A New Domino Reaction based on [4+2]-Cycloadditions of Pyrido[1,2-*a*]pyrazines with Azadienophiles

Thomas Billert [1], Rainer Beckert [1], Peer Fehling [2], Manfred Döring [2], Jörg Brandenburg [1], Helmar Görls [2] and Peter Langer [3]

[1] Institut für Organische und Makromolekulare Chemie, Friedrich-Schiller-Universität,
Humboldtstraße 10, 07743 Jena, Germany
[2] Institut für Anorganische und Analytische Chemie, Friedrich-Schiller-Universität,
August-Bebel-Straße 2, 07743 Jena, Germany
[3] Institut für Organische Chemie, Georg-August-Universität,
Tammannstraße 2, 37077 Göttingen, Germany

Received October 7, 1998

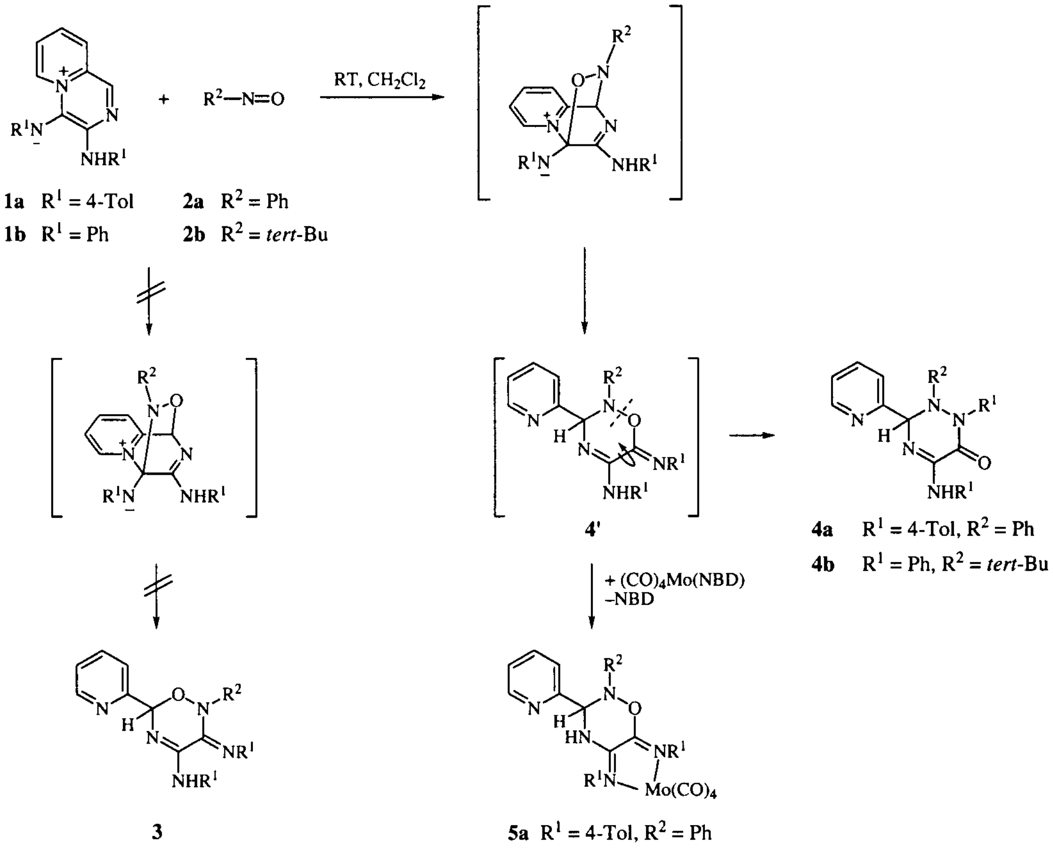
The reaction of pyrido[1,2-*a*]pyrazines **1** with nitroso compounds **2** provides pyridyl substituted 1,2,4-triazinones **4** *via* a domino reaction which involves a cycloaddition and a ring transformation reaction. The intermediate and regioselective formed oxadiazines **4'** were trapped by complexation yielding the $(CO)_4$Mo-complex **5**. Derivatives of diazene such as *N*-phenyltriazolindione **6a**, phthalazinedione **6b** or esters of azodicarboxylic acid **6c-6f** reacted with **1** to give different derivatives of 1,2,4-triazine **7a-f**. The use of oxygen gave oxadiazinones **8**.

J. Heterocyclic Chem., **36**, 627 (1999).

Introduction.

Ring transformation reactions constitute an efficient route for the synthesis of highly substituted cyclic compounds in the chemistry of natural products, in material sciences and in pharmaceutical chemistry [1]. In this context, nitrogen containing rings as tetrazines, triazines, pyridazines and related ring systems are among the most useful heterocycles and their utility has been widely demonstrated [2]. Recently, we described the facile preparation of pyrido[1,2-*a*]pyrazines **1** and their use as hetero-

Scheme 1



dienes in a cycloaddition/ring transformation sequence performed in one-pot [3]. As dienophiles derivatives of acetylene dicarboxylic acid, maleimides and quinones were used. Starting with juglone, cycloaddition was shown to proceed regioselectively [4]. These results encouraged us to study C-nitroso compounds and derivatives of diazene as dienophiles.

Results and Discussion.

The equimolar reaction of nitrosobenzene **2a** with **1a** under mild conditions resulted in the regioselective formation of the new heterocycle **4a** in very good yield. It is noteworthy, that triazinone **4a** was formed rather than the expected isomeric oxadiazine **4'** (Scheme 1).

Formation of **4a** can be described by the following mechanism: Initial [4+2]-cycloaddition of nitrosobenzene with **1** followed by a ring transformation *via* regeneration of the pyridine ring gave the intermediate **4'**. Subsequent Dimroth-rearrangement of **4'** in the course of aqueous work up finally afforded **4a**. As shown in Scheme 1, intermediate **4'** could be trapped by complexation. Adding $(CO)_4Mo$(norbornadiene) to the reaction mixture of **1a** and **2a** resulted in a deeply red colored solution, indicating the coordination of a 1,4-diazadiene moiety to the $Mo(CO)_4$ fragment [5]. The molybdenum complex **5a** was identified by spectroscopic methods and by elemental analysis. Starting from the final product **4a**, formation of an analogous complex has not been observed.

