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STUDIES ON THE SYNTHESES OF HETEROCYLIC COMPOUNDS—762†

SYNTHESIS OF 3-BENZYL-6-METHYL-2-OXO-3,6-DIAZABICYCLO[3.1.0]HEXANE AS A SYNTHETIC INTERMEDIATE OF MITOMYCINS

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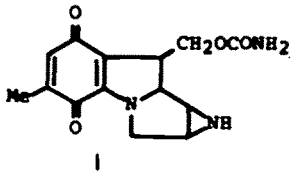
Abstract—(±)-1-Benzyl-3α-hydroxy-4β-methylamino-2-oxopyrrolidine (15) and its *cis*-isomer (16) were synthesised from 1-benzyl-4-ethoxycarbonyl-2,3-dioxopyrrolidine (2) in several steps. The former (15) was converted to 3-benzyl-6-methyl-2-oxo-3,6-diazabicyclo[3.1.0]hexane (17) with a mixture of triphenylphosphine, carbon tetrachloride and triethylamine.

RECENTLY we have reported a facile synthesis of mitosenes from 2-pyrrolidone.[1,2] As a preliminary experiment for the syntheais of mitosane (1) derivatives having an aziridine on ring C, the preparation of the title compound (17) was investigated. Among a number of procedures for the formation of aziridine, the cyclisation of β-aminoalcohols by simultaneous action of triphenylphosphine, carbon tetrachloride, and triethylamine[3] seems to be a choice of method because of its mild reaction condition and its convenient process. The *trans*-aminoalcohol (15) was prepared as shown in the Scheme from 1-benzyl-4-ethoxycarbonyl-2,3-dioxopyrrolidine (2) which was easily obtained by one pot reaction of benzylamine, ethyl acrylate and diethyl oxalate in the presence of sodium ethoxide.[4]



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Scheme 1.

Heating the lactam (2) with zinc powder gave two products which were seperable by recrystallisation. The stereochemistry of the major product (76% yield), m.p. 62–63.5°, and the minor one (23% yield), m.p. 107–109°, was determined as the *trans*-(3) and the *cis*-alcohol (4) respectively, on the basis of the following two reasons, namely the chemical shift due to 3-H and the chemical conversion. The proton at the C-3 position of the *trans*-isomer (3) was observed at the lower field, 4.68 ppm, than that of the *cis*-one (4), 4.57 ppm in the NMR spectra ($CDCl_3$), suggesting the assigned stereochemistry of these compounds.

Comparison of the coupling constants did not give us definite information. Both signals appeared as a distorted doublet or double doublet but after addition of deuterium oxide, these signals changed to clear doublets respectively. The coupling constant of the former (3) was 7.0 Hz, whereas that of the latter (4) was 7.3 Hz. The above coupling constants and chemical shifts were confirmed by addition of a shift reagent, tris(heptafluorobutanoylpivaloylmethanato)europium, and decoupling technique.

Both hydroxy-esters (3 and 4) were converted into the azides (6 and 12) and then subjected to Curtius reaction.[5] Namely reaction of the *trans*-ester (3) with hydrazine hydrate yielded the hydrazide (5; 99.9%), m.p. 137–138°, which was treated with sodium nitrite to afford the azide (6). Heating the azide (6) in ethanol gave the urethane (7), m.p. 120–122° (79% from 5). On the other hand, conversion of the *cis*-ester (4), via the *cis*-hydrazide (11), m.p. 237–238° (dec) (95% yield), into the *cis*-azide (12), followed by heating 12 in benzene or ethanol, furnished the pyrrolo[3,4-*d*]oxazole (13), m.p. 184–185° (87% yield). Since retension of configuration in the migrating group during Curtius reaction is well known,[6] it was verified that the relative configuration between the OH and the ester group of the major compound (3) was *trans*, while that of the minor one (4) was *cis*.

After protection of the OH group of the urthane (7) by the action with ethyl vinyl ether in the presence of hydrochloric acid,[7] the resulting acetal (8) was treated with methyl iodide in the presence of sodium hydride and hexamethylphosphoramide to give the N-Me product (9). Deprotection of the acetal group with diluted hydrochloric acid afforded the N-methylated urethane (10) (87% yield from 7). Methylation of the pyrrolo[3,4-*d*]oxazole (13) was carried out by treatment with methyl iodide in the presence of sodium hydride to furnish the N-Me compound (14) (99% yield).

