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Cycloaddition of Nitrile Oxides to Aza-analogues of Phenanthrene

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Abstract: Mesitonitrile oxide, but not benzonitrile oxide, adds to aza-analogues of phenanthrene to give low yields of monocycloadducts. Only phenanthridine reacts with the two nitrile oxides affording phenanthridinone. 4,7-phenanthroline also gives some other minor products among which the bisadduct to a pyridine ring was isolated. The reactivity of aza-analogues under examination is discussed in terms of FMO approximation. © 1998 Published by Elsevier Science Ltd. All rights reserved.

In the last two decades inter- and intra-molecular reactions of aromatic heterocycles with nitrile oxides have provided a powerful tool for the synthesis of complex heterocyclic systems.[1,2] Within reactions of these aromatic heterocycles those of pyridine, its aza-analogues and their benzo-derivatives with nitrile oxides have also been studied by our research group.[3] Against any predictions of a chemical inactivity, pyridine reacts with benzonitrile oxide in apolar solvents affording two biscycloadducts, which derive from the cycloaddition of the 1,3-dipole to each one of two double bonds of an initial unisolable monocycloadduct to the C=N double bond of pyridine. This monocycloadduct is viewed as a secondary product deriving from the electrocyclic closure of the unstable zwitterion, which arises from the addition of the 1,3-dipole to the nitrogen atom of pyridine.[3] However, these biscycloadducts are fragile with respect to the autoxidation and they fragment on standing in solution to give the corresponding amide and the 1,3-dipole nitrile.[3]

Pursuing our studies in this area and for a useful comparison with reactions of nitrile oxides and polycyclic aromatic hydrocarbons (PAHs),[4] which also show a dipolarophilic reactivity affording mono- and biscycloadducts in low yields,[5,6] we have examined the reactivity of some aza-analogues of phenanthrene (**1**) (aza-PHEs) [phenanthridine (**2a**), benzo[*h*]quinoline (**2b**), 1,10- (**2c**), 1,7- (**2d**) and 4,7-phenanthroline (**2e**)] towards benzo- (**3a**) and mesitonitrile oxide (**3b**). In addition to the influence of the introduction of one or two nitrogen atoms on the dipolarophilic reactivity of already studied **1**[5] and regiochemistry of the nitrile oxide addition in relation to the position of nitrogen atom(s), it was interesting to examine the reactivity of **3a**,**b** at the nitrogen atom(s) of pyridine rings of AZA-PHEs **2a**-**e** and finally discuss these phenomena in terms of the FMO approximation.[8] Because of the highest electronegativity of the nitrogen atom with respect to that of the carbon atom, by passing from **1** to **2a**-**e** the energy of the HOMO and LUMO (Table 1) lowers inverting the dominant interaction, which becomes HOMO(dipole) - LUMO(dipolarophile) and reducing the energetic gap with respect to that between **1** and **3a**,**b**. Therefore, a greater reactivity of aza-PHEs was expected and furthermore a regioselectivity in the cycloaddition with **2b**,**d** was expected because of different values of their orbital coefficients (Table 2).

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Table 1: HOMO and LUMO energies of **1**, **2a**-e and **3a**,b.

Energies	**1**	**2a**	**2b**	2c	**2d**	2e	3a	**3b**
LUMO	-0.535	-0.721	-0.695	-0.842	-0.894	-0.957	-0.295	-0.263
HOMO	-8.740	-9.118	-8.878	-9.149	-9.206	-9.284	-9.344	-9.014

Table 2: Orbital coefficients of Aza-PHE LUMOs and nitrile oxide HOMOs

Compd	Positions in Aza-PHEs										Nitrile oxides	
	1	2	3	4	5	6	7	8	9	10	C	N
2a	- 0.224	0.300	0.021	- 0.287	0.377	- 0.396	0.318	0.011	- 0.361	0.242		
2b	0.175	- 0.294	- 0.017	0.251	- 0.389	0.379	- 0.367	0.068	0.358	- 0.287		
2c	- 0.222	- 0.331	- 0.027	0.309	- 0.389	0.389	- 0.309	0.027	0.331	0.222		
2d	0.281	- 0.332	- 0.092	0.359	- 0.389	0.353	- 0.232	-0.043	0.328	-0.199		
2e	- 0.269	0.342	0.016	- 0.276	0.366	- 0.366	0.276	-0.016	- 0.342	0.269		
3a											0.336	- 0.382
3b											0.282	- 0.335

