1,3-DIPOLAR CYCLOADDITIONS OF POLYCYCLIC AROMATIC HYDROCARBONS WITH NITRILE OXIDES UNDER MICROWAVE IRRADIATION IN THE ABSENCE OF SOLVENT

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Abstract – In title cycloadditions microwave irradiation improves product yields and reduces dramatically reaction times in comparison with classical heating with and without refluxing solvents. In the double cycloaddition of nitrile oxides to anthracene a selectivity in favour of unsymmetrical bis-cycloadduct is observed.

Within our studies aimed at examining the reactivity of polycyclic aromatic hydrocarbons (PAHs) in order to find new derivatives for their potential use in the environmental chemistry, recently we reported that PAHs react with nitrile oxides[1,2] to give cycloadducts, which show peculiar properties towards reducing agents.

However, PAHs are poor dipolarophiles because their 1,3-dipolar cycloaddition reactions require a high cost of energy to overcome their resonance energy. In fact, we found that the most efficient nitrile oxides were mesitonitrile oxide and its 3,5-dichloro derivative with high reaction temperatures and times to afford low yields of cycloadducts (4.3-16.5%). In these conditions benzonitrile oxide undergoes the dimerization process rather than the cycloaddition process.[3]

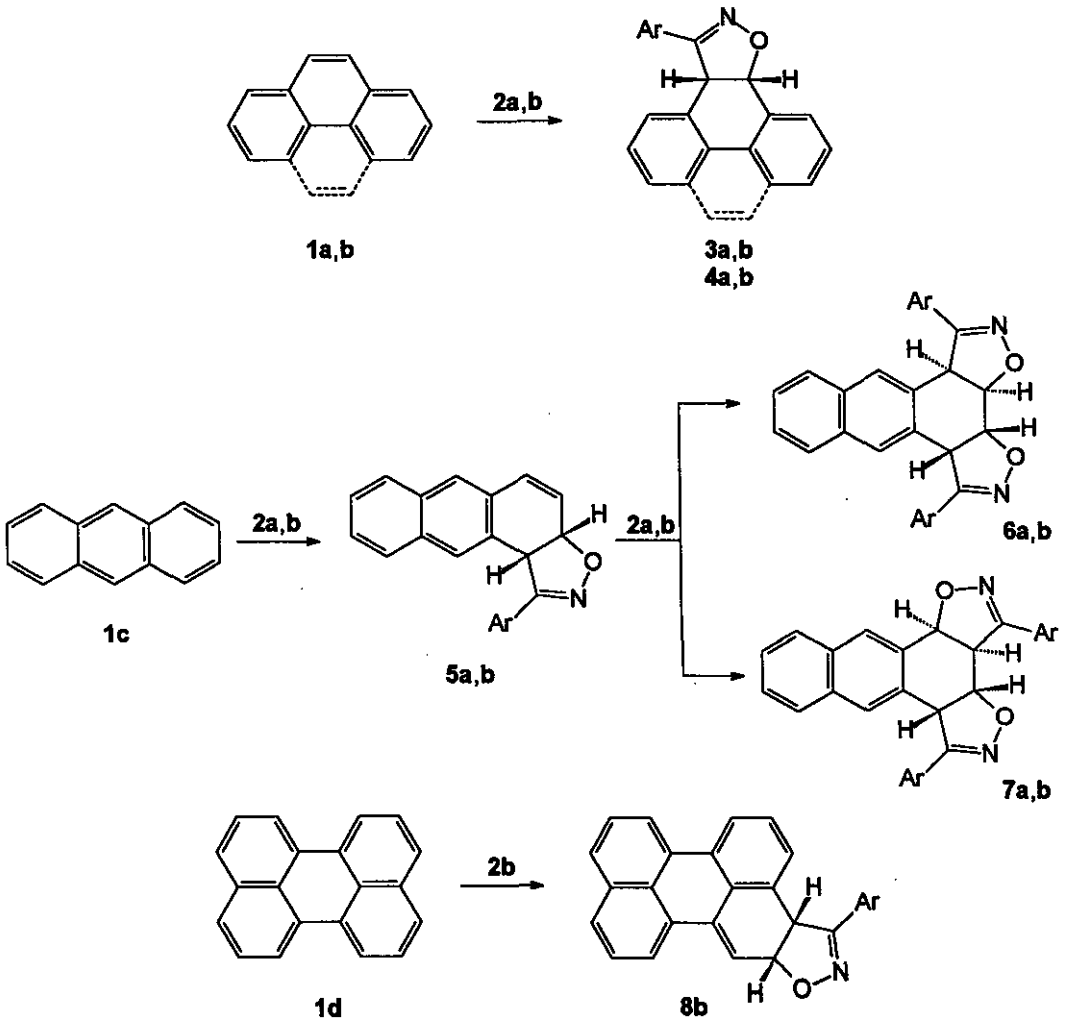
Then we decided to repeat the above reactions of PAHs with nitrile oxides under microwave heating under solvent free conditions because this technique proved to be efficient in some 1,3-dipolar cycloadditions of pyridinium dicyanomethylide with alkynes[4] and of nitrile oxides and nitrones with ketene acetals,[5,6] alkynes,[7] nitriles[8] and trifluoroacetoacetate or α-trifluoromethylstyrene.[9] In these reactions an acceleration of the reaction rate with consequent shortening reaction times and an improvement of the product purities and yields have been found. Moreover no changes in selectivity have been observed compared with the classical heating.

