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OXIDATION REACTIONS OF AZINES. 10*. SYNTHESIS, STRUCTURE, AND OXO-DIHYDROXYLATION OF 3-HYDROXYMETHYL-1-METHYL-4-PHENYL-1,2,3,6-TETRAHYDROPYRIDINE

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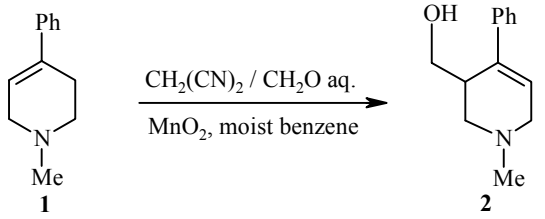
It has been established that oxidation of a mixture of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine and dicyanomethane or formaldehyde with manganese dioxide gives 3-hydroxymethyl-1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, the structure of which was confirmed by X-ray structural analysis. Some oxidative conversions by potassium permanganate of the product formed and its esters have been studied. These included lactamization, aromatization, and oxodihydroxylation.

Keywords: tetrahydropyridines, polyhydroxypiperidin-2-ones, hydroxymethylation, oxidation, oxodihydroxylation.

According to [2] the oxidation of a mixture of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (THP) (**1**) [3] and dicyanomethane with $KMnO_4$ leads to 2-dicyanomethylidenetetrahydropyridine, but on using MnO_2 the tetrahydropyridine hydroxymethylation product **2** is formed.



1 **2**

Data are given in the present study on confirmation of the structure of product **2**, possible routes for its formation, and the synthesis of a series of derivatives of polyhydroxypiperidin-2-one from it, the compounds which are of interest as potentially biologically active compounds. Hydroxymethyltetrahydropyridine **2** was obtained by us at room temperature by the manganese dioxide oxidation of a solution of THP **1** with dicyanomethane in moist benzene; the yield was 36.5% (on reacted THP **1**). Its structure was confirmed by spectral data. The position of the hydroxymethyl group at $C_{(3)}$ was established by analysis of the ^1H NMR spectral data using the COSY procedure. In the ^1H NMR spectrum there was a multiplet signal for the $C_{(5)}$

* For Part 9 see [1].

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vinyl proton (at 6.13 ppm), and signals for the two protons of the neighboring methylene group at 2.81 (dt) and 3.44 ppm (dd) with geminal spin-spin coupling constant J = 16.0 Hz, and the coupling constants with the vinyl proton J = 4.5 and J = 2.0 Hz. The signals of the protons of the second methylene group bound to nitrogen atom observed at 3.10 (br. d) and 2.67 ppm (ddd) and having geminal spin-spin coupling constant J = 4.4 Hz were retained. The methine proton 3-H was displayed as a sharp multiplet at 2.83 ppm. The spin-spin link between all the interacting protons of the tetrahydropyridine ring was confirmed by the presence of the corresponding cross peaks in the COSY spectrum. These data indicate the introduction of the hydroxymethyl grouping into position 3 of the ring. The hydroxyl proton of this group gives a broad signal with center at 4.4 ppm, but its methylene protons resonate at 3.65 and 3.89 ppm with a geminal spin-spin coupling constant J = 9.9 Hz and a coupling constant with the 3-H vinyl proton J = 3.5 Hz. The ^{13}C NMR spectrum and chromato-mass spectrometric analysis also confirmed the individuality and the structure of the compound being considered (see Experimental).

Since the melting point of compound **2** (82-84°C), obtained by us by the joint oxidation of THP **1** and dicyanomethane, differed significantly from the melting point of the substance of identical structure claimed in patent [4] (mp 98-100°C), an X-ray structural analysis of tetrahydropyridine **2** was carried out. The structure of the compound **2** molecule with the numbering of the atoms is shown in Fig. 1. The heterocyclic ring in the crystal is in a distorted *half-chair* conformation. The carbon atoms of its allyl fragment $C_{(3)}$–$C_{(5)}$ and the methylene group $C_{(6)}$ lie in one plane but the $N_{(1)}$ and $C_{(2)}$ atoms are displaced from this plane by 0.281 and -0.448 Å respectively. The hydroxymethyl group occupies a pseudoequatorial position with torsion angle $C_{(5)}$–$C_{(4)}$–$C_{(3)}$–$C_{(8)}$ equal to -106.4°*. The X-ray structural data therefore confirm the structure of compound **2** unambiguously.

