Alkaloids Asymmetric Synthesis from (*S*)-Pyroglutamic Acid. II [1]. Attempted Asymmetric Total Synthesis of *Trans*-5-ethyl-2-*n*-heptylpyrrolidine

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From the readily available (*S*)-pyroglutamic acid **1** the asymmetric synthesis of *trans* and *cis* 5-*n*-heptyl-2-(*S*)-hydroxymethylpyrrolidines **7**, some derivatives and transformations are described.

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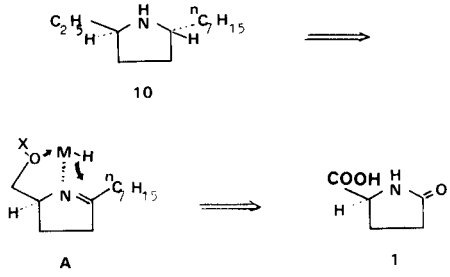
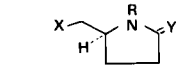
(*S*)-Pyroglutamic acid **1** is a cheap and readily available material in optically pure form, whose potential as a chiral template for alkaloids asymmetric synthesis, up to recently, has been practically neglected [2]. We have recently embarked on a project directed to the total asymmetric synthesis of pyrrolidine and piperidine alkaloids from this chiral substrate; here we present our first results in this field taking as the target molecule *trans*-5-ethyl-2-*n*-heptylpyrrolidine **10**, a component of the ant venom expelled by some *Solenopsis* species [3]. When this work was in progress Rapoport reported the first chiral synthesis of both enantiomers of *cis* and *trans*-5-butyl-2-heptylpyrrolidine from glutamic acid [2b].

In our retrosynthetic analysis of a *trans*-2,5-dialkylpyrrolidine we envisaged as the key intermediate, an endocyclic imine of type A (see Scheme 1) in which the orienting effect of the 5-hydroxymethyl group should direct the hydride attack from the β face giving compounds predominantly *trans*.

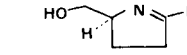


Scheme 1

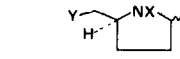
So starting from **1** and by known procedures [4], compound **2** was obtained, which by acetylation yielded the previously undescribed **3** as beautiful needles in 83% yield; followed by phosphorus pentasulfide treatment, the crystalline thiolactam **4** was obtained in 84% yield. Reaction of **4** with methyl iodide in methylene chloride at room temperature followed by a sodium methoxide/methanol reaction gave in one pot and 52% yield the thioimidate **5** (36% overall yield from **2** in three steps). Alkyl chain introduction at C-2 proceeded smoothly (81% yield) by reaction of **5** with *n*-heptylmagnesium bromide in methylene chloride [5], at reflux for 72 hours to yield the imine **6**. With this compound in hand we attacked the crucial step; we were pleased to find that diisobutylaluminium hydride reduction of **6** in methylene chloride at -78° gave **7a** + **7b**



2 X=OH, Y=O, R=H
3 X=OAc, Y=O, R=H
4 X=OAc, Y=S, R=H
14 X=OSi(CH$_3$)$_2$^{t}Bu, Y=O, R=H
15 X=OSi(CH$_3$)$_2$^{t}Bu, Y=O, R=CH$_2$Ø



5 R=SCH
6 R=n-C$_7$H$_{15}$

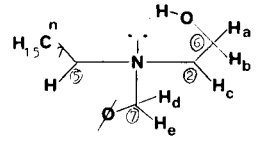


7a trans X=Y=H 7b cis
8a trans X=Y=CH$_2$Ø 8b cis
9 X=Y=OTs
11 trans X=Ts, Y=J
12 X=COCF$_3$, Y=H
13a trans X=COCF$_3$, Y=OTs 13b cis