The N-methylurethane (10) and the N-methylpyrrolo[3,4-*d*]oxazole (14) were hydrolysed by refluxing with aqueous methanolic potassium hydroxide respectively. The reactions were monitored by tlc and NMR spectroscopy. It is interesting that both compounds (10 and 14) gave a mixture of the same two components, both structures of which were assigned to be the *trans*-(15) and the *cis*-aminoalcohol (16). After refluxing for 5.5 hr, the utethane (10) yielded a mixture of 15 and 16 in a ratio of 0.73 : 1, and after 20 hr a mixture of 15 and 16 was obtained in a ratio of 1.91 : 1. Finally the *trans*-1,2-aminoalcohol (15) was isolated as a crystalline compound, m.p. 140–141°, in 51% yield from 10, after refluxing for 24 hr.

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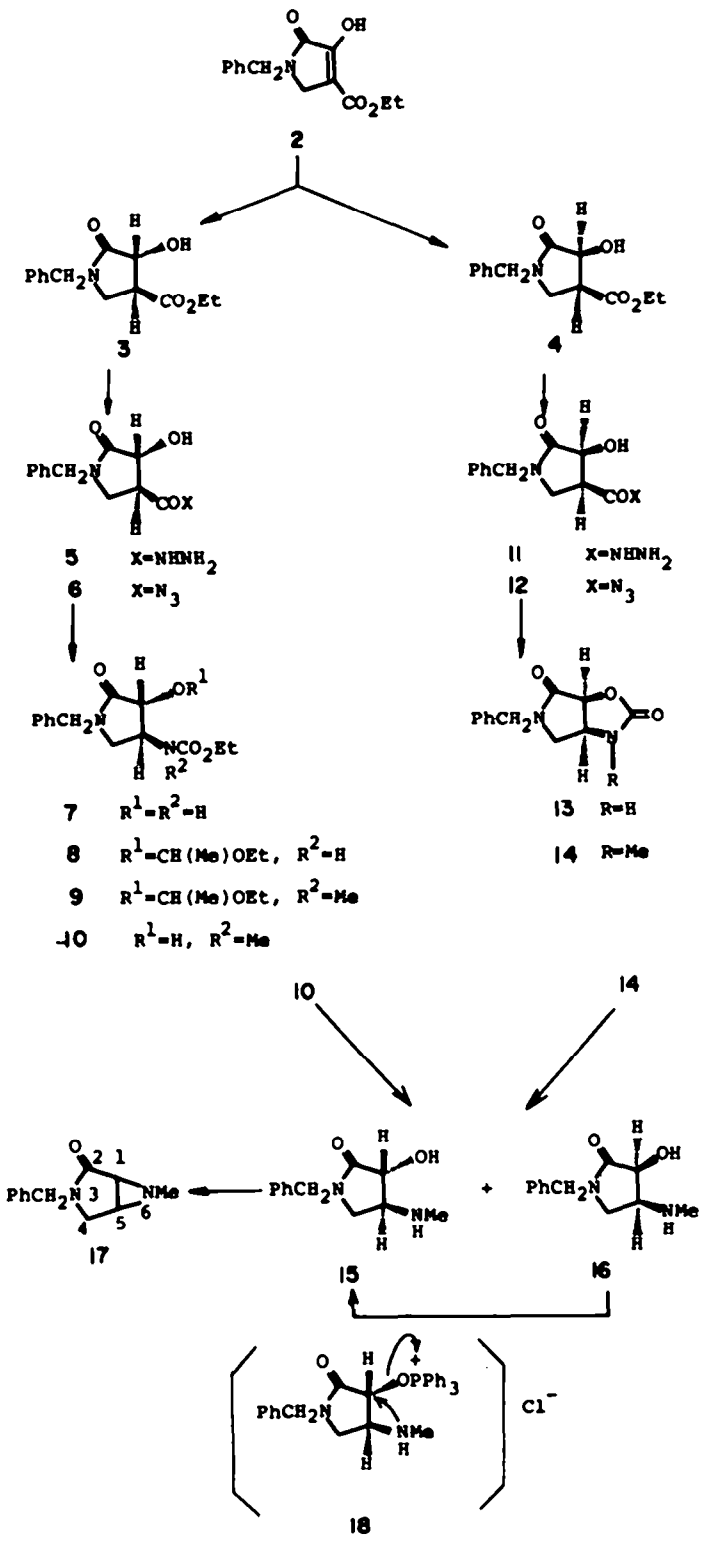

Scheme 2.