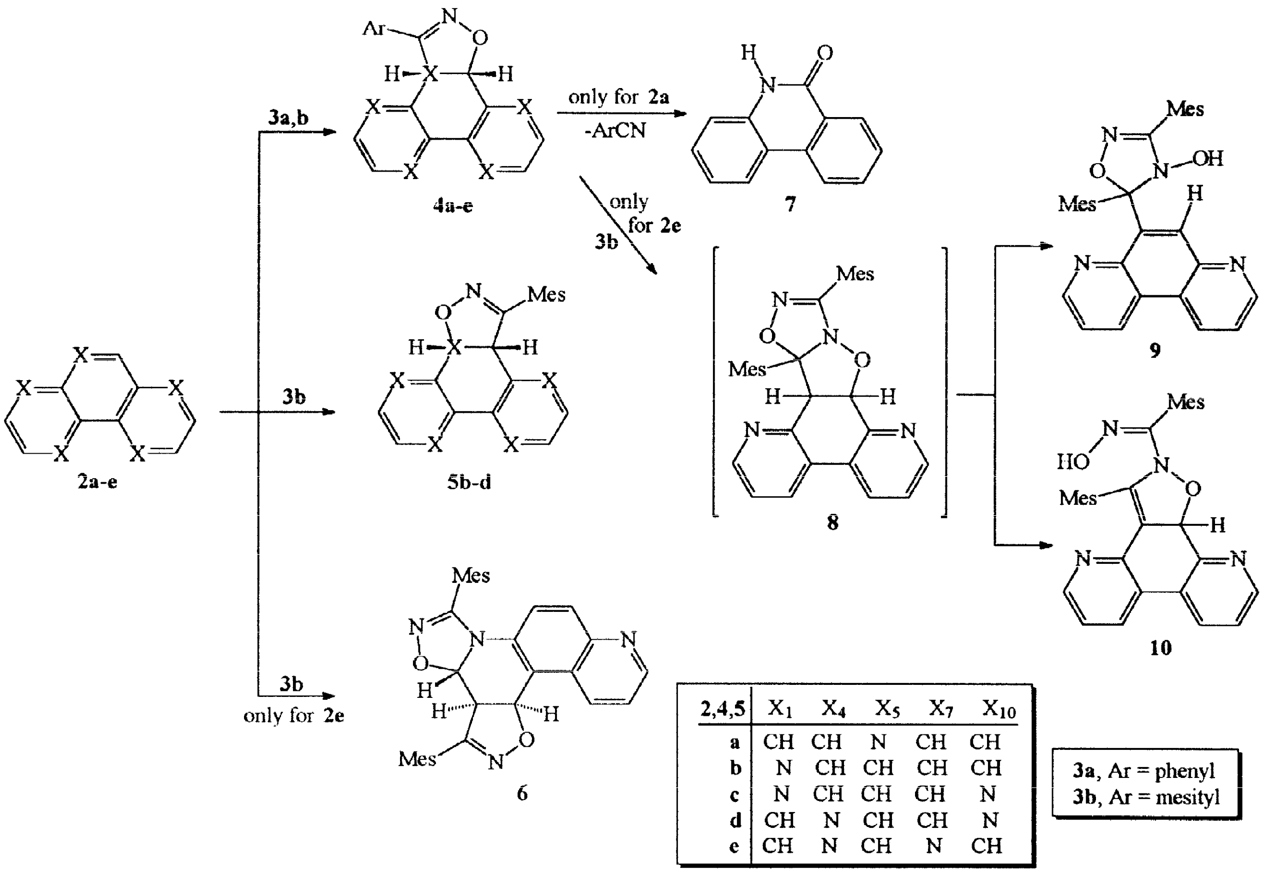
RESULTS AND DISCUSSION

In order to verify the reactivity of aza-PHEs **2a-e** at the nitrogen atom(s), their reactions with **3a** were conducted by adding very slowly triethylamine (two equiv.) to a solution of benzhydroximoyl chloride (two equiv.) and **2a-e** (one equiv.) in diethyl ether at - 10 °C and then allowing the reaction mixture to reach the room temperature which was maintained until the 1,3-dipole was consumed (ca. three days). However, under these conditions no reaction occurs with the exception of the reaction of **2a**, which afforded 6(5*H*)-phenanthridinone (**7**) with a yield of 46% and benzonitrile together with dimers of **3a**. On the contrary, reactions with **3b** were conducted by adding portion wise two equivalents of this 1,3-dipole to a refluxing solution of aza-PHEs **2a-e** in dichloromethane or benzene until **3b** was consumed (ca. 48 h for dichloromethane solutions and 24 h for benzene solutions). Also in this case, the reaction of **2a** with **3b** afforded **7** (49% yield for dichloromethane solution and 52% yield for benzene solution), but in all the other cases low yields (6.7-15%) of monocycloadducts were isolated. With the aim of increasing these yields, the same reactions were performed without solvent under irradiation in a simple microwave oven at 650 W and under heating in a silicon oil bath at 180 °C for short times, but these new conditions did not give the expected higher yields and did not lead to any variation in the site- and regio-selectivity of the addition, as in the cases of PAHs.[7] In particular the following results were obtained.