in 85% yield in a 4:1 ratio. This was followed by benzylation of the crude mixture and separation by careful flash-chromatography. To the less polar and major component **8a** the *trans* stereochemistry was assigned on the following grounds: in the 200 MHz ^{1}H-nmr spectrum, the methylene protons in the hydroxymethyl moiety appear as an A_2 system at 3.23 ppm (d, J = 3 Hz) and $\Delta\delta$ H_{de} = 0.2 ppm (J_{de} = 13.75 Hz); in contrast, the *cis*-**8b** isomer shows for the hydroxymethyl H_{abc} protons an ABX system δ H_a = 3.38 ppm (dd, J = 2.5 and 11.5 Hz); δ H_b = 3.54 ppm (dd, J = 3.5 and 11.5 Hz); the benzyl protons show $\Delta\delta$ = 0.1 ppm and J_{de} = 13.5 Hz.

A possible explanation of these features and the propos-

ed stereochemistry is that in the *cis* isomer only one invertomer must be largely predominant in the equilibrium (see Scheme 2); because of an intramolecular hydrogen bond as depicted and the coplanar side chain, the free rotation of the hydroxymethyl chain is severely restricted, so an ABX system is observed for the H_{abc} protons. On the other hand for the *trans* isomer, non bonded interactions between the alkyl chain and the benzyl group displaces the equilibrium to the invertomer in which no intramolecular hydrogen bond is possible, so the relative free rotation averages the chemical shifts for $H_{a \rightleftharpoons b}$. This assignment is also in good agreement with the observed $\Delta\delta$ H_{de} *cis* < $\Delta\delta$ H_{de} *trans* [6]. In the ^{13}C-nmr spectrum, interesting differences were also observed: for **8a**, δC_2, C_5 = 65.85, 65.76 ppm; δC_6 = 62.74 ppm and δC_7 = 57.81 ppm. In **8b**, δC_2, C_5 = 62.94, 62.06 ppm; δC_6 = 62.28 ppm and δC_7 = 51.91 ppm, the most striking being $\Delta\delta$ C_7 ~ 6 ppm.



CIS

TRANS

Scheme 2

So, at this stage we had successfully completed the introduction of the "east" side chain, the homologation to the ethyl "west" chain being an apparently simple task to solve.

In the preliminary experiments, working with the mixture **7a** + **7b**, we planned protection of the heterocyclic nitrogen and activation of the hydroxyl group by total tosylation. Thus compound **9** was obtained in 90% yield. Unfortunately, all efforts made in order to displace the tosyl group were unsuccessful, so, after the dimethyllithium cuprate reaction, **9** was recovered unchanged; reaction with methylmagnesium iodide, surprisingly, afforded, instead of the expected *N*-tosyl derivative of **10**, the iodide **11** in 18% yield. We cannot ascertain the reasons for this anomalous behavior. We assign tentatively the *trans* stereochemistry to **11**; this would be in good agreement with the $\delta(CH_2\text{-I})$ observed and recorded in the literature for analogous systems [7]. No related *cis* isomer could be detected. Other functionally similar derivatives, such as **13a** and **13b**, treated with the appropriate reagents as above also failed to yield the wanted products.

So another strategy was sought in which the essential features discovered in the preceeding study could be used, but the problematic "west" side chain introduction should be advanced in the synthetic plan, for example *via* organometallic addition to an aldehyde or acid chloride derived from **2**.

Silylation [8] of **2** gave **14** in 75% yield. Benzylation afforded **15** in a very low yield (17%); this fact and the, at this moment, known problems of racemization found by Rapoport [2b] in analogous oxidized derivatives, led us to abandon definitively our approach [9].

In summary, thus, from (*S*)-pyroglutamic acid a series of some new and original observations, the synthesis of some *cis* and *trans*-2,5-dialkylpyrrolidines, have been accomplished. We are currently investigating the transformation chiral pyrrolidine → chiral piperidine [7], aiming to a pseudoconhydrine chiral synthesis from an analogous chiral *n*-propyl derivative of **7**.

EXPERIMENTAL

The melting points were determined in a Kofler apparatus and are uncorrected. The ir spectra were recorded in a Perkin-Elmer 297 Spectrophotometer. The nmr spectra were obtained with a Brucker WP 80, 200 and 400 spectrometer using TMS as internal standard. Mass spectra were scanned with an AEI MS 50 at 70 eV.