In order to independently prove the regiochemistry, the structure of **4a** was confirmed by X-ray crystallographic analysis (Figure 1).

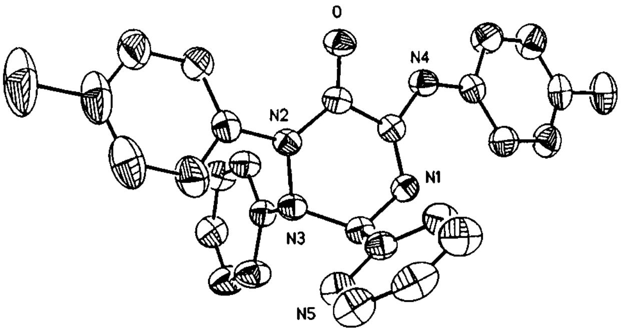


Figure 1. ORTEP drawing of the molecule **4a**.

Computational investigations confirmed the experimental results. HMO calculations of the π-energy E_π of the transition states **3** and **4'** clearly showed an energetical preference for the formation of **4'** [6]. The comparison of the heats of formation of **4'** and **4** by AM1 calculations [6] showed an energetical advantage of 21.2 kcal/mol for **4**. These results confirm the higher stability of the isolated Dimroth-rearranged compound **4** (Table 5) [7].

Table 1

Atomic Coordinates [x 10^4] and Equivalent Isotropic Displacement Parameters [$Å^2$ x 10^3] for **4a**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
O	2606(1)	-80(1)	3194(1)	62(1)
N(1)	3188(1)	-2200(1)	2236(1)	55(1)
N(2)	20540)	-1370(1)	2701(1)	52(1)
N(3)	2075(1)	-2269(1)	2254(1)	53(1)
N(4)	3547(1)	-570(2)	2227(1)	59(1)
N(5)	2171(1)	-3740(2)	3486(1)	68(1)
C(1)	2648(1)	-2782(2)	2420(1)	53(1)
C(2)	3123(1)	-1270(2)	2379(1)	52(1)
C(3)	2570(1)	-835(2)	27880)	51(1)
C(4)	4117(1)	-652(2)	1842(1)	58(1)
C(5)	4391(1)	-1526(2)	1646(2)	77(1)
C(6)	4952(1)	-1521(3)	1253(2)	88(1)
C(7)	5248(1)	-671(3)	1055(2)	76(1)
C(8)	4975(1)	192(3)	1263(2)	95(1)
C(9)	4413(1)	212(2)	1654(2)	85(1)
C(10)	5858(1)	-678(3)	633(2)	106(1)
C(11)	1473(1)	-1109(2)	3022(1)	60(1)
C(12)	1075(1)	-1841(3)	3251(2)	92(1)
C(13)	509(2)	-1593(4)	3539(2)	120(1)
C(14)	320(2)	-642(5)	3615(2)	119(2)
C(15)	722(2)	75(3)	3390(3)	127(2)
C(16)	1294(1)	-145(3)	3091(2)	97(1)
C(17)	-315(2)	-392(5)	3919(3)	189(3)
C(18)	1912(1)	-2158(2)	1405(1)	52(1)
C(19)	1781(1)	-3004(2)	971(2)	81(1)
C(20)	1626(2)	-2945(2)	154(2)	90(1)
C(21)	1588(1)	-2054(2)	-234(2)	77(1)
C(22)	1698(1)	-1218(2)	203(2)	76(1)
C(23)	1866(1)	-1261(2)	1021(1)	65(1)
C(24)	2653(1)	-3181(2)	3292(1)	56(1)
C(25)	3119(1)	-3013(2)	3830(2)	76(1)
C(26)	3085(2)	-3396(2)	4610(2)	94(1)
C(27)	2586(2)	-3939(2)	4826(2)	86(1)
C(28)	2150(2)	-4101(2)	4246(2)	80(1)

Table 2

Anisotropic Displacement Parameters [$Å^2$ x 10^3] for **4a**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[(ha^*)^2U_{11}+...+2hka^*b^*U_{12}]$.

	U11	U22	U33	U23	U13	U12
O	68(1)	57(1)	59(1)	-12(1)	7(1)	-6(1)
N(1)	60(1)	55(1)	50(1)	0(1)	4(1)	-1(1)
N(2)	57(1)	55(1)	45(1)	-7(1)	4(1)	-2(1)
N(3)	62(1)	52(1)	45(1)	-6(1)	-1(1)	-1(1)
N(4)	59(1)	56(1)	62(1)	-3(1)	13(1)	-7(1)
N(5)	77(1)	72(1)	54(1)	6(1)	10(1)	-2(1)
C(1)	62(1)	52(1)	45(1)	-2(1)	0(1)	1(1)
C(2)	56(1)	60(1)	40(1)	0(1)	2(1)	-2(1)
C(3)	61(1)	53(1)	39(1)	0(1)	2(1)	-5(1)
C(4)	55(1)	70(2)	48(1)	0(1)	1(1)	-4(1)
C(5)	62(2)	76(2)	93(2)	-3(2)	12(1)	-1(1)
C(6)	61(2)	103(2)	101(2)	-12(2)	10(2)	9(2)
C(7)	52(1)	111(2)	64(2)	8(2)	-2(1)	1(2)
C(8)	69(2)	102(3)	113(3)	23(2)	19(2)	-8(2)
C(9)	71(2)	73(2)	111(2)	9(2)	22(2)	-4(1)
C(10)	61(2)	165(4)	93(2)	16(2)	11(2)	5(2)
C(11)	56(1)	79(2)	46(1)	-13(1)	2(1)	-1(1)
C(12)	65(2)	110(2)	100(2)	10(2)	15(2)	-13(2)

Table 2 (continued)

