NEW PYRROLO[1,2-a][1,10]PHENANTHROLINE DERIVATIVES

F. Dumitrașcu*, C. Drăghici*, Loredana Barbu* and Christina Zălaru**

Abstract: The 1,3-dipolar cycloadditions between 1-(4-chlorophenacyl)-1,10-phenanthrolinium ylide 4 and dimethyl, diethyl or diisopropyl esters of acetylenedicarboxylic acid gave pyrrolo[1,2-a][1,10]phenantrolines 7a-c. The helical chirality of ethyl (7b) and isopropyl esters (7e) was put in evidence by 1H-NMR spectroscopy and the activation free energy was estimated from the coalescence. Treatment of ylide 4 with acetylenic esters at room temperature gave regio- and stereospecifically a mixture of cis-3,3a-dihydropyrrolophenantrolines 6 along with variable amounts of 7.

Introduction

The monosubstituted heteroaromatic N-ylides obtained in situ by deprotonation of the corresponding cycloimmonium salts in the presence of bases are 1,3-dipoles which undergo cycloaddition with acetylenic dipolarophiles resulting in the formation of fused five membered heterocycles [1-6].

Recently, we isolated and characterized the primary cycloadducts of monosubstituted phthalazinium and 1,10-phenanthrolinium phenacylides with dimethyl acetylene dicarboxylate [7]. Also, the rearrangement of primary cycloadducts was found to occur readily in the presence of triethylamine [7].

The present work describes the reaction of 1-(4-chlorophenacyl)-1,10-phenanthrolinium ylide 4 with esters of acetylenedicarboxylic acid giving new derivatives of pyrrolo[1,2-a][1,10]phenantrolines 7b,c. Compounds 7b,c were found to exhibit helical chirality. Also, the NMR characterization, previously described [7] is reported.

Experimental

All melting points were recorded with a Boetius microapparatus and are uncorrected. NMR spectra were recorded with a Varian Gemini 300BB instrument, operating at 300 MHZ for 1H and 75 MHz for 13C, the chemical shifts being expressed in δ values relative to TMS as internal standard.

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* To memory Dr. Ing. Dan Raileanu (1926-2002)
** Faculty of Chemistry, Department of Organic Chemistry, University of Bucharest, 90-94 Șos. Panduri, Bucharest, ROMANIA
Synthesis of diesters of 1-(4-chlorobenzoyl)-pyrrolo[1,2-a][1,10]phenanthroline-2,3-dicarboxylate (7a-c) - General procedure:

2.3 g (5 mmol) phenanthrolinium salt 3 were suspended in 25 mL dichloromethane and then 5.5 mmol of dimethyl (or diethyl, disopropyl) acetylenedicarboxylate were added. Under vigorous stirring 0.7 mL (5 mmol) of triethylamine (dissolved in 5 mL methylene chloride) were dropped. After 20 min. the reaction mixture was washed twice with water and the solvent evaporated. The residue was refluxed in ethanol for an hour and the precipitate was picked up by filtration.

Dimethyl ester, 1-(4-chlorobenzoyl)-pyrrolo[1,2-a][1,10]phenanthroline-2,3-dicarboxylate (7a) [7]

The product was recrystallized from nitromethane and yellow crystals were obtained. Yield 76%; m.p. 311 °C. Calcd. C 66.04; H 3.62; N 5.92. Found for C_{26}H_{17}ClN_{2}O_{5}: C 66.28; H 3.90; Cl 7.79; N 6.27.

^1^H-NMR (CDCl_{3}+TFA; δ, ppm; J, Hz): 3.77; 4.01 (2s, 6H, CH_{3}); 7.38 (d, 2H, 8.6, H-3', H-5); 7.41 (d, 2H, 8.6, H-2', H-6); 7.99 (d, 1H, 9.6, H-5); 8.23 (dd, 1H, 8.2; 6.3, H-9); 8.32 (d, 1H, 8.9, H-7); 8.39 (d, 1H, 9.6, H-6); 8.59 (d, 1H, 9.6, H-4); 9.17 (dd, 8.2; 1.2, H-8); 9.36 (dd, 6.3, 1.2, H-10).

^1^3^C-NMR (CDCl_{3}+TFA; δ, ppm): 53.2; 54.1 (2CH_{3}); 94.9 (C-3); 117.7; 118.8; 122.3; 126.3; 127.0; 128.5; 130.6 (C-1, C-2, C-3a, C-5a, C-7a, C-11a, C-11b); 124.7 (C-4, C-5, C-9); 126.1 (C-6); 126.9 (C-2', C-6'); 129.6 (C-3', C-5'); 130.3 (C-7); 138.0 (C-1); 139.1 (C-4'); 144.4 (C-10); 147.4 (C-8); 164.4; 166.9 (CO_{2}CH_{3}); 183.5 (COAr).

Diethyl ester, 1-(4-chlorobenzoyl)-pyrrolo[1,2-a][1,10]phenanthroline-2,3-dicarboxylate (7b)

The product was recrystallized from ethanol and yellow crystals were obtained. Yield 76%, m.p. 248-9 °C. Anal. Calcd. C 67.14; H 4.23; Cl 7.08; N 5.59. Found for C_{28}H_{21}ClN_{2}O_{5}: C 67.37; H 4.51; Cl 7.39; N, 5.87.

