Dedicated to the memory of
acad. Ecaterina Cioranescu-Nenitzescu

Isolation and X-Ray Structure of an Intermediate in 1,3-Dipolar Cycloaddition of 1,10-Phenanthrolinium N-Ylides with Alkynes: 1,2-Dihydropyrrolo-[1,2-a][1,10]phenanthroline

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We report the isolation and X-ray structure of a novel pyrroline derivative, trans diethyl 1-(4-bromobenzoyl)-1,2-dihydropyrrolo[1,2-a][1,10]phenanthroline-2,3-dicarboxylate, obtained by reaction between a 1,10-phenanthrolinium N-ylide and diethyl acetylene-dicarboxylate. The compound crystallizes in the space group C2/c (No.15) with a = 15.0144(2), b = 11.7567(2), c = 27.2246(4) Å, β = 98.633(1)° and Z = 8. The location of the double bond in the pyrrolinic moiety and the stereostructure of the cycloadduct were deduced from NMR data and confirmed by the X-ray analysis, which also revealed helicity of the phenanthroline system.

Keywords: 1,3-dipolar cycloaddition, 1,10-phenanthrolinium N-ylide, 1,2-dihydropyrrolophenanthroline, helicity

The cycloaddition reactions of heteroaromatic *N*-ylides and olefinic or acetylenic species involve interesting stereochemical and regiochemical aspects [1a-j, 2-4]. Firstly, the 1,3-dipolar cycloaddition reactions between heteroaromatic N-ylides **1** and acetylenic dipolarophile **2** gave the primary cycloadducts **3** which rearranged to pyrrolines **4** and/or **5** (scheme 1). Under the usual reaction conditions, intermediates **4**, **5** are generally unstable due to their tendency to dehydrogenate to yield fused pyrroles **6**. The position of the double bond in the pyrrolinic moiety, as well as the configuration of the pyrrolinic protons in **3**-**5** were established tentatively by NMR spectroscopy on the basis of the magnitudes of coupling constants between pyrrolidinic protons.

Recently, the cycloaddition of 1,10-phenanthrolinium *N*-ylides with esters of acetylene-dicarboxylic acids giving pyrrolo[1,2-a][1,10] phenanthroline derivatives was described [1f, 5-8]. In addition, the helical chirality of a representative pyrrolo[1,2-a][1,10] phenanthroline derivative was deduced from NMR spectroscopy in solution and confirmed by X-ray analysis [7,8].

Herein we report the isolation of a pyrroline derivative of type **5**, obtained by reaction between a 1,10-phenanthrolinium *N*-ylide and diethyl acetylene dicarboxylate (DEAD). The position of the double bond in the pyrrolinic moiety and the stereostructure of the cycloadduct were determined by X-ray analysis, and found to be consistent with the NMR data. Helical distortion of the phenanthroline unit was also confirmed by X-ray analysis.

Experimental part

Syntheses

2.3 g (5 mmol) phenanthrolinium salt **7** were suspended in 25 mL dichloromethane and then 5.5 mmol of diethylacetylenedicarboxylate were added. Under vigorous stirring, 1 mL (7.5 mmol) of triethylamine dissolved in 5 mL methylene chloride was added dropwise. After 10 min, the reaction mixture was washed twice with water and the solvent evaporated. The residue was triturated with ethanol and filtered; total yield 87%. The separation of the compounds **9** and **10** was achieved by column chromatography on neutral Al_2O_3 using CH_2Cl_2 as eluent.

Trans Diethyl 1-(4-bromobenzoyl)-1,2-dihydropyrrolo [1,2-a][1,10]phenanthroline-2,3-dicarboxylate (9). The product was recrystallized from acetonitrile as red crystals with m.p. 260-2 ^{0}C. Anal. $C_{28}H_{23}BrN_2O_5$. Calcd. C 61.44, H 4.24, Br 14.60, N 5.12. Found C 61.75, H 4.59, Br 15.01, N 5.38.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.24, 1.29 (2t, 6H, *J* = 7.1 Hz, $2CH_3$); 4.03 (d, 1H, *J* = 4.8 Hz, H-2); 4.09-4.3 (m, 4H, $2CH_2$); 7.20 (dd, 1H, *J* = 8.2, 4.2 Hz, H-9); 7.32, 7.45 (2d, 2H, *J* = 8.5 Hz, H-6, H-7); 7.39 (d, 1H, *J* = 9.5 Hz, H-5); 7.53 (d, 1H, *J* = 4.8 Hz, H-1); 7.73 (d, 2H, *J* = 8.6 Hz, H-3', H-5'); 7.89 (d, 1H, *J* = 9.5 Hz, H-4); 7.96-8.06 (m, 4H, H-8, H-10, H-2', H-6').