Phenanthridine (2a). As expected, **2a** undergoes the addition of **3a,b** to its $N_5=C_6$ double bond, which is the most reactive centre of the molecule,[9] to give cycloadducts **4a,b** (Scheme) which are not isolable because they undergo a rapid fragmentation giving **7** and the aromatic nitrile of the used nitrile oxide according to the autoxidation already observed in cycloadducts of pyridine, its aza-analogues and benzo-condensed derivatives.[3] According to literature data[2] and FMO approximation,[8] under the same conditions the $N_5=C_6$ double bond of **2a** shows a higher reactivity than that of the C_5=C_6 double bond of **1**.[5,7]

*Benzo[h]quinoline (**2b**).* In all the four methods **2b** reacts with **3b** to give a mixture (*ca.* 16% yield) of two regioisomeric monocycloadducts **4b** and **5b** in the 1:1 ratio (Scheme). These were identified through their ^1H, ^{13}C NMR spectra and NOEDS experiments which have allowed the observation of a strong interaction between dihydroisoxazole H_4 and H_5 protons and in the case of the regioisomer **4b**, a weak NOE effect among the dihydroisoxazole H_4 proton with benzoquinoline H_4 proton and protons of a methyl group of the mesityl moiety, while the dihydroisoxazole H_5 proton only weakly interacts with the benzoquinoline H_7 proton. In the case of the other regioisomer **5b**, the dihydroisoxazole H_4 shows a weak NOE effect with methyl protons of the mesityl group and the benzoquinoline H_7 proton, while the dihydroisoxazole H_5 only weakly interacts with the benzoquinoline H_4 proton.

Surprisingly, in contrast with the FMO approximation,[8] the introduction of a nitrogen atom in the position 1 of **1** does not affect the reactivity of the addition of **3b** and no regioselectivity was observed as it was the case with competitive experiments.



2,4,5	X_1	X_4	X_5	X_7	X_{10}
a	CH	CH	N	CH	CH
b	N	CH	CH	CH	CH
c	N	CH	CH	CH	N
d	CH	N	CH	CH	N
e	CH	N	CH	N	CH

3a, Ar = phenyl
3b, Ar = mesityl

Scheme

*1,10- (**2c**), 1,7- (**2d**) and 4,7-Phenanthroline (**2e**).* In the above conditions, phenanthrolines **2c-e** afforded cycloadducts **4c-e** and **5d** (ca. 15% yield for **4c**, ca. 18% yield for the mixture of **4d** and **5d** in the 1:1.7 ratio, and *ca.* 9.5% yield for **4e**) deriving from the addition of **2b** to the C_5=C_6 double bond of **2c-e** (Scheme).

Among the three phenanthrolines, however, **2e** was somewhat more reactive than the others because it gives, besides **4e**, minor yields of other products among which the biscycloadduct **6** (7.2%) and two products **9**

(5.1%) and **10** (3.0%) were isolated. These two latter compounds derive from the ring opening of the oxadiazole or isoxazole moiety of the biscycloadduct **8** arising from the addition of a second molecule of **3b** to the dihydroisoxazole C=N double bond of **4e**. However, like other cycloadducts of nitrile oxides to the C=N double bond of dihydroisoxazoles,[10] this is not stable to bases and it undergoes removal of the dihydroisoxazole H_4 proton by phenanthroline to give **9** restoring the aromaticity of **2e** and the dihydroisoxazole oxime **10** (Scheme).

The formation of this biscycloadduct **8** was not surprising because aza-PHEs are very poor dipolarophiles and then the C=N double bond of the dihydroisoxazole becomes competitive with respect to other dipolarophile sites in the molecule.[2]

While cycloadducts **4c** and **4e** were easily identified on the basis of their ^1H NMR spectra which show two doublets for dihydroisoxazole H_4 (4.97 and 5.28 ppm) and H_5 (6.19 and 6.20 ppm) protons and ^{13}C NMR spectra which show characteristic signals at 51.89, 76.91 and 158.24 ppm and 55.83, 80.06 and 158.64 ppm for dihydroisoxazole C_4, C_5 and C_3 carbon atoms, respectively, the structures of two regioisomers **4d** and **5d** were assigned by the help of NOEDS experiments as in the case of **4b** and **5b** (see Experimental).