^1^H-NMR (CDCl_{3}; δ, ppm; J, Hz): 1.10 (t, 3H, 7.1, 2-CH_{2}CH_{3}); 1.38 (t, 3H, 7.2, 3-CH_{2}CH_{3}); 3.76-4.02 (m, 2H, 7.1, 14.2, 2-CH_{2}CH_{3}, system ABX); 4.32-4.47 (m, 2H, 7.2, 14.4, 3-CH_{2}CH_{3}, system ABX); 7.35 (dd, 1H, 8.2, 4.3, H-9); 7.49 (d, 2H, 8.5, H-3', H-5); 7.68 (d, 1H, 9.2, H-5); 7.79 (d, 1H, 8.6, H-7); 7.85 (d, 1H, 8.6, H-6); 8.02 (dd, 1H, 4.3, 1.7, H-10); 8.10 (d, 2H, 8.5, H-2', H-6'); 8.17 (dd, 1H, 8.3, 1.7, H-8); 8.55 (d, 1H, 9.2, H-4).

^1^3^C-NMR (CDCl_{3}; δ, ppm): 13.7; 14.3 (2CH_{3}); 60.4; 61.5 (2CH_{3}); 104.2 (C-3); 120.3 (C-4); 122.5 (C-9); 138.4 (C-4'); 125.3 (C-7); 125.9 (C-5); 126.7 (C-6); 136.5 (C-1'); 131.3 (C-2', C-6'); 128.3 (C-3', C-5'); 136.1 (C-8); 125.7; 125.9; 127.7; 128.9; 130.1; 137.3; 137.4 (C-1, C-2, C-3a, C-5a, C-7a, C-11a, C-11b); 145.5 (C-10); 163.4; 165.4 (CO_{2}CH_{2}CH_{3}); 182.9 (COAr).

Disopropyl ester, 1-(4-chlorobenzoyl)-pyrrolo[1,2-a][1,10]phenanthroline-2,3-dicarboxylate (7c)

The product was recrystallized from nitromethane and yellow crystals were obtained. Yield 78%, m.p. 231-2 °C. Anal. Calcd. C 68.12; H 4.76; Cl 6.70; N 5.30. Found for C_{30}H_{25}ClN_{2}O_{5}: C 68.43; H 4.97; Cl 7.01; N 5.55.
Results and Discussion

1-(4-Chlorophenacyl)-1,10-phenanthrolinium bromide (3) was obtained by reaction between 1,10-phenanthroline monohydrate (1) and 2-bromo-4'-chloroacetophenone (2), in acetone at reflux, similarly to previous literature procedure [8–9].

The cycloimmonium ylide 4, being unstable was generated in situ by reaction between quaternary salt 3 and triethylamine. Ylide 4 has an amphionic structure and can act as 1,3-dipole, according to the structure 4B (Scheme 1), in reaction with acetylenic dipolarophiles, Treatment of 1-(4-chlorophenacyl)-1,10-phenantrolinium ylide (4) with dimethyl, diethyl or disopropyl esters of acetylenedicarboxylic in dichloromethane at room temperature gave a mixture consisting cis 6a-c and 7a-c. When the above mixture was heated in ethanol at reflux, pyrrolo[1,2-a][1,10]phenanthrolines 7a-c were obtained in good yields (Scheme 1). The structure proof for cis stereochemistry was assigned by 1H-NMR spectroscopy. The H-3 atom appeared as doublet with coupling constant $J = 13.8$ Hz, whereas H-3a gave a double triplet with coupling constants of 13.8, 2.6 and 2.1 Hz, the last two values corresponding to the coupling with H-4 and H-5 protons. The large value of the vicinal coupling constant between H-3 and H-3a indicated a cis configuration, in agreement similar values for other dihydroderivates [10–13].

The 1H- and 13C-NMR data for the compounds 7a-c were also in agreement with the structure assignment. Supplementary evidence was given by COSY, HETCOR and NOE experiments.

The most characteristic feature of 1H-NMR spectrum of the compound 7b is two distinct patterns ABX2 for the two methylenic protons in the ester groups. This behaviour can be explained by non-coplanarity between pyrrolic and pyridic moieties, rendering helical [14] conformation to the molecule 7b. A similar observation was made for compound 7c. At room temperature the methyl protons of each isopropyl radical appeared in the 1H-NMR spectrum as two doublets (Fig 1).
Scheme 1
On raising the temperature, coalesce occurred and finally only two doublets were observed. The activation free energy for the terminal rings flipping in 7c was found to cca. 70 kJ/mol\(^{-1}\) (coalescence temperature 60°C; solvent DMSO-\(d_6\)). Also, the methyl carbon of each isopropyl radical was found to be non-equivalent in the \(^1H\)-NMR spectrum.

**Conclusion**

The pyrrolo[1,2-a][1,10]phenanthrolines derivatives 7a-e were obtained by 1,3-dipolar cycloadition between 1,10-phenanthroline ylide 4 and acetylenic esters. The cis stereochemistry of dihydro-derivatives 6 was assigned by \(^1H\)-NMR spectroscopy. Based on \(^1H\)-NMR chemical shift non-equivalence of prochiral groups (ethyl, isopropyl) the pyrrolo[1,2-a][1,10]phenanthrolines 7b,c were found to posses helical chirality. In the case of 7c the activation free energy was determined by DNMR experiment.

**REFERENCES**