

1,3-Dipolar Cycloadditions of Mesitronitrile Oxide with (9-Fluorenylidene)aceto- and malono-nitriles. Synthesis of *Mono-* and *Bis-*1,2,4-Oxadiazolymethane Derivatives
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Received October 29, 1987

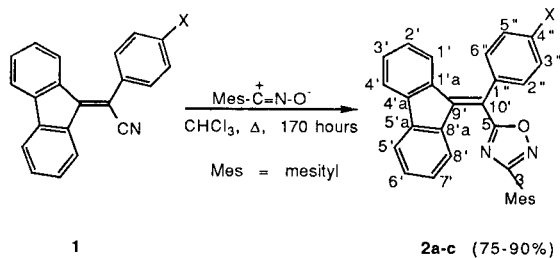
Mesitronitrile oxide reacts with $C\equiv N$ bond of (aryl)(9-fluorenylidene)acetonitriles **1** forming in very good yields the corresponding 1,2,4-oxadiazoles **2**. Analogously also proceeds the reaction of mesitronitrile oxide with 9-fluorenylidene malonodinitrile (**3**) with the formation of *bis*-1,2,4-oxadiazole derivative **4**.

J. Heterocyclic Chem., **25**, 1099 (1988).

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

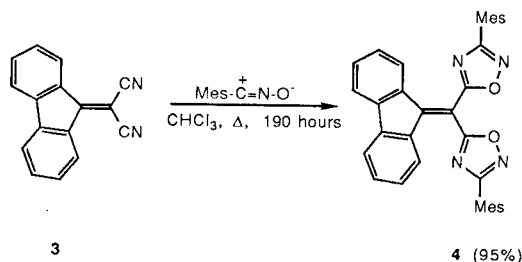
On the contrary the cycloaddition reaction of β -monoalkylamino- or β -aminocinnamionitriles with the above mentioned nitrile oxides mainly give the 1,2,4-oxadiazole derivatives [4], the higher reactivity of the $C\equiv N$ group in respect to the $C=C$ bond in this case being attributed to the assistance 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, mesitronitrile 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.



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

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



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

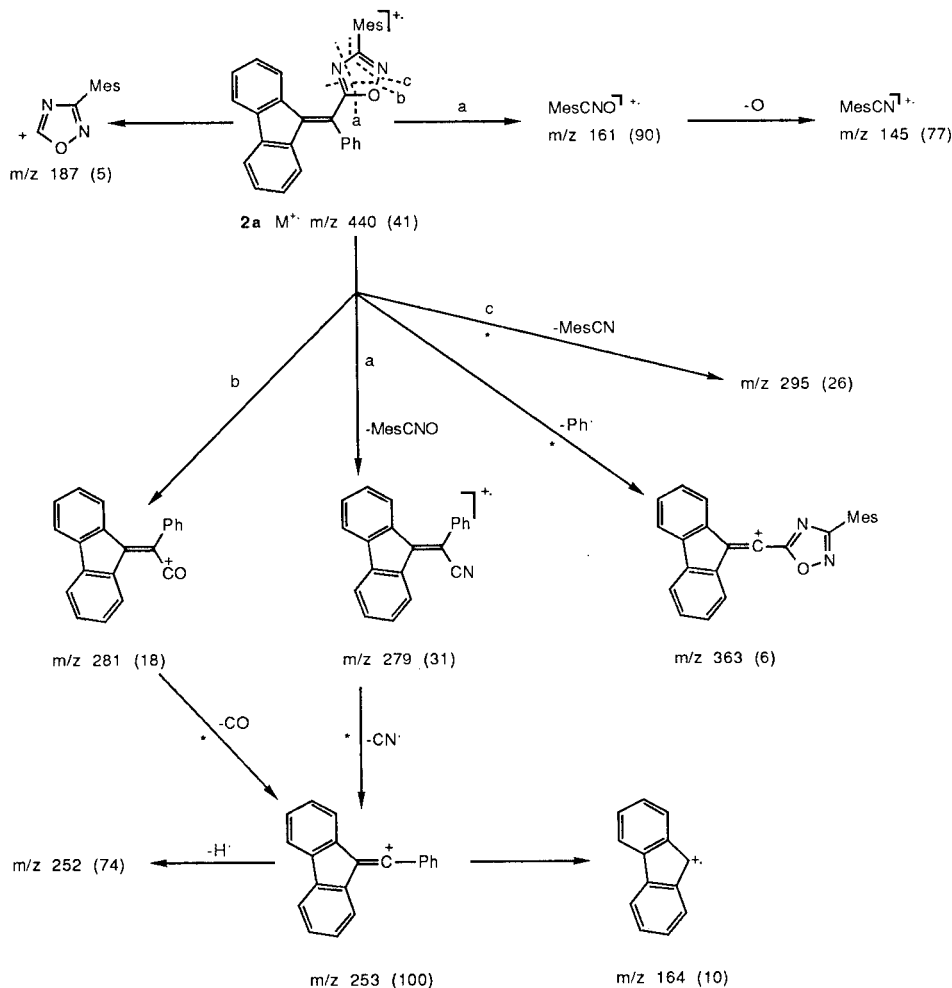
It is worth mentioning that from the reaction of dimethyl 9-fluorenylidene malonate after long refluxing in chloroform solution with an excess of mesitronitrile oxide, not one cycloaddition product was isolated.