The structure of the biscycloadduct **6** is based on its ^1H and ^{13}C NMR spectra which were confirmed by COSY, HETCOR and T-ROESY experiments. The phenanthroline H_1 proton (δ 5.93, d, J = 8.0 Hz) couples with H_2 proton (δ 3.59, dd, J = 8.0 and 9.2 Hz) which appears as a doublet of doublets because of the coupling of H_2 with H_3 proton (δ 6.11, d, J = 9.2 Hz). An *anti*-stereochemistry between the two five membered heterocycles resulted from the value of the coupling constant between the phenanthroline H_2 and H_3 protons and it was confirmed by T-ROESY experiments from which the H_2 proton gave a strong ROE with the H_1 proton and with protons of a methyl group of the mesityl moiety, but a very weak ROE with the H_3 proton. By saturation of the adjacent pyridine ring and for the shielding effect of the mesityl group, the doublet of the phenanthroline H_5 proton shifts from 8.25 ppm to 6.69 ppm, while that of the H_6 proton remains as doublet at 8.03 ppm.

Also the structures of *N*-hydroxyoxadiazole **9** and dihydroisoxazole oxime **10** are based on their spectral data. The ^1H NMR spectrum in deuterochloroform of **9** keeps the same pattern of **2e**, but with the signal at 8.21 ppm of phenanthroline H_6 proton which integrates for one proton and a broad signal at 7.80 ppm which is attributed to the hydroxyl proton of the *N*-hydroxy form or to the dihydrooxadiazole NH proton of *N*-oxide form. This proton exchanges with deuterium of D_2O and shifts on varying the concentration of the sample. The ^{13}C NMR spectrum contains two additional signals at 108.15 and 159.58 ppm which are characteristic of 4,5-dihydro-1,2,4-oxadiazole C_5 and C_3 carbon atoms, respectively. The IR spectrum shows a broad band centred at 3382 cm^{-1} for the hydroxyl group. The mass spectrum is characterized by intense molecular radical ion at *m/z* 502 and the main fragmentation corresponds to the loss of the hydroxyl radical.

The ^1H NMR spectrum of the dihydroisoxazole oxime **10** exhibits a singlet a 5.85 ppm for the dihydroisoxazole H_5 proton and a very broad singlet at 8.86 ppm for the oximic proton which disappears upon treatment with D_2O. Its ^{13}C NMR spectrum is characterized by signals at 58.15 and 159.13 ppm for dihydroisoxazole C_5 and oximic carbon atoms. The IR spectrum shows a strong broad peak centred at 3281 cm^{-1}. Besides the molecular peak at *m/z* 502, the mass spectrum contains two abundant fragment ions corresponding to the loss of the oximic and hydroxyl radical. The oxime structure was confirmed by obtaining the corresponding ketone by means of a deoximation process with chlorotrimethylsilane and sodium nitrite.[11]

As a consequence of the introduction of two nitrogen atoms, energy values of the phenanthroline HOMO and LUMO lower and then they were expected to be more reactive, but results of competitive experiments indicate for them a reactivity similar to that of **1** in contrast with predictions of FMO theory.[8] Indeed, **2e** is somewhat more reactive than **2c,d** because, besides **4e**, it affords minor products among which a biscycloadduct with the expected regioselectivity to its pyridine ring was isolated.

CONCLUSIONS

As expected, on the basis of the loss of the small resonance energy since two complete aromatic rings remain in the molecule, only the N_5=C_6 double bond of **2a** is reactive towards **3a,b** and the C_5=C_6 double bond of **2b-e** reacts only with **3b** as in the case of PAHs.[5] Nitrogen atoms of pyridine rings remain inactive toward **3a,b** with the exception of **2e** which behaves similarly to pyridine affording a sole possible biscycloadduct **6** with the expected regioselectivity. By comparison of the yield of the cycloadduct to the C_5=C_6 of **1** with that of **7** under the same conditions a difference arises which is in agreement with the FMO theory,[8] but there is not the same comparison with yields of **2b-e** which are similar in reactivity to **1** as it resulted by competitive experiments. The regioselectivity of the addition of **3b** to the C_5=C_6 double bond of **2b,d** is also in contrast with FMO theory,[8] because these afford a mixture of two regioisomers **4b,d** and **5b,d** in the ratio 1:1 and 1:1.7, respectively, against orbital coefficients of 0.389 - 0.379 and 0.389 - 0.353.

EXPERIMENTAL

Melting points were determined by a Kofler apparatus and are uncorrected. Elemental analyses were performed with a Perkin-Elmer elemental analyzer. IR spectra were recorded on a Perkin-Elmer Paragon 500 FT-IR Spectrometer using potassium bromide discs. NMR spectra were recorded on a Varian instrument at 200 or 500 MHz (^{1}H) and at 50 or 125 MHz (^{13}C) using deuterochloroform or dimethylsulfoxide-d_6 as solvent, chemical shifts are given in ppm (δ) from TMS as internal standard. Thin-layer chromatographic separations were performed on Merck silica gel 60-F_{254} precoated aluminium plates. Preparative separations were conducted by means of flash chromatography using Acros silica gel (0.035-0.070 mm) with cyclohexane-ethyl acetate mixture as eluents.

