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Reaction of *N*-Methyl-hydrazones as Azaenamines with Quinones

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Abstract—1,4-Naphthoquinone derivatives reacted with *N,N*-disubstituted hydrazones to give C adducts, whereas *N*-monoalkylhydrazones yielded N adducts which underwent ring closure to benzindazole-4,9-diones. Michael addition with methoxycarbonylbenzoquinone led to open chain mono- and disubstituted N adducts or phthalazin-1-one derivatives, depending on the hydrazone. N Adducts obtained from dimethylbenzoquinone cyclized by hetero Diels–Alder reaction to benzoxadiazines.

Introduction

A variety of natural or synthetic compounds containing a *p*-quinone moiety show strong biological activity due to their interference with metabolic processes of herbal and animal cells.[1,2] An outstanding example is given by the anthracycline antibiotics, which because of their antimitotic character[3] are presently some of the most important agents in the treatment of human cancers. In another area benzindazolequinones **1a** (Fig. 1) have been investigated for herbicide activity.[4] In this case the biological effect is based on the inhibition of photosynthesis.[5] The synthesis of benzindazolequinones **1** was achieved by reaction of quinone derivatives with diazomethane. Thus only indazoles **1a** unsubstituted in position 3 were available.[4] Hence the synthesis of new indazolequinones **1b** with various substituents in position 3 should be of great interest. We have recently reported two new syntheses of highly cytotoxic benzocarbazolequinones.[6,7] For example 2-methylamino-1,4-naphthoquinones reacted with 2,3-dimethylbenzoquinone to give 2-hydroxy-3,4,5-trimethyl-5*H*-benzo[*b*]carbazole-6,11-diones, with the naphthoquinones acting as enaminones in a new modification[6] of the Nenitzescu reaction (Fig. 1). Hydrazones react similarly to enamines[8,9,10,11] and can be regarded as azaenamines. Therefore it should be possible to achieve an analogous Michael addition of N^2-substituted hydrazones to 1,4-naphthoquinone followed by ring closure to the desired interesting indazole derivatives **1b**.

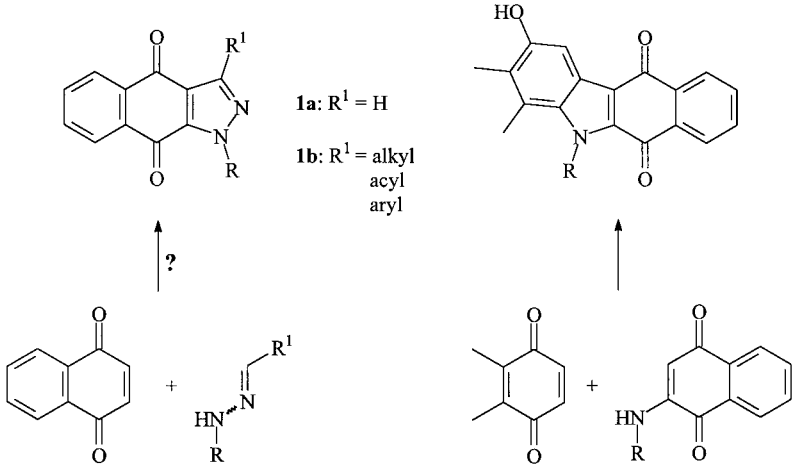

Figure 1.

Keywords: hydrazones; quinones; Michael and hetero Diels–Alder reactions; aza-enamines; Nenitzescu reaction.

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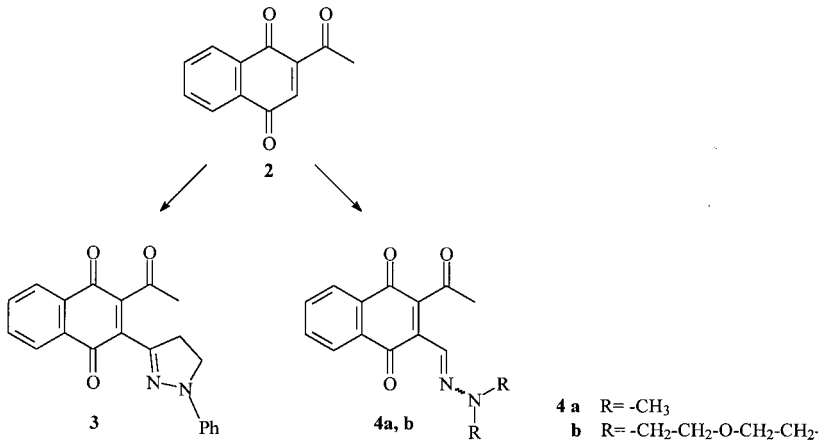

Figure 2.