The pyrrolo[3,4-*d*]oxazole (14) gave a mixture of 15 and 16 in a ratio of 0.2 : 1 after 2 hr and in a ratio of 2.26 : 1 after 24 hr. The *trans*-compound (15) was obtained in 65% yield from 14. The *cis*-aminoalcohol (15) was gained by the hydrolysis of 14 for 30 min followed by purification using high pressure liquid chromatography (HPLC). Further treatment of the *cis*-compound (16) with aqueous methanolic potassium hydroxide solution under the same condition gave the mixture containing predominantly *trans*-isomer (15), which would be thermodynamically more stable than *cis*-isomer (16). It was presumed that the production of the *cis*-isomer (16) from the *trans*-urethane (10) would be due to the formation of the pyrrolo[3,4-*d*]oxazole (14) as an inter-

mediate. This assumption was supported by tlc analysis of the product formed after refluxing **10** under the same condition as above for 5 min.

The *trans*-aminoalcohol (**15**) was treated with the complex prepared from triphenylphosphine and carbon tetrachloride in the presence of triethylamine[3] to give the aziridine (**17**), in 76% yield, *m/e* 202 (M^+). Two methine protons at C-1 and 5 positions were overlapped with the N-Me group at 2.40, and the methylene protons at C-4 position appeared at 3.31 ppm as a singlet. When the NMR spectrum was run in hexadeuteriobenzene, those protons were clearly visible as separate signals. Namely the proton at C-5 position was observed at 1.47 as a double doublet (J 7.0 and 3.0 Hz), while the proton at C-1 position appeared at 2.00 ppm as a double doublet (J 7.0 and 3.0 Hz). Furthermore the methylene protons at C-4 position were separately resonated at 2.60 as a double double doublet (J 10.4, 3.0 and 3.0 Hz) and at 2.93 as a doublet (J 10.7) and the N-Me signal was exhibited at 1.87 ppm as a singlet. The coupling constants were confirmed by decoupling analysis.

Reaction of the *cis*-isomer (**16**) under the same condition as above gave no aziridine (**17**) but the starting material was recovered. The mechanism for the formation of the aziridine ring by the above reaction had been discussed[3] and the above finding would support the proposed cyclisation by *trans*-elimination of the intermediate such as **18**.

EXPERIMENTAL

All m.ps were uncorrected. IR spectra were taken with a Hitachi 215 spectrophotometer, NMR spectra with a JNM-PS-100 spectrometer (TMS as an internal reference), and mass spectra with a Hitachi RMU-7 and JEOL JMS-01SG-2 spectrometers. Hplc's were carried out with a Hitachi 635 instrument (packing material: Hitachi gel 3011; column: 25 cm × 8 mm; mobile phase: methanol).

