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2,5-Diaryl-1,3,4-oxadiazin-6-ones **1** gave with nitrile oxides **2** 1,2,4-oxadiazole derivatives **4**. When mesitonitrile oxide **2a** was used, bis-adducts **3** were also formed. The cycloadditions showed a remarkable site selectivity towards one carbon nitrogen double bond. The structure of both adducts was fully characterized by X-ray analysis.

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1,3,4-Oxadiazin-6-ones are relatively new heterocyclic compounds and have recently attracted the interest of an increasing number of investigators in heterocyclic synthesis [3]. The first member of this class of compounds was synthesized by Steglich and co-workers [4] from phenyl glyoxilic acid benzoyl hydrazone and dicyclohexyl carbodiimide (DCC). Oxadiazinones have a 2,3-diaza-1,3-diene functionality and can act as π_4 components in inverse electron demand hetero Diels Alder reactions leading, after loss of nitrogen, to pyrone derivatives and other cyclic compounds [3,5-8]. Almost all of oxadiazinone chemistry concerns these cycloadditions recently reviewed by Christl [3].

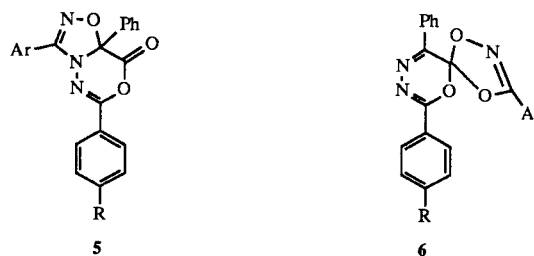
The purpose of this work was to study the dipolarophilic behaviour of oxadiazinones with nitrile oxides. It is obvious that the carbon nitrogen double bonds of **1** could form 1,2,4-oxadiazole ring systems leaving the lactone functionality free for subsequent transformations with nucleophiles. Thus these cycloadducts could be useful synthons for the preparation of highly substituted oxadiazole derivatives, which are known to be of great pharmacological interest [9].

Stable nitrile oxides **2** such as mesitonitrile oxide **2a**

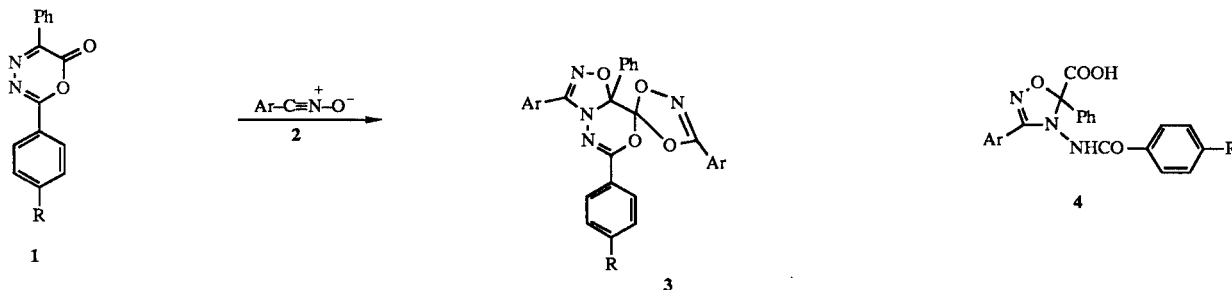
and 2,6-dichlorobenzonitrile oxide **2b** reacted with a series of 2,5-diaryl-1,3,4-oxadiazin-6-ones **1**, prepared according to Steglich procedure [4], in refluxing dry dichloromethane solution. Two main cycloadducts **3** and **4** were usually obtained (Scheme 1).

Compounds **4** were obtained in all cases while compounds **3** only when mesitonitrile oxide was used. Attempts to isolate the bis-adduct **3** with 2,6-dichlorobenzonitrile oxide failed. After prolonged heating of oxadiazinone **1a** with excess of 2,6-dichlorobenzonitrile oxide **2b** only the mono-adduct **4e** was isolated together with the corresponding furoxan, from the well known dimerization

Scheme 2



Scheme 1



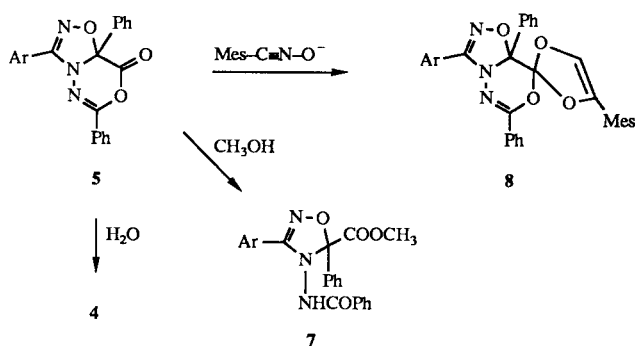
1a, R = H; **1b**, R = -CH₃; **1c**, R = -OCH₃; **1d**, R = -Cl; **1e**, R = -NO₂; **2a**, Ar = 2,4,6-(CH₃)₃C₆H₂; **2b**, Ar = 2,6-Cl₂C₆H₃; **3a**, Ar = 2,4,6-(CH₃)₃C₆H₂, R = H; **3b**, Ar = 2,4,6-(CH₃)₃C₆H₂, R = -CH₃; **3c**, Ar = 2,4,6-(CH₃)₃C₆H₂, R = -OCH₃; **3d**, Ar = 2,4,6-(CH₃)₃C₆H₂, R = -Cl; **3e**, Ar = 2,4,6-(CH₃)₃C₆H₂, R = -NO₂. **4a** Ar = 2,4,6-(CH₃)₃C₆H₂, R = H; **4b**, Ar = 2,4,6-(CH₃)₃C₆H₂, R = -CH₃; **4c**, Ar = 2,4,6-(CH₃)₃C₆H₂, R = -OCH₃; **4d**, Ar = 2,4,6-(CH₃)₃C₆H₂, R = Cl; **4e** Ar = 2,6-Cl₂C₆H₃, R = H; **4f**, Ar = 2,6-Cl₂C₆H₃, R = -CH₃; **4g**, Ar = 2,6-Cl₂C₆H₃, R = -OCH₃.

process of nitrile oxides, and other minor unidentified by-products. In contrast, when mesitonitrile oxide **2a** was used in excess and oxadiazinone **1e** only the bis-adduct **3e** was isolated.