	U11	U22	U33	U23	U13	U12
C(13)	68(2)	181(5)	111(3)	8(3)	21(2)	-25(3)
C(14)	58(2)	209(5)	89(2)	-55(3)	1(2)	7(3)
C(15)	66(2)	145(3)	170(4)	-84(3)	7(2)	9(2)
C(16)	64(2)	96(2)	131(3)	-45(2)	10(2)	2(2)
C(17)	65(2)	344(8)	157(4)	-92(5)	22(2)	14(3)
C(18)	55(1)	57(1)	44(1)	-3(1)	-1(1)	0(1)
C(19)	119(2)	59(2)	65(2)	-4(1)	-26(2)	-2(2)
C(20)	132(3)	71(2)	67(2)	-18(2)	-29(2)	10(2
C(21)	94(2)	89(2)	49(1)	-6(1)	-7(1)	4(2)
C(22)	101(2)	73(2)	55(2)	12(1)	-10(1)	-7(2)
C(23)	82(2)	60(2)	52(1)	1(1)	-5(1)	-6(1)
C(24)	68(2)	50(1)	49(1)	-1(1)	2(1)	0(1)
C(25)	98(2)	71(2)	59(2)	9(1)	-17(1)	-10(2)
C(26)	135(3)	86(2)	60(2)	7(2)	-26(2)	1(2)
C(27)	134(3)	75(2)	49(2)	5(1)	11(2)	22(2)
C(28)	98(2)	81(2)	60(2)	12(1)	23(2)	9(2)

Table 5

Comparison of the Calculated ΔH_f Values for **4** and **4'**

Compound	ΔH_f
4'	194.86 kcal/mol
4	173.96 kcal/mol

In further experiments, pyridopyrazines **1** were treated with nitroso-*tert*-butane **2b**. Under similiar conditions as in the formation of **4**, however employing significantly longer reaction times, only compound **4b** was isolated as colorless oil. The strong NOE between the proton in position three of the pyridine ring and the protons of the *tert*-butyl group clearly supports the structure of **4b**. All attempts to isolate the initially formed oxadiazine **4'** by variation of the solvent and/or the temperature were unsuccessful. Furthermore, we investigated the reaction of **1** with other azadienophiles. *N*-Phenyltriazolindione **6a** reacted with **1** at elevated temperature to give the bicyclic compound **7a**. The low yield is presumably caused by decomposition of **6a** to carbon monoxide, nitrogen and phenylisocyanate. Phthalazinedione **6b**, well known by its capacity to protect the 1,3-diene substructure in steroidal precursor molecules [8], was prepared *in situ* by oxidation of the sodium salt of phthalhydrazide with *tert*-butyl hypochlorite [9]. The reaction of **6b** and **1** was complex and only traces of the desired derivative **7b** were detected by mass spectrometry.

Table 3

Bond Lengths (Å) for **4a**

O-C(3)	1.223(3)	C(2)-C(3)	1.510(3)	C(14)-C(17)	1.522(5)
N(1)-C(2)	1.290(3)	C(4)-C(5)	1.369(4)	C(15)-C(16)	1.385(4)
N(1)-C(1)	1.456(3)	C(4)-C(9)	1.376(4)	C(18)-C(23)	1.373(3)
N(2)-C(3)	1.351(3)	C(5)-C(6)	1.393(4)	C(18)-C(19)	1.378(3)
N(2)-N(3)	1.423(2)	C(6)-C(7)	1.364(4)	C(19)-C(20)	1.379(4)
N(2)-C(11)	1.429(3)	C(7)-C(8)	1.359(4)	C(20)-C(21)	1.367(4)
N(3)-C(18)	1.440(3)	C(7)-C(10)	1.510(4)	C(21)-C(22)	1.362(4)
N(3)-C(1)	1.462(3)	C(8)-C(9)	1.395(4)	C(22)-C(23)	1.387(3)
N(4)-C(2)	1.354(3)	C(11)-C(16)	1.370(4)	C(24)-C(25)	1.366(4)
N(4)-C(4)	1.411(3)	C(11)-C(12)	1.375(4)	C(25)-C(26)	1.379(4)
N(5)-C(28)	1.338(3)	C(12)-C(13)	1.374(5)	C(26)-C(27)	1.367(4)
N(5)-C(24)	1.342(3)	C(13)-C(14)	1.361(6)	C(27)-C(28)	1.367(4)
C(1)-C(24)	1.526(3)	C(14)-C(15)	1.365(6)		

