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Effective and Mild Method for Preparation of Optically Active α -Amino Aldehydes *via* TEMPO Oxidation

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Abstract: The TEMPO oxidation method is successfully applied to preparation of variously protected, optically active α -amino aldehydes without racemization and in very good yield. © 1998 Elsevier Science Ltd. All rights reserved.

Aldehydes are important and versatile compounds, widely used in organic synthesis. In recent years has been a growing interest in chiral nonracemic aldehydes because of the development of new and effective methods for controlling stereochemistry of basic organic reactions. Protected α -amino aldehydes are of special interest, owing to their ready availability in both enantiomeric forms from natural sources (α -amino acids) and to their pronounced versatility due to the presence of both the formyl group and suitably protected amino functionality in the molecule.

 α -Amino aldehydes are mainly obtained from α -amino acids and only on occasion are they prepared from other chiral precursors. Usually the synthetic route proceeds *via* esters or active amides of α -amino acids, which are finally reduced.¹ A second approach is based on α -amino alcohols obtained from α -amino acids, which are oxidized to afford the desired α -amino aldehydes.¹

The N-protected α -amino alcohols are best obtained by borane-THF reduction of N-protected α -amino acids² or by sodium borohydride-lithium chloride³ or sodium borohydride-calcium chloride⁴ reduction of the corresponding methyl ester. Collin's reagent was the first oxidizing reagent shown to be efficient, offering a racemization-free procedure for Boc-L-leucinal synthesis.⁵ Various activated dimethyl sulfoxide oxidations are of special interest owing to their general nature. These methods can be applied for oxidation of relatively unstable derivatives of such a-amino acids as tryptophan and methionine.⁶ Among these oxidation methods,

the Parikh-Doering (DMSO/SO₃×Py) procedure is the best documented,^{4,7} and is effective not only in the synthesis of simple *N*-protected α -amino aldehydes, but also in the preparation of peptide C-terminal aldehydes. Recently, the Swern method⁸ was found to be very useful in preparation of *N*,*O*-protected L-serinals.⁹ Pyridinium dichromate (PDC) oxidation¹⁰ is suspected to cause racemization to various extents, depending on the type of α -amino aldehyde,⁵ whereas pyridinium chlorochromate (PCC) was found to be convenient for oxidation of *N*-benzyl-*N*-tosyl α -amino alcohols without racemization.¹¹ α -Amino alcohols with nonpolar side chains, such as L-leucinol, L-phenylalaninol, and L-valinol were found to be good substrates for alcohol dehydrogenase from horse liver, affording the respective α -amino aldehydes.¹²

There have been several reports on oxoammonium-promoted oxidation of alcohols to aldehydes and ketones.¹³⁻¹⁵ This method utilizes 2,2,6,6-tetramethyl-1-piperidinyloxy radical (TEMPO) with sodium hypochlorite as the oxidant. Recently, Leanna and coworkers¹⁶ have described the first application of this method towards the oxidation of α -heterosubstituted alcohols to the corresponding aldehydes. We have found¹⁷ that his method is also highly effective in the synthesis of variously *N*,*O*-protected L-serinals.



Scheme 1. Reagents and reaction conditions: (a) CbzCl, NaHCO₃, AcOEt, 0°C; (b) Boc₂O, NaHCO₃, RT; (c) TsCl, EtN₃, CH₂Cl₂, 0°C \rightarrow RT; (d) LiBH₄, EtOH-THF, 0°C; (e) TEMPO, NaOCl, NaBr, NaHCO₃, H₂O, toluene, AcOEt, 0°C; (f) PhCHO, EtN₃, MeOH, RT, then NaBH₄, RT.

Owing to mildness of the reaction conditions and to high stereochemical stability of products under such conditions,¹⁸ we decided to extend this oxidation method, leading to optically α -amino aldehydes, on other variously protected α -amino alcohols. Herein, we report on the successful application of this methodology to the important problem of the effective and mild synthesis of optically active active *N*-mono and *N*.*N*-diprotected α -amino aldehydes (Schemes 1, 2 and 3, Table 1).



Scheme 2. Reagents and reaction conditions: (a) CbzCl, NaHCO₃, AcOEt, 0°C; (b) Boc₂O, NaHCO₃, RT; (c) TsCl, EtN₃, CH₂Cl₂, 0°C \rightarrow RT; (d) TBSCl, imidazole, CH₂Cl₂/DMF, RT; (e) BOMCl, iPr₂EtN, CH₂Cl₂, RT; (f) LiBH₄, THF/EtOH, 0°C; (g) TEMPO, NaOCl, NaBr, NaHCO₃, H₂O, toluene, AcOEt, 0°C; (h) PhCHO, Et₃N, MeOH, RT, then NaBH₄, RT; (i) BnBr, Na₂CO₃, 18-crown-6 (cat.),acetone, reflux.



Scheme 3. (a) Ref. 19; (b) TEMPO oxidation.

| Entry | Alcohol | Aldehyde | Yield [%] | Entry | Alcohol | Aldehyde | Yield [%] |
|-------|------------|-----------|-----------|-------|------------|----------|----------------|
| 1 | 4a | 5a | 65 | 10 | 4j | 5j | 85 |
| 2 | 4b | 5b | 67 | 11 | 4 k | 5k | 90 |
| 3 | 4c | 5c | 36 | 12 | 41 | 51 | 9 7 |
| 4 | 4d | 5d | 73 | 13 | m | 5m | 99 |
| 5 | 4e | 5e | 70 | 14 | 4n | 5n | 93 |
| 6 | 4f | 5f | 98 | 15 | 40 | 50 | 87 |
| 7 | 4g | 5g | 98 | 16 | 4р | 5p | 97 |
| 8 | 4h | 5h | 99 | 17 | 4r | 5r | 90 |
| 9 | 4 i | 5i | 94 | | | | |

Table 1. TEMPO oxidation of protected α -aminc alcohols 4 to aldehydes 5.

The variously protected α -amino aldehydes 5 were conveniently prepared from the appropriate methyl esters 1, 2 in two simple steps. The reduction of the esters 3 with lithium borohydride in a mixture of ethanol and tetrahydrofuran. The final step involved oxidation of the resulting alcohols 4 with buffered commercial NaOCl solution in the presence of catalytic amounts of TEMPO radical and stoichiomeric amounts of NaBr, carried out in a biphasic (toluene - ethyl acetate - water) mixture, to afford the desired variously protected α -amino aldehydes 5. *N*-Protected α -amino aldehydes are relatively unstable both chemically and configurationally, particularly in solution.¹ For this reason we decided to examine the optical purities of 13 α -amino aldehydes 5, obtained *via* TEMPO oxidation (method A) and to compare them with those determined for α -amino aldehydes 5 prepared in two other routes: *via* Swern oxidation^{8,9} of alcohols 4 (method B) and DIBAL-H reduction^{9,31} of methyl esters 3 (method C) as shown in scheme 4 and in Table 2. Because of difficulty in direct determination of optical purity of α -amino aldehydes 5, we resolved to reduce them with LiBH₄ (Table 2, Entries 1-6 and 10), with NaBH₄ (Entries 7, 8, 11 and 12) or with LiAlH₄ (Entries 9 and 13) to appropriate alcohols 4. Enantiomeric purities of obtained α -amino alcohols 4 represent enantiomeric

purities of α -amino aldehydes 5 being reduced. Enantiomeric purities of alcohols 4 were determined by optical rotation measurements (method a) and/or by HPLC on CHIRACEL-OD-H chromatographic column (method b) as shown in Table 2.