Results and Discussion

Previous studies using the *N*,*N*-disubstituted hydrazones 1-phenyl-4,5-dihydro-pyrazole, methylene-morpholin-4-yl-amine and *N*,*N*-dimethyl-*N'*-methylene-hydrazine as aza-enamines in the reaction with quinone **2** have already shown, that this way azaenamine C adducts **3**[12], **4a** and **4b**[12] are available in methanol at room temperature (Fig. 2).

A recent publication by Granik[13] prompted us to report our own experiences with azaenamines. Granik has shown that *N*-phenylhydrazone **6** is able to act as an azaenamine, too.

Reaction with quinone **5** gave the hydroquinone-C-adduct **7** by Michael addition of the azomethine carbon. (Fig. 3). Cyclization of the adduct **7** was effected by oxidation leading directly to the the indazolequinone **8**.

In contrast to this result we were not able to detect C adducts **13a–d** when we carried out the aza-Nenitzescu reaction with *N*-methylhydrazones **10a–d** and 1,4-naphthoquinone **9** but obtained N adducts **11a–d** (Fig. 4). As proof for the structures **11a–d** we only mention the ^{1}H NMR spectrum e.g. of **11b**, in which the N=CH hydrogen at 7.86 ppm and 3-H at 7.05 ppm appeared as singlets and no NH signal was observed. Also, the UV/VIS spectra of **11a** and **4b**[12] were similar: both had two maxima at $\lambda(\log \epsilon)$=486 nm (3.90) (**11a**) resp. 476 nm (3.68) (**4b**) and λ=313 nm (4.40) (**11a**)

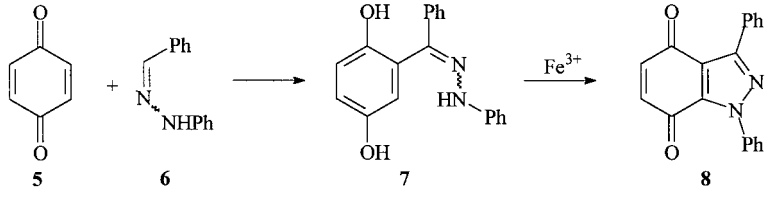

Figure 3.

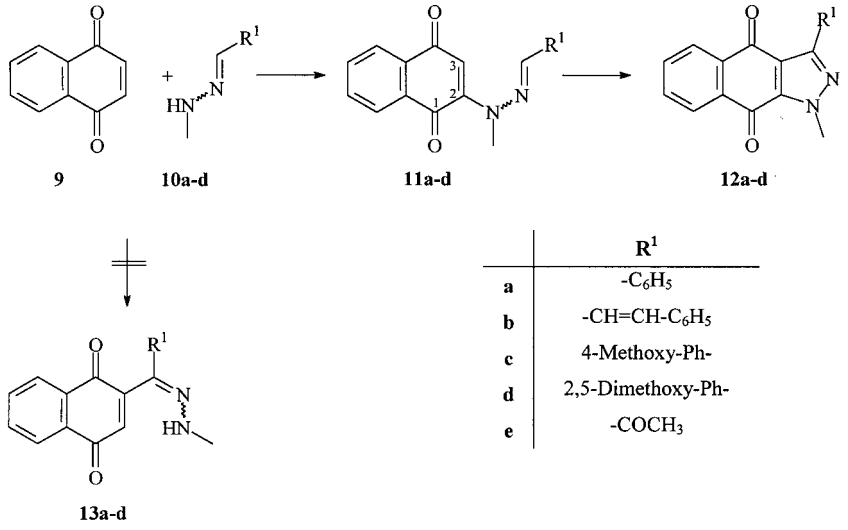

Figure 4.