(*S*)-5-Acetoxymethyl-2-pyrrolidinone (**3**).

Compound **2** (9.6 g, 83.4 mm) was treated in the usual manner with 10 ml of acetic anhydride and 20 ml of pyridine for 24 hours at room temperature. Evaporation of solvents and flash-chromatography (methylene chloride:methanol, 5%) yielded 11.1 g (83% yield) of **3**, mp (hexane:ethyl acetate) 67-69°; $[\alpha]_D^{25}$ + 48.6° (c 1.94, chloroform); ir (Nujol): 3100-3300 (N-H str), 1730, 1690 (CO str) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.62-2.25 (2H, m), 2.20 (3H, s), 2.37 (2H, m), 3.80-4.37 (3H, m), 7.00 (1H, br s); ^{13}C-nmr (deuteriochloroform): δ 178.31 (s), 170.71 (s), 66.95 (t), 52.85 (d), 29.63 (t), 23.21 (t), 20.68 (q); ms: m/z (M +1, 39), 97 (100), 86 (99), 69 (60), 56 (100).

Anal. Calcd. for $C_7H_{11}NO_3$: C, 53.42; H, 6.99; N, 8.90. Found: C, 53.50; H, 7.12; N, 8.79.

(*S*)-5-Acetoxymethyl-2-thiopyrrolidinone (**4**).

Compound **3** (8.6 g, 54.7 mmoles) was treated with 10 g (45.4 mmoles) of phosphorus pentasulfide in 90 ml of benzene, at reflux, under argon for 45 minutes. The liquid mass was decanted and the solid rest triturated with methylene chloride and filtered over Celite 545. The organic extract was washed with diluted aqueous bicarbonate solution and water, dried and evaporated. After flash-chromatography (hexane:ethyl acetate, 60%) pure **4** was obtained (7.9 g, 84% yield), mp (hexane:ethyl acetate) 73-75°; $[\alpha]_D^{25}$ + 80.0° (c 1.16, chloroform); ir (Nujol): 3150-3300 (N-H str), 1680-1740 (CO str) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.70-2.61 (3H, m), 2.10 (3H, s), 2.96 (2H, t, J = 7 Hz), 4.46-3.90 (3H, m); ^{13}C-nmr (deuteriochloroform): δ 205.77 (s), 170.47 (s), 65.62 (t), 60.74 (d), 42.70 (t), 25.32 (t), 20.63 (q); ms: m/z 173 (M, 52), 122 (32), 113 (22), 105 (32), 100 (100), 84 (43), 43 (30).

Anal. Calcd. for $C_7H_{11}NSO_2$: C, 48.55; H, 6.35; N, 8.09; S, 18.49. Found: C, 48.44; H, 6.36; N, 8.03; S, 18.27.

(*S*)-5-Hydroxymethyl-2-thiomethyl-1-pyrroline (**5**).

Compound **4** (7.9 g, 45 mmoles) was treated with 10 ml (0.16 mole) of

methyl iodide in 50 ml of methylene chloride at room temperature for 24 hours. The mixture was evaporated, dissolved in 40 ml of methanol and treated at 0° with 5.4 g (0.1 mole) of sodium methoxide for 45 minutes. The solvent was removed and the residual oil taken in methylene chloride, washed with brine, dried, evaporated and purified by flash-chromatography (methylene chloride:methanol, 5%) giving 3.3 g of **5** (52% yield), oil; $[\alpha]_D^{25}$ + 78.1° (c 2.16, chloroform); ir (neat): 3200 (O-H str), 1640 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.58-2.25 (2H, m), 2.43 (3H, s), 2.68 (2H, t, J = 7.5 Hz), 3.41 (1H, s), 3.53 (1H, dd, J = 6 and 12 Hz), 3.87 (1H, dd, J = 4 and 12 Hz), 4.16 (1H, m); ^{13}C-nmr (deuteriochloroform): δ 174.66 (s), 74.29 (d), 65.79 (t), 38.90 (t), 25.71 (t), 13.58 (q); ms: m/z 145 (M, 22), 128 (2), 114 (100), 100 (5), 98 (4), 74 (8), 61 (23).