The primary mono-adducts **5** and **6** could not be isolated, although equimolar amounts of the reacting species were used (Scheme 2). The cycloadduct **4** was apparently formed from hydrolysis of the primary mono-adduct **5** during the work up procedure. We note that the above mentioned ring opening occurs to a certain degree only and that an undetermined quantity of the primary cycloadduct **5** is present in the crude reaction mixture, since treatment of the reaction mixture with methanol affords the corresponding ester instead of the free acid (Scheme 3). This could be of interest since it is possible to obtain various 1,2,4-oxadiazole derivatives using different nucleophiles.

On the other hand, the mixed bis-adduct **8** was obtained if both 2,6-dichlorobenzonitrile oxide **2b** and mesitonitrile oxide **2a** were used. Thus 2,5-diphenyl-1,3,4-oxadiazin-6-one **1a** reacted first with an equimolar amount of 2,6-dichlorobenzonitrile oxide **2b**, under anhydrous conditions. After all nitrile oxide was consumed (tlc analysis) an equimolar amount of mesitonitrile oxide was added leading to the final mixed bis-adduct **8**. This is an indication that the formation of the bis-adduct **3** proceeds through the mono-adduct **5** instead of **6**.

Scheme 3



5a, Ar = 2,4,6-(CH_3)₃ C_6H_2 ; **5b**, Ar = 2,6- $\text{Cl}_2\text{C}_6\text{H}_3$; **7a**, Ar = 2,4,6-(CH_3)₃ C_6H_2 ; **7b**, Ar = 2,6- $\text{Cl}_2\text{C}_6\text{H}_3$; **8**, Ar = 2,6- $\text{Cl}_2\text{C}_6\text{H}_3$

Since there are at least two possible isomers for both mono- and the bis-adducts, in order to have an unambiguous structure determination X-ray crystallographic analyses were performed on compounds **3e** and **4f**. A summary of crystal and intensity collection data is given in Table 1.

The established molecular structure and the labeling sequence of **3a** is presented in the ORTEP drawing of Figure 1, which also illustrates the conformational geometry of the molecule. Selected values of bond distances and angles are listed in Table 2 and positional parameters in

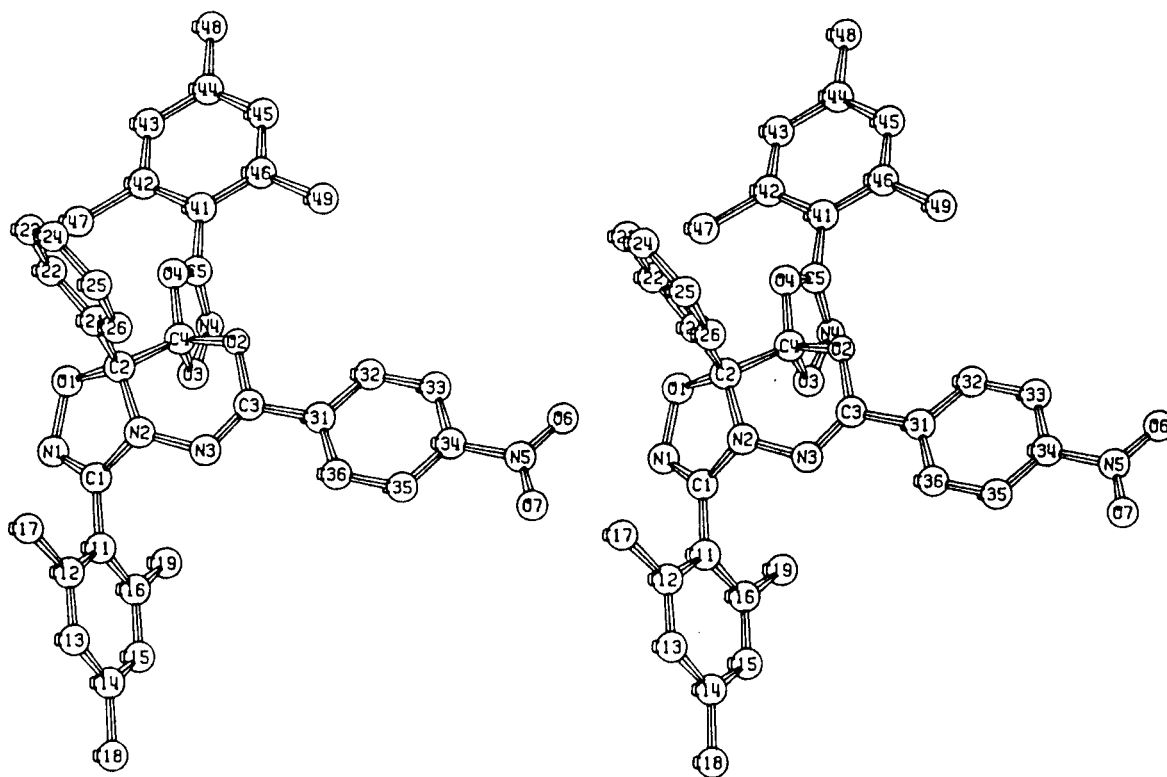
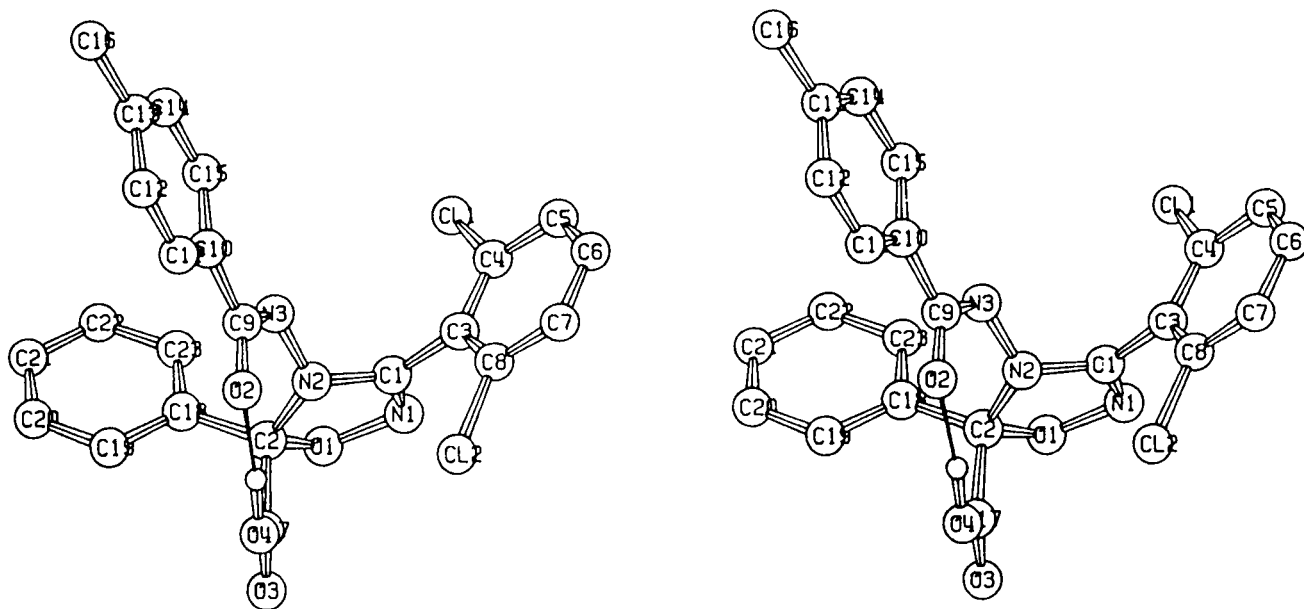
Table 1
Summary of Crystal and Intensity Collection Data