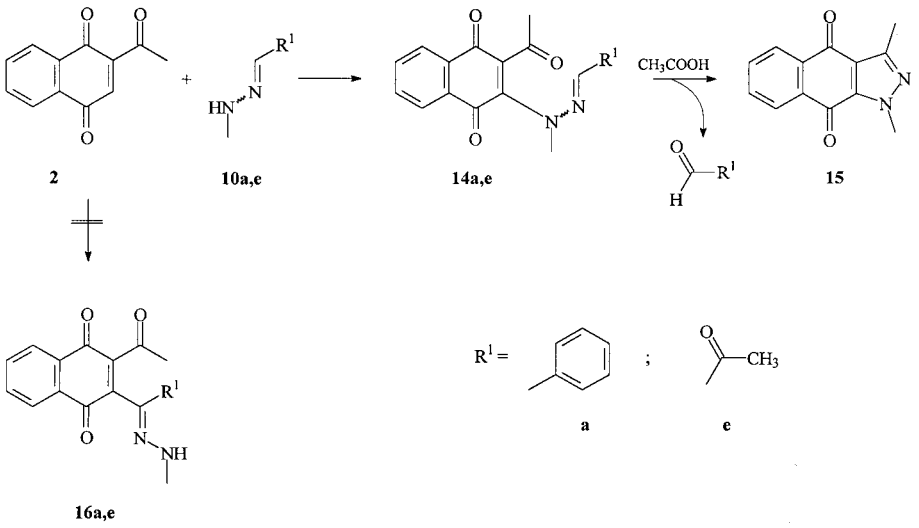

Figure 5.

resp. 290 nm (4.03) (**4b**), and agreed with the proposed structure. Apparently the nitrogen in *N*-methylhydrazones **10a–d** is more nucleophilic than in *N*-phenylhydrazone **6** and we only observed the formation of N adducts.

Ring closure of **11a–d** to benzindazole quinones was possible under drastic conditions. Heating the adducts above the melting point or in boiling xylene yielded the benzindazoles **12a–d**. The low reactivity is due to the presence of electron rich nitrogen substituent in position 2 which weakens the electrophilic character of the C-3 in **11a–d**. Moreover it is well-known that cyclizations of this type are disfavoured for stereochemical reasons[14]: the ring closure of **11a–d** can be regarded as a 5-*endo-trig* reaction, which is known to be an unfavorable process.

N-Methylhydrazones **10a,e** and acetylnaphthoquinone **2** gave similar products **14a,e** in good yields (Fig. 5). We were able to show that the amine nitrogen of azaenamines **10** attacked the quinone component **2** by nucleophilic addition. Only a singlet at 7.08 ppm was observed for the N=CH hydrogen in the ^{1}H NMR spectrum e.g. of **14e**, and neither the IR nor the ^{1}H NMR spectrum revealed the presence of an NH group. Hence we could exclude formation of the possible C adducts **16a,e**. The resulting quinone adducts **14a,e** were successfully cyclized by simple stirring in acetic acid. In both cases the same 1,3-dimethyl-benzindazole-4,9-dione **15** was obtained. We assumed that the ring closure proceeded by an intramolecular change of the hydrazone group. Thus benzindazole quinones substituted in position 3, e.g. **12a–d** and **15** are now available in good yield.

Investigations concerning the herbicide activity of **15** (spray chamber at a rate equivalent to 3000 g a.i./ha) showed that 21 days after treatment the test plants were destroyed 100% (*Sinapis alba*), 85% (*Lolium multiflorum*) and 60% (*Abutilon theophrasti*). Treating the plants with **15** caused foliar