Anal. Calcd. for $C_6H_{11}NOS$: C, 49.60; H, 7.57; N, 9.64; S, 22.04. Found: C, 49.42; H, 7.55; N, 9.88; S, 21.98.

2-*n*-Heptyl-(*S*)-5-hydroxymethyl-1-pyrroline (**6**).

Compound **5** (782 mg, 5.3 mmoles) dissolved in 41 ml of methylene chloride was treated at 0°, under argon, with *n*-heptylmagnesium bromide (79.5 mmoles, 4.5 *M* in ether) and refluxed for 72 hours, followed by careful hydrolysis at 0° with 20 ml of 15% aqueous solution of ammonium chloride; the mass was filtered over a short pad of Celite 545, diluted with methylene chloride, washed several times with brine, dried and evaporated. Flash-chromatography (methylene chloride:methanol, 5%) of the resultant oil gave 855 mg of **6** (81%) as an oil; $[\alpha]_D^{25}$ + 83.2° (c 0.99, chloroform); ir (neat): 3000-35000 (O-H str), 1620 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.88 (3H, t, J = 6.5 Hz), 1.13-2.03 (12H, m), 2.17-2.87 (4H, m), 3.55 (1H, dd, J = 6 and 12 Hz), 3.82 (1H, dd, J = 4 and 12 Hz), 4.20 (2H, m); ^{13}C-nmr (deuteriochloroform): δ 179.96 (s), 74.19 (d), 65.34 (t), 37.38 (t), 33.73 (t), 31.63 (t), 29.40 (t), 28.95 (t), 26.49 (t), 24.55 (t), 22.51 (t), 13.90 (q); ms: m/z 196 (M-1, 3), 180 (2), 166 (35), 140 (13), 126 (41), 113 (88), 82 (100).

Anal. Calcd. for $C_{12}H_{23}NO$: C, 73.00; H, 11.66; N, 7.09. Found: C, 72.90; H, 11.36; N, 6.90.

N-Benzyl-5-*n*-heptyl-(*S*)-2-hydroxymethylpyrrolidine (**8**).

Compound **6** (429 mg, 2.1 mmoles) dissolved in 4.5 ml of anhydrous methylene chloride was treated with 10.5 ml of diisobutylaluminium hydride (1 *M* in hexane) dropwise in 10 minutes at -78° under argon. It was warmed to room temperature overnight. Dilution with methylene chloride (10 ml) followed by treatment at 0° with 5.4 g of potassium fluoride and 1.2 ml of water, stirring for 30 minutes, filtration over Celite 545 and evaporation left 359 mg (85% yield) of 5-*n*-heptyl-2(*S*)-hydroxymethylpyrrolidine (**7**), which without further purification was treated with 0.22 ml of freshly distilled benzyl bromide (1.8 mmoles) and 150 mg of sodium bicarbonate, in 6 ml of anhydrous dimethylformamide at 60° for 30 minutes. The mixture was diluted with ether, washed several times with water, dried and evaporated to dryness. Flash-chromatography of the resultant oil gave 261 mg of **8a** and 61 mg of **8b** (61% yield).

Compound **8a**.

This compound was obtained as an oil; $[\alpha]_D^{25}$ + 44.5° (c 0.55, chloroform); ir (neat): 3100-3500 (O-H str); ^{1}H-nmr (deuteriochloroform): δ 0.89 (3H, t, J = 6.5 Hz), 1.10-1.41 (12H, m), 1.45-1.74 (4H, m), 2.75 (1H, m), 2.93 (1H, m), 3.23 (2H, d, J = 3 Hz), 3.66 (1H, d, J = 13.75 Hz), 3.86 (1H, d, J = 13.75 Hz), 7.25 (5H, s); ^{13}C-nmr (deuteriochloroform): δ 139.08-127.35 (aromatic), 65.85 (d), 65.76 (d), 62.74 (t), 57.81 (t), 35.24 (t), 31.88 (t), 30.26 (t), 29.87 (t), 29.31 (t), 27.03 (t), 26.33 (t), 22.68 (t), 14.10 (q); ms: m/z 272 (M-17, 9), 259 (100), 190 (34), 91 (56).