Since compound **2** was obtained previously [4] by boiling a mixture of THP **1** with aqueous formaldehyde in sulfuric acid (the Prince reaction), it is logically to assume that in our case the hydroxymethylation of THP **1** may occur due to the formation of formaldehyde on oxidizing the N-methyl group of the initial THP **1** or on hydrolysis and oxidative fission of dicyanomethane. To solve this problem an experiment was carried out first of all on the oxidative hydroxymethylation of THP **1** with aqueous formaldehyde in the absence of dicyanomethane. It was thereby established that the formation of compound **2**

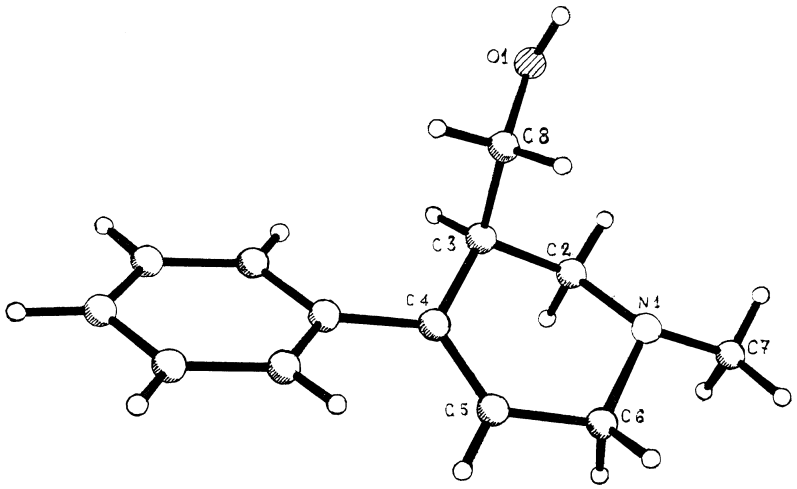
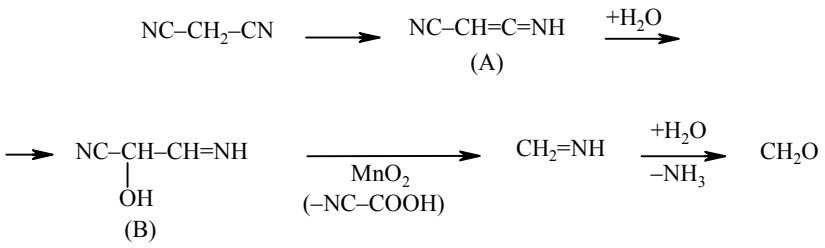


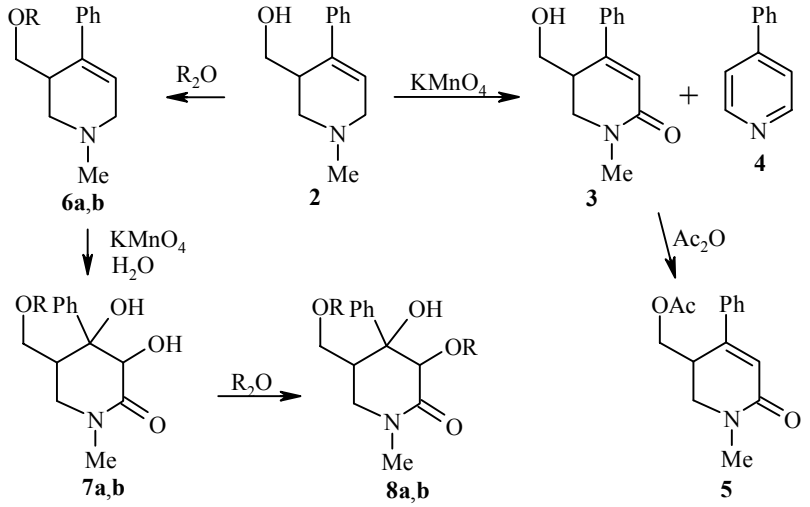
Fig. 1. Structure of the compound **2** molecule in the crystal.