Scheme 4. Reagents and reaction conditions: a) LiBH₄, EtOH-THF, 0°C or NaBH₄, MeOH, 0°C or LiAlH₄, EtOH, 0°C; b) DIBAL-H, Et₂O, -78°C, 1h; c) TEMPO, NaOCl, NaBr, NaHCO₃, H₂O, toluene, AcOEt; d) (COCl)₂, DMSO, CH₂Cl₂

We have demonstrated the configurational stability of several α -amino aldehydes 5. It should be noted that almost all α -amino aldehydes 5 can be prepared in optically pure form (Table 2, Entries 2, 3, 5-7, 9, 11, 13) using the TEMPO oxidation method. Our results show that all α -amino aldehydes 5 studied are configurationally stable under TEMPO oxidation conditions (method A) (Table 2, Entries 1-13). Moreover the presence of *t*-butoxycarbonyl (Table 2, Entries 2, 5, 8, 11) and tosyl protection (Entries 3, 6, 9) prevent racemization. *N*-Cbz-L-Alaninals (Table 2, Entries 1, 4) and *N*-Cbz-*N*-Bn-L-serinal (Table 2, Entry 10) are less stable.

For *N*-protected L-alaninals Swern oxidation (method B) (Table 2, Entries 2, 3, 5, 6) is as good as TEMPO oxidation (method A), contrary to DIBAL-H reduction (method C) (Table 2, Entries 2, 3, 5). For *N*, *O*-protected L-serinols **4** only TEMPO oxidation method led to enantiomerically pure α -amino aldehydes (Table 2, Entries 7-13). In the case of the Swern oxidation the high level of racemization was observed (Table 2, Entries 7, 8, 10-12).

| Entry | Aldehyde | Method for | preparation of a | Method for determination | |
|-------|------------|------------|------------------|--------------------------|--------------------------|
| | | А | В | С | of enantiomeric purity** |
| | | e.e.[%] | e.e. [%] | e.e. [%] | |
| 1 | 5a | 82 | 84 | - | a |
| 2 | 5b | 100 | 100 | 96 | а |
| 3 | 5c | 98 | - | 82 | а |
| 4 | 5f | 60 | - | - | a |
| 5 | 5g | 100 | 98 | 72 | a |
| 6 | 5h | 98 | 94 | - | a |
| 7 | 5 i | 100 | 76 | - | a,b |
| 8 | 5j | 100 | 24 | - | a,b |
| 9 | 5k | 100 | 100 | - | a,b |
| 10 | 5m | 88 | 38 | - | a,b |
| 11 | 5n | 96 | 24 | - | a,b |
| 12 | 5p | 82 | 36 | - | b |
| 13 | 5r | 100 | 100 | - | a, b |

Table 2. Optical purities of α -amino aldehydes 5.

* A - TEMPO oxidation, B - Swern oxidation, C - DIBAL-H reduction

** a - optical rotation b - chiral HPLC

These studies led to the conclusion that no racemization occurred under oxidation conditions. In summary, the TEMPO oxidation is a very good method for preparation of optically active, variously protected α -amino and α -amino- β -hydroxy aldehydes, practically without racemization. It seems to be much more efficient than routes previously used for synthesis of these unstable derivatives of α -amino acids.

Experimental

General

Melting points were determined using a Kofler hot stage apparatus and are uncorrected. Optical rotations were recorded using a JASCO DIP-360 polarimeter with a thermally jacketed 10 cm cell. ¹H NMR spectra were recorded using Bruker AM 500 (500 MHz) spectrometer, and ¹³C NMR spectra were recorded using also a Bruker AM 500 (125 MHz) or a Varian 200 (50 MHz) spectrometer. All chemical shifts are quoted in parts per million relative to tetramethylsilane (δ , 0.00 ppm), coupling constants (*J*) are measured in Hertz. Some spectra show additional signals as a consequence of restricted rotation around C-N bonds. IR

spectra were obtained on a Perkin-Elmer 1640 FTIR spectrophotometer. Mass spectra were recorded on an AMD-604 Intectra instrument using the electron impact (EI) or LSIMS technique. Flash-column chromatography was performed according to Still *et al.*²¹ on silica gel (Kieselgel-60, Merck, 200-400 mesh). HPLC measurements were performed on KNAUER HPLC PUMP 64 using KNAUER Variable Wavelenght Monitor and CHIRALCEL OD-H column.

N-Protection methods used in syntheses of variously N-protected methyl esters of α -amino acids. General procedures.

A. N-Benzylation reaction.

A solution of α -amino acid methyl ester hydrochloride (1 mmol) in methanol (1 mL) and triethylamine (1 mmol) at 0°C was treated with benzaldehyde (1 mmol). The reaction mixture was stirred at room temperature for 2h and then recooled to 0°C. Sodium borohydride (2 mmol) was added portionwise over a period of 30 min. The solution was partitioned between 4M hydrochloric acid (2 mL) and Et₂O (5 mL). The organic layer was extracted with 4M hydrochloric acid (2 x 1 mL). The combined aqueous layers were extracted with Et₂O (2 x 1 mL) and the ethereal phases were discarded. The aqueous phase was neutralized with solid NaHCO₃, and extracted with Et₂O (3 x 2 mL). Standard workup of the ethereal phase produced a desired *N*-benzyl derivative.

B. N-Benzyloxycarbonylation reaction.

Benzyl chloroformate (1.1 mmol) was added dropwise to a solution of the methyl ester of the α -amino acid (1 mmol) in ethyl acetate (3 mL) and saturated aqueous sodium bicarbonate (3 mL) at 0°C. The two-phase reaction mixture was stirred for 3 hours at room temperature and extracted with Et₂O (4 x 3 mL). The combined organic layers were washed with 1M hydrochloric acid (4 x 3 mL). Standard workup of the ethereal phase afforded a desired *N*-protected derivative.

C. N-tert-Butoxycarbonylation reaction.

Di-*tert*-butyl dicarbonate (1 mmol) was added to a solution of the methyl ester of the α -amino acid (1.1 mmol) in dry Et₂O (3 mL). The reaction mixture was stirred overnight at room temperature, washed with 0.1M hydrochloric acid (2 x 3 mL), and with saturated aqueous NaHCO₃ (3 mL). Standard workup of the ethereal phase gave a desired *N*-protected derivative.