Anal. Calcd. for $C_{19}H_{31}NO$: C, 78.89; H, 10.72; N, 4.84. Found: C, 78.60; H, 10.69; N, 4.83.

Compound **8b**.

This compound was obtained as an oil; $[\alpha]_D^{25}$ − 34.5° (c 1.08, chloroform); ir (neat): 3100-3500 (O-H str); ^{1}H-nmr (deuteriochloroform): δ 0.87 (3H, t, J = 6.5 Hz), 1.00-1.41 (12H, m), 1.41-2.09 (4H, m), 2.87-3.18 (2H, m), 3.38 (1H, dd, J = 2.5 and 11.5 Hz), 3.54 (1H, dd, J = 3.5 and 11.5 Hz), 3.71 (1H, d, J = 13.5 Hz), 3.81 (1H, d, J = 13.5 Hz), 7.25 (5H, s); ^{13}C-nmr (deuteriochloroform): δ 138.59-127.46 (aromatic), 62.94 (d), 62.28 (t), 62.06 (d), 51.91 (t), 31.88)t), 29.79 (t), 29.26 (t), 28.56 (t), 27.81 (t), 26.86 (t), 26.40 (t), 22.69 (t), 14.06 (q); ms: m/z 272 (M-17, 18), 258 (100), 190 (63), 91 (63).

Anal. Calcd. for $C_{19}H_{31}NO$: C, 78.89; H, 10.72; N, 4.84. Found: C, 78.70; H, 10.64; N, 4.83.

N-Tosyl-5-*n*-heptyl-(*S*)-2-tosyloxymethylpyrrolidine (**9**).

Compound **7** (278 mg, 1.4 mmoles) dissolved in 5 ml of methylene chloride was treated with 366 mg (3.08 mmoles) of *N,N*-dimethylaminopyridine and 571 mg (3.08 mmoles) of tosyl chloride at room temperature for 12 hours. Standard work-up and flash-chromatography (hexane:ethyl acetate, 20%) gave 608 mg (90% yield) of **9** as an oil; ir (neat): 3100, 2950, 1600, 1350, 1180, 1160 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.88 (3H, t, J = 6.5 Hz), 1.09-1.99 (16H, m), 2.43 (3H, s), 2.48 (3H, s), 3.52 (1H, m), 3.79 (1H, m), 3.96 (1H, dd, J = 8.5 and 10 Hz), 4.29 (1H, dd, J = 4 and 10 Hz), 7.34 (2H, d, J = 8 Hz), 7.40 (2H, d, J = 8 Hz), 7.69 (2H, d, J = 8 Hz), 7.87 (2H, d, J = 8 Hz); ^{13}C-nmr (deuteriochloroform): δ 145.03-127.04 (aromatic), 71.92 (t), 62.30 (d), 59.21 (d), 36.49 (t), 31.88 (t), 29.52 (t), 29.27 (t), 27.34 (t), 26.20 (t), 22.69 (t), 21.68 (q), 21.54 (q), 14.10 (q); ms: m/z 408 (34), 322 (100), 236 (15), 155 (42), 91 (63).

Anal. Calcd. for $C_{26}H_{37}NS_2O_5$: C, 61.46; H, 7.28; N, 2.75; S, 12.60. Found: C, 61.32; H, 7.32; N, 2.68; S, 12.72.

trans-*N*-Tosyl-5-*n*-heptyl-(*S*)-2-iodomethylpyrrolidine (**11**).

