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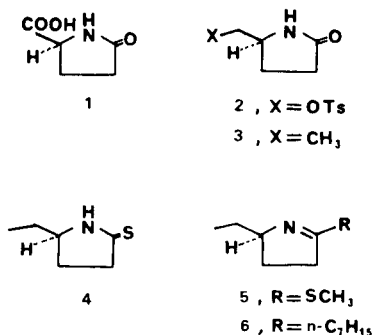
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From (*S*)-pyroglutamic acid (**1**) the asymmetric synthesis of (*S*)-5-ethyl-2-pyrrolidinone (**5**) in 30% yield is described.

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(*S*)-Pyroglutamic acid (**1**) is a simple, readily available heterocyclic chiral template. It is surprising to find the attention which it has received as a chiral building block for alkaloid asymmetric synthesis [1a-d]. In this communication we report the first asymmetric synthesis and some transformations of (*S*)-5-ethyl-2-pyrrolidinone (**3**) [2], which can be envisaged as a potentially useful intermediate for pyrrolidine alkaloid asymmetric synthesis. In contrast to the parent 5-alkylbutanolides, which have been largely investigated [3], the analogous chiral lactams remain, to the best of our knowledge, unknown.



So, starting from **1** and by the reported procedures [4, 1a] compound **2** was obtained in 61% yield. Side chain elongation was performed by the dimethylolithium cuprate reaction with **2** to give **3** in 48% yield. We could not improve this modest yield in spite of using several conditions, solvents, *etc.* In chloroform compound **3** had no measurable rotation [5].

Our initial objective was the synthesis of chiral 2,5-dialkylpyrrolidines, through imines of type **6**; both of them have been described as natural components of the ant venom expelled by some *Solenopsis* spp. [6].

This phosphorus pentasulfide treatment of **3** in benzene at reflux gave **4** in 61% yield, methyl thioimidate transformation of **6** to **5** was easily achieved by methyl iodide in methylene chloride at room temperature followed by alkaline treatment; the oily and unstable **5** was obtained in nearly 70% yield. Unfortunately, reaction of **5** with *n*-heptylmagnesium bromide failed to give the desired compound **6**.

In summary, the synthesis of (*S*)-5-ethyl-2-pyrrolidinone (**3**) is described by an efficient method that enables one to obtain other analogous 5-alkyllactams in optically pure form.

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 Bruker WP 200 spectrometer, using TMS as internal standard. Mass spectra were scanned with a AEI MS 50 apparatus at 70 eV.

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

Compound **2** (211 mg, 0.78 mmole) dissolved in 4 ml of anhydrous tetrahydrofuran was added dropwise at 0° under argon to a solution of dimethylolithium cuprate [3.90 mmoles, prepared from 4.8 ml of methylolithium (1.6 *M* in ether) and 742 mg (3.9 mmoles) of cuprous iodide] in 2 ml of dry tetrahydrofuran. The mixture was warmed to room temperature and allowed to stand overnight, then quenched at 0° by careful addition of 5 ml of 15% ammonium chloride solution; the mass was filtered over Celite, washed with ether, the organic phase extracted with brine several times, dried and evaporated. Flash-chromatography of the resultant oil gave 43 mg (48% yield) of **3**; ir (neat): 3200 (NH, str), 2900, 1670 cm⁻¹; ¹H nmr (deuteriochloroform): δ 0.95 (3H, t, J = 7 Hz), 1.27-1.83 (3H, m), 1.93-2.52 (3H, m), 3.58 (1H, qt, J = 6 Hz), 7.55 (1H, s); ¹³C nmr (deuteriochloroform): δ 178.72 (s), 56.13 (d), 30.41 (t), 29.50 (t), 26.69 (t), 9.94 (q); ms: m/z 113 (13), 84 (100), 58 (5), 56 (7), 41 (16).

Anal. Calcd. for C₈H₁₁NO: C, 63.64; H, 9.72; N, 12.37. Found: C, 63.51; H, 9.67; N, 12.21.

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

Compound **3** (205 mg) was treated with phosphorus pentasulfide (329 mg, 1.49 mmoles) in 6 ml of anhydrous benzene at reflux and for 40 minutes. The flask was cooled, the contents diluted with methylene chloride and washed with 10% sodium bicarbonate solution; the organic extract was dried and evaporated to give, after purification by flash-chromatography (hexane:ethyl acetate, 80%) 145 mg (61% yield) of **4**; mp (hexane:ethyl acetate): 61-63°; [α]_D²⁵ + 14° (c 1.33, chloroform); ir (nujol): 3150-3300 (NH, str), 1680-1700 (carbonyl, str) cm⁻¹; ¹H nmr (deuteriochloroform): δ 0.96 (3H, t, J = 7 Hz), 1.37-1.92 (2H, m), 2.07-2.55 (2H, m), 2.95 (2H, t, J = 7 Hz), 3.90 (1H, qt, J = 7 Hz), 9.15 (1H, s); ¹³C nmr (deuteriochloroform): δ 204.70 (s), 64.11 (d), 43.11 (t), 28.65 (t), 28.16 (t), 10.04 (q); ms: m/z 129 (100), 100 (43).

Anal. Calcd. for C₈H₁₁NS: C, 55.80; H, 8.52; N, 10.85. Found: C, 55.67; H, 8.51; N, 10.65.

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

Compound **4** (93 mg, 0.71 mmole) was treated with 1 ml of methyl iodide in 6 ml of methylene chloride at room temperature for 24 hours.

The mixture was washed with saturated sodium bicarbonate solution, dried and evaporated to give a red and unstable oil, **5** (70 mg, 70% yield), which showed no measurable rotation; we could not obtain a satisfactory microanalysis; ^1H nmr (deuteriochloroform): δ 0.95 (3H, t, $J = 7$ Hz), 1.25-1.90 (4H, m), 2.45 (3H, s), 2.00-2.75 (2H, m), 3.92 (1H, qt, $J = 7$ Hz); ^{13}C nmr (deuteriochloroform): δ 171.50 (s), 74.02 (d), 38.39 (t), 29.41 (t), 29.05 (t), 13.49 (q), 10.67 (q); ms: m/z 143 (22), 114 (56), 94 (100), 84 (39), 71 (22), 69 (22), 57 (33), 55 (33).

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[2] This compound and analogues have been previously synthesized in racemic form by reductive amination of γ -ketoesters; see; V. A. Sedavkina, *Metody Poluch. Khim. Reakt. Prep.*, **26**, 19 (1974); *Chem. Abstr.*, **86**, 89510n (1977).

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