Compound	3e	4f	4f'
Formula	$\text{C}_{34}\text{H}_{31}\text{N}_5\text{O}_5$	$\text{C}_{23}\text{H}_{17}\text{N}_3\text{O}_4\text{Cl}_2$	
rW	589.65	470.31	
a(Å)	10.711(3)	9.070(3)	9.682(3)
b(Å)	17.755(4)	13.352(4)	18.008(6)
c(Å)	16.595(4)	18.537(9)	13.205(3)
β (deg)	93.87(2)	98.52(3)	92.25(2)
$V(\text{Å}^3)$	3149(1)	2220(1)	2301(1)
Z	4	4	4
D _{calcd} (Mg m^{-3})	1.243	1.407	1.357
D _{meas} (Mg m^{-3})	1.23	1.40	1.35
Space group	$P2_1/c$	$P2_1/n$	$P2_1/c$
Radiation	Mo K α $\lambda = 0.71069$		
$\mu(\text{cm}^{-1})$	0.50	2.79	2.69
Scan speed (deg/min)	3.0-16.0	2.5-20.0	2.5-16.0
Scan range (deg)		1.6 plus α_1 - α_2	
Bkgd counting(s)	0.5	0.6	0.6
2θ limit (deg)	48.0	47.0	46.5
Data collected	5711	3962	3740
Data unique	4957	3301	3269
Data used	3898	2493	2619
$F_0 >$	$2\sigma(F_0)$	$4\sigma(F_0)$	$2\sigma(F_0)$
R _{int}	0.0216	0.0184	0.0102
Range of hkl	h 0,12; k 0,20; l -19,19	h 0,10; k -15,0 l -20,20	h -10,10; k -20,0; l -14,0
F(000)	1240	968	968
Nr [1]	491	304	304
$(\Delta/\sigma)_{\text{max}}$	0.029	0.017	0.034
$(\Delta\rho)_{\text{max}}$ ($\text{e}\text{Å}^{-3}$)	0.240	0.172	0.226
$(\Delta\rho)_{\text{min}}$ ($\text{e}\text{Å}^{-3}$)	-0.172	-0.260	-0.276
S [2]	1.11	0.83	1.06
R [3] (obsd)	0.0529	0.0416	0.0595
R [3] (all data)	0.0763	0.0598	0.0736
R _w [4] (obsd)	0.0476	0.0383	0.0521
R _w [4] (all data)	0.0620	0.0516	0.0601

[1] Nr = Number of refined parameters. [2] $S = [\sum w(\Delta F)^2 / (N-P)]^{1/2}$ P = Nb of parameters, N = Nb of observed reflections. [3] $R = \sum |\Delta F| / \sum |F_0|$. [4] $R_w = [\sum w(\Delta F)^2 / \sum w |F_0|^2]^{1/2}$.

Table 3. The intramolecular bond lengths and angles are in line with the hybridization expected to all atoms. The mesityl groups attached to C_1 of oxadiazoline ring and to C_5 dioxazole ring are almost perpendicular to the linked rings, while the *p*-nitrophenyl group adopts an almost coplanar conformation to the linked ring.