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^{-1} and 1580-1590 cm^{-1} for $C=C$ and $C=N$ bonds, whereas their ¹H nmr spectra gave the expected pattern according to their structure.

The ¹³C 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 δ about 169 ppm, whereas C-5 appears at δ 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 $M^{\bullet+}$ give peaks corresponding to retro-1,3-cycloaddition with the cleavage of mesitronitrile from the molecular ion, as well as mesitronitrile and the fragment $MesCN_2^{\bullet+}$. The base peak in the spectra studied corresponds to the $[M-187]^{\bullet+}$ ion, which is coming out from a cleavage of the mesityloxadiazoide fragment from the molecular ion. They also give peaks corresponding to the mesitronitrile oxide (m/z 161), mesityloxadiazoide (m/z 187), mesitronitrile (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 $M^{\bullet+}$ at m/z 550, of peaks at m/z 389 $[M-161]^{\bullet+}$, at m/z 363 $[M-187]^{\bullet+}$, 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 1H nmr spectra were obtained with either Varian CFT-20 (80 MHz) or Bruker AW-80 (80 MHz) spectrometers. The ^{13}C 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 Mesitronitrile Oxide.

(Aryl)9-fluorenylidene)acetonitrile **1a-c** (1 mmole), prepared as previously reported [9] and mesitronitrile oxide [12] (2.5 mmoles) were refluxed in dry and ethanol free chloroform (3 ml) for 150-190 hours, until tlc control experiments did not show the presence of free mesitronitrile 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 mesitronitrile oxide (0.436 g, 2.7 mmoles) in dry chloroform (3 ml) was refluxed for 190 hours and

(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^{-1} ; ^1H nmr: δ 2.25 (12H, s), 2.33 (6H, s), 6.96 (4H, s, H-Mes), 7.08-7.66 (8H, m); ^{13}C nmr: see Table; ms: m/z 550 (M^+ , 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 $\text{C}_{36}\text{H}_{30}\text{N}_4\text{O}_2$: C, 78.52; H, 5.49; N, 10.17. Found: C, 78.69; H, 5.52; N, 9.87.

Attempted Reaction of Dimethyl Fluorenylidene malonate with Mesitonitrile Oxide.

A solution of dimethyl fluorenylidene malonate [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 1a 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.

Acknowledgements.

We wish to express our thanks to Mr. D. Rigas, Mr. G. Barbaratsas and Mrs. Ch. Gartagani for their technical assistance and to Dr. J. Gallos (University of Florida) for some elemental analyses.

REFERENCES AND NOTES

- [1] P. Caramella and P. Grünanger, "1,3-Dipolar Cycloaddition Chemistry", Vol I, A. Padwa, ed, John Wiley and Sons, New York, 1984, p 361.
- [2] A. Corsaro, U. Chiacchio, G. Perrini, P. Caramella and G. Purrello, *J. Chem. Res (S)*, 402 (1984).
- [3] A. Corsaro, U. Chiacchio and G. Purrello, *J. Chem. Soc., Perkin Trans. 1*, 2154 (1977).
- [4] A. Corsaro, U. Chiacchio, A. Compagnini and G. Purrello, *J. Chem. Soc., Perkin Trans. 1*, 1635 (1980).
- [5] A. Corsaro, U. Chiacchio, G. Perrini, P. Caramella and G. Purrello, *J. Heterocyclic Chem.*, **22**, 797 (1985).
- [6] A. Corsaro, U. Chiacchio, P. Caramella and G. Purrello, *J. Heterocyclic Chem.*, **21**, 949 (1984).
- [7] J. E. Franz, R. F. Howe and H. K. Pearl, *J. Org. Chem.*, **41**, 620 (1976).
- [8] D. F. Ewing, *Org. Magn. Reson.*, **12**, 499 (1979).
- [9] P. S. Lianis, N. A. Rodios and N. E. Alexandrou, *Ann. Chem.*, 537 (1987).
- [10] L. B. Clapp, "Comprehensive Heterocyclic Chemistry", Vol 6, A. R. Katritzky and C. W. Rees, eds, Pergamon Press, New York, 1984, p 379.
- [11] Q. N. Porter, "Mass Spectrometry of Heterocyclic Compounds", 2nd Ed, John Wiley and Sons, New York, 1985, p 887.
- [12] C. Grundmann and R. Richter, *J. Org. Chem.*, **33**, 476 (1968).
- [13] H. D. Hartzler, *J. Org. Chem.*, **31**, 2654 (1966).
- [14] W. Lehnert, *Tetrahedron*, **29**, 635 (1973).
- [15] K.-C. Liu, B. R. Shelton and R. K. Howe, *J. Org. Chem.*, **45**, 3916 (1980).
- [16] S. Papadopoulos and J. Stephanidou-Stephanatou, *Ann. Chem.*, 1697 (1985).