* A detailed discussion of the data of the X-ray structural analysis will be published separately.

occurs at room temperature and it was isolated in 22% yield (on reacted THP **1**). In the absence of oxidizing agent this did not occur and THP **1** was isolated from the reaction mixture in quantitative yield. On attempting to oxidize a solution of THP **1** in aqueous benzene with MnO_2 in the absence of formaldehyde and dicyanomethane, the hydroxymethylation did not take place and 84% of initial THP **1** were recovered. These results indicate that, under the conditions studied for the joint oxidation of THP **1** and dicyanomethane, dicyanomethane is the source of formaldehyde. It is not excluded that as a result of hydration of its tautomeric form (A), hydroxyimine (B) is formed, undergoing oxidative fission with the formation of formaldimine, which is hydrolyzed to formaldehyde. (There are literature data on the instability of the cyano group in the presence of manganese compounds [5].) Formaldehyde generated in this way attacks the double bond of THP **1**, which probably assists the possible formation of carboxylic acids (particularly formic) on destructive oxidation of dicyanomethane. It is most probable that hydroxymethylation occurs with rearrangement of the double bond in the heterocyclic ring, since the hydroxymethyl group turns out to be in the allyl position.



The presence of a double bond and a hydroxymethyl group in THP **2** offers the possibility of a change from the tetrahydropyridine system to analogs of amino sugars in the event of successful oxodihydroxylation of THP **2** with potassium permanganate by the method developed by us previously [6,7]. However attempts at a similar polyfunctionalization of THP **2** led to its oxidation only to the intermediate 5-hydroxymethyl-2-oxotetrahydropyridine (**3**) in 50% yield. 4-Phenylpyridine (**4**) was also isolated (10% yield) from the reaction mixture. The formation of the latter is, as far as we know, the first example of oxidative aromatization of tetrahydropyridine ring proceeding under such mild conditions (at room temperature) with splitting of the hydroxymethyl and N-methyl groups and dehydrogenation. The presence of the amide fragment in lactam **3** was confirmed by its ^{13}C NMR spectrum, in which a signal for the C=O group was observed at 165.19 ppm. Oxidation of the methylene group of the allylamine fragment was indicated by the ^{1}H NMR spectrum, in which the signal of the vinyl 3-H proton has the form of a narrow singlet (at 6.23 ppm).



7, **8 a** R = COMe; **b** R = COEt

Esters **5** and **6a,b** were obtained to increase the stability of alcohols **2** and **3** towards the action of potassium permanganate and also to raise the potential of their biological action. The oxodihydroxylation reaction was carried out on substrates **6a,b** for which acyl protection of the hydroxyl group was used. In this case polyfunctionalization occurred successfully and the expected 5-acyloxymethyl-3,4-dihydroxypiperidin-2-ones **7a,b** were isolated in yields of 37.5 and 23.5% respectively. The action of an excess of acylating agent on them gave esterification of only the most available secondary hydroxyl group and diesters **8a,b** were formed. In the ^{1}H NMR spectrum of lactam diol **7a** two singlet signals were observed for the protons of the two methyl groups (at 1.98 and 3.00 ppm). The protons of the two hydroxyl groups were displayed as a broad signal with center at 3.30 ppm and a narrow singlet at 4.60 ppm. The methine proton on the $C_{(5)}$ atom was recorded as a multiplet with center at 2.50 ppm. One of the protons on the $C_{(6)}$ atom forms a doublet-doublet signal at 3.22 ppm with spin-spin coupling constants J = 13.10 and J = 2.50 Hz. The remaining aliphatic protons resonate as overlapping multiplets with an integrated intensity of four proton units at 3.70-4.00 ppm. In the IR spectrum of this diol there is one narrow (at 3550 cm^{-1}) and one broad (with center at 3555 cm^{-1}) absorption band for the hydroxyl groups. In its mass spectrum a low intensity (13%) peak was observed for the molecular ion with *m/z* 293 and a peak for the $[PhCO]^+$ ion of maximal intensity.

