1,3-Dipolar Cycloadditions of Mesitonitrile Oxide with (9-Fluorenylidene)-aceto- and malono-nitriles. Synthesis of *Mono*- and *Bis*-1,2,4-Oxadiazolylmethane Derivatives

Pygmalion S. Lianis, Nestor A. Rodios and Nicholas E. Alexandrou\*

Laboratory of Organic Chemistry, University of Thessaloniki,
Thessaloniki, Greece
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Mesitonitrile oxide reacts with  $C \equiv N$  bond of (aryl)(9-fluorenylidene)acetonitriles 1 forming in very good yields the corresponding 1,2,4-oxadiazoles 2. Analogously also proceeds the reaction of mesitonitrile oxide with 9-fluorenylidenemalonodinitrile (3) with the formation of bis-1,2,4-oxadiazole derivative 4.

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It has been shown previously that the cycloaddition reaction of acrylonitrile [1], cinnamonitrile [2] and  $\beta$ -dialkylaminocinnamonitrile [3] with benzo- and mesitonitrile oxides mainly give cyanoisoxazolines, thus proving that the  $C \equiv N$  group is a poorer dipolarophile than the C = C bond [1,2,3].

On the contrary the cycloaddition reaction of  $\beta$ -monoalkylamino- or  $\beta$ -aminocinnamonitriles with the above mentioned nitrile oxides mainly give the 1,2,4-oxadiazole derivatives [4], the higher reactivity of the  $C \equiv N$  group in respect to the C = C bond in this case being attributed to the assistance of hydrogen bonding between the N-H group and the oxygen of the nitrile oxide moiety in the intermediate cycloadduct [5,6].

It has been found in this work that although benzonitrile oxide is unreactive, mesitonitrile oxide reacts with (aryl)(9-fluorenylidene)acetonitriles 1a-c to give the corresponding (aryl)(9'-fluorenylidene)(3-mesityl-1,2,4-oxadiazol-5-yl)methanes 2a-c in very good yields (75-90%), the cycloaddition proceeding exclusively on the  $C \equiv N$  bond.

a, X = H; b,  $X = OCH_3$ ; c, X = CI

The reaction takes place in refluxing chloroform solution with 2.5 molecular equivalents of the mesitonitrile oxide, until the nitrile oxide is not detectable by tlc control experiments (150-190 hours).

In a similar way also proceeds the cycloaddition between mesitonitrile oxide and (9-fluorenylidene)malononitrile 3, giving the bis-1,2,4-oxadiazole derivative 4.

The cycloaddition of the mesitonitrile oxide with the present unsaturated aceto- 1 and malononitriles 3 is electronically governed by the same factors as in tetracycanoethylene [7] which also gives 1,2,4-oxadiazole derivatives.

It is worth mentioning that from the reaction of dimethyl 9-fluorenylidenemalonate after long refluxing in chloroform solution with an excess of mesitonitrile oxide, not one cycloaddition product was isolated.

The structure of the cycloadducts 2 and 4 was elucidated on the basis of their analytical and spectral data. Thus, the compounds 2 show in their ir spectra bands at 1610 cm<sup>-1</sup> and 1580-1590 cm<sup>-1</sup> for C = C and C = N bonds, whereas their <sup>1</sup>H nmr spectra gave the expected pattern according to their structure.

The  $^{13}$ C nmr spectra of 2 are very complicated, especially in the aromatic region (110-140 ppm). However, their assignment has been based on shift additivities [8], off-resonance and hydrogen coupled spectra, peak heights as well as by comparison to analogous compounds [9], and are given in the Table. It is also mentioned that in compounds 2 and 4 the chemical shifts of C-3 of the oxadiazole ring appear at  $\delta$  about 169 ppm, whereas C-5 appears at  $\delta$  about 176 ppm in 2 but at  $\delta = 172.8$  ppm in 4. The 3.7 ppm diamagnetic shift of C-5 in 4 in respect to 2a is rather due to the displacement of the aryl group at C-10' of compounds 2 by the oxadiazole function in compound 4.