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 14.2, 14.7 (2 CH_3); 49.7 (C-2); 58.8, 61.5 (2 CH_2); 71.0 (C-1); 88.5 (C-3); 119.7, 120.7, 121.8, 126.8, 136.3, 136.5 (C-4, C-5, C-6, C-7, C-8, C-9); 122.0, 128.4, 130.3, 132.7, 135.6, 137.3 (C-5a, C-7a, C-11a, C-11b, C-1', C-4'); 130.8, 132.1 (C-2', C-3', C-5', C-6); 146.3 (C-10); 155.1 (C-3a); 165.5 (3-CO_2Et); 173.4 (2-CO_2Et); 189.5 (COAr).

Diethyl 1-(4-bromobenzoyl)-pyrrolo[1,2-a][1,10] phenanthroline-2,3-dicarboxylate (10)

The product was recrystallized from dimethylformamide and yellow crystals with m.p. 257-9 ^{0}C were obtained. Anal. Calcd. ($C_{28}H_{21}BrN_2O_5$): C 61.66, H 3.88, Br 14.65, N 5.14. Found: C 61.91, H 4.11, Br 14.97, N 5.32.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.10 (t, 3H, *J* = 7.1 Hz, 2-$CH_2C\mathbf{H_3}$); 1.38 (t, 3H, *J* = 7.2 Hz, 3-$CH_2C\mathbf{H_3}$); 3.76-4.02 (m, 2H, *J* = 7.1, 14.2 Hz, 2-$C\mathbf{H_2}CH_3$, system ABX_3); 4.34-4.44 (m, 2H, *J* = 7.2, 14.4 Hz, 3-$C\mathbf{H_2}CH_3$, system ABX_3); 7.36 (dd, 1H, *J* = 8.3, 4.3 Hz, H-9); 7.66 (d, 2H, *J* = 8.5 Hz, H-3', H-5'); 7.70 (d, 1H, *J* = 9.2 Hz, H-5); 7.81 (d, 1H, *J* = 8.5 Hz, H-7); 7.87 (d, 1H, *J* = 8.5 Hz, H-6); 8.03 (d, 2H, *J* = 8.5, H-2', H-6'); 8.03 (dd, 1H, *J* = 4.3, 1.7 Hz, H-10); 8.18 (dd, 1H, *J* = 8.3, 1.7 Hz, H-8); 8.56 (d, 1H, *J* = 9.2 Hz, H-4).

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Table 1
CRYSTAL DATA AND REFINEMENT PARAMETERS FOR COMPOUND **9**

Chemical formula	$C_{28}H_{23}BrN_2O_5$
Formula weight	547.39
Crystal Color, Habit	red, needle
Crystal Dimensions	0.15 x 0.15 x 0.10 mm^3
Crystal System	Monoclinic
Lattice Type	C-centered
Space Group	C2/c (#15)
Lattice Parameters	a = 15.0144(2) Å
	b = 11.7567(2) Å
	c = 27.2246(4) Å
	β = 98.633(1)°
Volume	4751.2(1) $Å^3$
Z value	8
D_{calc}	1.530 g/cm^3
F(000)	2240
μ(Mo-Kα)	1.774 mm^{-1}
Reflections/restraints/parameters	5719/0/327
Residuals: R1, wR2 [I > 2σ(I)]	0.0424, 0.0792
Goodness of Fit, S	1.017
Max. shift/error	0.001
Max. peak in final Δρ synthesis	0.46
Min. peak in final Δρ synthesis	-0.38

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 13.7, 14.3 ($2CH_3$); 60.4, 61.6 ($2CH_2$); 104.3 (C-3); 120.4 (C-4); 122.5 (C-9); 125.3 (C-4'); 125.4 (C-7); 126.0 (C-5); 126.8 (C-6); 127.1 (C-1'); 131.4 (C-2', C-6'); 131.5 (C-3', C-5'); 136.1 (C-8); 125.7; 126.7; 127.7; 128.9; 130.1; 136.9, 137.3 (C-1, C-2, C-3a, C-5a, C-7a, C-11a, C-11b); 145.6 (C-10); 163.4, 165.4 ($CO_2CH_2CH_3$); 183.2 (COAr).