In the case of **4f** in the crystallization dish there were two kinds of morphologically different crystals. We solved the structure of both and then turned out to be two phases **4f** and **4f'** of the same compound crystallizing in different space groups (Table 1). Positional parameters for **4f** and **4f'** are given in Tables 4 and 5 and Figure 2 an ORTEP drawing of **4f** illustrates the assigned structure and the labeling sequence. Selected bond distances and angles of **4f** are listed in Table 6. Few corresponding bond distances and angles in structures **4f** and **4f'** differ by more than 2 esds' and none by more than 3 esds'. Most of the corre-

Figure 1. ORTEP drawing for compound **3e**.Figure 2. ORTEP drawing for compound **4f**.

sponding torsion angles differ by less than four degrees. The only exception (Table 6) are the torsion angles at bonds around which free rotation is allowed (N_2-N_3 , N_3-C_9 , C_9-C_{10} , C_1-C_3 and C_2-C_{16}). The differences in these torsion

angles range between 15 and 25 degrees and it is probably these differences that led to the two different phases **4f** and **4f'**. There are two hydrogen bonds in **4f** and **4f'**; one very strong intramolecular, $O_4-H_4 \cdots O_2$, and one intermolec-

Table 2

Selected Bond Distances and Angles for Compound 3e

a. Bond distances (Å)

O ₁ -N ₁	1.445(3)	C ₄ -C ₂	1.531(4)
N ₁ -C ₁	1.275(4)	C ₂ -C ₂₁	1.520(4)
C ₁ -N ₂	1.401(4)	C ₃ -C ₃₁	1.471(4)
N ₂ -C ₂	1.462(4)	C ₄ -O ₄	1.393(3)
C ₂ -O ₁	1.424(4)	C ₅ -O ₄	1.375(3)
C ₁ -C ₁₁	1.476(4)	C ₅ -N ₄	1.266(4)
N ₂ -N ₃	1.381(3)	N ₄ -O ₃	1.445(3)
N ₃ -C ₃	1.275(4)	O ₃ -C ₄	1.398(4)
C ₃ -O ₂	1.379(3)	C ₅ -C ₄₁	1.469(4)
C ₄ -O ₂	1.425(3)		

b. Angles (°)

O ₁ -N ₁ -C ₁	107.2(2)	O ₂ -C ₄ -C ₂	108.7(2)
N ₁ -C ₁ -N ₂	113.6(3)	C ₄ -C ₂ -N ₂	106.2(2)
C ₁ -N ₂ -C ₂	106.5(2)	N ₃ -C ₃ -C ₃₁	121.1(2)
N ₂ -C ₂ -O ₁	103.5(2)	C ₄ -O ₃ -N ₄	106.8(2)
C ₂ -O ₁ -N ₁	109.0(2)	O ₃ -N ₄ -C ₅	105.1(2)
C ₁₁ -C ₁ -N ₁	124.8(3)	N ₄ -C ₅ -O ₄	115.2(3)
C ₂₁ -C ₂ -O ₁	110.6(2)	C ₅ -O ₄ -C ₄	104.8(2)
C ₂ -N ₂ -N ₃	123.4(2)	O ₄ -C ₄ -O ₃	106.3(2)
N ₂ -N ₃ -C ₃	116.9(2)	O ₄ -C ₅ -C ₄₁	118.9(2)
N ₃ -C ₃ -O ₂	124.8(2)	N ₄ -C ₅ -C ₄₁	125.8(3)
C ₃ -O ₂ -C ₄	112.7(2)		

Table 3

Positional Parameters (x 10⁴) for Carbon Nitrogen and Oxygen Atoms of 3e

Atom	X	Y	Z
O(1)	1640(2)	2342(1)	9451(1)
N(1)	1397(3)	1541(2)	9436(2)
C(1)	1994(3)	1257(2)	10053(2)
N(2)	2627(2)	1791(1)	10549(1)
C(2)	2366(3)	2525(2)	10174(2)
N(3)	3766(2)	1603(1)	10937(1)
C(3)	4585(3)	2124(2)	11017(2)
O(2)	4453(2)	2835(1)	10689(1)
C(4)	3634(3)	2849(2)	9976(2)
O(3)	4169(2)	2441(1)	9367(1)
N(4)	4703(3)	2983(1)	8840(2)
C(5)	4322(3)	3617(2)	9071(2)
O(4)	3587(2)	3596(1)	9719(1)
C(11)	2013(3)	448(2)	10259(2)
C(12)	1171(3)	171(2)	10792(2)
C(17)	202(3)	677(2)	11133(2)
C(13)	1223(3)	-587(2)	10982(2)
C(14)	2074(3)	-1072(2)	10662(2)
C(18)	2076(4)	-1908(2)	10862(3)
C(15)	2884(3)	-784(2)	10132(2)
C(16)	2866(3)	-28(2)	9919(2)
C(19)	3734(4)	269(2)	9310(2)
C(21)	1646(3)	3051(2)	10697(2)
C(22)	906(4)	3618(3)	10339(3)
C(23)	273(5)	4105(3)	10813(5)
C(24)	382(5)	4046(3)	11633(4)
C(25)	1098(4)	3489(2)	11998(3)
C(26)	1722(3)	2991(2)	11522(2)
C(31)	5787(3)	1998(2)	11480(2)
C(32)	6780(3)	2493(2)	11434(2)
C(33)	7899(3)	2362(2)	11868(2)
C(34)	8015(3)	1733(2)	12346(2)
N(5)	9190(3)	1599(2)	12837(2)
O(6)	10045(2)	2039(2)	12785(2)

O(7)	9261(2)	1047(2)	13270(2)
C(35)	7058(3)	1229(2)	12398(2)
C(36)	5939(3)	1362(2)	11964(2)
C(41)	4548(3)	4345(2)	8686(2)
C(42)	3659(3)	4602(2)	8095(2)
C(47)	2471(4)	4159(3)	7877(3)
C(43)	3915(3)	5265(2)	7692(2)
C(44)	5000(3)	5665(2)	7860(2)
C(48)	5254(4)	6365(2)	7375(2)
C(45)	5838(3)	5407(2)	8467(2)
C(46)	5639(3)	4752(2)	8891(2)
C(49)	6588(3)	4479(2)	9543(2)