Starting materials. Benzohydroximoyl chloride[12] required for benzonitrile oxide generation and mesitonitrile oxide[13] were prepared following literature methods.

General procedure for cycloaddition reactions of Aza-PHEs 2a-e with 3a. To a stirred solution of aza-PHEs **2a-e** (20 mmol) and benzohydroximoyl chloride (40 mmol) in dry diethyl ether (40 ml) two equivalents of triethylamine in the same solvent were added at - 10 °C over 24 hours. The reaction mixture was then allowed to reach the room temperature and maintained until the 1,3-dipole was consumed (*ca.* three days), the reaction course being monitored by ^{1}H NMR spectroscopy. Among aza-PHEs, only **2a** afforded 6(5*H*)-phenanthridinone **7** which partially precipitated together with triethyl ammonium chloride. The residual part was also isolated by flash chromatography of the residue obtained by removal of the solvent from the reaction mixture.

5,6-Dihydrophenanthridin-6-one (7). Yield 46%; mp 292-293 °C (Lit.[14] 295-296 °C), white crystals from ethyl acetate (Found: C, 80.01; H, 4.68; N, 7.21. $C_{13}H_9NO$ requires: C, 79.98; H, 4.65; N, 7.17%); ν_{max} (KBr) 3166, 3048, 1665, 1631, 1609, 1425, 1370 cm^{-1}; δ_H (DMSO-d_6) 7.21-7.88 (m, 5H, aromatic H), 8.30-8.52 (m, 3H, aromatic H), 11.70 (s, 1H, NH); δ_C (DMSO-d_6) 116.62, 118.06, 122.79, 123.14, 123.77, 126.17, 127.98, 128.45, 130.09, 133.33, 134.76, 137.05, 161.34; ms: *m/z* 195 (M^+), 179, 167.

General procedure for cycloaddition reactions of Aza-PHEs 2a-e with 3b. To a solution of aza-PHEs **2a-e** (20 mmol) in dry dichloromethane or benzene (40 ml) two equivalents of **3b** were added portionwise and the reaction mixture was refluxed for 48 or 24 h, respectively. After removing the solvent, the reaction mixture was subjected to flash chromatography to give the cycloadducts, whose physical and spectral data are given below, where the following abbreviations were used: ME for methyl, MES for mesityl, PHE for phenanthroline, DHI for dihydroisoxazole, BQ for benzoquinoline, DHO for dihydrooxadiazole, AR for aromatic. In the case of **2a** the reaction mixture gave **7**, 49% yield for dichloromethane solution and 52% for benzene solution.

3-Mesityl-3a,11b-dihydrobenzo[h]isoxazolo[4,5-f]quinoline (4b). Yield 8%; mp 232-234 °C, yellow crystals from diethyl ether (Found: C, 81.11; H, 5.95; N, 8.19. $C_{23}H_{20}N_2O$ requires: C, 81.15; H, 5.92; N, 8.23%); ν_{max} (KBr) 2960, 1610, 1470, 1430 cm^{-1}; δ_H ($CDCl_3$) 1.35 (s, 3H, ME H), 1.40 (s, 3H, ME H), 2.41 (s, 3H, ME H), 5.00 (d, 1H, J = 11.03 Hz, DHI H_4), 6.14 (d, 1H, J = 11.03 Hz, DHI H_5), 6.63 (m, 1H, BQ H), 6.91 (s, 1H, MES H), 6.92 (s, 1H, MES H), 6.94 (m, 1H, BQ H), 7.50 (m, 2H, BQ H), 7.71 (m, 1H, BQ H), 8.54 (m, 1H, BQ H), 8.56 (m, 1H, BQ H); δ_C ($CDCl_3$) 18.43, 19.03 and 21.05 (ME C), 52.68 (DHI C_4), 77.71 (DHI C_5), 123.28, 125.03, 128.53, 128.89, 129.56, 130.05, 135.07, 136.01, 136.94, 138.85, 139.25, 149.77 (AR C), 159.31 (DHI C_3); ms: *m/z* 340 (M$^+$), 324, 309, 179.