Compound **9** (105 mg) dissolved in 3 ml of dry methylene chloride was treated at 0°, under argon, with 2 ml of methylmagnesium iodide (1.8 *M* in ether), at room temperature overnight. Hydrolysis at 0° with 5 ml of saturated solution of ammonium chloride and extraction with ether gave, after drying and evaporation an oil that was purified by flash-chromatography (hexane:ethyl acetate, 10%) to give 25 mg of **11** (18% yield) as an oil; $[\alpha]_D^{25}$ − 44.2° (c 2.71, chloroform); ir (neat): 3025, 2850, 1600, 1460, 1350, 1260, 1160 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.89 (3H, t, J = 6.5 Hz), 1.08-1.93 (16H, m), 2.44 (3H, s), 3.13 (2H, t, J = 10 Hz), 3.69 (2H, m), 7.29 (2H, d, J = 8 Hz), 7.68 (2H, d, J = 8 Hz); ^{13}C-nmr (deuteriochloroform): δ 143.09-127.03 (aromatic), 63.07 (d), 62.25 (d), 36.97 (t), 31.87 (t), 30.95 (t), 29.50 (t), 29.38 (t), 29.26 (t), 26.30 (t), 22.68 (t), 21.53 (q), 14.09 (q), 11.47 (t); ms: m/z 364 (11), 336 (3), 322 (6), 252 (6), 238 (100), 105 (60).

Anal. Calcd. for $C_{19}H_{30}INSO_2$: C, 49.02; H, 6.45; N, 3.01; S, 6.88. Found: C, 48.93; H, 6.41; N, 2.97; S, 6.79.

N-Trifluoromethyl-5-*n*-heptyl-(*S*)-2-tosyloxymethylpyrrolidine (**13**).

Compound **7** (851 mg, 4.2 mmoles) of **7** dissolved in 10 ml of anhydrous methanol was treated with 0.55 ml (4.62 mmoles) of ethyl trifluoroacetate and 0.64 ml of triethylamine at room temperature for 22 hours. After evaporation the residual oil, **12** was treated with tosyl chloride as usual. Flash-chromatography (hexane:ethyl acetate, 10%) gave 920 mg of **13a** and 230 mg of **13b** (61% overall yield).

Compound **13a**.

This compound was obtained as an oil; $[\alpha]_D^{25}$ − 18.6° (c 2.75, chloroform); ir (neat): 2925, 1690 (CO str), 1600, 1450, 1370, 1230, 1200, 1190 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.89 (3H, t, J = 6.5 Hz), 1.09-1.55 (12H, m), 1.70-1.95 (2H, m), 2.00-2.22 (2H, m), 2.45 (3H, s), 3.97 (1H, m), 4.16 (2H, d, J = 8 Hz), 4.33 (1H, q, J = 5 Hz), 7.29 (2H, d, J = 8 Hz), 7.68 (2H, d, J = 8 Hz); ^{13}C-nmr (deuteriochloroform): δ 145.16-128.00 (aromatic), 68.05 (t), 59.88 (d), 31.79 (t), 29.18 (t), 28.89 (t), 27.93 (t), 26.69 (t), 24.25 (t), 22.64 (t), 21.59 (q), 14.03 (q); ms: m/z 365 (4), 350 (11), 278 (10), 264 (100), 196 (5), 178 (38), 166 (10), 91 (10).

Anal. Calcd. for $C_{21}H_{30}F_3NO_4$: C, 55.94; H, 6.66; N, 3.10; S, 7.10. Found: C, 55.86; H, 6.50; N, 3.05; S, 7.06.

Compound **13b**.