Table 4

Positional Parameters (x 10⁴) for Non-hydrogen Atoms of 4f

Atom	X	Y	Z
CL(1)	-3245(1)	2712.7(9)	6897.6(9)
CL(2)	-2924(2)	622(1)	9826(1)
C(1)	-2069(4)	2059(2)	8860(3)
N1	-2289(3)	2658(2)	9332(2)
O(1)	-957(2)	2926(1)	9699(2)
C(2)	17(3)	2334(2)	9622(2)
N(2)	-720(3)	1815(2)	8920(2)
C(3)	-3178(4)	1642(2)	8331(3)
C(4)	-3810(4)	1901(3)	7442(3)
C(5)	-4887(5)	1526(4)	6954(4)
C(6)	-5321(6)	877(5)	7368(6)
C(7)	-4725(7)	590(4)	8241(6)
C(8)	-3654(5)	975(3)	8720(4)
N(3)	-141(3)	1507(2)	8073(2)
C(9)	467(4)	835(2)	8181(3)
O(2)	557(3)	527(2)	9014(2)
C(10)	1010(4)	484(2)	7257(3)
C(11)	1558(5)	-211(2)	7328(3)
C(12)	2132(5)	-547(2)	6509(3)
C(13)	2158(5)	-196(2)	5600(3)
C(14)	1590(6)	484(3)	5526(4)
C(15)	1000(6)	827(3)	6334(3)
C(16)	2852(7)	-548(3)	4702(4)
C(17)	177(4)	1975(3)	10685(3)
O(3)	164(3)	2357(2)	11428(2)
O(4)	334(4)	1257(2)	10740(2)
C(18)	1370(4)	2629(2)	9259(3)
C(19)	2624(5)	2377(3)	9675(4)
C(20)	3834(6)	2671(5)	9319(6)
C(21)	3811(8)	3192(5)	8577(6)
C(22)	2585(7)	3433(4)	8153(4)
C(23)	1353(5)	3153(3)	8500(3)

ular, N₃-H₃...O₃ [O₄...O₂ = 2.647(4) Å (4f) and 2.624(3) Å (4f'), O₄-H₄...O₂ = 168(5)° (4f) and 174(3)° (4f'); N₃...O₃ = 3.008(4) Å (4f) and 2.998(3) Å (4f'), N₃-H₃...O₃ = 173(3)° (4f) and 170(3)° (4f').

Analytical and spectral data (ir, ¹H nmr, ms), are summarized in Tables 7 and 8. As regards mono-adducts 4 unusually high frequencies (about 1750 cm⁻¹) are observed for the carbonyl group, band which is usually assigned to monomer form of carboxylic acids. This is in line with the already mentioned very strong intramolecular hydrogen bond observed (O₄-H₄...O₂) and also to the shorter length (C₁₇-O₃ = 1.198(5) Å for 4f and 1.202(4) Å 4f') of carboxylic carbon oxygen double bond, comparing with a typical

Table 5
Positional Parameters ($\times 10^4$) for Non-hydrogen Atoms of **4f**

Atom	X	Y	Z
CL(1)	6323(1)	2428.5(7)	7621.1(6)
CL(2)	5793(1)	5702.4(8)	5910.9(6)
C(1)	5050(3)	4441(2)	7147(2)
N(1)	5379(3)	5011(2)	7696(1)
O(1)	4006(2)	5217(2)	7967(1)
C(2)	2776(3)	4883(2)	7445(2)
N(2)	3541(2)	4271(2)	6950(1)
C(3)	6176(3)	4030(2)	6730(2)
C(4)	6851(3)	3115(2)	6909(2)
C(5)	7953(4)	2743(3)	6539(2)
C(6)	8358(4)	3294(4)	5982(3)
C(7)	7709(4)	4196(4)	5778(2)
C(8)	6626(4)	4568(3)	6153(2)
N(3)	3036(3)	3364(2)	6641(1)
C(9)	2439(3)	3348(2)	5929(2)
O(2)	2014(3)	4127(2)	5609(1)
C(10)	2333(3)	2359(2)	5561(1)
C(11)	1372(3)	2230(3)	4919(2)
C(12)	1265(4)	1311(3)	4571(2)
C(13)	2128(4)	513(2)	4846(2)
C(14)	3122(4)	657(2)	5463(2)
C(15)	3230(4)	1564(2)	5822(2)
C(16)	1999(5)	-504(3)	4474(2)
C(17)	2074(4)	5823(2)	7042(2)
O(3)	1909(3)	6573(2)	7379(1)
O(4)	1656(3)	5772(2)	6338(2)
C(18)	1675(3)	4330(2)	7837(2)
C(19)	203(3)	4622(2)	7792(2)
C(20)	-719(3)	4135(3)	8211(2)
C(21)	-180(4)	3362(3)	8664(2)
C(22)	1263(4)	3057(2)	8702(2)
C(23)	2188(3)	3544(2)	8294(2)