Here we report the results of reactions conducted under microwave irradiation under solvent-free condi-

tions between phenanthrene (**1a**), pyrene (**1b**), anthracene (**1c**), and perylene (**1d**) with 2,4,6-trimethyl- (**2a**) and 3,5-dichloro-2,4,6-trimethylbenzonitrile oxide (**2b**) in the same ratio used in the classical heating.

RESULTS AND DISCUSSION

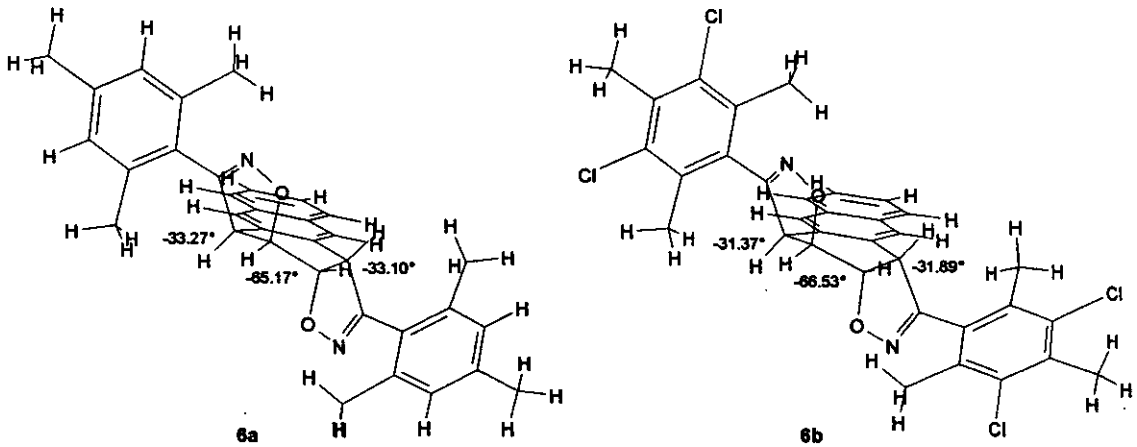
Reactions were performed in a simple microwave oven at 650 W without solvent by using two equivalents of the 1,3-dipole for PAH which are the same equivalents as the previous reactions conducted in refluxing benzene or toluene.[1,2] The results are summarized in Table 1. By chromatography of reaction crudes, the same cycloadducts obtained by the classical heating were also isolated and moreover the symmetrical bis-cycloadduct (**6a**) was isolated, too. Previously, this latter was too small amount to isolate (Scheme). As shown in Table 2 (Experimental), ^{1}H NMR data of all reaction products (**3a,b-7a,b** and **8b**) are reported.



3a-7a: Ar = 2,4,6-trimethylphenyl
3b-8b: Ar = 3,5-dichloro-2,4,6-trimethylphenyl

Scheme

Compound (**6a**) was identified on the basis of its spectral data. Particularly, the ^{1}H NMR spectrum exhibits two doublets at δ 4.949 and 4.951 (J = 8.08 and 8.12 Hz) for isoxazolinic 4-H protons and two double doublets at δ 5.378 and 5.382 (J = 3.38 and 3.42 Hz) for isoxazolinic 5-H protons, because the structure (**6a**), like (**6b**), are not symmetrical as it also appears by their minimized geometries calculated with MM4[10] program (Figure). An anti-stereochemistry is suggested for **6a,b** by the small coupling constant (3.09-3.11 and 3.38-3.42 Hz) through the bond connecting the two five-membered heterocyclic rings.



Figure

The most important differences between the two reaction conditions concern cycloadduct yields and reaction times (Table 1).