D. N-Tosylation reaction.

Tosyl chloride (2 mmol) was added to a solution of the methyl ester of the α -amino acid (1 mmol) in methylene chloride (3 mL). To the cold (0°C) solution, triethylamine (0.5 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 20 h. Then it was diluted with water (10 mL) and extracted with methylene chloride (5 mL). Standard workup of the organic layer produced a desired *N*-protected derivative.

E. N-Benzylation reaction of compound 3k.

To a solution of 3k (23 mmol) in acetone (35mL) was added Na₂CO₃ (89 mmol), benzyl bromide (34 mmol) and 18-crown-6 (100 mg). The reaction mixture was refluxed for 48h. Then it was diluted with water (50 mL) and extracted with ether (3 x 50 mL). A standard workup of the combined organic layers afforded the desired derivative 3p in 83% yield.

O-Protection methods used in syntheses of variously N,O-protected L-serine methyl esters. General Procedures.

A. O-tert-Butyldimethylsilylation reaction.

A solution of *tert*-butyldimethylchlorosilane (1.5 mmol) in methylene chloride (5 mL) was added dropwise to a solution of *N*-protected L-serine methyl ester (1 mmol) and imidazole (4 mmol) in dry DMF (5 mL). The reaction mixture was stirred at room temperature for 3 h and diluted with Et_2O (20 mL). Standard workup of the organic layer afforded a desired *N*,*O*-protected derivative.

B. O-Benzyloxymethylation reaction.

A solution of N-protected L-serine methyl ester (1 mmol) and diisopropylethylamine (1.5 mmol) in methylene chloride (5 mL) was treated with benzyl chloromethyl ether (1.5 mmol) and stirred overnight at room temperature. Then the reaction mixture was diluted with Et_2O (20 mL). Standard workup of the organic layer afforded a desired N,O-protected derivative.

Analytical and spectral data of protected α -amino acid methyl esters.

Data for methyl esters of α -amino acids 3a,²¹ 3b,²⁻²² 3g,²³⁻²⁵ 3h,¹¹⁻²⁶ 3i,²⁷ 3j,²⁸ 3k,²⁹ 3o,⁹ and $3r^{19,30}$ were identical with those already published.

A. Methyl ester 3c: $[\alpha]_D^{20}$ =+0.99 (c 1.2, CHCl₃); m.p. 65-66°C (from *n*-hexane-ether); IR (KBr), v(cm⁻¹): 3231, 1733, 1439, 1338, 1229, 1166, 1135, 1091, 992, 698; ¹H-NMR (200 MHz, CDCl₃), δ : 7.74 (dAB_2 , J =8.2, 2H, (Ar)), 7.30 (dAB_2 , J = 8.2, 2H, (Ar)), 5.58 (d, J = 8.5, 1H, NH), 4.1-3.9 (m, 1H, CH), 3.53 (s, 3H, OCH₃), 2.42 (s, 3H, CH₃(Ar)), 1.37 (d, J = 7.2, 3H, CH₃); ¹³C-NMR (50 MHz, CDCl₃), δ : 172.4, 143.4, 137.7, 129.5, 127.0, 52.4, 51.3, 21.3, 19.5; Analysis calculated for C₁₁H₁₅NO₄S: C, 51.36%, H, 5.85%; N, 5.44%; found: C, 51.37%; H, 6.10%; N, 5.45%.

B. Methyl ester 3d: $[\alpha]_D^{20}$ =+46.8 (c 1.2, CHCl₃); IR (film), v(cm⁻¹): 3343, 2953, 1723, 1612, 1513, 1248, 1214, 1035, 824, 740; ¹H-NMR (200 MHz, CDCl₃), δ : 7.33 (s, 5H, (Ar)), 7.0-6.8 (m, 4H, (Ar)), 5.25 (d, J = 8.2, 1H, NH), 5.1 (m, 2H, OCH₂(Cbz), 4.7-4.6 (m, 1H, CH), 3.76 (s, 3H, CH₃O(Ar)), 3.70 (s, 3H, OCH₃), 3.2-3.0 (m, 2H, CH₂(Ar)); ¹³C-NMR (50 MHz, CDCl₃), δ : 172.0, 158.7, 136.2, 130.2, 128.5, 128.4, 128.1, 128.0, 127.6, 114.0, 66.9, 55.2, 54.9, 52.2, 37.3; EIMS (m/z): 343 (M)⁺, 202, 192, 121, 91; EIMS HR (m/z) calculated for C₁₉H₂₁NO₅ (M)⁺: 343.1420, found: 343.1415.

C. Methyl ester 3e: $[\alpha]_D^{20}$ =+59.2 (c 1.8, CHCl₃); IR (KBr), v(cm⁻¹): 3397, 2982, 1740, 1704, 1613, 1517, 1504, 1247, 1223, 1171, 1034, 839, 825, 789; ¹H-NMR (200 MHz, CDCl₃), δ : 7.1-6.8 (m, 4H, (Ar)), 4.95 (d, J = 9.4, 1H, NH), 4.6-4.5 (m, 1H, CH), 3.78 (s, 3H, CH₃O(Ar)), 3.71 (s, 3H, OCH₃), 3.1-2.9 (m, 2H, CH₂(Ar)), 1.41 (s, 9H, C(CH₃)₃); ¹³C-NMR (50 MHz, CDCl₃), δ : 172.4, 158.6, 155.0, 130.2, 127.9, 113.9, 79.8, 55.2, 54.5, 52.1, 37.1, 28.3; EIMS (m/z): 309 (M)⁺, 253, 236, 192, 121; EIMS HR calculated for C₁₆H₂₃NO₅ (M)⁺: 309.1576, found: 309.1579.

D. Methyl ester 3f: $[\alpha]_D^{20}$ =-32.8 (c 1.9, CHCl₃); IR (film), v(cm⁻¹): 2950.1, 1744.9, 1703.2, 1453.6, 1413.7, 1218.9, 1068.6, 699.0; ¹H-NMR (500 MHz, CDCl₃), δ : 7.4-7.2 (m, 10H, Ar), 5.2-5.1 (m, 2H, OCH₂(Cbz)), 4.59 (m, 2H, NCH₂(Ar)), 4.5-4.4 (m, 0.6H, CH), 4.2 (m, 0.4H, CH), 3.63 (s, 1.7H, OCH₃), 3.44 (s, 1.3H, OCH₃), 1.4-1.3 (m, 3H, CH₃); ¹³C-NMR (125 MHz, CDCl₃), δ : 172.2, 172.0, 156.2, 138.1, 137.7, 136.2, 128.3, 127.9, 127.8, 127.7, 127.6, 127.2, 127.0, 67.4, 67.3, 55.1, 55.0, 52.0, 51.8, 50.8, 49.4, 15.8, 15.2; Analysis calculated for C₁₉H₂₁NO₄: C, 69.72%; H, 6.42%; N, 4.28%; found: C, 69.69%; H, 6.56%; N, 4.25%.