In the mass spectra of the compounds 2 the whole fragmentation pattern is in agreement with their structure and with the pattern expected for the 1,2,4-oxadiazole ring system [10,11]. Thus, all the compounds besides the molecu-

#### Scheme

Main fragmentation pattern in the mass spectrum of the compound 2a.

lar ion M<sup>+</sup> give peaks corresponding to retro-1,3-cycload-dition with the cleavage of mesitonitrile oxide from the molecular ion, as well as mesitonitrile and the fragment MesCN<sub>2</sub><sup>7</sup>. The base peak in the spectra studied corresponds to the [M-187]<sup>+</sup> ion, which is coming out from a cleavage of the mesityloxadiazole fragment from the molecular ion. They also give peaks corresponding to the mesitonitrile oxide (m/z 161), mesityloxadiazole (m/z 187), mesitonitrile (m/z 145) and to the fluorenyl fragment (m/z 164). A general fragmentation pattern of the compound 2a is given in the Scheme. Compound 4 gave an analogous mass spectrum with the appearance, besides the molecular ion M<sup>+</sup> at m/z 550, of peaks at m/z 389 [M-161]<sup>+</sup>, at m/z 363 [M-187]<sup>+</sup>, m/z 187, m/z 161 and m/z 145 (100).

### **EXPERIMENTAL**

Melting points were determined on a Kofler hot-stage apparatus and

are uncorrected. The ir spectra were recorded as Nujol mulls on a Perkin-Elmer 297 spectrometer. The 'H nmr spectra were obtained with either Varian CFT-20 (80 MHz) or Bruker AW-80 (80 MHz) spectrometers. The '3C nmr spectra were obtained using a Varian CFT-20 spectrometer. All spectra were recorded using tetramethylsilane (TMS) as internal standard in deuteriochloroform solutions. The mass spectra were recorded at 70 eV with a Hitachi-Perkin-Elmer RMU-6L spectrometer and elemental analyses were performed with a Perkin-Elmer 240B CHN analyser. Silica gel (Merck 60, 70-230 mesh) was used for column chromatography.

General Procedure for the Cycloadditions of (Aryl)(9-fluorenylidene)-acetonitriles 1a-c with Mesitonitrile Oxide.

(Aryl)(9-fluorenylidene)acetonitrile 1a-c (1 mmole), prepared as previously reported [9] and mesitonitrile oxide [12] (2.5 mmoles) were refluxed in dry and ethanol free chloroform (3 ml) for 150-190 hours, until tle control experiments did not show the presence of free mesitonitrile oxide. Evaporation of the solvent and addition of petroleum ether (bp 60-80°) afforded the corresponding cycloadducts 2.

(9-Fluorenylidene)(phenyl)(3-mesityl-1,2,4-oxadiazol-5-yl)methane (2a).

A solution of 1a (0.335 g, 1.2 mmoles) and mesitonitrile oxide (0.436 g, 2.7 mmoles) in dry chloroform (3 ml) was refluxed for 190 hours and

 $Table $$^{13}C$ Chemical Shifts of Compounds $2a$-c and $4$ (in Deuteriochloroform, $\delta$ ppm from TMS)$ 

	2a	2b	2c	4		2a	<b>2</b> b	<b>2</b> c	4
C-3	169.13	169.09	169.14	169.35	C-1"	137.10	129.34	_	_
C-5	176.51	176.84	176.12	172.81	C-2"	129.40	131.10	131.0	-
					C-6"				
C-8'	124.29	24.29 124.12	124.31	126.24	C-3"	129.40	114.75	129.68	-
C-1'	125.98	125.75	125.82		C-5"				
C-2'	127.27	127.16	127.21	127.93	C-4"	[4]	160.54	135.55	_
C-7′			127.33						
C-3'	129.91	129.71	130.10	132.21	X	-	55.36	-	-
C-6'									
						<b>M</b> esityl-carbons			
C-4'	119.73	119.67	119.83	120.18	C-1	123.72 [3]	123.73 [3]	123.52	123.18
C-5′	119.84	119.77	119.03	120.10					
C-4a'	141.35	141.20	141.34	142.45	C-2	137.78	137.69	137.69	137.85
[1] C-5a'	141.73	141.56	141.79		C-6				
C-la'	136.56 136.66 137.24 137.25	136.66	136.32	135.60	C-3	128.66	128.57	128.62	128.68
[1] C-8a'		137.25	136.76		C-5				
C-9' [2]	124.0 [3]	123.82 [3]	122.40	100.14	C-4	139.83	139.86	139.98	140.12
C-10' [2]	142.42	141.94	142.96	151.61	CH <sub>3</sub>	20.36	21.20	20.23	20.28
						21.29	21.42	21.19	21.21