Table 4

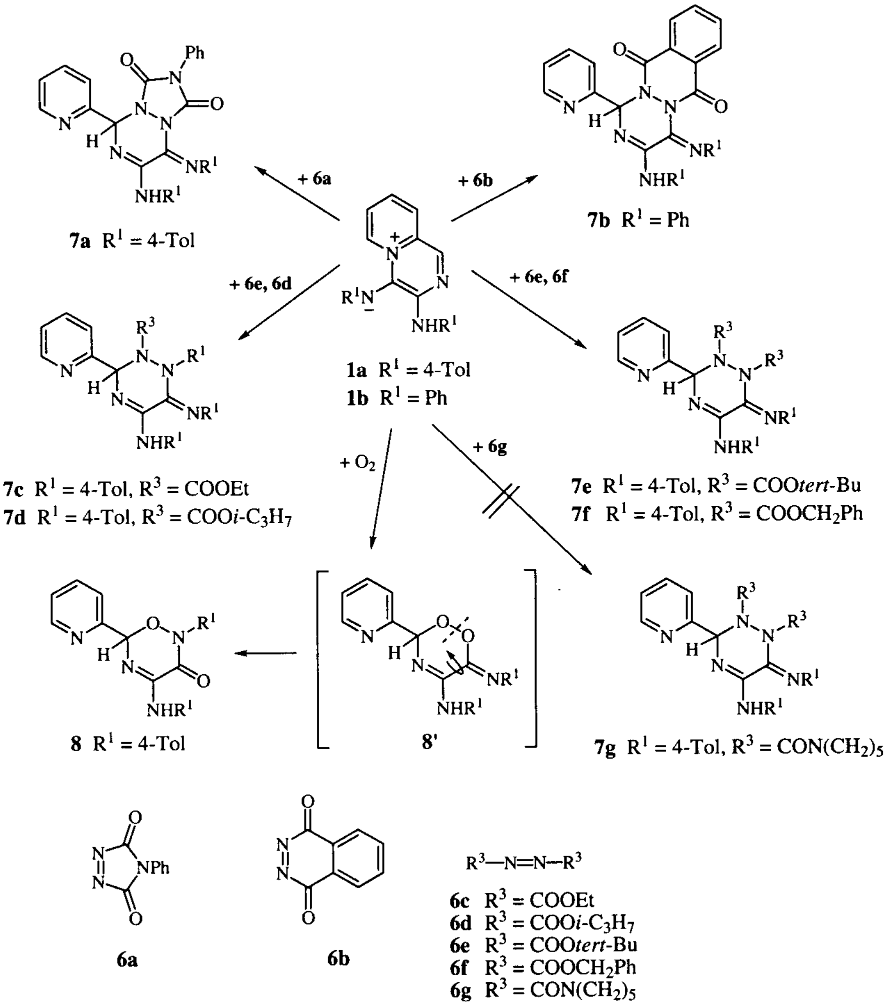
Bond Angles (°) for **4a**

C(2)-N(1)-C(1)	113.6(2)	C(4)-C(9)-C(8)	120.4(3)
C(3)-N(2)-N(3)	119.0(2)	C(16)-C(11)-C(12)	119.0(3)
C(3)-N(2)-C(11)	125.4(2)	C(16)-C(11)-N(2)	121.5(2)
N(3)-N(2)-C(11)	115.6(2)	C(12)-C(11)-N(2)	119.5(2)
N(2)-N(3)-C(18)	113.4(2)	C(13)-C(12)-C(11)	119.6(4)
N(2)-N(3)-C(1)	110.0(2)	C(12)-C(13)-C(14)	122.7(4)
C(18)-N(3)-C(1)	115.9(2)	C(15)-C(14)-C(13)	116.9(3)
C(2)-N(4)-C(4)	129.9(2)	C(15)-C(14)-C(17)	121.6(5)
C(28)-N(5)-C(2	117.3(2)	C(13)-C(14)-C(17)	121.4(5)
N(1)-C(1)-N(3)	113.9(2)	C(14)-C(15)-C(16	122.1(4)
N(1)-C(1)-C(24)	112.6(2)	C(11)-C(16)-C(15)	119.7(3)
N(3)-C(1)-C(24)	110.0(2)	C(23)-C(18)-C(19)	119.2(2)
N(1)-C(2)-N(4)	125.1(2)	C(23)-C(18)-N(3)	123.4(2)
N(1)-C(2)-C(3)	123.5(2)	C(19)-C(18)-N(3)	117.4(2)
N(4)-C(2)-C(3)	111.3(2)	C(18)-C(19)-C(20)	120.0(3)
O-C(3)-N(2)	124.0(2)	C(21)-C(20)-C(19)	121.0(3)
O-C(3)-C(2)	121.2(2)	C(22)-C(21)-C(20)	118.8(2)
N(2)-C(3)-C(2)	114.8(2)	C(21)-C(22)-C(23)	121.1(3)
C(5)-C(4)-C(9)	118.5(2)	C(18)-C(23)-C(22)	119.8(2)
C(5)-C(4)-N(4)	124.4(2)	N(5)-C(24)-C(25)	122.0(2)
C(9)-C(4)-N(4)	117.1(2)	N(5)-C(24)-C(1)	114.9(2)
C(4)-C(5)-C(6)	119.6(3)	C(25)-C(24)-C(1)	123.0(2)
C(7)-C(6)-C(5)	122.6(3)	C(24)-C(25)-C(26)	119.3(3)
C(6)-C(7)-C(8)-	117.2(3)	C(27)-C(26)-C(25)	119.3(3)
C(6)-C(7)-C(10)	121.9(3)	C(28)-C(27)-C(26)	117.9(3)
C(8)-C(7)-C(10)	120.9(3)	N(5)-C(28)-C(27)	124.1(3)
C(7)-C(8)-C(9)	121.7(3)		

Using diethyl azodicarboxylate **6c**, the reaction gave 1,2,4-triazine derivative **7c**, which is presumably formed in an analogous mechanism as described above in Scheme 1. The structure of the derivative **7c** bearing a pattern of substituents different from that expected from an initial [2+4]-cycloaddition reaction/ring transformation sequence was deduced from its NOESY spectrum. The observed NOEs of the protons of both ethyl groups and of the aromatic protons of the substituent R^1 support the structure of **7c**.

Similarly, the diisopropyl ester **6d** was readily converted into derivative **7d**. In contrast, the *tert*-butyl and benzyl substituted diazenes **6e** and **6f** did not undergo such a rearrangement reaction. In the nmr spectra of the

Scheme 2



products **7e,f** the signals of the pyridine substructure are most diagnostic. Beyond that, the spectra showed a high degree of dynamic processes by a high number of broad signals. This behavior can be explained by the interconversion of different prototropic isomers. The mass spectra of **7e,f** as well as their elemental analyses showed that **1a** and **6e,f** reacted in a 1:1 stochiometry. We propose, that in this case, a Dimroth-rearrangement cannot take place, due to the bulky substituents. On the other hand, the diamide **6g** (R^3 = $CON(CH_2)_5$) did not react with **1** at all, even at higher temperatures (boiling toluene). After several weeks of standing in methylene chloride at room temperature only the oxygen adduct **8** was isolated in moderate yield. Similar experiments without the diazene derivative **7g** gave similar results, the oxygene derivative **8** was furnished again. As expected NOESY experiments with **8** pointed towards a Dimroth-rearrangement, as shown in Scheme 2. The triplet oxygen was presumably transformed into singlet oxygen by sensitization (by the colored educt **1** or corresponding colored intermediates) which underwent the cycloaddition/ring transformation sequence leading to **8'**. Finally, this cyclic peroxide gave the more stable oxadiazinone **8** [10].