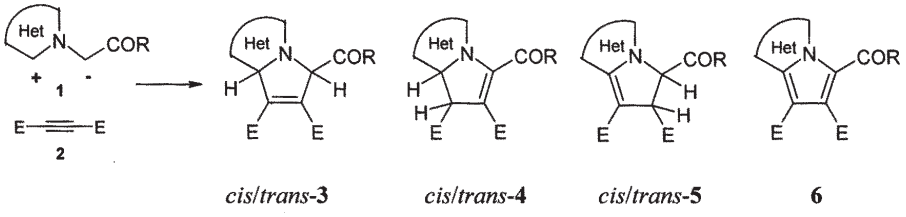
X-ray analysis of **9**

A cubic fragment was cut from a needle and mounted on a Nonius Kappa CCD four-circle diffractometer for intensity data-collection at -160°C with Mo-Ka radiation (λ = 0.71073Å). Data-collection strategy (program COLLECT [11]) involved 1.0° ϕ- and ω-scans. Program DENZO-SMN [12] was used for lattice parameter refinement (30347 reflections in the θ-range 1.02-27.88°) and data reduction. The data were corrected for absorption using program SADABS [13]. Structure solution by the direct method with program SHELXS86 [14] and full-matrix least-squares (LS) refinement on F^2 with program SHELXL97 [15] followed routinely, all non-H atoms being treated anisotropically. All H atoms were located in difference electron density maps and were added in idealized positions in a riding model with U_{iso} values equal to 1.2 times those of their parent atoms. LS weights of the form $w = [\sigma^2(F_o)^2 + (aP)^2 + bP]^{-1}$ with $P = [\max(F_o^2, 0) + 2F_c^2]/3$ were used in the final stages of refinement. Molecular parameters were computed with program PLATON [16] and program ORTEP-3 [17] was used for the figure. Final crystal and refinement data are listed in table 1. CCDC-272065 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Centre, 12 Union Road, Cambridge CB2 1EZ, UK: fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

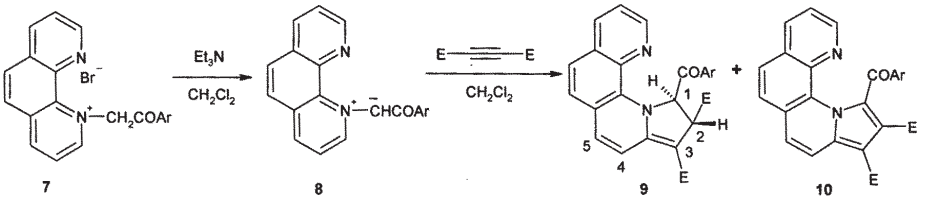
Results and discussion

Treatment of the 1,10-phenanthrolinium bromide **7** [9-10] with diethyl acetylenedicarboxylate (DEAD) in the presence of an excess of triethylamine gave pyrrolophenanthroline **10** along with dihydroderivative **9** (scheme 2). The ratio between the compounds **9** and **10** determined by H-NMR spectroscopy was found to be 60:40. *N*-Ylide **8**, generated from salt **7** by the action of triethylamine, acts as a 1,3-dipole in the reaction with dipolarophile DEAD giving the primary cycloadduct of type **3** (scheme 1), which in the presence of excess triethylamine rearranged to compound **9**. Under the reaction conditions reported, the dihydroderivative **9** was partially aromatized to the pyrrolophenanthroline **10**. The compounds **9** and **10** were separated by column chromatography and their structures were assigned by elemental analysis and NMR spectroscopy. Similar results were obtained when DEAD was replaced with dimethyl- or diisopropyl acetylenedicarboxylate.