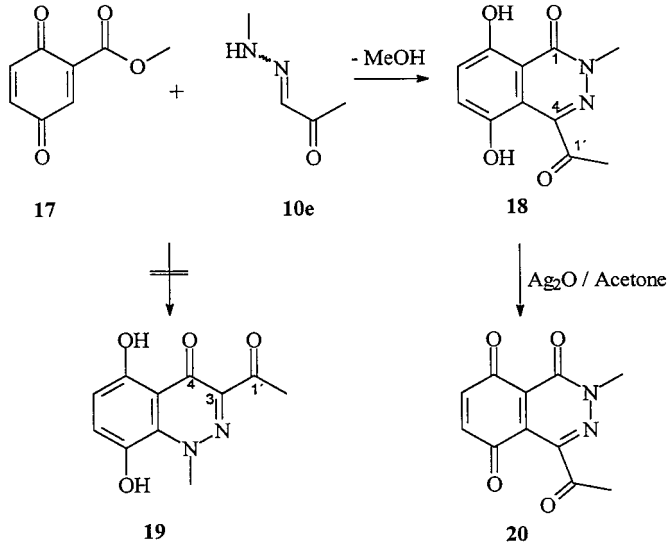

Figure 6.

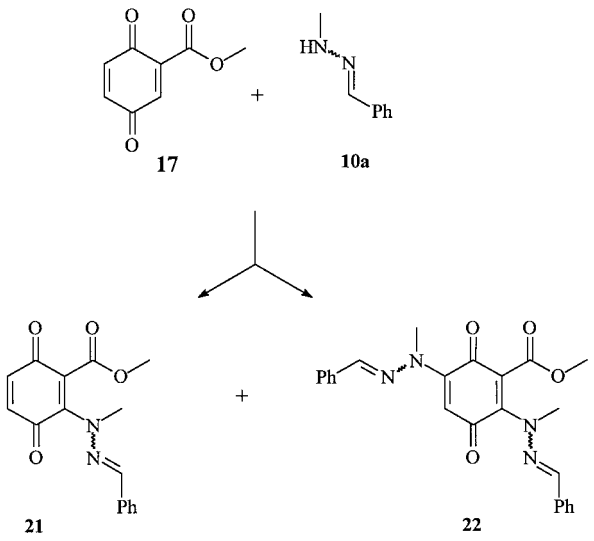

Figure 7.

necrosis similar to observations with 1-alkyl-3*H*-naphthindazole-4,9-diones (**1**), known to inhibit photosynthesis.[5]

The reaction of 2-methoxycarbonyl-benzoquinone **17** as a more reactive quinone component with methylhydrazonopropanone **10e** led to a product with mass spectral data and microanalysis in agreement with the structure of the phthalazine derivatives **18** or **19** (Fig. 6).

The formation of **18** was corroborated by ^{13}C NMR spectroscopy. In the case of the cinnoline derivative **19**, carbonyl carbons 1′ and 4 were supposed to show signals with similar shifts due to their chemical analogy. However, we found two different signals at 203.5 ppm (C-1′) and 163.3 ppm (C-1) confirming the structure of **18**.

The phthalazine derivative **18** was successfully transformed into phthalazine-5,8-dione **20**. As a result of the oxidation the two singlets for the OH hydrogens at 12.04 and 11.07 ppm (**18**) disappeared. The UV/VIS maximum was shifted from $\lambda(\log \epsilon)$=366 nm (3.95) (**18**) to 425 nm (3.54) (**20**). In this case phthalazine **18** was the product of a Michael addition of hydrazone structure **10e**, with the carbon atom as active site demonstrating the ambient reactivity of hydrazones. Again, the benzaldehyde hydrazone **10a** reacted at the nitrogen leading to the mono- and disubstituted hydrazino compounds **21** and **22**. (Fig. 7).

In addition, we have examined the behavior of 2,3-dimethyl-benzoquinone **23**. This quinone was selected in order to avoid double reaction which seemed to complicate the use of simple *p*-benzoquinone.