EXPERIMENTAL

All reagents were of commercial quality (Aldrich, Fluka, Merck). Solvents were dried and purified using standard techniques. Reactions were monitored by thin layer chromatography (tlc), on plastic plates coated with silica gel and flourescent indicator (Polygram SIL G/UV_{254} from Macherey-Nagel) or plastic plates coated with neutral alumina with flourescence indicator (Polygram ALOX N/UV_{254} from Macherey-Nagel). Flash chromatography was carried out on silica gel (Merck, Silica gel 60, particle size 0.063 mm-0.2 mm, 70-230 mesh ASTM) or neutral alumina (Merck, aluminium oxide 90 active neutral, activity V, particle size 0.063 mm-0.2 mm, 70-230 mesh ASTM). Melting points were measured with a Galen III (Boëtius system) from Cambridge Instruments, and are uncorrected. The uv-vis spectra were obtained using a Perkin Elmer Lambda 19 spectrophotometer. Infrared spectra were recorded on a Nicolet Impact 400 spectrometer (potassium bromide). The ^1H nmr and ^{13}C nmr spectra were obtained on Bruker DRX 400 (400 MHz) and Bruker AC 250 (250 MHz) spectrometers. Mass spectra were taken from measurements on a Finnigan MAT SAQ 710 mass spectrometer. Elemental analyses were carried out using an automatic analyzer LECO CHNS 932.

2,3-Dihydro-1-(4-methylphenyl)-5-[(4-methylphenyl)amino]-2-phenyl-3-(2-pyridinyl)-1,2,4-triazin-6(1*H*)-one (**4a**, R^1 = tolyl).

Compound **1** (R^1 = tolyl, 10 mmoles, 3.40 g) was dissolved in 40 ml of dichloromethane and a solution of nitrosobenzene **2a** (10 mmoles, 1.07 g) in 20 ml of dichloromethane was added. After stirring for 24 hours in air at room temperature the solvent was evaporated *in vacuo*. The residue was recrystallized from *tert*-butylmethylether. Compound **4a** was obtained as colorless needles, 3.85 g (86%), mp 195°; ir (nujol): ν NH 3327, CO 1663, 1626, 1596, CN 1547 cm^{-1}; ^1H nmr (deuteriodichloromethane): δ 2.28 (s, 3H), 2.30 (s, 3H), 6.72 (s, 1H), 7.00-7.14 (m, 5H), 7.24-7.39 (m, 7H), 7.51 (d, 1H, J = 8 Hz), 7.63 (d, 2H, J = 8 Hz), 7.73 (t, 1H, J = 6 Hz), 8.14 (s, 1H, N-H), 8.69 ppm (d, 1H, J = 4 Hz); ^{13}C nmr (deuteriodichloromethane): δ 20.9, 21.0, 79.6, 118.8, 119.5, 122.3, 123.0, 123.8, 124.1, 129.4, 129.7, 129.8, 133.1, 136.7, 137.0, 137.2, 137.3, 148.0, 148.2, 150.1, 156.3, 157.2 ppm (C=O); ms: m/z 448 (M^+).

Anal. Calcd. for $C_{28}H_{25}N_5O$: C, 75.15; H, 5.63; N, 15.65. Found: C, 75.08; H, 5.50; N, 15.48.

The X-ray crystallography of **4a** had molecular formula $C_{28}H_{25}N_5O$; formula weight = 447.5; monoclinic; space group C2/c; Z = 8; a = 21.961 (2), b = 13.563 (1), c = 16.361 (2) Å, β = 90.37 (1) °, V = 4873.1 (8) Å^3; calculated density = 1.22 g cm^3, absorption coefficient μ = 770 cm^{-1}. Intensity data were collected on a clear prism 0.40 x 0.40 x 0.25 mm^3 mounted on a glass fiber on a NONIUS CAD4 diffractometer. Graphite monochromatized Mo*Kα* radiation was used, [λ(Mo*Kα*] = 0.71069 Å], with maximum 2Θ = 51.3°. Intensity data were measured at room temperature using ω/2Θ scans with scan widths = 0.8 +0.350 tanΘ and a scan rate varied from 2 to 10°/minute (in omega). Moving-crystal moving-counter background counts were made by scanning an additional 25% above and below the scan width range. Thus, the ratio of peak counting time to background counting time was 2:1. Of 4627 unique reflections measured, 2831 had intensities > 3σ. As a check on crystal and electronic stability 3 representative reflections were measured every 60 minutes. The intensities of these standards remained constant within experimental error throughout data collection. No decay correction was applied. Cell parameters were determined by least squares fit of $K\alpha_1$ 2Θ values ($\lambda K a_1$ = 0.71069 Å) for 25 high 2Θ reflections. Lorentz and polarization corrections were applied to the data. No absorption correction was made [11]. The structure was solved by direct methods, using SHELXS [12]. A total of 30 atoms were located from an E-map. The remaining atoms were located in succeeding difference Fourier syntheses. The structure was refined in full-matrix least-squares on F^2 (SHELXL-93 [13]) where the function minimized in the refinement was $\Sigma w(F_0^2-F_c^2)^2$, where weights *w* were defined $w=1/[\sigma^2(F_02) + (0.0771 + P)^2 + 2.2395+P]$ where $P = (F_o^2+2F_c^2)/3)$. Hydrogen atoms were calculated and added to the structure factor calculation. Temperature factors for hydrogens were assigned as one-half unit higher than the equivalent isotropic temperature factors for the attached atoms. The final refinement included 310 variable parameters and converged (largest parameter shift was 0.00 times is esd) with unweighted and weighted agreement factors of:

$$R1 = \Sigma ||F_o| - |F_c|| / \Sigma |F_o| = 0.046$$

$$wR2 = [\Sigma [w(F_o2 - F_c^2)^2] / \Sigma [wF_o^2)^2]]^{1/2} = 0.121.$$

XP [14] was used for structure representations.

The atomic coordinates and thermal parameters of **11c** are shown in Tables 1 and 2, and the bond lengths, and angles, are listed in Tables 3 and 4. Further details of the crystal structure investigations are available on requests from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen, on quoting the depository number CSD-408612, the names of the authors, and the journal citation.

Tetracarbonyl-molybdenum Complex of Compound **4'** (**5a**, R^1 = tolyl).

