toluenesulfonyl chloride (0.21g; 0.64 mmol) in pyridine (5 ml) was dropped to a solution of aziridine **2** (0.137g; 0.64 mmol) in pyridine (5 ml) at -5°C and under N_2 atmosphere. After stirring for 12h at rt. the reaction solution was poured onto ice-water (20ml) and extracted with 10 ml of $CHCl_3$ (3 times). The collected $CHCl_3$ extracts were washed with water, dried over $MgSO_4$ and evaporated in vacuo. The residue was recrystallized (n-hexane/isopropanol) to give colourless needles (0.208g, 81%). Selected data for (*2S,3S,4S*)-**7**: $[\alpha]^{20}_D$ = +24.7° (c = 1, $CHCl_3$); m.p. 83°C; ^{1}H NMR ($CDCl_3$, HMDS): δ 1.12 (3H,t); 1.26 (3H,s); 1.35 (3H,s); 2.35 (3H,s); 3.62 (1H,dd); 3.88 (4H,m); 4.24 (1H,d); 4.39 (1H,m); 5.29 (1H,d); 7.23-7.69 (4H,m); ^{13}C NMR ($CDCl_3$, HMDS): δ 13.8; 21.1; 25.0; 26.1; 56.5; 56.6; 62.3; 65.9; 73.7; 109.9; 127.1; 129.5; 137.8; 143.6; 167.9; (*2R;3R;4R*)-**7**: $[\alpha]^{20}_D$ = -23.8° (c = 1, $CHCl_3$).

(*Received in Germany* 1 *July* 1994; *accepted* 15 *August* 1994)