E. Methyl ester 3I: $[\alpha]_D^{20}$ =+4.75 (*c* 1.18, CHCl₃); IR (film) v(cm⁻¹): 3334, 3023, 2952, 2888, 1752, 1724, 1517, 1212, 1039, 740, 699; ¹H-NMR (200 MHz, CDCl₃), δ : 7.4-7.3 (*m*, 10H, Ar), 5.70 (*d*, *J*=8.0, 1H, NH), 5.12 (*s*, 2H, OCH₂(Cbz)), 4.72 (*s*, 2H, OCH₂O), 4.6-4.5 (*m*, 1H, CH), 4.53 (*s*, 2H, OCH₂(BOM)), 4.11 (*d*, *d* J = 3.2, J = 10.1, 1H, CH_AH_B), 3.82 (*d*, *d* J = 3.0, J = 10.1, 1H, CH_AH_B), 3.76 (*s*, 3H, OCH₃); ¹³C-NMR (50 MHz, CDCl₃), δ : 170.7, 156.0, 137.3, 136.2, 128.5, 128.5, 128.2, 128.1, 127.9, 94.7, 69.6, 68.2, 67.1, 54.3, 52.6; LSIMS (m/z): 769 (2M+Na)⁺, 747 (2M+H)⁺, 396 (M+Na)⁺, 374 (M+H)⁺; LSIMS HR (m/z) calculated for C₂₀H₂₄NO₆ (M+H)⁺: 374.1604, found: 374.1604.

F. Methyl ester **3m**: $[\alpha]_D^{20}$ =+44.7 (c 1.8, CHCl₃); IR (film) v(cm⁻¹): 2953, 2856, 1744, 1462, 1252, 1116, 1076, 1005, 838, 778, 698; ¹H-NMR (500 MHz, 90°C, toluen-d₈), δ : 7.2-7.0 (m, 10H, Ar), 5.06 (bs, 2H, OCH₂(Cbz)), 4.9-4.8 (m, 1H, CH), 4.56 (s, 1H, NC<u>H</u>_AH_B(Ar)), 4.52 (s, 1H, NCH_A<u>H</u>_B(Ar)), 4.07 (s, 2H, CH₂OTBS), 3.29 (bs, 3H, OCH₃), 0.87 (s, 9H, SiC(CH₃)₃), -0.03 (s, 3H, SiCH₃), -0.4 (s, 3H, SiCH₃); ¹³C-NMR (125 MHz, 90°C, toluen-d₈), δ : 169.8, 156.6, 137.6, 137.4, 129.1, 128.9, 51.3, 26.1, 18.5, -5.5; LSIMS (m/z): 480 (M+Na)⁺, 458 (M+H)⁺; LSIMS HR (m/z) calculated for C₂₅H₃₆NO₅Si (M+H)⁺: 458.2363, found: 458.2360.

G. Methyl ester 3n: $[\alpha]_D^{20} = -47.5$ (c 1.6, CH₂Cl₂); IR (film) v(cm⁻¹): 3485, 2953, 1744, 1699; ¹H NMR (200 MHz, CDCl₃) δ : 7.4-7.2 (m, 5H, (Ar)), 4.72 (d_{AB_2} , J = 16.2, 1H, NCH_AH_B(Ar)), 5.0-4.2 (m, 1H, CH), 4.20 (d_{AB_2} , J = 16.2, 1H, NCH_AH_B(Ar)), 5.0-4.2 (m, 1H, CH), 4.20 (d_{AB_2} , J = 16.2, 1H, NCH_AH_B(Ar)), 4.20-3.92 (m, 2H, CH₂OTBS), 3.63 (m, 3H, OCH₃), 1.5-1.3 (m, 9H, OC(CH₃)₃), 1.0-0.8 (m, 9H, SiC(CH₃)₃), 0.1-(-0.1) (m, 6H, Si(CH₃)₂); ¹³C NMR (50 MHz, CDCl₃) δ : 170.3, 155.7, 155.1, 139.3, 138.1, 128.1, 128.0, 127.0, 126.6, 80.63, 80.43, 62.4, 62.0, 61.3, 61.2, 51.8, 51.3, 28.3, 25.8, 18.1, -3.6, 5.6; EIMS (m/z) 423 9(M)⁺, 367, 350, 322, 310; EIMS HR (m/z) calculated for C₂₂H₃₇NO₅Si

 $(M)^+: 423.2441$, found: 423.2441, calculated for $C_{11}H_{22}NO_4Si$ (M-CO₂Me)⁺: 322.1838, found: 322.1834, calculated for $C_{11}H_{22}NO_4Si$ (M-Bu⁴)⁺: 350.1788, found: 350.1787.

H. Methyl ester **3***p*: $[\alpha]_{D}^{20}$ =+31.3 (c 1.1, CHCl₃); m.p. 63-65°C (from hexane - AcOEt); IR (KBr) v(cm⁻¹): 2951, 1747, 1734, 1471, 1343, 1250, 1165, 1090, 838, 777; ¹H-NMR (200 MHz, CDCl₃), δ : 7.7-7.6 (*m*, 2H, C₆H₄), 7.4-7.2 (*m*, 7H, Ar), 4.68 ($d_{AB_{22}}$, *J* = 16.5, 1H, C<u>H_AH</u>_B(Ar)), 4.65 (*t*, *J* = 5.6, 1H, CH), 4.52 ($d_{AB_{22}}$, *J* = 16.5, 1H, CH_AH_B(Ar)), 3.89 (*d*, *J* = 5.7, 2H, CH₂OTBS), 3.50 (*s*, 3H, OCH₃), 2.41 (*s*, 3H, CH₃(Ar)), 0.76 (*s*, 9H, SiC(CH₃)₃), -0.09 (*s*, 3H, SiCH₃), -0.12 (*s*, 3H, SiCH₃); ¹³C-NMR (50 MHz, CDCl₃), δ : 169.6, 143.3, 137.6, 137.1, 129.3, 128.1, 127.8, 127.7, 127.5, 127.2, 62.7, 61.3, 51.8, 50.2, 25.6, 21.5, 18.0, -5.8, -5.9; LSIMS (m/z): 500 (M+Na)⁺, 478 (M+H)⁺; LSIMS HR (m/z) calculated for C₂₄H₃₆NO₅SSi (M+H)⁺: 478.2083, found: 478.2084.

Reduction of methyl esters 3 to alcohols 4. General procedure.

Lithium borohydride (5 mmol) was added portionwise to a cold (0°C) solution of a methyl ester of α amino acid (1 mmol) in a mixture of THF and ethanol (1:9 v/v, 10 mL). The reaction mixture was stirred at 0°C or at room temperature for 20 h. Then to this mixture was slowly added 0.5 M hydrochloric acid (20 mL) and extracted with Et₂O (3 x 10 mL). The combined etheral extracts were washed with saturated aqueous NaHCO₃ (10 mL) and brine (10 mL), dried (MgSO₄), evaporated to dryness and chromatographed using a mixture of *n*-hexane and ethyl acetate.

Analytical and spectral data of protected α -amino alcohols.