3-Mesityl-3a,11b-dihydrobenzo[h]isoxazolo[5,4-f]quinoline (5b). Yield 8%; mp 239-241 °C, yellow crystals from diethyl ether (Found: C, 81.19; H, 4.89; N, 8.27. $C_{23}H_{20}N_2O$ requires: C, 81.15; H, 5.92; N, 8.23%); ν_{max} (KBr) 2921, 1609, 1468, 1432 cm^{-1}; δ_H ($CDCl_3$) 1.25 (s, 3H, ME H), 2.22 (s, 3H, ME H), 2.23 (s, 3H, ME H), 4.97 (d, 1H, J = 11 Hz, DHI H_4), 6.18 (d, 1H, J = 11 Hz, DHI H_5), 6.64 (m, 1H, BQ H), 6.86 (m, 2H, MES H), 7.10 (m, 1H, BQ H), 7. 34 (m, 2H, BQ H), 8.05 (d, 1H, BQ H), 8.54 (m, 1H, BQ H), 8.67 (d, 1H, BQ H); δ_C ($CDCl_3$) 17.60, 19.88, 20.82 (ME C), 52.08 (DHI C_4), 77.57 (DHI C_5), 122.35, 124.65, 128.19, 128.38, 129.16, 129.46, 131.90, 136.67, 137.43, 139.07, 148.66, (AR C), 159.17 (DHI C_3); ms: *m/z* 340 (M$^+$), 324, 309, 179.

3-Mesityl-3a,11b-dihydroisoxazolo[4,5-f][1,10]phenanthroline (4c). Yield 15%; mp 187-190 °C, white crystals from ethyl acetate (Found: C, 77.45; H, 4.58; N, 12.27. $C_{22}H_{19}N_3O$ requires: C, 77.40; H, 5.61; N, 12.31%); ν_{max} (KBr) 2916, 1609, 1568, 1463, 1429 cm^{-1}; δ_H ($CDCl_3$) 1.99 (s, 3H, ME H), 2.25 (s, 3H, ME H), 2.41 (s, 3H, ME H), 4.97 (d, 1H, J = 11 Hz, DHI H_4), 6.19 (d, 1H, J = 11 Hz, DHI H_5), 6.66 (s, 1H, MES H), 6.92 (s, 1H, MES H), 6.95 (dd, 1H, J = 7.8, 1.6 Hz, PHE H_3), 7.04 (dd, 1H, J = 7.8, 4.4 Hz, PHE H_2), 7.44 (dd, 1H, J = 7.8, 4.4 Hz, PHE H_7), 8.07 (m, 1H, J = 7.8, 1.6 Hz, PHE H_6), 8.07 (m, 1H, J = 4.4, 1.6 Hz, PHE H_1), 8.86 (m, 1H, J = 4.4, 1.6 Hz, PHE H_8); δ_C ($CDCl_3$) 19.02, 19.83, 21.02 (ME C), 51.89 (DHI C_4), 76.91 (DHI C_5), 122.97, 123.61, 123.86, 124.55, 126.61, 128.35, 128.48, 128.53, 128.80, 135.81, 135.91, 136.63, 137.37, 137.83 139.24, 146.05, 148.81, 150.02, 150.18 and 151.19, (AR C), 158.24 (DHI C_3); ms: *m/z* 341 (M$^+$), 325, 310, 180.

3-Mesityl-3a,11b-dihydroisoxazolo[5,4-f][1,7]phenanthroline (4d). Yield 6.7%; mp 213-215 °C, white crystals from ethyl acetate (Found: C, 77.37; H, 5.57; N, 12.29. $C_{22}H_{19}N_3O$ requires: C, 77.40; H, 5.61; N, 12.31%); ν_{max} (KBr) 2960, 1609, 1593, 1577, 1429 cm^{-1}; δ_H ($CDCl_3$) 1.42 (s, 3H, ME H), 2.23 (s, 3H, ME H), 2.46 (s, 3H, ME H), 5.18 (d, 1H, J = 10.7 Hz, DHI H_4), 6.21 (d, 1H, J = 10.7 Hz, DHI H_5), 6.99 (s, 2H, MES H), 7.26 (m, 1H, PHE H_3), 7.38 (m, 1H, PHE H_9), 8.08 (m, 1H, PHE H_4), 8.32 (s, 1H, PHE H_{10}), 8. 70 (s, 2H, PHE H_2 and H_8); δ_C ($CDCl_3$) 19.30, 20.82, 21.01 (ME C), 65.84 (DHI C_4), 78.90 (DHI C_5), 122.31, 123.39, 128.22, 128.77, 132.65, 136.82, 137.51, 137.96, 138.64, 149.97, 150.11, 150.63, (AR C), 158.15 (DHI C_3); ms: *m/z* 341 (M$^+$), 325, 310, 180.