Table 6
Selected Bond Distances and Angles for Compound **4f**

a. Bond distances (Å)			
C ₁ -N ₁	1.268(5)	C ₁₇ -O ₃	1.198(5)
N ₁ -O ₁	1.443(4)	C ₂ -C ₁₈	1.509(5)
O ₁ -C ₂	1.430(4)	C ₂ -N ₂	1.480(4)
C ₂ -C ₁₇	1.548(5)	N ₂ -C ₁	1.377(4)
C ₁₇ -O ₄	1.305(5)	N ₂ -N ₃	1.386(4)
b. Angles (°)			
N ₁ -C ₁ -N ₂	114.8(3)	N ₃ -C ₉ -O ₂	120.8(3)
O ₁ -N ₁ -C ₁	106.5(3)	O ₂ -C ₉ -C ₁₀	121.8(3)
C ₂ -O ₁ -N ₁	108.1(2)	N ₃ -C ₉ -C ₁₀	117.4(3)
N ₂ -O ₂ -O ₁	102.3(2)	N ₂ -C ₁ -C ₃	122.6(3)
C ₂ -N ₂ -C ₁	105.5(3)	N ₂ -C ₂ -C ₁₈	115.3(3)
N ₁ -C ₁ -C ₃	122.5(3)	C ₂ -C ₁₇ -O ₄	118.1(3)
C ₁ -N ₂ -N ₃	119.6(3)	C ₂ -C ₁₇ -O ₃	120.0(4)
N ₂ -N ₃ -C ₉	117.5(3)	O ₄ -C ₁₇ -O ₃	121.9(4)
c. Torsion angles for 4f and 4f' (°)			
	4f	4f'	
C ₁ -N ₂ -N ₃ -C ₉	-127.7(4)	-109.9(3)	
N ₁ -C ₁ -C ₃ -C ₄	71.5(6)	90.9(5)	
N ₁ -C ₁ -C ₃ -C ₈	-107.1(6)	-87.3(5)	
O ₁ -C ₂ -C ₁₇ -O ₃	-37.3(6)	-42.2(5)	
O ₁ -C ₂ -C ₁₇ -O ₄	143.1(4)	138.7(3)	
N ₂ -C ₁ -C ₃ -C ₄	111.4(5)	-90.0(4)	
N ₂ -C ₁ -C ₃ -C ₈	70.1(6)	89.8(5)	
N ₂ -C ₂ -C ₁₇ -O ₃	-147.3(4)	-152.1(4)	
N ₂ -C ₂ -C ₁₇ -O ₄	33.1(6)	28.8(5)	

Table 7
Analytical and Spectral Data of **3**

Compound	Mp °C	Yield %	Molecular Formula	Analysis %			Spectral Data
				Calcd.	Found		
				C	H	N	
3a	218-221	15	C ₃₅ H ₃₂ N ₄ O ₄ M.W. 572.6	73.41	5.63	9.79	ir (nujol): 1640, 1610 (C=N) cm ⁻¹ ; ¹ H nmr (deuteriochloroform): δ 2.3, 2.4 (s, 18H), 6.9 (s, 4H), 7.1-7.9 (m, 10H); ms: m/z 382, 264, 222, 161, 145, 130 (base), 119, 105, 103, 77.
				73.58	5.94	10.01	
3b	225-228	18	C ₃₆ H ₃₄ N ₄ O ₄ M.W. 586.7	73.70	5.84	9.55	ir (nujol): 1630, 1610 (C=N) cm ⁻¹ ; ¹ H nmr (deuteriochloroform): δ 2.3, 2.4 (s, 21H), 6.9 (s, 4H), 7.0-7.75 (m, 9H); ms: m/z 397, 264, 236, 161, 145 (base), 133, 130, 119, 117, 105, 103, 91, 77.
				73.46	5.67	9.76	
3c	212-215	34	C ₃₆ H ₃₄ N ₄ O ₅ M.W. 602.7	71.74	5.69	9.30	ir (nujol): 1640, 1610 (C=N) cm ⁻¹ ; ¹ H nmr (deuteriochloroform): δ 2.3, 2.4 (s, 18H), 3.75 (s, 3H), 6.8-7.8 (m, 13H); ms: m/z 440, 413, 280, 264, 252, 235, 161, 149, 145 (base), 133, 130, 117, 106, 105, 103, 77.
				71.86	5.66	9.52	
3d	220-221	20	C ₃₅ H ₃₁ N ₄ O ₄ Cl M.W. 607.1	69.24	5.15	9.23	ir (nujol): 1640, 1600 (C=N) cm ⁻¹ ; ¹ H nmr (deuteriochloroform): δ 2.35, 2.45 (s, 18H), 6.95 (b s, 4H), 7.15-7.9 (m, 9H); ms: m/z 606 (M ⁺), 416, 274, 264, 235, 161, 145, 139, 137, 130, 105, 103, 91, 77.
				69.39	5.09	9.14	
3e	233-235	35	C ₃₅ H ₃₁ N ₅ O ₆ M.W. 617.6	68.05	5.05	11.33	ir (nujol): 1640, 1605 (C=N) cm ⁻¹ ; ¹ H nmr (deuteriochloroform): δ 2.35, 2.43 (s, 18H), 6.91 (b s, 4H), 7.2-8.3 (m, 9H); ms: m/z 264, 164, 161, 145, 130 (base), 115, 105, 103, 91, 77.
				68.05	4.96	11.14	