(±) - 1 - *Benzyl* - 4*β* - *ethoxycarbonyl* - 3*β* - *hydroxy* - 2 - *oxopyrrolidine* (**4**) *and* (±) - 1 - *Benzyl* - 4*β* - *ethoxycarbonyl* - 3*α* - *hydroxy* - 2 - *oxopyrrolidine* (**3**). To a stirred soln of **2**[4] (26.1 g) in AcOH (200 ml) was added Zn powder (32.5 g) in small portions at 100° under N_2 and the mixture was stirred at the same temp. for 30 min. After cooling to room temp., the filtrate was taken up into $CHCl_3$, which was washed with water and brine, and dried over Na_2SO_4. Evaporation of the solvent and the excess AcOH gave an oil, which was triturated with EtOAc to give a suspension of the solid which was removed by filtration. Evaporation of the filtrate followed by trituration of the residue with ether-hexane gave a crystalline mass. Recrystallisation from CCl_4 gave *cis*- **4** as colourless needles (6.039 g., 23%), m.p. 107–109° (Found: C, 63.76; H, 6.40; N, 5.29. $C_{14}H_{17}NO_4$ requires: C, 63.86; H, 6.51; N, 5.32%); IR ($CHCl_3$): 1720 sh and 1700 (C=O) cm^{-1}; NMR ($CDCl_3$)[6]: *δ* 1.24 (3H, t, J 6.7 Hz, CH_2CH_3), 2.23 (1H, br s, OH, disappeared with D_2O), 3.1–3.8 (3H, m, 4-H and 5-H_2), 4.17 (2H, q, J 6.9 Hz, CH_2CH_3), 4.49 (2H, s, $PhCH_2$), 4.57 (1H, distorted d, J 7.3 Hz, 3-H), 7.29 (5H, s, ArH); MS *m/e* 263 (M^+). Evaporation of the above mother liquor gave a syrup, which was partitioned between benzene and a sat $NaHCO_3$aq. The benzene layer was washed with water and brine, dried over Na_2SO_4 and evaporated to give *trans*- **3** as an oil (20 g, 76%), recrystallisation of which from ether gave colourless scales, m.p. 62–63.5° (Found: C, 63.81; H, 6.52; N, 5.37. $C_{14}H_{17}NO_4$ requires: C, 63.86; H, 6.51; N, 5.32%); IR ($CHCl_3$): 1730 and 1700 (C=O) cm^{-1}; NMR ($CDCl_3$): *δ* 1.23 (3H, t, J 6.7 Hz, CH_2CH_3), 3.0–3.6 (3H, m, 4-H and 5-H_2), 4.17 (2H, q, J 6.7 Hz, CH_2CH_3), 4.45 (2H, s, $PhCH_2$), 4.68 (1H, dd, J 7.0 and 4.0 Hz, 3-H), 5.36 (1H, d, J 4.0 Hz, OH, disappeared with D_2O), 7.23 (5H, s, ArH); MS *m/e* 263 (M^+).

(±) - 1 - *Benzyl* - 4*β* - *carbazoyl* - 3*α* - *hydroxy* - 2 - *oxopyrrolidine* (**5**). To a stirred soln of *trans*- **3** (13 g) in EtOH (100 ml) was added 90% hydrazine hydrate (30 ml) at room temp. and the mixture was stirred for 2 hr at the same temp. Evaporation of the solvent and the excess of hydrazine hydrate gave **5** as a crystalline mass (12.3 g, 99.9%), recrystallisation from EtOH gave colourless needles, m.p. 137–138° (Found: C, 57.88; H, 5.94; N, 16.80. $C_{12}H_{15}N_3O_3$ requires: C, 57.82; H, 6.07; N, 16.86%); IR (Nujol): 3325–3150 ($NHNH_2$), 1685 and 1625 (C=O) cm^{-1}; MS *m/e* 249 (M^+).

(±) - 1 - *Benzyl* - 4*β* - *ethoxycarbonylamino* - 3*α*- -*hydroxy* - 2 - *oxopyrrolidine* (**7**). To a stirred mixture of crude **5** (2.49 g) in 1 N HCl (60 ml) and $CHCl_3$ (60 ml) was added a soln of $NaNO_2$ (0.96 g) in cold water (11 ml) dropwise over a period of 10 min at 0°. The mixture was stirred for 3 hr at 0°. The separated organic layer was washed with water and brine, and dried over Na_2SO_4. Evaporation of the solvent gave the crude **6** as a colourless oil, IR ($CHCl_3$): 2145 (CON_3) and 1700 (C=O) cm^{-1}.

A soln of the crude **6** in EtOH was refluxed for 2 hr. Evaporation of the solvent gave a crystalline mass, recrystallisation from benzene afforded **7** as colourless needles (2.197 g, 79%), m.p. 120–122° (Found: C, 60.51; H, 6.51; N, 9.90. $C_{14}H_{18}N_2O_4$ requires: C, 60.42; H, 6.52; N, 10.07%); IR ($CHCl_3$): 1705 (C=O) cm^{-1}; NMR ($CDCl_3$): *δ* 1.17 (3H, t, J 7.2 Hz, CH_2CH_3), 2.9–3.2 and 3.5–3.8 (each 1H, each distorted t, J 8.2 Hz, 5-H_2), 4.07 (2H, q, J 7.2 Hz, CH_2CH_3), 4.43 (2H, s, $PhCH_2$), 5.23 (1H, br s, OH, disappeared with D_2O), 6.05 (1H, br s, NH), 7.24 (5H, s, ArH); MS *m/e* 278 (M^+).