A solution of equimolar amounts of **1** (R = tolyl) and nitrosobenzene **2a** in dry dichloromethane was allowed to stand at room temperature under argon for 24 hours, until **1** cannot be detected by tlc anymore. A solution of (norbornadiene)Mo(CO)$_4$ complex in dry dichloromethane was then added and the mixture was stirred for 3 hours, while the color changed from yellowish brown to red. The solution was concentrated to approximately one quarter. Cooling to -30° afforded red crystals of **5a** overnight, which were isolated by filtration; ir (nujol): ν NH 3357, 2009, 1881, CO 1816, 1678, 1620, 1599, 1523, 1502; ^1H nmr (deuteriodichloromethane): δ 2.32, 2.34, 2.36, 2.40 (4s, 6H), 6.64-6.83 (m, 3.8H), 7.07-7.39 (m, 8H), 7.45-7.70 (m, 3.5H), 7.79-7.90 (m, 1.8H), 8.04 (s, 0.5H), 8.38 (s, 0.6H), 8.82 (d, 0.6H, J = 6 Hz), 8.95 (d, 0.4H, J = 6 Hz); ^{13}C nmr (deuteriodichloromethane): δ 21.0, 21.1, 82.6, 84.8, 118.7, 120.7, 121.4, 121.7, 122.6, 123.3, 124.3, 124.5, 125.0, 125.9, 126.0, 129.7, 130.1, 130.2, 130.7, 132.9, 136.0, 136.4, 136.9, 137.0, 137.3, 137.5, 138.4, 138.9, 144.6, 147.7, 152.8, 153.1, 154.2, 155.1, 155.9, 156.5, 157.4, 157.6, 205.4, 206.0, 206.9, 208.2 (CO_{ax}), 220.0, 221.3, 221.7, 224.1 ppm (CO_{eq}).

Anal. Calcd. for $C_{32}H_{25}N_5O_5Mo$: C, 58.63; H, 3.84; N, 10.68. Found: C, 58.89; H, 3.96; N, 10.45.

2,3-Dihydro-1-(4-methylphenyl)-5-[(4-methylphenyl)amino]-2-*tert*-butyl-3-(2-pyridinyl)-1,2,4-triazin-6(1*H*)-one (**4b**, R = phenyl).

Dimer nitroso-*tert*-butane (5 mmoles, 0.87 g) in 20 ml of dichloromethane was added to a solution of 10 mmoles (3.12 g) of **1** (R^1 = phenyl) in 40 ml of dichloromethane. The mixture was allowed to stand on air at room temperature for several weeks, until tlc shows no trace of **1** anymore. The reaction was complete after four weeks. The resulting triazinone **4b** can be detected by tlc. After removal of the solvent the residue was dissolved in 30 ml of toluene and purified by column chromatography (alumina, Toluene/Acetone 9:1). Removal of the solvent resulted in a colorless or light brown viscoseous oil or amorphous solid, 2.88 g (72%); ^1H nmr (deuteriodichloromethane): δ 1.10 (s, 9H), 6.13 (s, 1H), 7.00 (t, 1H), 7.15 (t, 1H), 7.23-7.38 (m, 8H), 7.67-7.77 (m, 3H), 8.37 (s, 1H, N-H), 8.58 (d, 1H); ^{13}C nmr (deuteriodichloromethane): δ 27.1, 61.0, 75.4, 119.3, 122.8, 123.5, 123.6, 124.0, 125.6,129.0, 129.1, 136.9, 139.9, 144.1, 146.0, 146.3, 149.4, 158.7 ppm; ms: m/z 400 (M^+), 344, 329, 312, 240, 163.

Anal. Calcd. for $C_{24}H_{25}N_5O$: C, 72.16; H, 6.31; N, 17.53. Found: C, 72.00; H, 6.20; N, 17.44.

5,8-Dihydro-7-[(4-methylphenyl)amino]-8-[(4-methylphenyl)imino]-2-phenyl-5-(2-pyridinyl)-1*H*-[1,2,4]triazolo[1,2-*a*][1,2,4]triazine-1,3(2*H*)-dione (**7a**, R^1 = tolyl).

A solution of **1** (R^1 = tolyl) (5 mmoles, 1.7 g) and **6a** (5 mmoles, 0.88 g) in 50 ml of toluene was heated at reflux for 5 hours. After removal of the solvent *in vacuo*, the residue was dissolved in acetone (100 ml). The acetone was then evaporated to 30 ml, while a yellowish solid separated. It was collected and dried *in vacuo*, yellowish solid, 0.47 g (18%), mp 203-205° dec; ^1H nmr (deuteriodichloromethane): δ 2.29, 2.33 (2s, 6H), 6.87 (d, 2H, J = 8.2 Hz), 7.05 (s, 4H), 7.18 (d, 2H, J = 8.2 Hz), 7.35-7.41 (m, 5H), 7.65 (d, 3H, J = 7.4 Hz), 7.81 (t, 1H, J = 7 Hz), 7.94 (s, 1H), 8.72 (d, 1H, J = 4.1 Hz); ^{13}C nmr (deuteriodichloromethane): δ 21.0, 21.1, 119.4, 121.1, 124.7, 129.0, 129.2, 129.6, 130.0, 134.1, 135.2, 135.9, 138.0, 150.1, 152.1, 158.4 ppm; ms: m/z 516 (M^+), 120 ($(PhNCO+1)^+$).

Anal. Calcd. for $C_{31}H_{26}N_6O_2$: C, 72.36; H, 5.09; N, 16.33. Found: C, 72.12; H, 5.05; N, 16.22.

1,4-Dihydro-3-(phenylamino)-4-(phenylimino)-1-(2-pyridinyl)[1,2,4]triazino[1,2-*b*]phthalazine-6,11-dione (**7b**, R^1 = phenyl).