Data for α -amino alcohols 4a,²¹ 4b,² 4g,²⁵ 4h,²⁶ 4i,²⁷ 4j,²⁸ 4k,²⁹ 4o⁹ and 4r³⁰ were identical with those already published.

A. α -Amino alcohol 4c: $[\alpha]_D^{20}$ =-6.6 (c 1.0, CHCl₃); m.p. 55-57°C (from hexane - AcOEt); IR (KBr) v(cm⁻¹): 3475, 3192, 1437, 1300, 1289, 1161, 1140, 1076, 1023, 971, 816, 669; ¹H-NMR (500 MHz, CDCl₃), δ : 7.79 (m, 2H, (Ar)), 7.28 (m, 2H, (Ar)), 5.84 (d, J = 7.6, 1H, NH), 3.6-3.3 (m, 4H, CH₂, CH, OH), 2.39 (s, 3H, CH₃(Ar)), 0.97 (d, J = 6.7, 3H, CH₃); ¹³C-NMR (125 MHz, CDCl₃), δ : 143.1, 137.5, 129.5, 126.8, 65.8, 51.2, 21.2, 17.1; Analysis calculated for C₁₀H₁₅NO₃S: C, 52.38%; H, 6.59%; N, 6.11%; S, 13.98%; found C, 52.35%; H, 6.82%; N, 6.06%; S, 13.94%.

B. α -Amino alcohol **4d**: $[\alpha]_{D}^{20}$ =-12.5 (c 1.0, CHCl₃); IR (KBr) v(cm⁻¹): 3453, 3398, 3311, 2951, 1691, 1661, 1612, 1545, 1511, 1301, 1245, 1035, 815, 740; ¹H-NMR (200 MHz, CDCl₃), δ : 7.32 (s, 5H, (Ar)), 7.1-6.8 (m, 4H, (Ar)), 5.07 (s, 2H, OCH₂(Cbz)), 5.00 (d, J = 8.2, 1H, NH), 4.0-3.8 (m, 1H, CH), 3.78 (s, 3H, CH₃O(Ar)), 3.7-3.5 (m, 2H, CH₂O), 2.79 (d, J = 7.1, 2H, CH₂(Ar)); ¹³C-NMR (50 MHz, CDCl₃), δ : 158.4, 156.5, 136.4, 130.2, 129.5, 128.5, 128.4, 128.1, 128.0, 114.1, 66.8, 64.0, 55.2, 54.3, 36.5; EIMS (m/z): 315 (M)⁺, 194, 164, 150, 121, 91; EIMS HR (m/z) calculated for C₁₈H₂₁NO₄ (M)⁺: 315.1471, found: 315.1472.

C. α -Amino alcohol **4e**: $[\alpha]_D^{20}$ =-22.9 (*c* 1.0, CHCl₃); IR (KBr) v(cm⁻¹): 3359, 2960, 1687, 1527, 1514, 1246, 1170, 1036, 1003, 816; ¹H-NMR (200 MHz, CDCl₃), δ : 7.1-6.8 (*m*, 4H,(Ar)), 4.74 (*d*, *J* = 7.7, 1H, NH), 3.78 (*s*, 3H, CH₃O(Ar)), 3.7-3.4 (*m*, 3H, CH, CH₂O), 2.77 (*d*, *J* = 7.0, 2H, CH₂(Ar)), 2.45 (*bs*, 1H, OH), 1.41 (*s*, 9H, C(CH₃)₃); ¹³C-NMR (50 MHz, CDCl₃), δ : 158.1, 156.1, 130.2, 129.8, 113.8, 79.6, 63.9, 55.2, 53.8, 36.5, 28.3; EIMS (m/z): 281 (M)⁺, 225, 208, 164, 121; EIMS HR (m/z) calculated for C₁₅H₂₃NO₄ (M)⁺: 281.1627, found: 281. 1634.

D. α -Amino alcohol **4f**: $[\alpha]_D^{20}$ =+4.8 (c 1.9, CHCl₃); ¹H-NMR (500 MHz, CDCl₃), δ : 7.4-7.1 (m, 10H, Ar), 5.2-5.1 (m, 2H, OCH₂(Ar)), 4.5-4.4 (m, 2H, NCH₂(Ar)), 4.1-4.0 (m, 1H, CH), 3.6-3.3 (s, 2H, CH₂O), 2.7-2.4 (m, 1H, OH), 1.1-1.0 (m, 3H, CH₃); ¹³C-NMR (125 MHz, CDCl₃), δ : 156.8, 138.7, 136.7, 128.3, 128.2, 127.7, 127.6, 127.1, 126.9, 126.8, 67.1, 64.8, 55.2, 54.6, 48.4, 15.3, 15.0, 14.4; EIMS m/z: 299 (M⁺), 268, 224, 191, 181, 108, 104, 91, 79; EIMS HR (m/z) calculated for C₁₈H₂₁NO₃: 299.1521, found: 299.1517.

E. α -*Amino alcohol* **4***l*: $[\alpha]_D^{20} = -1.0$ (*c* 1.06, CHCl₃); IR (film) v(cm⁻¹): 3412, 3340, 3032, 2946, 2884, 1702, 1528, 1455, 1241, 1107, 1044, 739, 698; ¹H-NMR (200 MHz, CDCl₃) δ : 7.30 (*m*, 10H, Ar), 5.42 (*d*, *J* = 7.3, 1H, NH), 5.09 (*s*, 2H, OCH₂(Cbz)), 4.74 (*s*, 2H, OCH₂O), 4.57 (*s*, 2H, OCH₂(BOM)), 3.95-3.60 (*m*, 5H, 2xCH₂. CH), 2.9-2.4 (*bs*, 1H, OH); ¹³C-NMR (50 MHz, CDCl₃), δ : 156.4, 137.4, 136.2, 128.5, 128.4, 128.1, 128.1, 127.8, 95.0, 69.8, 67.9, 66.9, 63.0, 52.0; LSIMS (m/z): 368 (M+Na)⁺, 346 (M+H)⁺; LSIMS HR (m/z) calculated for C₁₉H₂₄NO₅ (M+H)⁺: 346.1655, found: 346.1655.

F. α -*Amino alcohol* **4m**: $[\alpha]_D^{20} = +5.2$ (*c* 1.1, CHCl₃); IR (film) v(cm⁻¹): 3440, 2928, 2856, 1697, 1681, 1471, 1252, 1107, 1006, 837, 777, 698; ¹H-NMR (500 MHz, CDCl₃), δ : 7.4-7.2 (*m*, 10H, Ar), 5.16 (*bs*, 2H, OCH₂(Cbz)), 4.76 (*d*, *J* = 16.2, 1H, NCH_AH_B(Ar)), 4.43 (*d*, *J* = 16.2, 1H, NCH_AH_B(Ar)), 4.0-3.6 (*m*, 5H, CH₂CHCH₂), 3.20 (*bs*, 1H, OH), 0.87 (*s*, 9H, SiC(CH₃)₃), 0.01 (*s*, 6H, Si(CH₃)₂); ¹³C-NMR (125 MHz, CDCl₃), δ : 157.0, 136.3, 128.8, 128.9, 128.5, 128.0, 127.9, 127.2, 67.5, 63.0, 62.4, 55.4, 46.4, 25.8, 18.1, -5.6; LSIMS (m/z): 881 (2M+Na)⁺, 452 (M+Na)⁺, 430 (M+H)⁺; LSIMS HR (m/z) calculated for C₂₄H₃₆NO₄SSi (M+H)⁺: 430.2414, found: 430.2413.