Table 1. Comparison of reactions of **1a-d** with **2a,b** by classical heating and under microwave irradiation.

PAH	Classical Heating with solvent[a]		Classical Heating without solvent[b]	Microwave irradiation		
	products (yield %)[c]		products (yield %)[d]	time (min)	products (yield %)[d]	
1a	**3a** (15.0)	**3b** (6.5)	**3b** (8.5)	3.5	**3a** (17.6)[e]	**3b** (20.6)
1b	**4a** (8.0)	**4b** (15.9)	**4b** (20.7)	5	**4a** (17.0)	**4b** (30.8)
1c	**5a** (15.7)	**5b** (16.5)	**5b** (10.8)	6	**5a** (11)	**5b** (10.4)
	6a (trace)	**6b** (4.3)	**6b** (9.2)		**6a** (10.2)	**6b** (16.5)
	7a (4.6)	**7b** (4.3)	**7b** (9.8)		**7a** (32.7)	**7b** (34.8)
1d		**8b** (8.5)	**8b** (12.2)	10		**8b** (19.32)

[a]PAHs **1a-d** and **2a,b** in the 1:2 ratio were refluxed for 24 h in dry benzene or toluene;[1] [b]PAHs **1a-d** and **2b** in the 1:2 ratio were placed in a silicon oil bath preheated at 180 °C until **2b** was consumed (5-10 min); [c]Isolated yields from ref. 1 and 2; [d]Isolated yields; [e]By employing a 1:4 ratio yield improved to 25.1%.

As shown in Table 1, reaction times were shortened dramatically from 24 hours to 3-10 minutes by passing from heating at reflux to microwave irradiation. Approximately, yields of cycloadducts (**4a,b**) and (**8b**) redouble, and those of **3b**, **6a,b** and **7a,b** increase of a 3, 4 and 7.5 factor, respectively, while those of **5a,b** reduce of a third. There is, then, a selectivity in favour of unsymmetrical bis-cycloadducts (**7a,b**) that previously was not observed because bis-cycloadducts were minor products. The highest yields of bis-cycloadducts on that of mono-cycloadducts suggested that these could be due to the effect of the lowest temperature used in classical heating. So we repeated the reaction of PAHs with **2b** in neat conditions and in refluxing decalin, but we found that from mixtures of PAHs and two equivalents of **2b**, placed in a silicone oil bath preheated at 180 °C until **2b** was consumed (5-10 min), yields of compounds (**6b**) and (**7b**) redouble and that of **5b** reduces of a third, while those of compounds (**3b, 4b** and **8b**) are only *ca.* 30% higher than those obtained by classical heating in refluxing toluene (Table 1). A failure was observed in the case of reactions in refluxing decalin because the 1,3-dipole preferentially undergoes the degradation process rather than the cycloaddition process.

As in the classical heating (with and without solvent), perylene does not react with **2a**, as well as naphthalene and triphenylene do not react with **2a,b** under microwave irradiation in the absence of solvents.

EXPERIMENTAL

Melting points were determined with a Kofler hot-stage apparatus and are uncorrected. IR spectra were taken on a Perkin-Elmer 281 spectrophotometer using potassium bromide discs, ^{1}H and ^{13}C NMR spectra were recorded on a Bruker W P 80 spectrometer using tetramethylsilane as internal standard and deuterochloroform as solvent. Elemental analyses were performed on a Carlo Erba Elemental Analyser 1106. Thin layer chromatography was performed on Merck silica gel 60-F_{254} precoated aluminium plates and flash chromatography was performed on Merck silica gel 60 by using mixtures of cyclohexane-ethyl acetate as eluents. Microwave irradiations were conducted in a Moulinex FM 5745 A domestic oven at 650 W.

Staring materials. Mesitonitrile oxide[11] and 3,5-dichloro-2,4,6-trimethylbenzonitrile oxide[12] were prepared following literature methods. PAHs were purchased from Aldrich Co.

General procedure for cycloaddition reactions. a) Microwave irradiation conditions. The PAH and two equivalents of the 1,3-dipole were mixed in a pyrex vessel and irradiated at 650W for the indicated time (see Table 1) and the products were isolated from the crude mixture by flash chromatography. Physical and spectral data of cycloadducts have been already given,[1,2] however, ^{1}H NMR data of all reaction products (**3a,b-7a,b** and **8b**) are reported in Table 2. From the reaction mixture of **1c** and **2a** the symmetrical bis-cycloadduct (**6a**) was also isolated. Previously this was not found because it was in so small amount that it escaped isolation. b) Neat conditions. The PAH and two equivalents of the **2b** were mixed in a pyrex

vessel and placed into a silicon oil bath preheated at 180 °C until **2b** was consumed (5-10 min). The same products,[1,2] which were obtained under microwave irradiation, were isolated by flash chromatography of the crude mixtures and identified by their physical and spectral data.