[1] Shifts of C-4a', C-5a' and C-1a', C-8a' may be interchanged. [2] Shifts of C-9' and C-10' may be interchanged. [3] Shifts of C-9' and C-1(Mes) may be interchanged. [4] Masked under the peak of C-3", C-5".

treated as above to give **2a** (0.47 g, 89%), mp 169-171° as yellow crystals (from ether-petroleum ether); ir (nujol): 1610, 1590, 1540 cm<sup>-1</sup>; <sup>1</sup>H nmr:  $\delta$  2.24 (6H, s), 2.28 (3H, s), 6.92 (2H, s, H-Mes), 6.6-7.7 (13H, m); <sup>13</sup>C nmr: see Table; ms: m/z 440 (M\*, 41), 439 (31), 409 (2), 363 (6), 336 (3), 335 (10), 295 (26), 281 (18), 279 (31), 278 (46), 254 (51), 253 (100), 252 (74), 187 (5), 165 (10), 164 (10), 161 (90), 160 (33), 159 (15), 146 (61), 145 (77), 132 (25), 130 (82), 104 (18), 103 (33), 91 (51), 77 (46).

Anal. Calcd. for C<sub>31</sub>H<sub>24</sub>N<sub>2</sub>O: C, 84.52; H, 5.49; N, 6.36. Found: C, 84.42; H, 5.32; N, 6.29.

(9-Flurylidene)(p-methoxyphenyl)(3-mesityl-1,2,4-oxadiazol-5-yl)methane (2b).

A solution of **1b** (0.383 g, 1.24 mmoles) and mesitonitrile oxide (0.499 g, 3.09 mmoles) in dry chloroform (3 ml) was refluxed for 190 hours and treated as above to give **2b** (0.38 g, 65%), mp 141-143° as yellow crystals (from ether-petroleum ether); ir (nujol): 1610, 1540 cm<sup>-1</sup>, <sup>1</sup>H nmr:  $\delta$  2.26 (6H, s), 2.31 (3H, s), 3.88 (3H, s, OCH<sub>3</sub>), 6.94 (2H, s, H-Mes), 6.67-7.70 (12H, m); <sup>13</sup>C nmr: see Table; ms: m/z 470 (M<sup>+</sup>, 27), 469 (10), 440 (1), 364 (1), 363 (1), 336 (1), 335 (3), 325 (13), 311 (4), 309 (10), 308 (8), 294 (3), 284 (92), 283 (58), 269 (29), 268 (50), 264 (6), 253 (17), 252 (23), 241 (13), 239 (100), 226 (10), 213 (17), 165 (12), 164 (13), 161 (23), 160 (88), 159 (71), 146 (23), 145 (90), 132 (27), 130 (60), 126 (17), 115 (21), 104 (33), 103 (42), 91 (40), 77 (60).

Anal. Calcd. for  $C_{32}H_{26}N_2O_2$ : C, 81.68; H, 5.57; N, 5.95. Found: C, 81.68; H, 5.70; N, 6.00.

The petroleum ether washings were chromatographed on a silca gel column, using petroleum ether-methylenechloride (2:1) as eluant, from which **2b** (0.06 g, 10%) and the starting material **1b** (0.06 g, 15.7%) were isolated, the whole yield on **2b** being 75%.

(p-Chlorophenyl)(9-fluorenylidene)(3-mesityl-1,2,4-oxadiazol-5-yl) methane (2e).