G. α -Amino alcohol **4n**: $[\alpha]_D^{20} = -10.9$ (c 1.2, CH₂Cl₂); IR (film) v(cm⁻¹): 3432, 2929, 1693, 1671; ¹H NMR (200 MHz, CDCl₃) δ : 7.3-7.2 (*m*, 5H, (Ar)), 4.8-4.1 (*m*, 2H, CH₂(Ar)), 4.0-3.5 (*m*, 5H, 2xCH₂, CH), 2.95 (*bs*, 1H, OH), 1.41 (*s*, 9H), 0.85 (*s*, 9H, SiC(CH₃)₃), 0.01 (*s*, 6H, Si(CH₃)₂); ¹³C NMR (50 MHz, CDCl₃) δ : 156.6, 139.2, 128.5, 128.2, 127.1, 80.5, 63.3, 62.0, 61.9, 52.4, 28.4, 25.9, 25.6, 18.2, -5.6; LSIMS HR (m/z) calculated for C₂₁H₃₈NO₄Si (M+H)⁺: 396.2570, found: 396.2570.

H. α -Amino alcohol **4***p*: $[\alpha]_{D}^{20}$ =-17.3 (*c* 1.3, CHCl₃); m.p. 59-60°C (from hexane - AcOEt); IR (KBr) v(cm⁻¹): 3520, 2952, 2927, 2884, 2856, 1327, 1308, 1146, 1094, 854, 835, 773, 726; 658; ¹H-NMR (200 MHz, CDCl₃), δ : 7.8-7.7 (*m*, 2H, Ar), 7.5-7.2 (*m*, 7H, Ar), 4.56 (dAB_{22} , J= 16.0, 1H, NC<u>H</u>_AH_B(Ar)), 4.44 (dAB_{22} , J= 15.8, 1H, NCH_AH_B(Ar)), 4.0-3.9 (*m*, 1H, CH), 3.7-3.4 (*m*, 4H, CH₂OTBS, CH₂O), 2.39 (*s*, 3H, CH₃(Ar)), 1.3-1.2 (*m*, 1H, OH), 0.79 (*s*, 9H, SiC(CH₃)₃), -0.07 (*s*, 3H, SiCH₃), -0.08 (*s*, 3H, SiCH₃); ¹³C-NMR (50 MHz, CDCl₃), δ : 142.9, 138.0, 137.6, 129.4, 128.2, 128.0, 127.9, 127.8, 127.4, 127.3, 127.1, 126.9, 65.5, 62.0, 61.6, 61.2, 48.6, 25.5, 21.2, 17.8, -5.9, -5.10; LSIMS (m/z): 921 (2M+Na)⁺, 472 (M+Na)⁺, 450 (M+H)⁺; LSIMS HR (m/z) calculated for C₂₃H₃₆NO₄SSi (M+H)⁺: 450.2134, found: 450.2134.

TEMPO oxidation of alcohols 4 to aldehydes 5. General procedure.

To a cold (0°C), rapidly stirred (> 1000 rpm) biphasic mixture consisted of an alcohol 4 (1 mmol), TEMPO free radical (0.02 mmol), sodium bromide (1 mmol), toluene (3 mL), ethyl acetate (3 mL) and water (0.5 mL), an aqueous solution of NaOCl (1.1 mmol) containing NaHCO₃ (2.9 mmol) was added dropwise over a period of 1-2 h. The aqueous layer was separated and washed with Et_2O (5 mL). The combined organic layers were washed with a solution of KI (8 mg) dissolved in 10% aqueous KHSO₄ (2 mL), then with 10% aqueous sodium thiosulfate (1 mL), brine (2 mL), and dried (MgSO₄). Filtration and concentration in vacuo afforded a desired aldehyde 5 which was immediately used for further reactions.

Swern oxidation of alcohols 4 to aldehydes 5. General procedure.

To a stirred solution of oxalyl chloride (1.5 mmol, 131 μ L) in dry CH₂Cl₂ (5 mL) at -78°C was added a solution of dry DMSO (4.5 mmol, 320 μ L) in CH₂Cl₂ (1.5 mL). After 15 min, a solution of alcohol **2** (1 mmol) in CH₂Cl₂ (1 mL)was added over 10-min period of time, resulting in a cloudy solution which was stirred for additional 30 min. Triethylamine (5 mmol, 0.7 mL) was added and then the cooling bath was removed. After the reaction mixture reached room temperature, solvent was evaporated and a remaining mixture was extracted with Et₂O (3x10 mL). The combined organic layers were washed with HCl_{aq} (0.1 M, 10 mL), saturated NaHCO_{3 aq} (30 mL) and brine (30 mL). Finally the solution was dried over MgSO₄ and evaporated in vacuo.

Reduction of esters 3 to aldehydes 5 using DIBAL-H. General procedure.

A precooled solution of DIBAL-H (2 mmol, 1.3 mL, 1.5 M in toluene) was added dropwise under argon to a cold (-78°C) stirred solution of an α -amino methyl ester (1 mmol) in dry Et₂O (6 mL). Stirring was continued at -78°C for one hour. Then methanol (2 mL) and aqueous solution of sodium-potasium tartrate (5 mL) was added. The reaction temperature was then increased to room temperature and the reaction mixture was stirred untill the phases were completely separated. After separation, the organic layer was washed with brine (5 mL), dried (MgSO₄) and evaporated in vacuo.

Analytical and spectral data of protected α -amino aldehydes.

Data for α -amino aldehydes 5a,²¹ 5b,²² 5g,²³⁻²⁵ 5h,^{11,26} 5i,²⁷ 5j,²⁸ 5k,²⁹ 5o⁹ and 5r^{19,30} were identical with those already published.

A. Aldehyde Sc: IR (film) v(cm⁻¹): 3473, 3286, 1598, 1451, 1327, 1162, 1092, 1031, 815, 667; ¹H-NMR (500 MHz, CDCl₃), δ : 9.45 (d, J = 0.5, 1H, CHO), 7.75 (m, 2H, (Ar)), 7.30 (m, 2H, (Ar)), 5.77 (d, J = 5.2, 1H, NH),

3.84 (*m*, 1H, CH), 2.41 (*s*, 3H, CH₃(Ar)), 1.27 (*d*, J = 7.4, 3H, CH₃); ¹³C-NMR (125 MHz, CDCl₃), δ : 198.6, 143.8, 136.7, 129.7, 129.6, 127.0, 57.3, 21.4, 15.5; LSIMS (m/z): 477 (2M+Na)⁺, 455 (2M+Na)⁺, 250 (M+Na)⁺, 228 (M+H)⁺; LSIMS HR (m/z) calculated for C₁₀H₁₄NO₃ (M+H)⁺: 228.0694, found: 228.0694.

