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NOTE

Elegant synthesis of novel pyrroles and dipyrrylmethane of biosynthetic importance

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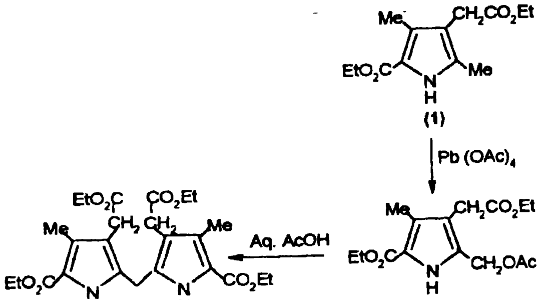
Ethyl 4-ethoxycarbonylmethyl-3,5-dimethylpyrrole-2-carboxylate (1) has been synthesized by extension and modification of Knorr pyrrole synthesis. Its acetoxymethyl derivative (2) has also been synthesized. Diethyl 3,3′-bis(ethoxycarbonylmethyl)-4,4′-dimethyl-2,2′-dipyrrylmethane-5,5′-dicarboxylate has been synthesized by self-condensation of 2.

Tri- and tetra-substituted pyrroles are essential starting substances for the synthesis of symmetrical as well as unsymmetrical dipyrrylmethanes which are invaluable intermediates for the synthesis of porphyrins of biosynthetic importance[1]. Syntheses of two new pyrroles, ethyl 4-ethoxycarbonylmethyl-3,5-dimethylpyrrole-2-carboxylate, ethyl 5-acetoxymethyl-4-ethoxycarbonylmethyl-3-methylpyrrole-2-carboxylate and a new dipyrrylmethane, diethyl 3,3′-bis(ethoxycarbonylmethyl)-4,4′-dimethyl-2,2′-dipyrrylmethane-5,5′-dicarboxylate are reported here.

Results and Discussion

In continuation of our earlier work[2], pyrrole **1** was synthesized by the nitrosation of ethyl acetoacetate with sodium nitrite and glacial acetic acid, followed by reductive condensation with ethyl 3-acetyl-4-oxopentanoate in presence of zinc and acetic acid. Its 5-acetoxymethyl derivative was prepared by oxidation with lead tetraacetate[3] (Scheme 1).



Scheme 1

Diethyl 3,3′-bis(ethoxycarbonylmethyl)-4,4′-dimethyl-2,2′-dipyrrylmethane-5,5′-dicarboxylate (**3**) was synthesized by self-condensation[4] of pyrrole **2** in presence of aqueous acetic acid.

Experimental

M.ps. are uncorrected. NMR spectra were determined on a Varian A-60 instrument relative to TMS as internal standard. All the solutions in the water-immiscible solvents were dried over sodium sulfate prior to evaporation TLC was carried out on silica gel G (Merck) using either chloroform or chloroform-methanol. Ethyl 3-acetyl-4-oxopentanoate[5] was synthesized by reported procedure.

Ethyl 4-ethoxycarbonylmethyl-3,5-dimethylpyrrole-2-carboxylate (**1**) : An aqueous solution of sodium nitrite (7.5 g) in water (25 ml) was added to a cooled and stirred solution of ethyl acetoacetate (13 g) in glacial acetic acid (50 ml) below 10°. The solution was further stirred at this temperature for 3 h and left overnight at room temperature. The nitroso compound so obtained was added to ethyl 3-acetyl-4-oxopentanoate (18.6 g) in acetic acid (30 ml) with stirring followed by Zn dust (15 g) in small portions at 60–65°. After heating the mixture for 2 h at 90–95°, it was decanted from any excess of zinc and then poured on crushed ice. The resulting solid was washed with cold water and crystallized from aqueous ethanol as colourless needles (12 g, 47%), m.p. 93–94° (Found : C, 61.80; H, 7.28; N, 5.24. $C_{13}H_{19}NO_4$ requires : C, 61.66; H, 7.51; N, 5.53%); ^1H NMR δ ($CDCl_3$) δ 9.5 (1H, s, NH), 4.2 (4H, q, 2 × OCH_2CH_3), 3.28 (2H, s, $CH_2CO_2CH_2CH_3$), 2.2 (6H, s, ring methyls), 1.26 (6H, t, 2 × OCH_2CH_3).

Ethyl 5-acetoxymethyl-4-ethoxycarbonylmethyl-3-methylpyrrole-2-carboxylate (**2**) : To pyrrole **1** (6 g) dissolved in glacial acetic acid (40 ml), lead tetraacetate (9 g) was added in small portions during 30 min with stirring. It was further stirred for ~3.5 h. The solution was then diluted with ice-cold water. The resulting white solid was crystallized from ethyl acetate/light petroleum, (5.3 g), m.p. 83–84° (Found : C, 57.88; H, 6.71; N, 4.44. $C_{15}H_{21}NO_6$ requires : C, 57.87; H, 6.75; N, 4.50%); ^{1}H NMR δ ($CDCl_3$) 9.5 (1H, s, NH), 5.04 (2H, s, CH_2OCOCH_3), 4.2 (4H, q, 2 × OCH_2CH_3), 3.28 (2H, s, $CH_2CO_2C_2H_5$), 2.2 (3H, s, ring methyl), 2.06 (3H, s, CH_2OCOCH_3), 1.26 (6H, t, 2 × CH_2CH_3).

Diethyl 3,3′-bis(ethoxycarbonylmethyl)-4,4′-dimethyl-2,2′-dipyrrylmethane-5,5′-dicarboxylate (**3**) : Pyrrole **2** (5 g) dissolved in aqueous acetic acid (45 ml; 80%) was heated at 90–95° for 3 h with stirring when the product was precipitated. The reaction mixture was then cooled and diluted. The resulting solid was crystallized from ethanol as colourless plates (3.6 g), m.p. 155–156° (Found : C, 61.15; H, 6.98; N, 5.62. $C_{25}H_{34}N_2O_8$ requires : C, 61.22; H, 6.93; N, 5.71%); ^{1}H NMR δ ($CDCl_3$) 9.4 (1H, NH), 9.18 (1H, NH), 4.2 (8H, overlapping, q, 4 × OCH_2CH_3), 3.85 (2H, CH_2), 3.28 (4H, s, $CH_2CO_2C_2H_5$), 2.2 (6H, s, 2 × ring methyl), 1.26 (12H, t, OCH_2CH_3).

References

1. V. Singh, A. Baqi and P. C. Gupta, *J. Indian Chem. Soc.*, 1999, **73**, 269.
2. P. S. Clezy, T. T. Hai and P. C. Gupta, *Aust. J. Chem.*, 1976, **29**, 393.
3. E. Bullock, A. W. Johnson, E. Markham and K. B. Shaw, *J. Chem. Soc.*, 1958, 1430.
4. P. S. Clezy and A. J. Liepa, *Aust. J. Chem.*, 1970, **23**, 2443.
5. J. B. Garner, G. A. Reddick and G. I. Fink, *J. Am. Chem. Soc.*, 1909, **31**, 668.