3-Mesityl-3a,11b-dihydroisoxazolo[4,5-f][1,7]phenanthroline (5d). Yield 11.3%; mp 226-228 °C, white crystals from ethyl acetate (Found: C, 77.46; H, 5.63; N, 12.27. $C_{22}H_{19}N_3O$ requires: C, 77.40; H, 5.61; N, 12.31%); ν_{max} (KBr) 2959, 1610, 1593, 1579, 1430 cm^{-1}; δ_H ($CDCl_3$) 1.45 (s, 3H, ME H), 2.28 (s, 3H, ME H), 2.45 (s, 3H, ME H), 5.10 (d, 1H, J = 11.5 Hz, DHI H_4), 6.18 (d, 1H, J = 11.5 Hz, DHI H_5), 6.71 (s, 1H, MES H), 6.92 (d, 1H, J = 7.5 Hz, PHE H), 6.95 (s, 1H, MES H), 6.98 (t, 1H, PHE H), 7.48 (t, 2H, PHE H), 8.57 (d, 1H, J = 3.5 Hz, PHE H), 8. 81 (d, 1H, J = 3.5 Hz, PHE H) 8.89 (d, 1H, J = 7.5 Hz, PHE H); δ_C ($CDCl_3$) 19.23, 20.04, 21.14 (ME C), 52.15 (DHI C_4), 77.52 (DHI C_5), 123.49, 124.28, 124.94, 128.21, 128.67, 134.25, 136.24, 137.00, 138.05, 139.49, 148.54, 148.81, 150.29, 150.31, (AR C), 157.26 (DHI C_3); ms: *m/z* 341 (M^+), 325, 310, 180.

3-Mesityl-3a,11b-dihydroisoxazolo[4,5-f][4,7]phenanthroline (4e). Yield 9.5%; mp 170-172 °C, white crystals from ethyl acetate (Found: C, 77.44; H, 4.58; N, 12.27. $C_{22}H_{19}N_3O$ requires: C, 77.40; H, 5.61; N, 12.31%); ν_{max} (KBr) 2920, 1610, 1439, 1411 cm^{-1}; δ_H (CDCl$_3$) 1.25 (s, 3H, ME H), 2.24 (s, 6H, ME H), 5.28 (d, 1H, J = 11 Hz, DHI H_4), 6.20 (d, 1H, J = 11 Hz, DHI H_5), 6.72 (s, 1H, MES H), 6.85 (s, 1H, MES H), 7.25 (m, 1H, PHE H_9), 7.45 (m, 1H, PHE H_2), 8.15 (m, 2H, PHE H_1 and H_{10}), 8.32 (d, 1H, J = 4.6 Hz, PHE H_8), 8.87 (m, 1H, J = 4.6 Hz, PHE H_3); δ_C (CDCl$_3$) 19.11, 21.12, 29.65 (ME C), 55.83 (DHI C_4), 80.06 (DHI C_5), 122.97, 124.21, 125.56, 125.85, 128.26, 128.85, 130.50, 130.91, 132.24, 137.73, 138.57, 148.21, 149.62, 150.01, 150.65, (AR C), 158.64 (DHI C_3); ms: *m/z* 341 (M^+), 325, 310, 180.

3,6-Dimesityl-3a,13c-dihydro-3bH-isoxazolo[5,4-a][1,2,4]oxadiazolo[5,4-c][4,7]phenanthroline (6). Yield 7.2%; mp 278-280 °C, yellow crystals from ethyl acetate (Found: C, 76.52; H, 5.99; N, 11.11. $C_{32}H_{30}N_4O_2$ requires: C, 76.47; H, 6.02; N, 11.15%); ν_{max} (KBr) 2918, 1612, 1587, 1490, 1422 cm^{-1}; δ_H (CDCl$_3$) 1.88 (s, 3H, ME H), 2.33 (s, 3H, ME H), 2.36 (s, 3H, ME H), 2.42 (s, 6H, ME H), 2.45 (s, 3H, ME H), 3.59 (dd, 1H, J = 8.0, 9.2 Hz, DHI H_4), 5.93 (d, 1H, J = 8.0 Hz, DHI H_5), 6.11 (d, 1H, J = 9.2 Hz, DHO H_5), 6.69 (d, 1H, J = 9.5 Hz, PHE H_5), 6.83 (s, 1H, MES H), 6.98 (s, 2H, MES H), 7.08 (s, 1H, MES H), 7.64 (m, 1H, PHE H_9), 8.03 (d, 1H, PHE H_6), 8.84 (s, 1H, PHE H_8), 8.85 (s, 1H, PHE H_{10}); δ_C (CDCl$_3$) 19.34, 19.85, 20.20, 21.17, 21.18 (ME C), 50.91 (DHI C_4), 75.20 (DHI C_5), 90.61 (DHO C_5), 114.33, 119.60, 122.55, 124.82, 128.98, 129.27, 136.44. 137.18, 138.33, 139.57, 141.58, 145.38(AR C), 150.83 (DHO C_3), 159.948 (DHI C_3); ms: *m/z* 502 (M^+), 473, 457, 444, 357, 340.