Table 2. ^{1}H NMR data of cycloadducts (**3a,b-7a,b** and **8b**).

Compound	δ_H ($CDCl_3$)	Ref.
3a	1.39 (s, 3H, methyl H), 2.24 (s, 3H, methyl H), 2.42 (s, 3H, methyl H), 4.75 (d, 1H, J = 10.6 Hz, isoxazolinic 4-H), 6.06 (d, 1H, J = 10.6 Hz, isoxazolinic 5-H), 6.64 (s, 1H, aromatic H), 6.90 (s, 1H, aromatic H), 6.63-7.91 (m, 8H, aromatic H)	1
3b	1.38 (s, 3H, methyl H), 2.47 (s, 3H, methyl H), 2.48 (s, 3H, methyl H), 4.85 (d, 1H, J = 10.8 Hz, isoxazolinic 4-H), 6.14 (d, 1H, J = 10.8 Hz, isoxazolinic 5-H), 6.60 (m, 1H, aromatic H), 7.04 (m, 1H, aromatic H), 7.30 (m, 1H, aromatic H), 7.43 (m, 2H, aromatic H), 7.82 (m, 3H, aromatic H)	2
4a	1.12 (s, 3H, methyl H), 2.26 (s, 3H, methyl H), 2.50 (s, 3H, methyl H), 5.30 (d, 1H, J = 11.2 Hz, isoxazolinic 4-H), 6.40 (d, 1H, J = 11.2 Hz, isoxazolinic 5-H), 6.62 (s, 1H, aromatic H), 6.95 (s, 1H, aromatic H), 6.80-7.94 (m, 8H, aromatic H)	1
4b	1.07 (s, 3H, methyl H), 2.52 (s, 3H, methyl H), 2.57 (s, 3H, methyl H), 5.24 (d, 1H, J = 11.3 Hz, isoxazolinic 4-H), 6.47 (d, 1H, J = 11.3 Hz, isoxazolinic 5-H), 6.79 (m, 1H, aromatic H), 7.34 (m, 2H, aromatic H), 7.79 (m, 3H, aromatic H), 8.00 (m, 2H, aromatic H)	2
5a	1.41 (s, 3H, methyl H), 2.18 (s, 3H, methyl H), 2.43 (s, 3H, methyl H), 4.96 (d, 1H, J = 11.7 Hz, isoxazolinic 4-H), 5.80 (ddd, 1H, J = 11.7, 3.0 and 1.2 Hz, isoxazolinic 5-H), 6.05 (dd, 1H, J = 9.9 and 3.0 Hz, vinylic H), 6.50 (s, 1H, aromatic H), 6.79 (d, 1H, J = 9.9 Hz, vinylic H), 6.91 (m, 2H, aromatic H), 7.35 (m, 3H, aromatic H), 7.51 (s, 1H, aromatic H), 7.73 (m, 1H, aromatic H)	2
5b	1.46 (s, 3H, methyl H), 2.44 (s, 3H, methyl H), 2.49 (s, 3H, methyl H), 4.93 (d, 1H, J = 11.4 Hz, isoxazolinic 4-H), 5.86 (ddd, 1H, J = 11.4, 2.8 and 1.3 Hz, isoxazolinic 5-H), 6.06 (dd, 1H, J = 9.8 and 2.8 Hz, vinylic H), 6.81 (d, 1H, J = 9.8 Hz, vinylic H), 6.91 (s, 1H, aromatic H), 7.44 (m, 4H, aromatic H), 7.74 (m, 1H, aromatic H)	2
6a	1.30 (s, 6H, methyl H), 2.30 (s, 6H, methyl H), 2.48 (s, 6H, methyl H), 4.949 (d, 1H, J = 8.08 Hz, isoxazolinic 4-H), 4.951 (d, 1H, J = 8.12 Hz, isoxazolinic 4'-H), 5.378 (dd, 1H, J = 8.08 and 3.42 Hz, isoxazolinic 5-H), 5.382 (dd, 1H, J = 8.12 and 3.38 Hz, isoxazolinic 5'-H), 6.65 (s, 2H, aromatic H), 6.93 (s, 2H, aromatic H), 7.00 (s, 2H, aromatic H), 7.33 (s, 4H, aromatic H)	
6b	1. 26 (s, 6H, methyl H), 2.55 (s, 6H, methyl H), 2.57 (s, 6H, methyl H), 4.898 (d, 1H, J = 8.29 Hz, isoxazolinic 4-H), 4.902 (d, 1H, J = 8.31 Hz, isoxazolinic 4'-H), 5.467 (dd, 1H, J = 8.29 and 3.09 Hz, isoxazolinic 5-H), 5.473 (dd, 1H, J = 8.31 and 3.11 Hz, isoxazolinic 5'-H), 6.92 (s, 2H, aromatic H), 7.38 (s, 4H, aromatic H)	
7a	1.32 (s, 3H, methyl H), 2.01 (s, 6H, methyl H), 2.24, 2.28 (s, 3H, methyl H), 2.33(s, 3H, methyl H), 4.53 (dd, 1H, J = 9.0 and 2.4 Hz, isoxazolinic 4-H), 4.67 (d, 1H, J = 10.5 Hz, isoxazolinic 4'-H), 4.97 (dd, 1H, J = 10.5 and 2.4 Hz, isoxazolinic 5'-H), 5.99 (d, 1H, J = 9.0 Hz, isoxazolinic 5-H), 6.61 (s, 1H, aromatic H), 6.90 (m, 3H, aromatic H), 7.42 (m, 4H, aromatic H), 7.86 (m, 1H, aromatic H), 8.27 (s, 1H, aromatic H)	2
7b	1.32 (s, 6H, methyl H), 2.42 (s, 6H, methyl H), 2.51 (s, 3H, methyl H), 2.54 (s, 3H, methyl H), 4.44 (dd, 1H, J = 9.2 and 2.4 Hz, isoxazolinic 4-H), 4.65 (d, 1H, J = 10.4 Hz, isoxazolinic 4'-H), 5.00 (dd, 1H, J = 10.4 and 2.4 Hz, isoxazolinic 5'-H), 6.03 (d, 1H, J = 9.2 Hz, isoxazolinic 5-H), 6.88 (s, 1H, aromatic H), 7.48 (m, 3H, aromatic H), 7.88 (m, 1H, aromatic H), 8.28 (s, 1H, aromatic H)	2
8b	1.26 (s, 3H, methyl H), 2.54 (s, 3H, methyl H), 2.59 (s, 3H, methyl H), 4.47 (d, 1H, J = 8.9 Hz, isoxazolinic 4-H), 5.03 (dd, 1H, J = 8.9 and 2.2 Hz, isoxazolinic 5-H), 5.45 (d, 1H, J = 2.2 Hz, vinylic H), 6.45 (m, 1H, aromatic H), 7.27 (m, 1H, aromatic H), 7.73 (m, 2H, aromatic H), 7.99 (m, 3H, aromatic H), 8.16 (m, 1H, aromatic H), 8.34, (m, 1H, aromatic H)	2