Reaction of the *N*-methylhydrazones **10a,c** with dimethylbenzoquinone **23** in methanol gave only the N adducts **24a,c** and no C adducts. The absence of the NH hydrogen in the ^1H NMR spectrum and the observed singlet due to the N-CH_3 group at 3.55 ppm (**24a**) resp. 3.53 ppm (**24c**) indicated that again the N adduct has been formed. The N=CH hydrogen at 7.78 ppm (**24a**) resp. 7.75 ppm (**24c**) and the fact that no N–H group was present in the IR spectra supported our conclusion. The UV/VIS spectra showed maxima at $\lambda(\log \epsilon)$=314 nm (4.33) and 510 nm (3.83) (**24a**) and 312 nm (4.38) and 526 nm (3.93) (**24c**), respectively. Purifying the resulting crystals by stirring in boiling methanol,

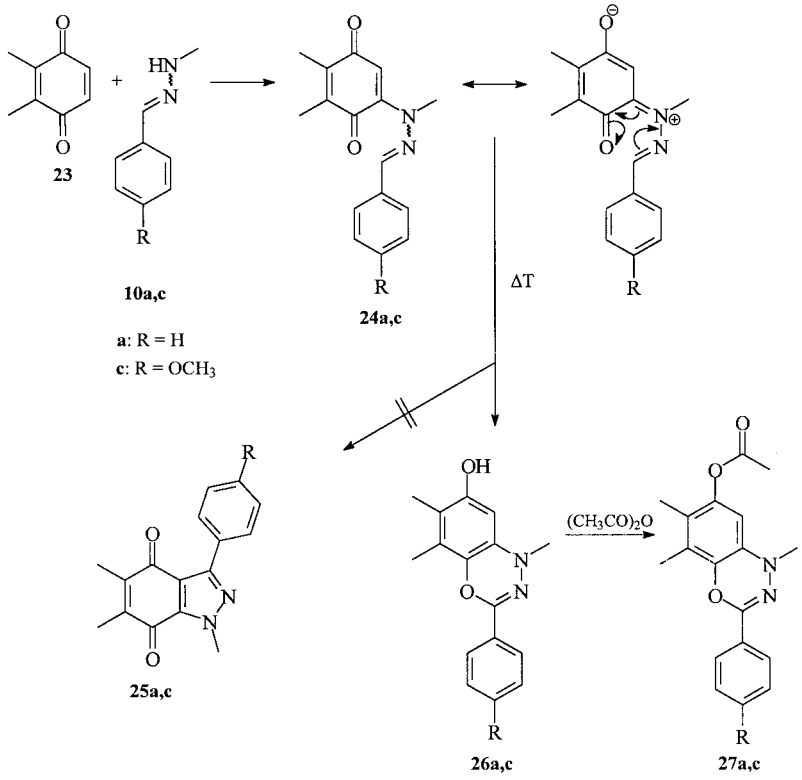

Figure 8.

2-propanol or toluene gave a yellow colored solution from which the benzoxadiazine derivatives **26a,c** were isolated. The signal for N=CH hydrogen in the ^{1}H NMR spectrum was absent; however, an additional signal for OH hydrogen at 9.07 ppm (**26a**) or 9.03 ppm (**26c**) appeared. The IR spectrum showed OH bands at 3280 and 3480 cm^{-1} instead of signals for C=O. To prove the structures of **26a,c**, the acetyl derivatives **27a,c** were prepared. Apparently the N adducts **24** suffered ring closure to benzoxadiazine by intramolecular hetero Diels–Alder reaction (Fig. 8). Again the nitrogen in *N*-methylhydrazones **10** showed a more nucleophilic character than in *N*-arylhydrazones **6**.

Conclusion

Our results demonstrate the ambient character of the *N*-alkylhydrazone structure. The reaction of *N*-alkylhydrazones with quinones opens new ways to heterocyclic compounds, such as benzindazolones, benzoxadiazines and phthalazines.

Experimental

NMR spectra were recorded using Bruker AC 200 (^{1}H: 200 MHz; ^{13}C: 50 MHz) with TMS as internal standard. Mass spectra were performed using Finnigan 4000 mass-spectrometer (EI, 70 eV). IR spectra: Perkin Elmer FT-IR-1600 spectral photometer. Melting points were measured with Gallenkamp-apparatus and are uncorrected. TLC-control: Merck Silica gel 60 F_{254}. Microanalyses were performed by Zentrale Einrichtung der Chemie/Pharmazie -Mikroanalyse- der Heinrich-Heine-Universität Düsseldorf. All solvents were purified and dried by known methods. Chemicals that are not specially mentioned were commercially available products.