A solution of 1 mmole (0.31 g) of **1** (R^1 = phenyl) in 10 ml of dry acetone was added dropwise to a freshly prepared solution of phthalazinedione **6b** in acetone [9] at -78°. After addition of **1** the reaction mixture was stirred for another 30 minutes at -78° and was then allowed to slowly warm up to room temperature. Thin layer chromatography of the solution showed a wide range of products. The orange-brown product with a R_F value of 0.5 (silica gel, toluene:*iso*-propanole 5:1) was isolated by preparative tlc and gave a mass spectrum with the desired molecular mass peak of the product **7b**. The yield was approximately 5% and nmr studies showed that the isolated product was not pure; ms: m/z 473 $(M+1)^+$, 326, 270, 163 $(Ph(CO)_2(NH)_2+1)^+$, 148 $(Ph(CO)_2(NH)+1)^+$, 123, 94.

General Procedure for the Cycloaddition Reaction between the Pyrido[1,2-*a*]pyrazine **1** and the Azodicarboxylates **6c-f**.

A solution of 1 mmole of the pyrido[1,2-*a*]pyrazine **1** (R^1 = tolyl) and 1 mmole of the azodicarboxylate **6c-f** in 50 ml of dichloromethane was stirred at room temperature for several days. The reaction progress was controlled by tlc. After the detection of completeness, the solvent was removed *in vacuo*, and the residue was chromatographed on neutral alumina using toluene:acetone 10:1. The products **7c** and **7d** were obtained as colorless or slightly grey solids after removing most of the eluent, addition of some ml of *n*-hexane and cooling. The products **7e** and **7f** are yellowish amorphous solids or viscoseous oils, which were yielded by removing the eluent *in vacuo* and carefully drying the residue.

Ethyl 6-[Ethoxycarbonyl)imino]-3,6-dihydro-1-(4-methylphenyl)-5-[(4-methylphenyl)amino]-3-(2-pyridinyl)-1,2,4-triazine-2(1*H*)-carboxylate (**7c**, R^1 = tolyl).

This compound was obtained after a reaction time of two days as a greyish solid, yield 71%, mp 172-175°; ^1H nmr (deuteriodichloromethane): δ 0.68 (t, 3H, J = 7.0 Hz), 1.42 (t, 3H, J = 7.2 Hz), 2.30 (s, 3H), 2.34 (s, 3H), 3.32 (m, 1H), 3.61 (m, 1H), 4.34 (q, 2H, J = 7.1 Hz), 7.03-7.26 (m, 6H), 7.41 (d, 3H, J = 7.8 Hz), 7.59-7.74 (m, 3H), 8.54 (d, 1H, J = 4.0 Hz), 8.61 (s, 1H); ^{13}C nmr (deuteriodichloromethane): δ 13.8, 14.7, 20.9, 21.2, 63.5, 63.9, 71.6, 119.8, 122.6, 122.8, 123.8, 129.6, 129.8, 132.7, 135.5, 136.7, 137.1, 137.3, 143.7, 145.7, 149.9, 151.4, 155.5, 156.5 ppm; ms: m/z 515 (M^+).

Anal. Calcd. for $C_{28}H_{30}N_6O_4$: C, 65.37; H, 5.84; N, 16.34. Found: C, 65.62; H, 5.75; N, 16.28.

iso-Propyl 6-[*iso*-Propylcarbonyl)imino]-3,6-dihydro-1-(4-methylphenyl)-5-[(4-methylphenyl)amino]-3)-(2-pyridinyl)-1,2,4-triazine-2(1*H*)-carboxylate (**7d**, R^1 = tolyl).

This compound was obtained as a pale greyish solid after a reaction time of four days, yield 69%, mp 195-198°; ^1H nmr (deuteriodichloromethane): δ 0.44 (d, 3H, J = 4.9 Hz), 0.92 (d, 3H, J = 6.2 Hz), 1.39 (d, 3H, J = 6.2 Hz), 1.42 (d, 3H, J = 6.2 Hz), 2.32 (s, 3H), 2.36 (s, 3H), 4.27 (m, 1H), 5.13 (m, 1H), 7.00-7.71 (m, 12H), 8.55 (d, 1H, J = 4.0 Hz), 8.64 (s, 1H); ^{13}C nmr (deuteriodichloromethane): δ 20.2, 20.5, 20.8, 21.3, 21.9, 22.0, 70.0, 71.4, 119.2, 122.4, 123.4, 128.1, 129.2, 129.3, 132.2, 134.9, 136.4, 136.7, 136.9, 143.2, 145.3, 149.5, 150.4, 154.3, 156.1 ppm; ms: m/z 543 (M^++1), 93.

Anal. Calcd. for $C_{30}H_{34}N_6O_4$: C, 66.42; H, 6.27; N, 15.50. Found: C, 66.68; H, 6.15; N, 15.38.

Bis(*tert*-butyl) 3,6-Dihydro-5-[(4-methylphenyl)amino]-6-[(4-methylphenyl)imino]-3-(2-pyridinyl)-1,2,4-triazine-1,2-dicarboxylate (**7e**, R^1 = tolyl).

This compound was obtained after a reaction time of four days as a yellowish oil or an amorphous solid, yield 72%; ^1H nmr (deuteriodichloromethane): δ 0.85 (s, 4H), 1.43 (s, 5H), 1.47 (s, 5H), 1.57 (s, 4H), 2.26 (s, 3H), 2.31, 2.32 (2s, 3H), 6.32 (t, 0.7H), 6.73 (d, 13H, J = 8 Hz), 6.99-7.22 (m, 6H), 7.39 (t, 2H), 7.61-7.71 (m, 1.5H), 7.81 (t, 0.6H), 8.06 (s, 0.4H, N-H), 8.52 (d, 0.5H, J = 5 Hz), 8.61 (s, 1H, N-H); ^{13}C nmr (deuteriodichloromethane): δ 20.8, 21.1, 27.4, 28.2, 28.3, 28.5, 81.9, 82.5, 83.2, 119.2, 119.5, 120.8, 122.9, 123.5, 124.0, 127.2, 129.5, 129.6, 129.8, 132.1, 132.2, 132.4, 136.3, 137.0, 137.4, 137.5, 143.5, 145.9, 149.9, 155.6, 156.9 ppm; ms: m/z 571 (M^++1).

Anal. Calcd. for $C_{32}H_{38}N_6O_4$: C, 67.37; H, 6.67; N, 14.74. Found: C, 67.58; H, 6.35; N, 14.48.