In the ^{1}H NMR spectrum of diester **8a** one further singlet signal appeared (compared with the spectrum of its precursor **7a**) for the protons of the acetyl group (at 2.15 ppm). The signal for the 3-H methine proton underwent a significant shift towards low field (singlet at 6.05 ppm) due to the deshielding effect of the neighboring acetoxy group. The signal of the hydroxyl proton at $C_{(4)}$ has the form of a broadened singlet at 2.80 ppm. The remaining aliphatic protons form multiplet signals in approximately the same regions as in the case of monoester **7a**.

Analysis of the ^{1}H NMR spectra of the polysubstituted piperidones **7** and **8,** with regard to the ^{1}H NMR and X-ray data of their simplified analogs [6,7] and of THP **2,** indicates that the piperidine ring in piperidones **7** and **8** has the conformation of a flattened *chair* with equatorial orientation of the phenyl and acyloxymethyl groups and two vicinal *cis*-disposed hydroxyl groups.

The conversions studied therefore enable a transition to be effected from the tetrahydropyridine system to a structural analogs of the polyhydroxypiperidine alkaloids such as nojirimycin, its metabolite mannonolactam, and others which possess important chemotherapeutic potential [8].

EXPERIMENTAL

The NMR spectra of compounds were recorded in $CDCl_3$ on a Bruker WM 250 instrument with operating frequency of 250 (^{1}H) and 75 (^{13}C) MHz, internal standard was TMS. The IR spectra were taken on a UR 20 instrument in paraffin oil (compounds **3**, **5**, and **6a**) or in KBr disks (compounds **2**, **7a**, and **8a**). The mass spectra were obtained on a MX 1303 instrument with direct insertion of the sample into the ion source (energy of ionizing electrons 70 eV). A check on the course of reactions and the homogeneity of compounds was carried out by TLC on Silufol UV 254 plates, visualizing with iodine vapor. Resolution and purification of substances was effected by column chromatography on L-60 silica gel (40/100).

3-Hydroxymethyl-1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (2). A. Activated MnO_2 (5 g, 58 mmol) was added during 15 min at room temperature to solution of compound **1** (1 g, 5.8 mmol) with dicyanomethane (0.38 g, 5.8 mmol) in moist benzene (50 ml). The mixture was stirred for 2 h, the solid MnO_2 was removed, and washed with benzene (90 ml). The solvent from the combined filtrates was distilled in vacuum, and the residue subjected to column chromatography (eluent acetone). Initial THP **1** (0.44 g, 44%) was isolated and then alcohol **2** (0.24 g, 36.5% calculated on reacted THP **1**) was obtained as colorless crystals; mp 82-84°C (mp 98-100°C [4]), R_f 0.33 (acetone) and 0.10 (ether). IR spectrum, ν, cm^{-1}: 3153 (br, OH), 1640, 1570 (C=C). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.4 (3H, s, Me); 2.67 (1H, ddd, J = 11.0, J = 4.0, and J = 2.5,

2-H); 2.81 (1H, dt, J = 16.0 and J = 2.0, 6-H); 2.83 (1H, n. m, 3-H); 3.10 (1H, br. d, J = 11.0, 2-H); 3.44 (1H, dd, J = 16.0 and J = 4.5, 6-H); 3.65 and 3.89 (1H and 1H, two dt, J = 9.9 and J = 2.5, 3-CH_2O); 4.40 (1H, br. s, OH); 6.13 (1H, n. m, 5-H); 7.25-7.42 (5H, m, Ph). ^{13}C NMR spectrum, δ, ppm: 38.26 (Me); 45.31 ($C_{(3)}$); 55.27 ($C_{(2)}$); 58.07 ($C_{(6)}$); 65.95 (CH_2O); 124.48 ($C_{(5)}$); 126.17, 127.33 and 128.47 (Ph); 136.2 and 139.9 (C_{quat}). Mass spectrum, *m/z* (*I*, %): 203 (55) $[M]^+$, 202 (17), 184 (6), 173 (19), 172 (100), 170 (54), 144 (23), 142 (16), 128 (21), 117 (19), 115 (28). Found, %: C 77.03; H 8.81; N 6.75. $C_{13}H_{17}NO$. Calculated, %: C 76.85; H 8.37; N 6.90. The structure of alcohol **2** was established by X-ray structural analysis.