2-Acetylnaphthoquinone (2). See Refs. 15,16

Formaldehyde dimethylhydrazone. See Ref. 17

2-Acetyl-3-(dimethyl-hydrazonomethyl)-[1,4]naphthoquinone (4a). Formaldehyde dimethylhydrazone (0.25 g, 1.7 mmol) was added slowly to **2** (0.20 g, 1 mmol) in methanol (5 ml) and stirred 1 h. The mixture was cooled overnight at −20°C and violet crystals (20 mg, 7,5%) were filtered off and dried. Mp 148°C. MS (70 eV): *m/z* (%): 270 (1) [M$^+$], 227 (1), 212 (2), 182 (1), 157 (1), 127 (2), 101 (1), 58 (44), 43 (100). IR (KBr): ν=2924, 1699, 1665, 1620, 1590 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=307 (4,51), 506 (4.18) nm. ^{1}H NMR ($CDCl_3$): 2.48 (s 3H; $COCH_3$), 3.20 (s 6H, two CH_3), 7.18 (s 1H, N=CH), 7.75–7.78 (m 2H, 6,7-H), 8.05–8.12 (m 2H, 5,8-H). Anal. calcd for $C_{15}H_{14}N_2O_2$: C, 66.66; H, 5.22; N, 10.36. Found: C, 66.74; H, 5.33; N, 9.97.

Benzaldehyde methylhydrazone (10a). See Ref. 18

Cinnamaldehyde methylhydrazone (10b). See Ref. 19

Anisaldehyde methylhydrazone (10c). See Ref. 20

2,5-Dimethoxy-benzaldehyde methylhydrazone (10d). Methylhydrazine (4.61 g, 0.10 mol) was slowly added to 2,5-dimethoxy-benzaldehyde (16.60 g, 0.10 mol) in 100 ml diethyl ether. $MgSO_4$ (5 g) was added and the mixture heated 3 h under reflux. The solvent was removed and the pale yellow oil was purified by Kugelrohr distillation at 235°C/23 mbar to give white crystals (16.5 g, 70%). For identification the unstable hydrazone was stirred 30 min in acetic acid anhydride and then treated with water to give the acylated product as pale white crystals. Mp 89°C. MS (70 eV): *m/z* (%): 236 (10) [M$^+$], 193 (3), 178 (4), 163 (100), 148 (34), 135 (11), 121 (9), 107 (7), 91 (11), 77 (20), 43 (91). IR (KBr): ν=3038, 2998, 2922, 2836, 1666, 1617, 1595, 1571 cm^{-1}. ^{1}H NMR ($CDCl_3$): 2.46 (s 3H, $COCH_3$), 3.36 (s 3H, NCH_3), 3.82, 3.85 (d 6H, two OCH_3), 6.84–6.95 (m 2H, 3′,4′-H), 7.46 (d 1H, 6′-H), 8.03 (s 1H, N=CH). Anal. calcd for $C_{12}H_{16}N_2O_3$: C, 61.00; H, 6.83; N, 11.86. Found: C, 61.19; H, 6.84; N, 11.81.

1-Methylhydrazonopropanone (10e). See Ref. 21

2-(*N*′-benzylidene-*N*-methyl-hydrazino)-[1,4]naphthoquinone (11a). Benzaldehyde methylhydrazone **10a** (2.72 g, 20.4 mmol) in methanol (5 ml) was added slowly to a suspension of 1,4-naphthoquinone **9** (1.92 g, 12 mmol) in methanol (15 ml). After being stirred for 15 min the precipitate (2.50 g, 72%) was filtered off, washed with methanol and dried. Red needles from toluene. Mp 175°C. MS: *m/z* (%): 290 (19), 261 (7), 233 (6), 186 (38), 158 (49), 130 (23), 106 (100), 77 (71), 51 (35). IR (KBr): ν=3075, 3057, 2941, 1672, 1632, 1590, 1557 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=313 (4.40), 486 (3.90) nm. ^{1}H NMR ($CDCl_3$): 3.68 (s 3H, CH_3), 7.05 (s 1H, 3-H), 7.37–7.47 (m 3H, C_6H_5), 7.62–7.78 (m 4H, C_6H_5, 6,7-H), 7.86 (s 1H, N=CH), 8.04–8.10 (m 2H, 5,8-H). ^{13}C NMR ($CDCl_3$): 183.92 (s, C-4 or C-1), 182.77 (s, C-1 or C-4), 150.27 (s, C-2), 140.29 (d, N=CH), 134.75 (s, C-4a), 133.88 (d, C-6 or C-7), 132.56 (d, C-7 or C-6), 132.47 (s, phenyl-C), 132.28 (s, C-8a), 129.84 (d, phenyl-CH), 128.77 (d, phenyl-CH), 127.29 (d, phenyl-CH), 126.61 (d, C-5 or C-8), 125.53 (d, C-8 or C-5), 115.61 (d, C-3), 36.31 (q, CH_3). Anal. calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.19; H, 4.82; N, 9.55.