In the H-NMR spectrum of dihydroderivative **9** the pyrrolinic protons (H-1 and H-2) appeared as two doublets with a coupling constant of 4.8 Hz. In principle, it should be possible to deduce the stereochemistry of such cycloadducts from the magnitude of the coupling constant between pyrrolinic protons (being larger for a *cis*-arrangement than for a *trans*-arrangement, in accordance with the dihedral angle). However, when only a single



Scheme 1



Ar = 4-BrC_6H_4; E = $CO_2C_2H_5$

Scheme 2

stereoisomer is present the coupling constant values are unreliable indicators of stereochemistry. Interestingly, in the H-NMR spectrum of **9** the methylenic protons in the esters groups appeared as two ABX_3 patterns. The magnetic non-equivalence of the methylenic protons can be explained either on the basis of helical distortion or the presence in the molecule of two chiral centres C-1 and C-2, respectively. The X-ray structure of compound **9** clearly indicated the *trans*-configuration of the two pyrrolinic protons, as well as the helicity of the molecule.

The molecular structure and conformation of **9** are shown in figure 1. Analysis of the geometry of the novel pyrroline ring system (labeled 1) shows that it is not planar but adopts an envelope conformation with the flap at atom C16 (a distance of only 0.185(4) Å, however, above the plane of the other four ring atoms). Bond distances in this ring are consistent with structure **9** in scheme 2, the shortest being the formal double bond C2-C17 (1.368(3) Å) and the longest C15-C16 (1.555(3) Å) indicating saturation. The other distances characterizing ring 1 are: N1-C2 1.388(3), N1-C15 1.473(3) and C16-C17 1.501(3) Å. The *trans*-configuration of the substituents at C15 and C16 is also evident.

Intramolecular strain, primarily due to the abnormally short non-bonded contact N10 ··· C28 (2.578(3) Å), contributes to the observed helicity of the phenanthroline ring system, which adopts a convex shape. This is evident from the acute angles between the least-squares planes 2-4, which are 4.6(1)° for 2 ^ 4, 2.2(1)° for 4 ^ 3, and 6.6(1)° for 2 ^ 3.

In the molecule of **9**, containing the dihydropyrrolo system, the degree of helicity is considerably smaller than that observed in the related compound ethyl 1-(4-phenylbenzoyl)-pyrrolo[1,2-a][1,10]phenanthroline-3-carboxylate [4], where the bond equivalent to C15-C28 is formally coplanar with the pyrrolo ring, leading to a remarkably short intramolecular contact N10 ··· C28 of only 2.465(2) Å and correspondingly greater distortion of the phenanthroline system.

In the crystal of **9**, stacking of the phenanthroline rings of symmetry-related molecules leads to two distinct π–π interactions with centroid ··· centroid (Cg ··· Cg) distances shorter than 4 Å. These occur between symmetry-related rings 2 and 4 (3.689 Å) and between ring 3 and its symmetry related counterpart (3.961 Å).

In conclusion, the novel dihydropyrrolo ring system occurring in the intermediate **9** has been characterized by

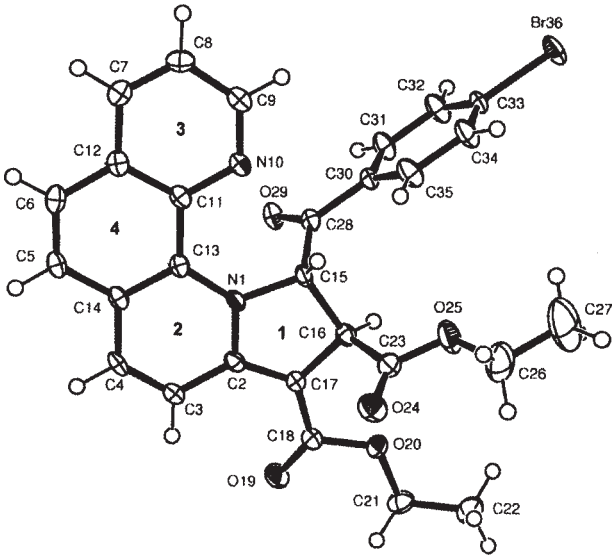


Fig. 1. Molecular strucuture of **9** with thermal ellipsoids drawn at the 50% probability level

H-NMR and X-ray crystallographic techniques. To our knowledge, this is the first example of structural elucidation of an intermediate from the 1,3-dipolar cycloaddition reactions of heteroaromatic N-ylides with alkynes. In addition, the nature and extent of helicity in the molecule of **9** have been elucidated.

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