3a,9a12a,12b-Tetrahydro-3,10-dimesitylanthraceno[1,2-*d*][4,3-*d*]diisoxazole (6a). Yield 10.2 %; mp 278 °C (decomp) from ethyl acetate (Anal. Calcd. For $C_{34}H_{32}N_2O_2$: C, 81.57; H, 6.44; N, 5.60. Found: C, 81.54; H, 6.47; N, 5.59.); ν_{max} (KBr) 1450, 1380 cm^{-1}; δ_H ($CDCl_3$) 1.30 (s, 6H, methyl H), 2.30 (s, 6H, methyl H), 2.48 (s, 6H, methyl H), 4.949 (d, 1H, J = 8.08 Hz, isoxazolinic 4-H), 4.951 (d, 1H, J = 8.12 Hz, isoxazolinic 4'-H), 5.378 (dd, 1H, J = 8.08 and 3.42 Hz, isoxazolinic 5-H), 5.382 (dd, 1H, J = 8.12 and 3.38 Hz, isoxazolinic 5'-H), 6.65 (s, 2H, aromatic H), 6.93 (s, 2H, aromatic H), 7.00 (s, 2H, aromatic H), 7.33 (s, 4H, aromatic H); δ_C ($CDCl_3$) 19.14, 20.03 and 21.14 (methyl C), 50.78 (isoxazolinic C-4), 77.46 (isoxazolinic C-5), 124.87, 126.26, 127.22, 127.84, 128.49, 132.11, 136.07, 138.00, 139.17 (aromatic C), 160.75 (isoxazolinic C-3).

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