Table 8
Analytical and Spectral Data of 4

Compound	Mp °C	Yield %	Molecular Formula	Analysis %			Spectral Data
				Calcd./Found	C	H	
4a	223-225	20	C ₂₅ H ₂₃ N ₃ O ₄ M.W. 429.5	69.91	5.40	9.79	ir (nujol): 3280 (NH), 1750 (C = O), 1640, 1630 (C = O and/or C=N) cm ⁻¹ ; ¹ H nmr (deuteriochloroform/DMSO-d ₆): δ 2.15 (s, 3H), 2.4 (s, 6H), 6.8 (s, 2H), 7.2-7.85 (m, 10H), 9.4 (b s, 1H); ms: m/z 385, 264, 240, 223, 161, 145, 117, 105 (base) 103.
				70.07	5.31	9.86	
4b	187-190	22	C ₂₆ H ₂₅ N ₃ O ₄ M.W. 443.5	70.41	5.68	9.48	ir (nujol): 3250 (NH), 1740 (C = O), 1630, 1620 (C = O and/or C = N) cm ⁻¹ ; ¹ H nmr (deuteriochloroform): δ 2.1 (s, 3H), 2.2 (s, 6H), 6.85 (s, 2H), 6.9-7.8 (m, 9H), ms: m/z 399, 264, 254, 236, 161, 145, (base), 130, 119, 117, 105, 103, 77.
				70.67	5.38	9.37	
4c	186-189	32	C ₂₆ H ₂₅ N ₃ O ₅ M.W. 459.5	67.69	5.48	9.15	ir (nujol): 3250 (NH), 1740, 1720 (C = O), 1610, inflections at 1620, 1640 (C = O and/or C = N) cm ⁻¹ ; ¹ H nmr(deuteriochloroform): δ 2.22 (s, 3H), 2.36 (s, 6H), 3.74 (s, 3H), 6.7 (d, 2H, J = 8 Hz) 6.86 (s, 2H), 7.15-7.78 (m, 7H), ms: m/z 415, 270, 264, 161, 145, 135, 133, 130 (base), 119, 115, 105, 103, 92, 77.
				67.78	5.31	8.91	
4d	185-188	20	C ₂₅ H ₂₂ N ₃ O ₄ Cl M.W. 463.9	64.72	4.78	9.05	ir (nujol): 3250 (NH), 1750 (C = O), 1630, 1610 (C = O and/or C=N) cm ⁻¹ ; ¹ H nmr (DMSO, d ₆): 2.2 (s, 3H), 2.4 (s, 6H), 6.8 (s, 2H), 7.2-7.6 (m, 7H), 7.65-7.94 (m, 2H), 9.2 (b s, 1H); ms: m/z 419, 274, 264, 161, 145 (base), 139, 137, 130, 119, 105, 103, 77.
				64.70	4.68	9.15	
4e	190-193	32	C ₂₂ H ₁₅ N ₃ O ₄ Cl ₂ M.W. 456.3	57.94	3.31	9.21	ir (nujol): 3220 (NH), 1750 (C = O), 1640, 1630 (C = O and/or C=N) cm ⁻¹ ; ¹ H nmr (deuteriochloroform): δ 7.2-7.8 (m); ms: m/z 411, 290, 240, 187, 171 (base), 136, 121, 119, 105, 103.
				57.81	3.48	9.04	
4f	180-183	55	C ₂₃ H ₁₇ N ₃ O ₄ Cl ₂ M.W. 470.3	58.73	3.64	8.93	ir (nujol): 3280 (NH), 1760 (C = O), 1625, 1605 (C = O and/or C=N) cm ⁻¹ ; ¹ H nmr (deuteriochloroform): δ 2.28 (s, 3H), 6.8-7.8 (m, 12H), ms: m/z 425, 290, 254, 187, 171 (base), 136, 119, 105, 103.
				58.55	3.65	8.69	
4g	182-185	37	C ₂₃ H ₁₇ N ₃ O ₅ Cl ₂ M.W. 486.3	56.80	3.52	8.64	ir (nujol): 3220 (NH), 1750 (C = O), 1625, 1605 (C = O and/or C=N) cm ⁻¹ ; ¹ H nmr (deuteriochloroform): δ 3.55 (s, 3H), 6.7-7.9 (m, 12H); ms: m/z 441, 290, 270, 224, 187, 171 (base), 136, 135, 105, 103.
				57.11	3.50	8.67	

one of carboxylic acids (about 1.23 Å). Analogous high frequency carbonyl absorption has been observed in the case of a closely related isoxazoline carboxylic acid [10]. In the mass spectra, a M-44 fragment is observed instead of the molecular ion together with other decomposition fragments. In respect to the bis-adducts **3** there is no carbonyl absorption but instead a C=N absorption at 1630-1620 cm⁻¹ is observed. In the mass spectra there is no peak for the molecular ion. A peak arising from the molecular ion by splitting off a nitrile oxide molecule (m/z 161) and carbon dioxide is observed at high mass units.

All reactions studied showed a remarkable site selectivity. There are three dipolarophilic centers in oxadiazinone molecule, two carbon nitrogen double bonds and one carbon oxygen double bond. The carbon nitrogen double bond which is adjacent to the carbonyl group is the more reactive dipolarophilic center, since it is activated by the adjacent electron-withdrawing carbonyl group and thus has more double bond character. This is consistent with the fact that all the mono-adducts as well as the bis-adducts that were isolated are the results of cycloaddition to this carbon nitrogen double bond.

The other carbon nitrogen double bond which is next to the oxygen atom seems to be unreactive. Surprisingly, in contrast to early statements [11,12], the carbonyl double bond is the next most reactive dipolarophilic center. To the best of our knowledge, this is the first reported cycloaddition of a nitrile oxide to an "ester type" carbonyl double bond. It has been assumed that the bis-adduct **3** arises through intermediate **5**. If this is true, then the oxadiazole ring seems to activate the carbonyl double bond. Nevertheless, steric factors could also be invoked to explain this peculiar behaviour.

As regards the different behaviour of 2,6-dichloro benzonitrile oxide which gives only mono-adducts **4**, we note that we have already observed [13,14] analogous differences, where mesitonitrile oxide reacts more readily with carbon oxygen double bond, than 2,6-dichloro benzonitrile oxide. This seems to be reasonable if one considers that cycloadditions to carbonyl double bond are HOMO-dipole controlled reactions [10]. It is evident that these reactions proceed better with mesitonitrile oxide which has higher HOMO energy and consequently, is more nucleophilic than 2,6-dichlorobenzonitrile oxide [15]. Besides,

the lowering of LUMO energy caused by chlorine atoms in 2,6-dichlorobenzonitrile oxide favours LUMO dipole controlled reactions leading to mono-adducts **4**.

EXPERIMENTAL

All melting points are uncorrected and they were obtained with a hot stage apparatus. The ir spectra were obtained with a Perkin-Elmer 297 spectrometer. The ¹H nmr spectra, reported in δ units, (TMS), were recorded with a Bruker AW 80 spectrometer, whereas mass spectra were measured with a Hitachi-Perkin-Elmer Model RMU-6L spectrometer with an ionization energy of 70 eV. Mesitronitrile oxide **2a** and 2,6-dichlorobenzonitrile oxide **2b** were prepared according to Grundmann procedure [16], while oxadiazinones **1** were prepared as reported [4] from the corresponding phenyl glyoxylic acid aroyl hydrazones and dicyclohexyl carbodiimide.