B. Aldehyde **5d**: IR (film) v(cm⁻¹): 3330, 2927, 1713, 1612, 1513, 1248, 1034, 837, 741; ¹H-NMR (200 MHz, CDCl₃), δ : 9.62 (s, 1H, CHO), 7.34 (s, 5H, (Ar)), 7.1-6.8 (m, 4H, (Ar)), 5.28 (d, J = 6.5, 1H, NH), 5.11 (s, 2H, CH₂(Cbz)), 4.47 (dt, $J_1 = 6.7$, $J_2 = 6.5$, 1H, CH), 3.77 (s, 3H, CH₃O), 3.08 (d, J = 6.5, 2H, CH₂(Ar)); ¹³C-NMR (50 MHz, CDCl₃), δ : 201.9, 158.0, 156.4, 140.9, 130.1, 129.7, 128.2, 127.8, 126.7, 113.7, 64.7, 63.2, 55.0, 40.2; EIMS (m/z): 313 (M)⁺, 284, 240, 162, 121, 91; EIMS HR calculated for C₁₈H₁₉NO₄ (M)⁺: 313.1314, found 313.1319.

C. Aldehyde **5e**: IR (KBr) v(cm⁻¹): 3364, 2978, 1704, 1613, 1514, 1367, 1248, 1164, 1034, 835, 770; ¹H-NMR (500 MHz, DMSO-d₆), δ : 9.49 (*s*, 1H, CHO), 7.3-7.2 (*m*, 1H, NH), 7.1-6.8 (*m*, 4H, (Ar)), 4.0 (*m*, 1H, CH), 3.70 (*s*, 3H, CH₃O), 3.00 (*dd*, $J_I = 13.0$, $J_2 = 4.8$, 1H, CH_AH_B(Ar)), 2.65 (*dd*, $J_I = 13.0$, $J_2 = 10.0$, 1H, CH_AH_B(Ar)), 1.34 (*s*, 9H, C(CH₃)₃); ¹³C-NMR (125 MHz, DMSO-d₆), δ : 201.3, 157.8, 155.5, 130.1, 129.5, 113.6, 78.3, 61.0, 54.9, 32.5, 28.1; EIMS (m/z): 279 (M)⁺, 150,136, 121; EIMS HR calculated for C₁₅H₂₁NO₄ (M)⁺ 279.1471, found 279.1470.

D. Aldehyde **5***f*: IR (film) v(cm⁻¹): 1738, 1696, 1453, 1424, 1242, 1027, 699; ¹H-NMR (500 MHz, CDCl₃), δ : 9.49 (*s*, 0.6H, CHO), 9.39 (*s*, 0.4H, CHO), 7.4-7.3 (*m*, 10H, Ar), 5.20 (*s*, 2H, OCH₂(Cbz)), 4.8-4.7 (*m*, 1H, NCH_AH_B(Ar)), 4.4-4.3 (*m*, 1H, NCH_AH_B(Ar)), 3.8-3.6 (*m*, 1H, CH), 1.3-1.2 (*m*, 3H, CH₃); ¹³C-NMR (125 MHz, CDCl₃), δ : 199.2, 199.1, 156.0, 137.3, 136.0, 128.7, 128.5, 128.2, 128.1, 128.0, 127.7, 27.5, 67.9, 67.8, 61.9, 61.5, 51.5, 50.6, 12.7, 11.8; LSIMS (m/z): 320 (M+Na)⁺, 298 (M+H)⁺; LSIMS HR (m/z) calculated for C₁₈H₂₀NO₃ (M+H)⁺: 298.1443, found: 298.1445.

E. Aldehyde **51**: IR (film) v(cm⁻¹): 3330, 3032, 2948, 2887, 1719, 1521, 1455, 1242, 1166, 1114, 1044, 741, 698; ¹H-NMR (200 MHz, CDCl₃), δ : 9.58 (*s*, 1H, CHO), 7.4-7.3 (*m*, 10H, Ar), 5.8-5.6 (*m*, 1H, NH), 5.13 (*s*, 2H, OCH₂(Cbz)), 4.72 (*s*, 2H, OCH₂O), 4.53 (*s*, 2H, OCH₂(BOM)), 4.42 (*m*, 1H, CH), 4.18 (*d*, *d* J = 3.2, J = 10.4, 1H, CH_AH_BOTBS), 3.82 (*d*, *d* J = 3.7, J = 10.4, 1H, CH_AH_BOTBS); ¹³C-NMR (50 MHz, CDCl₃), δ : 198.2, 156.1, 137.3, 136.0, 128.5, 128.5, 128.4, 128.3, 128.1, 127.9, 127.9, 95.0, 94.8, 69.9, 69.7, 67.2, 67.1, 65.8, 65.6, 60.3; LSIMS (m/z): 344 (M+H)⁺; LSIMS HR (m/z) calculated for C₁₉H₂₂NO₅ (M+H)⁺: 344.1498, found: 344.1493.

F. Aldehyde **5m**: IR (KBr) $v(cm^{-1})$: 3033, 2954, 2857, 1737, 1694, 1468, 1427, 1363, 1117, 1017, 839,778, 699; ¹H-NMR (200 MHz, CDCl₃), δ : 9.45 (*s*, 0.6H, CHO), 9.31 (*s*, 0.4H, CHO), 7.4-7.2 (*m*, 10H, Ar), 5.19 (*s*, 2H, OCH₂(Cbz)), 5.03 (*d*, *J* = 16.0, 1H, NC<u>H</u>_AH_B(Ar)), 4.34 (*d*, *J* = 16.0, 1H, NCH_A<u>H</u>_B(Ar)), 4.2-3.7 (*m*, 3H, CH₂. CH), 0.86 (*s*, 5.4H, SiC(CH₃)₃), 0.85 (*s*, 3.6H, SiC(CH₃)₃), 0.00 (*s*, 3.6H, Si(CH₃)₂), -0.05 (*s*, 2.4H, Si(CH₃)₂); ¹³C-NMR (50 MHz, CDCl₃), δ : 198.2, 198.0, 155.8, 137.5, 137.4, 136.0, 135.6, 128.8, 128.5, 128.4, 128.0, 127.8, 127.7, 127.6, 68.0, 67.8, 67.6, 67.1, 61.3, 60.7, 53.0, 52.5, 25.8, 18.1, -5.6; LSIMS (m/z):

450 $(M+Na)^+$, 428 $(M+H)^+$; LSIMS HR (m/z) calculated for C₂₄H₃₄NO₄Si $(M+H)^+$: 448.2257, found: 448.2256.