B. Aqueous 37% formaldehyde solution (0.5 g, 5.8 mmol) and 10% NaOH solution (1 ml) were added to solution of THP **1** (1 g, 5.8 mmol) in benzene (50 ml), and then after 15 min activated MnO_2 (5 g, 58 mmol) was added. The mixture was stirred for 1 h 30 min at 20-40°C, then MnO_2 was separated, and washed with hot benzene (90 ml). The filtrates were evaporated, and after chromatographic separation of the residue the initial compound **1** (0.37 g, 37%) and alcohol **2** (0.16 g, 22% calculated on reacted THP **1**) were obtained .

C. Mixture of THP **1** (0.5 g, 2.9 mmol) with MnO_2 (2.5 g, 29 mmol) in moist benzene (20 ml) was stirred for 3 h at room temperature. According to TLC only the initial THP **1** was present in the reaction mixture and was isolated in 84% yield (0.42 g) by the standard treatment. Replacement of benzene by other solvents (acetone, ethanol, acetonitrile) did not lead to the oxidation of THP **1** under analogous conditions.

5-Hydroxymethyl-1-methyl-2-oxo-4-phenyl-1,2,3,6-tetrahydropyridine (3). Suspension of potassium permanganate (0.4 g, 2.6 mmol) in water (2 ml) was added during 20 min to solution of alcohol **2** (0.35 g, 1.7 mmol) in acetonitrile (50 ml) and the mixture obtained was stirred for 1 h 30 min at room temperature. After the standard treatment and chromatographic separation lactam **3** (0.19 g, 50%) and 4-phenylpyridine (0.027 g, 10%) were obtained. Lactam **3** was isolated as a colorless oil; R_f 0.65 (acetone). IR spectrum, ν, cm^{-1}: 3370 (OH), 1642 and 1592 (NC=O and C=C). ^1H NMR spectrum, δ, ppm: 3.0 (3H, s, Me); 3.05 (1H, m, 5-H); 3.55 (2H, m, 6-H); 3.67 (2H, m, 5-CH_2O); 4.21 (1H, br. s, OH); 6.23 (1H, s, 3-H); 7.32 and 7.50 (3H and 2H, two m, Ph). ^{13}C NMR spectrum, δ, ppm: 34.33 ($C_{(5)}$); 39.22 (Me); 48.35 ($C_{(6)}$); 60.47 (CH_2OH); 119.89 ($C_{(3)}$); 126.07, 128.78, 129.6, and 150.09 (Ph); 136.0 ($C_{(4)}$); 165.19 (C=O). Mass spectrum, *m/z* (*I*, %): 217 (60) $[M]^+$, 186 (50), 185 (100). Found, %: C 71.4; H 7.38; N 6.12. $C_{13}H_{15}NO_2$. Calculated, %: C 71.89; H 6.91; N 6.45.

Phenylpyridine 4 was obtained as colorless crystals of mp 76-78°C [9]. R_f 0.48 (acetone). ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.36-7.70 (5H, m, Ph); 7.44 and 8.58 (2H and 2H, AA'BB' system, J = 5.8 and J = 1.6, Het). Mass spectrum, *m/z* (*I*, %): 155 (100) $[M]^+$, 128 (74), 127 (67), 115 (70), 102 (78).

3-Acetoxymethyl-1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (6a). Acetic anhydride (0.3 g, 1.98 mmol) was added to a cooled (0°C) solution of alcohol **2** (0.4 g, 1.98 mmol) in anhydrous pyridine (3 ml). The mixture was maintained at room temperature for 48 h, then poured onto ice, and extracted with chloroform. After chromatographic purification of the extract, acetate **6a** (0.36 g, 75%) was isolated as a dense colorless oil darkening with time; R_f 0.57 (acetone). IR spectrum, ν, cm^{-1}: 1730 (C=O), 1640, 1596 (C=C). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.98 (3H, s, COMe); 2.30 (3H, s, NMe); 2.50 and 2.80 (1H and 1H, two dd, J = 11 and 4.5 and J = 11 and 3.0 respectively, 2-CH_2); 3.05 (1H, br. s, 3-H); 2.90 and 3.30 (1H and 1H, two br. d, J = 18, 6-CH_2); 4.03 (2H, m, 3-CH_2O); 5.95 (1H, br. t, J = 3.0, 5-H); 7.10-7.40 (5H, m, Ph). Mass spectrum, *m/z* (*I*, %): 245 (100) $[M]^+$, 184 (76), 172 (99), 170 (30), 91 (35), 77 (19). Found, %: C 73.51; H 7.93; N 5.77. $C_{15}H_{19}NO_2$. Calculated, %: C 73.47; H 7.76; N 5.71.