(±) - 1 - *Benzyl* - 4*β* - *ethoxycarbonylmethylamino* - 3*α* - *hydroxy* - 2 - *oxopyrrolidine* (**10**). To a stirred soln of **7** (1.39 g) and ethyl vinyl ether (0.54 g) in dry CH_2Cl_2 (50 ml) was added dry ether (0.5 ml), which had been previously saturated with dry HCl at 0°. The resulting mixture was stirred at 0° for 41 hr. After addition of triethylamine, the mixture was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave (±)-**8** (1.75 g) as a pale yellowish oil, which was used in the next reaction without purification, IR ($CHCl_3$): 1705 (C=O) cm^{-1}; NMR ($CDCl_3$): *δ* 1.16 (6H, t, J 7.2 Hz, 2 × CH_2CH_3), 1.38 (3H, d, J 5 Hz, $CHCH_3$), 2.9–3.2 (1H, distorted t, J 8.2 Hz, 5-H), 3.4–3.8 (3H, m, $CHOCH_2CH_3$ and 5-H), 4.08 (2H, q, J 7.2 Hz, $CO_2CH_2CH_3$), 4.43 (2H, s, $PhCH_2$), 5.17 (1H, q, J 5.0 Hz, $CHCH_3$), 5.93 (1H, br d, J 6.0 Hz, NH), 7.27 (5H, s, ArH); MS *m/e* 278 ($M^+ - C_4H_6O$).

A mixture of the dried **8** (1.75 g), 50% NaH in mineral oil (434 mg), dry hexamethylphosphoramide (0.9 ml), and dry THF (90 ml) was stirred at room temp. for 4 hr under N_2. To the resulting mixture MeI (0.8 ml) was added and the mixture was stirred at room temp. for 4 hr. After addition of ammonium chloride (480 mg), evaporation of the solvent gave a residue which was extracted with benzene. The benzene extract was washed with water several times and brine, and dried over Na_2SO_4. Evaporation of the solvent afforded (±)-**9** as a pale yellowish oil, which was used in the next step without purification, IR ($CHCl_3$): 1695 (C=O) cm^{-1}; NMR ($CDCl_3$): *δ* 1.1–1.5 (9H, m, 3 × Me). 2.88(3H, s, NMe), 3.2–3.9 (4H, m, $CHOCH_2CH_3$ and 5-H_2) 4.13 (2H, q, J 7.2 Hz, $CO_2CH_2CH_3$), 4.45 (2H, s, $PhCH_2$), 4.8–5.4 (1H, m, $CHCH_3$), 7.27 (5H, s, ArH); MS *m/e* 292 ($M^+ - C_4H_6O$).

A mixture of the crude methylated **9**, 10% HCl (10 ml) and benzene (20 ml) was stirred at room temp. for 1 hr under N_2. After addition of benzene, the organic layer was washed with sat. $NaHCO_3$aq and brine, and dried over Na_2SO_4. Evaporation of the solvent gave a residue (1.7 g) which was chromatographed on silica gel (51 g). Elution with benzene–EtOAc (1 : 1 v/v) afforded **10** as a syrup (1.274 g, 87%), which was further purified by hplc (flow rate: 3.5 ml/min, Rt: 4.2 min) to give a syrup (Found: C, 59.92; H, 7.03; N, 8.97. $C_{15}H_{20}N_2O_4$. 0.5 H_2O requires: C, 59.78; H, 7.02; N, 9.30%); IR ($CHCl_3$): 1695 (C=O) cm^{-1}; NMR ($CDCl_3$): *δ* 1.55 (3H, t, J 7.2 Hz, CH_2CH_3), 2.91 (3H, s, NMe), 3.17–3.86 (2H, m, 5-H_2), 4.11 (2H, q, J 7.2 Hz, CH_2CH_3), 4.47 (2H, s, $PhCH_2$), 4.68 (1H, d, J 8.5 Hz, 3-H), 5.46 (1H, br s, OH, disappeared with D_2O), 7.28 (5H, s, ArH); MS *m/e* 292 (M^+).