G. Aldehyde **5n**: IR (film) ν (cm⁻¹): 2930, 1736, 1685; ¹H-NMR (200 MHz, CDCl₃) & 9.65(*s*, 0.5H, CHO), 9.34(*s*, 0.5H, CHO), 7.4-7.2 (*m*, 5H, Ar), 4.4-3.8 (*m*, 4H, CH₂OTBS, NCH₂(Ar)), 3.65 (*dd*, *J*,=4.7, *J*₂=7.9, 0.5H, CH), 3.61 (*dd*, *J*,=4.7, *J*₂=7.9, 0.5H, CH), 1.45 (*s*, 9H, OC(CH₃)₃), 0.90 (*s*, 9H, SiC(CH₃)₃), 0.06 (*s*, 6H, Si(CH₃)₂); ¹³C-NMR (50 MHz, CDCl₃) & 198.4, 155.5, 154.7, 138.3, 137.9, 128.8, 128.7, 128.2, 127.6, 127.5, 81.7, 81.2, 67.4, 66.9, 61.5, 60.9, 52.8, 52.5, 28.2, 28.0, 25.8, 18.1, -5.6; EIMS (m/z): 393 (M)⁺, 364, 308, 280; EIMS HR (m/z) calculated for C₂₀H₃₄NO₃Si (M-CHO)⁺: 364.2253, found: 364.2254.

H. Aldehyde 5p: IR (film) v(cm⁻¹): 3443, 2928, 2856, 1732, 1332, 1157, 1106, 838, 783; ¹H-NMR (200 MHz, CDCl₃), δ : 9.49 (s, 1H, CHO), 7.8-7.7 (m, 2H, Ar), 7.4-7.3 (m, 7H, Ar), 4.61 ($d_{AB_{2}}$, J = 15.1, 1H, NCH_AH_B(Ar)), 4.50 ($d_{AB_{2}}$, J = 15.0, 1H, NCH_AH_B(Ar)), 4.2-4.0 (m, 1H, CH), 4.0-3.9 (m, 2H, CH₂OTBS), 2.45 (s, 3H, CH₃(Ar)), 0.80 (s, 9H, SiC(CH₃)₃), -0.03 (s, 3H, SiCH₃), -0.04 (s, 3H, SiCH₃); ¹³C-NMR (50 MHz, CDCl₃), δ : 198.2, 143.7, 137.2, 136.2, 129.7, 128.8, 128.5, 128.2, 127.4, 67.2, 60.5, 51.2, 25.6, 21.5, 18.0, -5.8; LSIMS (M)⁺: 917 (2M+Na)⁺, 895 (2M+H)⁺, 470 (M+Na)⁺, 448 (M+H)⁺; LSIMS HR (m/z) calculated for C₂₃H₃₄NO₄SSi (M+H)⁺: 448.1978, found 448.1988.

REFERENCES AND NOTES

- 1. Jurczak, J; Gołębiowski, A. Chem. Rev. 1989, 89, 149.
- 2. Stanfield, C. F.; Parker, J. E.; Kanellis, P. J. Org. Chem. 1981, 46, 4799.
- 3. Hamada, Y.; Shioiri, T. Tetrahedron Lett. 1982, 23, 1193.
- 4. Luly, J. R.; Dellaria, J. F.; Plattner, J. J.; Soderquist, J. L.; Yi, N. J. Org. Chem. 1987, 52, 1487.
- 5. Rittle, K. E.; Homnick, C. F.; Ponticello, G. S.; Evans, B. E. J. Org. Chem. 1982, 47, 3016.
- 6. Tourve, D. Janssen Chim. Acta 1985, 3, 3.
- 7. Hamada, Y.; Shioiri, T. Chem. Pharm. Bull. 1982, 30, 1921.
- 8. Mancuso, A. J.; Swern, D. Synthesis 1981, 165.
- 9. Gołębiowski, A.; Gorins, G.; Johnson, C. R.; Kiciak, K. Polish J. Chem. 1993, 67, 685.
- 10. Stanfield, C. F.; Parker, J. E.; Kanellis, P. J. Org. Chem. 1981, 47, 4797.
- 11. Pyne, S. G.; Hensel, M. J.; Fuchs, P. L. J. Am. Chem. Soc. 1982, 104, 5719.
- 12. Andersson, L.; Wolfenden, R. Anal. Biochem. 1982, 124, 150.
- 13. Semmelhack, M. F.; Chou, C. S.; Cortes, D. A. J. Am. Chem. Soc. 1983, 105, 4492.
- 14. Anelli, P. L.; Biffi, C. B.; Montanari, F.; Quici, S. J. Org. Chem. 1987, 52, 2559.
- 15. Tong, G.; Perich, J. W.; Johns, R. B. Tetrahedron Lett. 1990, 31, 3759.
- 16. Leanna, M. R.; Sowin, T. J.; Morton, H. E. Tetrahedron Lett. 1992, 33, 5029.
- 17. Jurczak, J.; Prokopowicz, P.; Gołębiowski, A. Tetrahedron Lett. 1993, 34, 7107.
- 18. Jurczak, J.; Gryko, D.; Kobrzycka, E.; Gruza, H.; Prokopowicz, P., in preparation.
- 19. Garner, P.; Park, J. M. J. Org. Chem. 1990, 55, 3772.
- 20. Still, W. C.; Kahn, M.; Mitra, A. J. Org. Chem. 1978, 43, 2923.
- 21. Kokotos, G. Synthesis 1990, 299.
- 22. Gołębiowski, A.; Jacobson, U.; Jurczak, J. Tetrahedron 1987, 43, 3063.
- 23. Gołębiowski, A.; Raczko, J.; Jurczak, J. Bull. Pol. Ac.: Chem. 1988, 36, 209.
- 24. Gołębiowski, A.; Jacobsson, U.; Raczko, J.; Jurczak, J. J. Org. Chem. 1989, 54, 3759.
- 25. Hormuth, S.; Reissig, H-U.; Dorsch, D. Liebigs Ann. Chem. 1994, 121.
- 26. Fuij, N.; Nahai, K.; Tamamura, H.; Otaka, A.; Mimura, N.; Miwa, Y.; Toga, T.; Yamamota, Y.; Ibuka, T. J. Chem. Soc. Perkin Trans 1 1995, 1359.
- 27. Konradi, A. W.; Kemp, S. J.; Pedersen, S. F. J. Am. Chem. Soc. 1994, 116, 1316.
- 28. Gonda, A. J.; Helland, A. C.; Ernst, B.; Bellus, D. Synthesis 1993, 729.
- 29. Fuji, N.; Nakai, K.; Bashita, H.; Hotta, Y.; Tamamura, H.; Otaka, A.; Ibuka, H. Chem. Pharm. Bull. 1994, 42, 2241.
- 30. Williams, L.; Zhang, Z.; Shao, F.; Carroll, P.; Joullie, M. M. Tetrahedron 1996, 52, 11673.
- 31. Ito. A.; Takahashi, R.; Baba, Y. Chem. Pharm. Bull. 1975, 23, 3081.