General Procedure for the Cycloaddition Reactions of Oxadiazinones **1** with Nitrile Oxides.

A solution of oxadiazinone (3 mmoles) and nitrile oxide (3.2 mmoles) in methylene chloride (20 ml) was refluxed for about six days. The course of the reaction was monitored by tlc. The dichloromethane was partly removed *in vacuo*. Hexane was added and compounds **4** were crystallized out. Recrystallization with dichloromethane-hexane gave pure analytical samples. Analytical as well as spectral data for all compounds **4** are given in Table 8. The filtrates after evaporation of the solvent were chromatographed on Silica gel column using a 30% ethyl acetate-hexane mixture to give bis-adducts **3** in all reactions with mesitronitrile oxide **2a**. Analytical samples were obtained after recrystallization with dichloromethane-hexane mixtures. As regards bis-adduct **3e** this was prepared by the same way using excess of mesitronitrile oxide (1:2). Under these conditions mono-adduct **4** could not be isolated. Spectral and analytical data for all compounds **3** are given in Table 7.

Preparation of Methyl Esters **7**.

Oxadiazinone **1a** (0.4 g, 1.6 mmoles) and mesitronitrile oxide **2a** (0.275 g, 1.7 mmoles) in dry dichloromethane (20 ml) was refluxed for 6 days. At the end of the reaction (tlc) methanol (10 ml) was added and the mixture was refluxed for half an hour. A part of bis-adduct **3a** was crystallized out and the residue was subjected to silica gel chromatography, using a 35% ethyl acetate-hexane mixture as the eluant to give compound **3a** (total yield 10%) and the methyl ester **7a** in 39% yield, mp 179-182° (dichloromethane-hexane); ir (Nujol): 3325 (NH), 1720, 1705, inflection at 1690 (C=O), 1610 (C=N) cm⁻¹; ¹H nmr (deuteriochloroform): δ 2.2 (s, 3H), 2.45 (s, 6H), 3.9 (s, 3H), 6.95 (s, 2H), 7.2-7.95 (m, 10H), 8.4 (s, 1H); ms: m/z 443, 384, 282, 264, 223, 161, 145, 130, 105 (base) 103, 91, 77.

Anal. Calcd. for C₂₆H₂₅N₃O₄ (MW 443.48): C, 70.41; H, 5.68; N, 9.48. Found: C, 70.56; H, 5.60; N, 9.69.

Methyl ester **7b** was prepared in a similar way described above using excess of 2,6-dichlorobenzonitrile oxide **2b**. Silica gel chromatography of crude reaction mixture using a 30% ethyl acetate-hexane mixture as the eluant gave the methyl ester **7b** in 80% yield; mp 191-193° (dichloromethane-hexane); ir (Nujol): 3310 (NH), 1735, 1700, 1660 (C=O), 1610 (C=N) cm⁻¹; ¹H nmr (deuteriochloroform): δ 3.9 (s, 3H), 7.2-7.9 (m, 13H), 8.8 (s, 1H); ms: m/z 470, 411, 307, 290, 223, 187, 171, 136, 105 (base), 103, 77.

Anal. Calcd. for C₂₅H₁₇N₃O₄Cl₂ (MW 471.3): C, 58.73; H, 3.64; N, 8.93. Found: C, 58.89; H, 3.84; N, 8.93.

Preparation of Mixed bis-Adduct **8**.

Oxadiazinone **1a** (0.4 g, 1.6 mmoles) and 2,6-dichlorobenzonitrile oxide **2b** (0.3 g, 1.6 mmoles) in dry dichloromethane (20 ml) was refluxed for three days. Then mesitronitrile oxide (0.26 g, 1.6 mmoles) was added and refluxed for four days. The crude reaction mixture was chromatographed on silica gel using a 30% ethyl acetate-hexane mixture as the eluant to give bis-adduct **8** in a 20% yield, mp 194-196° (dichloromethane-hexane); ir (nujol): 1635, 1610 (C=N) cm⁻¹; ¹H nmr (deuteriochloroform): δ 2.31 (s, 3H), 2.46 (s, 6H), 6.95 (s, 2H), 7.19-7.94 (m, 13H); ms: m/z 290, 222, 187, 171, 161, 145, 130, 119 (base), 105, 103, 91, 77.

Anal. Calcd. for C₃₂H₂₄N₄O₄Cl₂ (MW 599.4): C, 64.11; H, 4.03; N, 9.35. Found: C, 64.31; H, 4.11; N, 9.30.

Crystallographic Analysis.

Crystals suitable for X-ray were obtained by slow evaporation of dichloromethane-hexane solutions. Photographic investigation indicated the space group of all three crystals (Table 3). The data were collected on a Syntex P2₁ diffractometer. Lattice parameters were refined by a least-square procedure using 15 automatically controlled reflections. Periodically monitored reference reflections showed no significant changes in intensities for **3e**, but a systematic decrease in intensities (10%) for **4f** and **4f'**. A correction for this was applied during data reduction. Lorentz and polarization but no absorption corrections were applied. All three structures were solved by direct methods using SHELXS 86 [17] and all non-hydrogen atom were located from the E-maps. The methyl hydrogen of **3a** and all the hydrogens of **4f** and **4f'** except H₃ and H₄ were located from a ΔF synthesis and refined isotropically, while the non-hydrogen atoms were refined anisotropically using unit weights and the program SHELX 76 [18]. The atomic scattering factors were taken from the International Tables [19]. Lists of Positional parameters of the hydrogen atoms, thermal parameters for all atoms and structure factor amplitudes may be obtained from the author (A. T.).

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