1-Methyl-3-phenyl-1*H*-benzo[*f*]indazole-4,9-dione (12a). **11a** (1.00 g, 3.4 mmol) was dissolved in xylene (50 ml) and refluxed 48 h (TLC control). The solvent was removed and the residue was suspended in boiling methanol. After 5 min the mixture was filtered and the solution stored at −20°C. Yellow crystals (0.25 g, 25%). Mp 130°C. MS: *m/z* (%): 288 (100) [M$^+$], 257 (7), 232 (6), 204 (9), 176 (4), 144 (13), 129 (42), 102 (40), 77 (75), 51 (25). IR (KBr): ν=3058, 3007, 2949, 1676, 1662, 1594 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=246 (4.57), 268 (4.42), 339 (3.75) nm. ^{1}H NMR ($CDCl_3$): 4.40 (s 3H, CH_3), 7.44–7.51 (m 3H, C_6H_5), 7.72–7.81 (m 2H, 6,7-H), 8.13–8.30 (m 4H, 5,8-H, C_6H_5). Anal. calcd for $C_{18}H_{12}N_2O_2$: C, 74.99; H, 4.20; N, 9.72. Found: C, 74.87; H, 4.07; N, 9.68.

2-[*N*-Methyl-*N*′-(3-phenyl-allylidene)-hydrazino]-[1,4]-naphthoquinone (11b). Cinnamaldehyde methylhydrazone **10b** (2.72 g, 17 mmol) in methanol (5 ml) was added slowly to a suspension of 1,4-naphthoquinone **9** (1.60 g, 10 mmol) in methanol (15 ml). After being stirred for 15 min the precipitate (2.10 g, 65%) was filtered off, washed with

methanol and dried to give violet needles from toluene. Mp 159°C. MS: *m/z* (%): 316 (11) [M^+], 289 (4), 259 (4), 225 (11), 197 (3), 187 (22), 158 (18), 130 (100), 129 (25), 115 (24), 103 (30), 89 (33), 82 (35), 77 (66), 63 (17), 51 (47). IR (KBr): ν=3026, 1672, 1646, 1630, 1592, 1556 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=336 (4.33), 500 (3.78) nm. ^1H NMR ($CDCl_3$): 3.63 (s 3H, N-CH_3), 6.88–7.13 (m 3H, allyl system), 7.31–7.52 (m 5H, C_6H_5), 7.64–7.73 (m 3H, 6,7-H, 3-H), 8.04–8.10 (m 2H, 5,8-H). Anal. calcd for $C_{20}H_{16}N_2O_2$: C, 75.93; H, 5.10; N 8.85. Found: C, 75.74; H, 5.13; N,8.,82.