This compound was obtained as an oil; $[\alpha]_D^{25}$ − 9.0° (c 1.21, chloroform); ir (neat): 2925, 2850, 1680 (CO str), 1600, 1470, 1440, 1370, 1210, 1200, 1190 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.87 (3H, t, J = 6.5 Hz), 1.10-1.60 (12H, m), 1.81 (1H, m), 2.00 (1H, m), 2.05-2.13 (2H, m),

2.43 (3H, s), 4.08 (2H, m), 4.30 (2H, m), 7.29 (2H, d, J = 8 Hz), 7.68 (2H, d, J = 8 Hz); ^{13}C-nmr (deuteriochloroform): δ 145.15-127.91 (aromatic), 67.79 (t), 60.14 (d), 57.88 (d), 35.91 (t), 35.74 (t), 29.20 (t), 29.08 (t), 28.96 (t), 26.72 (t), 24.42 (t), 22.60 (t), 21.56 (q), 13.92 (q); ms: m/z 365 (27), 350 (50), 322 (18), 292 (18), 278 (36), 264 (54), 196 (27), 178 (100), 168 (64), 100 (50), 91 (54).

Anal. Calcd. for $C_{21}H_{30}F_3NO_4S$: C, 55.94; H, 6.66; N, 3.10; S, 7.10. Found: C, 55.80; H, 6.62; N, 3.00; S, 7.14.

(*S*)-5-*t*-Butyldimethylsilyloxymethyl-2-pyrrolidinone (**14**).

Compound **2** (232 mg, 2 mmoles) dissolved in 3 ml of dimethylformamide was treated with *t*-butyldimethylsilyl chloride (361 mg, 2.4 mmoles) and 340 mg (5 mmoles) of imidazole at room temperature for 24 hours. The mixture was extracted with water-ether, dried, concentrated and submitted to flash-chromatography (ethyl acetate) to give 304 mg (75% yield) of **14** as an oil; $[\alpha]_D^{25}$ + 43.0° (c 1.39, chloroform); ir (neat): 1700 (CO str) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.85 (9H, s), 1.51-2.50 (5H, m), 3.30-3.83 (3H, m); ^{13}C-nmr (deuteriochloroform): δ 178.27 (s), 66.41 (t), 55.67 (d), 29.74 (t), 25.96 (q), 25.65 (t), 22.78 (s), -5.66 (q); ms: m/z 214 (M-15, 4), 172 (100), 156 (3), 155 (5), 154 (3), 128 (12), 116 (13), 84 (31), 75 (24), 73 (23), 59 (8).

Anal. Calcd. for $C_{11}H_{23}NO_2Si$: C, 57.55; H, 18.02; N, 6.10. Found: C, 57.50; H, 17.96; N, 5.87.

N-Benzyl-(*S*)-5-*t*-butyldimethylsilyloxymethyl-2-pyrrolidinone (**15**).

Compound **14** (187 mg, 0.82 mmoles) dissolved in 3 ml of anhydrous dimethylformamide was treated with 75 mg of sodium hydride (50% oil dispersion, 1.5 mmoles) for 1 hour at room temperature; then 0.08 ml of benzyl bromide was added and the flask was warmed at 60° overnight. The mixture was quenched with water and extracted with ether, dried and evaporated. After flash-chromatography (hexane:ethyl acetate, 30%) **15** was obtained (50 mg 17% yield) as an oil; $[\alpha]_D^{25}$ + 50.5° (c 1.41, chloroform); ir (neat): 1695 (CO str) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.85 (9H, s), 1.75-2.21 (2H, m), 2.25-2.63 (2H, m), 3.32-3.77 (3H, m), 4.03 (1H, d, J = 15 Hz), 4.92 (1H, d, J = 15 Hz), 7.25 (5H, s); ^{13}C-nmr (deuteriochloroform): δ 175.51 (s), 137.18-127.38 (aromatic), 63.66 (t), 58.53 (d), 44.71 (t), 30.33 (t), 25.86 (q), 21.60 (t), 18.20 (s), -5.51 (q); ms: m/z 320 (M + 1, 2), 304 (5), 262 (99), 174 (100), 91 (99).

Anal. Calcd. for $C_{18}H_{29}NO_2Si$: C, 67.60; H, 9.07; N, 4.38. Found: C, 67.53; H, 8.99; N, 4.32.

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[9] Other attempts made in order to oxidize compound **6** and correlate it with some intermediates described by Rapoport [2b] also failed.