1-Methyl-4-phenyl-3-propionyloxy-1,2,3,6-tetrahydropyridine (6b) was obtained in much the same way from alcohol **2** (1.6 g, 7.88 mmol) and propionic anhydride (3 g, 23.6 mmol). Ester **6b** (1.7 g, 85%) was isolated as a viscous yellow oil. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.10 and 2.25 (3H and 2H, t and q respectively, J = 7.6, Et); 2.53 (3H, s, NMe); 2.92 (2H, d, J = 5, 2-H); 3.20-3.35 (3H, m, 3- and 6-H); 3.95-4.15 (2H, m, CH_2O); 5.91 (1H, m, 5-H); 7.22-7.35 (5H, m, Ph). ^{13}C NMR spectrum, δ, ppm: 9.37 and 27.3 (Et); 35.78 (NMe); 44.05 ($C_{(3)}$); 53.10 and 53.33 ($C_{(2)}$ and $C_{(6)}$); 122.92 ($C_{(5)}$); 125.97, 127.58, 128.47 (Ph); 136.3 and 139.1 ($C_{(4)}$); 174.1 (C=O). Mass spectrum, *m/z* (*I*, %): 259 (33) $[M]^+$, 202 (11), 185 (41), 184 (100), 172 (97), 115 (30), 91 (46). Found, %: N 5.22. $C_{16}H_{21}NO_2$. Calculated, %: N 5.41.

5-Acetoxymethyl-1-methyl-2-oxo-4-phenyl-1,2,3,6-tetrahydropyridine (5) was obtained in much the same way from lactam **3** (0.35 g, 1.6 mmol) and acetic anhydride (1.6 mmol). Ester **5** (0.27 g, 65%) was isolated as a viscous yellow oil (darkening on storage). IR spectrum, ν, cm^{-1}: 1722 (C=O), 1644 ((NC=O), 1600 (C=C). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.00 (3H, s, COMe); 3.05 (3H, s, NMe); 3.25 (1H, m, 5-H); 3.45 (1H, dd, *J* = 14.0 and *J* = 2.0, 6-H); 3.75 (1H, dd, *J* = 14.0 and *J* = 6.0, 6-H); 4.10 (2H, m, CH_2O); 6.30 (1H, s, 5-H); 7.15-7.80 (5H, m, Ph). Mass spectrum, *m/z* (*I*, %): 259 (30) $[M]^+$, 230 (11), 186 (100), 170 (51), 155 (48), 145 (33), 129 (31), 105 (45), 91 (44). Found, %: C 69.24; H 7.01; N 5.30. $C_{15}H_{17}NO_3$. Calculated, %: C 69.50; H 6.56; N 5.41.

5-Acetoxymethyl-3,4-dihydroxy-1-methyl-2-oxo-4-phenylpiperidine (7a). Suspension of potassium permanganate (0.42 g, 2.44 mmol) in water (5 ml) was added during 20 min to solution of acetate **6a** (0.3 g, 1.22 mmol) in acetonitrile (30 ml) and the mixture was stored at room temperature for 2 h. After the standard treatment lactam diol **7a** (0.11 g, 37.5%) was obtained; mp 154-156°C. IR spectrum, ν, cm^{-1}: 3550 narrow and 3355 br (OH), 1716 (C=O), 1644 and 1626 (NC=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.98 (1H, s, C–Me); 2.50 (1H, m, 5-H); 3.00 (3H, s, NMe); 3.22 (1H, dd, *J* = 13.1 and *J* = 2.5, 6-H); 3.32 (1H, br. s, OH); 3.70-4.00 (4H, overlapping m, 3-, 6-H, and 5-CH_2O); 4.60 (1H, s, 4-OH); 7.30-7.50 (5H, m, Ph). Mass spectrum, *m/z* (*I*, %): 293 (13) $[M]^+$, 203 (17), 174 (75), 144 (33), 105 (100). Found, %: C 61.53; H 6.74; N 4.71. $C_{15}H_{19}NO_5$. Calculated, %: C 61.43; H 6.49; N 4.78.