A solution of 1c (0.389 g, 1.24 mmoles) and mesitonitrile oxide (0.499 g, 3.09 mmoles) in dry chloroform (3 ml) was refluxed for 150 hours and treated as above to give 2c (0.54 g, 91%), mp 157-159° as yellow crystals (from ether-petroleum ether); ir (nujol): 1610, 1580 cm<sup>-1</sup>; <sup>1</sup>H nmr:  $\delta$  2.26 (6H, s), 2.33 (3H, s), 6.97 (2H, s, H-Mes), 6.70-7.70 (12H, m); <sup>13</sup>C nmr: see Table; ms: m/z 476/474 (M\* , 40), 461/459 (1), 446/444 (3), 363 (14), 362 (20), 348 (20), 335 (17), 331/329 (15), 315 (23), 313 (20), 289/287 (32), 278 (23), 277 (20), 253 (23), 252 (100), 251 (17), 250 (31), 187 (12), 164 (9), 161 (89), 160 (17), 159 (6), 146 (60), 145 (28), 132 (29), 130 (43), 126 (11), 119 (17), 105 (20), 104 (14), 103 (14), 91 (46), 77 (57).

Anal. Calcd. for C<sub>31</sub>H<sub>23</sub>ClN<sub>2</sub>O: C, 78.39; H, 4.88; N, 5.90. Found: C, 78.25; H, 4.73; N, 5.58.

(9-Fluorenylidene)-bis-(3-mesityl-1,2,4-oxadiazol-5-yl)methane (4).

A solution of (9-fluorenylidene)malonodinitrile (3) [13] (0.137 g, 0.6 mmoles) and mesitonitrile oxide (0.302 g, 1.87 mmoles) in dry chloroform (3 ml) was refluxed for 190 hours and treated as above to give 4 0.313 g, 95%), mp 191-193° as yellow crystals (from benzene-ethanol); ir (nujol): 1630, 1610, 1595 cm<sup>-1</sup>; <sup>1</sup>H nmr:  $\delta$  2.25 (12H, s), 2.33 (6H, s), 6.96 (4H, s, H-Mes), 7.08-7.66 (8H, m); <sup>13</sup>C nmr: see Table; ms: m/z 550 (M<sup>+</sup>; 3), 549 (1), 415 (1), 391 (1), 389 (3), 363 (32), 362 (28), 348 (11), 336 (10), 335 (38), 321 (32), 287 (45), 286 (15), 281 (45), 262 (25), 205 (13), 187 (18), 165 (18), 164 (18), 161 (37), 160 (70), 159 (49), 146 (31), 145 (100), 132 (15), 130 (81), 126 (14), 119 (17), 105 (27), 104 (15), 103 (25), 91 (38), 77 (54).

Anal. Calcd. for  $C_{26}H_{30}N_4O_2$ : C, 78.52; H, 5.49; N, 10.17. Found: C, 78.69; H, 5.52; N, 9.87.

Attempted Reaction of Dimethyl Fluorenylidenemalonate with Mesitonitrile Oxide.

A solution of dimethyl fluorenylidenemalonate [14] (0.353 g, 1.2 mmoles) and mesitonitrile oxide (0.29 g, 1.8 mmoles) in dry chloroform (3 ml) was refluxed for 240 hours. After evaporation of the solvent and washing of the residue with petroleum ether, the starting material was isolated in 80% yield. The washings gave an oily product which consisted (tlc) of starting material and mesitoisocyanate.

# Attempted Reaction of la with Benzonitrile Oxide.

To a stirred solution of **1a** (0.335 g, 1.2 mmoles) and benzhydroxymoyl chloride [15] (0.28 g, 1.8 mmoles) in dry methylenechloride (4 ml) a solution of triethylamine (0.243 g, 2.4 mmoles) in methylenechloride (2 ml) was slowly added. After standing the reaction mixture for 24 hours, it was treated as described elsewhere [16] to give the starting material **1a** in 96% yield.

The same reaction was repeated in dry methylenechloride with refluxing for 24 hours. The reaction mixture after treating in the similar way as above gave the starting material 1a in 93% yield.

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