(±) - 1 - *Benzyl* - 4*β* - *carbazoyl* - 3*β* - *hydroxy* - 2 - *oxopyrrolidine* (**11**). To a stirred suspension of *cis*-**4** (5.953 g) in EtOH (45 ml) was added 90% hydrazine hydrate (13.6 g) at room temp. and the mixture was stirred for 2 hr at the same temp. Evaporation of the solvent and the excess of hydrazine hydrate

gave a crystalline mass, which was washed with cold EtOH and ether to give the pure 11 as colourless needles (5.317 g, 95%), m.p. 237–238° dec. (Found: C, 57.84; H, 6.04; N, 16.86. $C_{12}H_{15}N_3O_3$ requires C, 57.82; H, 6.07; N, 16.86%); IR (Nujol): 3325 ($NHNH_2$), 1680 and 1645 (C=O) cm^{-1}; MS *m/e* 249 (M^+).

5 - *Benzyl* - 2,6 - *dioxopyrrolo*[3,4 - *d*]*oxazole* (13). To a stirred mixture of 11 (5.317 g) in 1 N HCl (107 ml) and $CHCl_3$ (100 ml) was added a soln of $NaNO_2$ (1.8 g) in cold water (21 ml) dropwise over a period of 10 min at 0°. The mixture was stirred for 2 hr at 0°. Separated organic layer was washed with water and brine, and dried over Na_2SO_4. Evaporation of the solvent gave the crude 12 as a colourless crystalline mass, IR ($CHCl_3$): 2149 (CON_3) and 1710 (C=O) cm^{-1}.

A soln of crude 12 in dry benzene (200 ml) was refluxed for 2 hr. The crystalline mass formed was recrystallised from EtOH to give 13 as colourless needles (4.307 g, 87%), m.p. 184–185° (Found: C, 61.95; H, 5.15; N, 12.06. $C_{12}H_{12}N_2O_3$ requires: C, 62.06; H, 5.21; N, 12.06%), IR (Nujol): 1740 and 1670 (C=O) cm^{-1}; NMR (CF_3CO_2H): δ 3.3–4.1 (2H, m, 4-H_2), 4.50 and 4.80 (each 1H, each d, J 15 Hz, $PhCH_2$), 5.70 (1H, d, J 8 Hz, 6a-H), 7.35 (5H, s, ArH); MS *m/e* 232 (M^+).

5 - *Benzyl* - 3 - *methyl* - 2,6 - *dioxopyrrolo*[3,4 - *d*]*oxazole* (14). To a stirred soln of 13 (2.32 g) in dry DMF was added 50% NaH in mineral oil (576 mg) at room temp. in one portion and the mixture was stirred at the same temp. for 1 hr under N_2. After cooling to 0°, to the resulting mixture was added MeI (0.76 ml) in small portions and the mixture was stirred for 2 hr. After addition of ammonium chloride, evaporation of the solvent gave a residue, which was extracted with $CHCl_3$. The extract was washed with water and brine, and dried over Na_2SO_4. Evaporation of the solvent gave a crystalline mass, recrystallisation of which from EtOH afforded 14 as colourless needles (2.444 g, 99%), m.p. 161–162.5° (Found: C, 63.43; H, 5.61; N, 11.34. $C_{13}H_{14}N_2O_3$ requires: C, 63.40; H, 5.73; N, 11.38%); IR ($CHCl_3$): 1765 and 1715 (C=O) cm^{-1}; NMR ($CDCl_3$): δ 2.80 (3H, s, NMe), 3.1–3.7 (2H, m, 4-H_2), 4.30 (1H, ddd, J 8.0, 4.8 and 1.4 Hz, 3a-H), 4.50 (2H, s, $PhCH_2$), 4.98 (1H, d, J 8.0 Hz, 6a-H), 7.27 (5H, s, ArH); MS *m/e* 246 (M^+).

(±) - 1 - *Benzyl* - 3*α* - *hydroxy* - 4*β* - *methylamino* - 2 - *oxopyrrolidine* (15). (A) A mixture of 10 (55 mg), 0.85 N methanolic KOH (2 ml), MeOH (4 ml), and water (0.5 ml) was refluxed under N_2 for 24 hr. Evaporation of the solvent gave a residue which was dissolved in 10% ammonia. After addition of crystalline NaCl, the mixture was extracted with EtOAc, and dried over Na_2SO_4. Evaporation of the solvent gave a crystalline mass, which was recrystallised from benzene to afford the *trans*-15 as colourless needles (21 mg, 51%), m.p. 140–141° (Found: C, 65.07, H, 6.94; N, 12.27. $C_{12}H_{16}N_2O_2$ requires: C, 65.43; H, 7.32; N, 12.72%); IR ($CHCl_3$): 1695 cm^{-1}; NMR ($CDCl_3$):[8] δ 2.47 (3H, s, NCH_3), 2.93 (2H, s, NH and OH, disappeared with D_2O), 2.9–3.6 (3H, m, 4-H and 5-H_2), 4.23 (1H, d, J 8 Hz, 3-H), 4.48 (2H, s, $PhCH_2$), 7.28 (5H, s, ArH). (B) A mixture of 14 (50 mg), 0.85 N methanolic KOH (2 ml), MeOH (4 ml), and water (0.5 ml) was refluxed under N_2 for 24 hr. The same work-up as above gave the *trans*- 15 as colourless needles (29 mg, 65%), m.p. 140–141°, which was identified by comparison with the sample prepared by method A (m. m.p., IR and NMR spectra).