3,5-Dimesityl-5-[4,7]phenanthrolin-5-yl-4,5-dihydro-1,2,4-oxadiazol-4-ol (9). Yield 5.1%; mp 163-165 °C, yellow crystals from ethyl acetate (Found: C, 76.41; H, 6.05; N, 11.09. $C_{32}H_{30}N_4O_2$ requires: C, 76.47; H, 6.02; N, 11.15%); ν_{max} (KBr) 3382 (br), 2919, 1611, 1589, 1491, 1473 cm^{-1}; δ_H (CDCl$_3$) 2.26 (s, 3H, ME H), 2.31 (s, 9H, ME H), 2.42 (s, 6H, ME H), 6.90 (s, 2H, MES H), 6.95 (s, 2H, MES H), 7.59 (dd, 1H, J = 4.0 and 8.0 Hz, PHE H_2), 7.61 (dd, 1H, J = 4.0 and 8.0 Hz, PHE H_9), 7.80 (s, 1H, hydroxyl H), 8.21 (s, 1H, PHE H_6), 8.86 (d, 1H, J = 8.0 Hz, PHE H_1), 8.94 (d, 1H, J = 4.0 Hz, PHE H_8), 9.01 (d, 1H, J = 8.0 Hz, PHE H_{10}), 9.04 (d, 1H, J = 4.0 Hz, PHE H_3); δ_C (CDCl$_3$) 18.17, 20.75, 20.91, 21.08 (ME C), 108.15, 122.65, 122.83, 128.96, 129.23, 129.98, 130.59, 131.07, 131.64, 133.19, 135.40, 137.03, 137.86, 139.66, 144.08, 150.58, 153.33, 159.58 (AR C), (DHO C_3); ms: *m/z* 502 (M^+), 458, 443, 413, 398, 341, 325, 309, 297.

Mesityl(3-mesityl-2,11b-dihydroisoxazolo[4,5-f][4,7]phenanthrolin-2-yl)methanone oxime (10). Yield 3%; mp 268-270 °C, white crystals from ethyl acetate (Found: C, 76.46; H, 6.01; N, 11.16. $C_{32}H_{30}N_4O_2$ requires: C, 76.47; H, 6.02; N, 11.15%); ν_{max} (KBr) 3281 (br), 2918, 1553, 1517, 1441, 1407 cm^{-1}; δ_H (CDCl$_3$) 1.47 (s, 3H, ME H), 2.28 (s, 6H, ME H), 2.33 (s, 6H, ME H), 2.50 (s, 3H, ME H), 5.85 (s, 1H, DHI H_5), 6.77 (s, 1H, MES H), 6.91 (s, 2H, MES H), 6.96 (s, 1H, MES H), 7.28 (m, 1H, PHE H), 7.47 (m, 1H, PHE H), 8.22 (t, 1H, PHE H), 8.31 (d, 1H, J = 3.4 Hz, PHE H) 8.74 (d, 1H, J = 3.4 Hz, PHE H), 8.86 (bs, 1H, oxime H); δ_C (CDCl$_3$) 18.47, 20.28, 20.94, 21.20 (ME C), 58.94 (DHI C_5), 118.56, 120.98, 124.73, 124.81, 126.58, 128.18, 128.69, 128.96, 130.24, 131.01, 131.67, 135.09, 136.50, 137.40, 137.60, 149.42, 150.41, 151.11 (AR C), 156.51 (DHI C_3); ms: *m/z* 502 (M^+), 485, 472, 446, 367, 341, 296, 207, 196.

*General procedure for cycloaddition reactions of Aza-PHEs **2a-e** with **3b** under microwave irradiation and neat conditions.* a) Microwave irradiation conditions: an Aza-PHEs **2a-e** (8 mmol) and two equivalents of **3b** were mixed in a pyrex vessel and irradiated in a microwave oven at 650 W for 5 min. b) Neat conditions: an Aza-PHEs **2a-e** (8 mmol) and two equivalents of **3b** were mixed in a pyrex vessel and placed into a silicon oil bath preheated to 180 °C until **3b** was consumed (5-10 min).

Cycloadducts which were the same of those obtained under the above conditions, were isolated by flash chromatography of crude mixtures and identified by their physical and spectral data. Their yields were very similar to those obtained in benzene solutions.

Competition experiments. For competitive experiments between **1** and **2c-e**, a solution of these latter (2 mmol each one) with **3b** (2 mmol) in dry benzene (10 ml) was refluxed with stirring for 24 hours. The yields of the two cycloadducts were determined by GC analysis of three different reaction mixtures following the method of internal standard. The maximum deviation from the average of triplicate runs was ± 3%.

Method of calculations. The calculations were performed by means of the semiempirical PM3 method[15] available in the MOPAC computation package distributed by QCPE (QCPE program n. 455, version 6.0).

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