3,4-Dihydroxy-1-methyl-2-oxo-4-phenyl-5-propionyloxymethylpiperidine (7b). Diol **7b** (0.48 g, 23.5%) was obtained in much the same way by the oxodihydroxylation of tetrahydropyridine **6b** (1.70 g, 6.6 mmol) with potassium permanganate (1.60 g, 9.9 mmol), and was isolated as colorless crystals; mp 104-106°C; R_f 0.65 (acetone). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.06 and 2.20 (3H and 2H, t and q respectively, *J* = 7.6, Et); 2.50 (1H, m, 5-H); 3.00 (3H, s, NMe); 3.20 (1H, dd, *J* = 12.0 and *J* = 2.4, 6-H); 3.35 and 4,65 (1H and 1H, two s, 3- and 4-OH); 3.50-4.00 (3H, m, CH_2O and 6-H); 4.12 (1H, s, 3-H); 7.20-7.50 (5H, m, Ph). M^+ 307 (mass spectrometrically). Found, %: N 4.49. $C_{16}H_{21}NO_5$. Calculated, %: N 4.56.

3-Acetoxy-5-acetoxymethyl-4-hydroxy-1-methyl-2-oxo-4-phenylpiperidine (8a). Acetic anhydride (0.4 ml, 0.40 mmol) and acetyl chloride (0.3 ml, 0.42 mmol) were added to solution of diol **7a** (60 mg, 0.20 mmol) in benzene (30 ml). The mixture was boiled for 5 h, the solvents were then distilled off in vacuum, and the residue was separated chromatographically (eluent ether). Diester **8a** (47 mg, 61%) was obtained as colorless crystals; mp 148-149°C; R_f 0.55 (acetone). IR spectrum, ν, cm^{-1}: 1741, 1711, 1691, 1661 (all C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.93 and 2.15 (3H and 3H each, two s, 2 COMe); 2.50 (1H, m, 5-H); 2.80 (1H, br. s, OH); 3.20 (1H, dd, *J* = 13.0 and *J* = 3.0, 6-H); 3.70-4.10 (3H, overlapping m, 6-H and 5-CH_2O); 6.05 (1H, s, 3-H); 7.01-7.40 (5H, m, Ph). M^+ 335 (mass spectrometrically). Found, %: C 60.52; H 6.65; N 4.03. $C_{17}H_{21}NO_6$. Calculated, %: C 60.90; H 6.27; N 4.18.

4-Hydroxy-1-methyl-2-oxo-4-phenyl-3-propionyloxy-5-propionyloxymethylpiperidine (8b). Mixture of diol **7b** (0.37 g, 1.2 mmol), propionic anhydride (0.50 g, 3.8 mmol), and pyridine (2 ml) was stored for 48 h at room temperature, then poured onto ice (50 g), and extracted with chloroform. The extract was washed with water (2 × 20 ml), and dried. Diester **8b** (0.25 g, 62%) was isolated after distilling off the solvent, as colorless crystals; mp 110-112°C; R_f 0.75 (acetone). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.10 and 2.25 (6H and 4H, t and q respectively, two Et); 2.50 (1H, m, 5-H); 2.93 (1H, br. s, 4-OH); 3.00 (3H, s, NMe); 3.25 (1H, dd, *J* = 12.0 and *J* = 2.2, 6-H); 3.80-4.20 (3H, m, CH_2O and 6-H); 6.21 (1H, s, 3-H); 7.40-7.50 (5H, m, Ph). M^+ 363 (mass spectrometrically). Found, %: N 3.61. $C_{19}H_{25}NO_6$. Calculated, %: N 3.86.

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