(C) A mixture of the *cis*- 16 (42 mg), 0.85 N methanolic KOH (2 ml), MeOH (4 ml), and water (0.5 ml) was refluxed for 25 hr under N_2. The same work-up as above afforded *trans*- 15 as colourless needles (25 mg, 60%), m.p. 140–141°, which was identified by comparison with the sample prepared by method A (m. m.p., IR and NMR spectra).

(±) - 1 - *Benzyl* - 3*β* - *hydroxy* - 4*β* - *methylamino* - 2 - *oxopyrrolidine* (16). A mixture of 14 (100 mg), 0.85 N methanolic KOH (4 ml), and water (1 ml) was refluxed for 30 min under N_2. The same work-up as above gave a syrup (89 mg). Further purification by hplc (flow rate: 3.0 ml/min) gave the *cis*- 16 (Rt; 4.14 min) as a colourless syrup (37.2 mg) (Found: M^+ 220.1212 $C_{12}H_{16}N_2O_2$ requires: M^+ 220.1212); IR ($CHCl_3$): 1695 (C=O) cm^{-1}; NMR ($CDCl_3$):[8] δ 2.43 (3H, s, NMe), 2.9–3.5 (5H, m, 4-H, 5-H_2, NH and OH), 4.37 and 4.67 (each 1H, each d, J 14.4 Hz, $PhCH_2$), 4.42 (1H, d, J 6.0 Hz, 3-H), 7.32 (5H, s, ArH) and the *trans*- 15 as a colourless solid (7.3 mg) whose spectral data (IR and NMR) were identical with those of the above sample (15).

3 - *Benzyl* - 6 - *methyl* - 2 - *oxo* - 3,6 - *diazabicyclo*[3.1.0]*hexane* (17). To a stirred soln of triphenylphosphine (185 mg) in dry acetonitrile (20 ml) was added CCl_4 (1 ml) at room temp. and the mixture was stirred for 25 min at the same temp. under N_2. To the resulting mixture was added *trans*- 15 (50 mg) in dry $CHCl_3$ (10 ml) and dry Et_3N (0.1 ml), and the mixture was stirred at room temp. for 19 hr under N_2. Evaporation of the solvent and the excess of Et_3N gave a solid which was subjected to hplc (flow rate: 3.5 ml/min, R_t: 6.09 min) to afford 17 (35 mg, 76%) as a colourless semi-crystalline mass (Found: M^+ 202.1107. $C_{12}H_{14}N_2O$ requires: M^+ 202.1107), IR ($CHCl_3$): 1690 (C=O) cm^{-1}; NMR (benzene-d_6): δ 1.47 (1H, dd, J 7.0 and 3.0 Hz, 5-H), 1.87 (3H, s, NMe), 2.00 (1H, dd, J 7.0 and 3.0 Hz, 1-H), 2.60 (1H, ddd, J 10.4, 3.0 and 3.0 Hz, 4-H), 2.93 (1H, d, J 10.4 Hz, 4-H), 4.19 (2H, s, $PhCH_2$), 7.07 (5H, s, ArH); NMR ($CDCl_3$): δ 2.40 (5H, s, NMe, 1 and 5-H), 3.31 (2H, br s, 4-H_2), 4.16 and 4.59 (each 1H, each d, J 15.0 Hz), 7.28 (5H, s, ArH); MS *m/e* 202 (M^+).

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[8]Assignments were verified by addition of a shift reagent, tris-(heptafluorobutanoylpivaloylmethanato)europium, and decoupling technique.