Bis(phenylmethyl) 3,6-Dihydro-5-[(4-methylphenyl)amino]-6-[(4-methylphenyl)imino]-3-(2-pyridinyl)-1,2,4-triazine-1,2-dicarboxylate (**7f**, R^1 = tolyl).

This compound was obtained after the mixture was allowed to react for about a week as a yellow oil, which solidified upon drying to a yellow amorphous solid, yield 75%, mp 71-75°; ^1H nmr (deuteriodichloromethane): δ 0.90 (m, 2H), 1.30 (m, 2.5H), 2.27 (m, 6.5H), 4.10 (d, 1H, J = 12 Hz), 4.68 (d, 1H, J = 12 Hz), 5.29 (s, 1H), 6.60-7.60 (m, 18H), 8.39 (s, 0.8H), 8.58 (s, 1H), 9.32 (s, 0.2H); ^{13}C nmr (deuteriodichloromethane): δ 14.3, 20.9, 21.0, 21.2, 23.0, 32.0, 68.7, 69.5, 70.8, 119.7, 120.1, 122.2, 122.7, 123.9, 128.5, 128.6, 128.9, 129.0, 129.6, 129.8, 130.0, 132.7, 135.1, 135.6, 137.1, 137.2, 143.2, 145.5, 149.8, 154.9, 156.1, 158.0 ppm; ms: m/z 639 (M^++1), 269, 91.

Anal. Calcd. for $C_{38}H_{34}N_6O_4$: C, 71.47; H, 5.33; N, 13.17. Found: C, 71.69; H, 5.05; N, 13.03.

2-(4-Methylphenyl)-4-[(4-methylphenyl)amino]-6-(2-pyridinyl)-2*H*-1,2,5-oxadiazin-3(6*H*)-one (**8**, R^1 = tolyl).

A solution of 10 mmoles (3.4 g) of **1** (R^1 = tolyl) and 10 mmoles (2.5 g) of **6g** in 50 ml of dichloromethane was allowed to stand on air at room temperature for several weeks, until tlc detected completeness of the reaction. The solvent was then removed *in vacuo* and the residue was chromatographed on neutral alumina using toluene, yielding 1.1 g (30%) of **8**. The compound was also obtained in similar yields from a solution of **1a** in dichloromethane, which was allowed to stand for several weeks on air at room temperature. Compound **8** was yielded as a white crystalline solid after chromatographic work up by adding n-hexane to the toluene solution, mp 159-162° dec; ^{1}H nmr (deuteriodichloromethane): δ 2.33 (s, 3H), 2.35 (s, 3H), 6.64 (s, 0.8H), 7.16-7.22 (m, 4H), 7.35 (t, 1H, J = 5.5 Hz), 7.57 (d, 2H, J = 8.6 Hz), 7.68 (d, 2H, J = 6.6 Hz), 7.73 (d, 1H, J = 7.1 Hz), 7.80 (t, 1H, J = 7.6 Hz), 8.04 (s, 1H), 8.67 (d, 1H, J = 4.0 Hz), 9.32 (s, 0.2H); ^{13}C nmr (deuteriodichloromethane): δ 20.9, 21.1, 93.0, 119.6, 120.1, 120.7, 123.0, 124.6, 129.8, 130.0, 133.5, 135.9, 136.5, 137.3, 146.0, 149.9, 154.1, 156.2 ppm; ms: m/z 373 (M^++1), 251.

Anal. Calcd. for $C_{22}H_{20}N_4O_2$: C, 70.97; H, 5.38; N, 15.05. Found: C, 71.05; H, 5.25; N, 14.93.

Acknowledgements.

This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

REFERENCES AND NOTES

[1] H. C. van der Plas, Ring Transformations of Heterocycles, Vol **1** and **2**, Academic Press, New York, NY, 1973.

[2] D. L. Boger and S. M. Weinreb, Hetero-Diels-Alder Methodology in Organic Synthesis, Academic Press, San Diego, 1987.

[3] J. Brandenburg, R. Beckert, P. Fehling, and M. Döring, *J. Prakt. Chem./Chem.-Ztg.*, **338**, 430 (1996).

[4] T. Billert, R. Beckert, P. Fehling, and M. Döring, *Tetrahedron*, **53**, 5455 (1997).

[5] G. van Koten and K. Vrieze, *Adv. Organomet. Chem.*, **21**, 151 (1982).

[6] The parameters of the heteroatoms have been quoted according to: A. Streiwieser, Molecular Orbital Theory, Wiley: New York, 1967. See also: R. Hoffmann, *J. Chem. Phys.*, **39** 1397 (1963). For the calculation of the relative stability of the activated complexes ethylene was used as dienophile.

[7] The configurations of the isomers were generated and the energies were subsequently minimized using the MM+ force field which is implemented in release 3.0 of HyperChem®. MM+ supplements the standard MM2 parameters (N. L. Allinger, *J. Am. Chem. Soc.*, **99**, 8127 (1977)). The minima obtained from the search were further optimized using the AM1 wavefunction, M. J. S. Dewar, E. G. Zoebisch, E. F. Healy and J. J. P. Stewart, *J. Am. Chem. Soc.*, **107**, 3902 (1985) and the RHF approximation.

[8] N. A. Bogolovskii, G. E. Litvinova, and G. I. Samochvalov, *Zh. Obshch. Khim.*, **48**, 908 (1978).

[9] T. J. Kealy, *J. Am. Chem. Soc.*, **84**, 966 (1962).

[10] A. de Meijere, D. Kaufmann, and I. Erden, *Tetrahedron*, **42**, 6487 (1986).

[11] MOLEN, An Interactive Structure Solution Procedure, Enraf-Nonius, Delft, The Netherlands, 1990.

[12] G. M. Sheldrick, *Acta Crystallogr. Sect. A*, **46**, 467 (1990).

[13] G. M. Sheldrick, University of Göttingen, Germany, 1993.

[14] G. M. Sheldrick, SHELXTL/PC, Siemens Analytical X-Ray Instruments, Inc., Madison, WI, 1992.