1-Methyl-3-(3-phenyl-propenyl)-1*H*-benzo[*f*]indazole-4,9-dione (12b). 11b (0.32 g, 1 mmol) was dissolved in xylene (50 ml) and stirred 5 days under reflux (TLC control). The solvent was removed, the residue treated with dichloromethane (1 ml) and chromatographed on silica gel (0.06–0.2 mm) with eluent dichloromethane. Yellow needles from methanol. Mp 144°C. MS: *m/z* (%): 314 (7) [M^+], 285 (1), 245 (1), 231 (2), 215 (1), 172 (9), 149 (9), 129 (100), 102 (43), 76 (32), 51 (53), 43 (24). IR (KBr): ν=3060, 3022, 2947, 1673, 1635, 1589, 1576, 1525, 1501 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=250 (4.51), 310 (4.34), 412 (3.78) nm. ^1H NMR ($CDCl_3$): 4.36 (s 3H, N-CH_3), 7.28–7.45 (m 3H), 7.61–7.92 (m 6H) (allyl system, C_6H_5, 6,7-H), 8.21–8.30 (m 2H, 5,8-H). Anal. calcd for $C_{20}H_{14}N_2O_2$: C, 76.41; H, 4.49; N, 8.91. Found: C, 76.46; H, 4.67; N, 8.99.

2-[*N′*-(4-methoxy-benzylidene)-*N*-methyl-hydrazino]-[1,4]-naphthoquinone (11c). Anisaldehyde methylhydrazone **10c** (2.80 g, 17 mmol) in methanol (5 ml) was added slowly to a suspension of 1,4-naphthoquinone **9** (1.60 g, 1 mmol) in methanol (15 ml). After being stirred for 15 min the precipitate (1.40 g, 44%) was filtered off, washed with methanol and dried to give red needles from toluene. Mp 148–151°C. MS: *m/z* (%): 320 (49) [M^+], 291 (10), 263 (7), 233 (2), 187 (24), 158 (19), 135 (100), 104 (27), 77 (47), 44 (20). IR (KBr): ν=3064, 2998, 2975, 2938, 2838, 1673, 1625, 1607, 1593, 1554, 1512 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=304 (4.49), 321 (4.51), 503 (4.03) nm. ^1H NMR ($CDCl_3$): 3.68 (s 3H, N-CH_3), 3.87 (s 3H, O-CH_3), 6.91–6.98 ('d' 2H, 3′,5′-H, *AA′*BB′), 7.03 (s 1H, 3-H), 7.63–7.76 (m 4H, 2′,6′-H from AA′*BB′*, 6,7-H), 7.85 (s 1H, N=CH), 8.04–8.10 (m 2H, 5,8-H). Anal. calcd for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.74. Found: C, 71.13; H, 5.11; N, 8.57.

3-(4-Methoxy-phenyl)-1-methyl-1*H*-benzo[f]indazole-4,9-dione (12c). See **12a**. Yellow crystals from methanol (0.27 g, 27%). Mp 173°C. MS: *m/z* (%): 318 (100) [M^+], 303 (21), 275 (20), 247 (2), 219 (3), 190 (3), 165 (4), 159 (8), 114 (5), 105 (6), 76 (15), 50 (14). IR (KBr): ν=3089, 2940, 2842, 1669, 1609, 1593, 1576 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=248 (4.74), 272 (4.43), 412 (3.68) nm. ^1H NMR ($CDCl_3$): 3.88 (s 3H, O-CH_3), 4.38 (s 3H, N-CH_3), 6.96–7.07 ('d' 2H, 3′,5′-H *AA′*BB′), 7.70–7.84 (m 2H, 6,7-H), 8.17–8.31 (m 4H, 5,8-H and 2′,6′-H AA′*BB′*). Anal. calcd for $C_{19}H_{14}N_2O_3$: C, 71.69; H, 4.43; N, 8.80. Found: C, 71.81; H, 4.54; N, 8.64.

2-[*N′*-(2,5-dimethoxy-benzylidene)-*N*-methyl-hydrazino]-[1,4]naphthoquinone (11d). 2,5-Dimethoxy-benzaldehyde methylhydrazone **10d** (1.32 g, 6.8 mmol) was added slowly to a suspension of 1,4-naphthoquinone **9** (0.64 g, 4 mmol) in methanol (15 ml) under stirring. After 30 min the violet precipitate (0.64 g, 46%) was filtered off, washed with methanol and dried. Mp 186°C (methanol). MS: *m/z* (%): 350 (24) [M^+], 319 (24), 293 (7), 263 (5), 236 (2), 187 (36), 163 (32), 148 (100), 105 (47), 77 (97), 50 (64). IR (KBr): ν=3068, 3030, 3006, 2948, 2909, 2836, 1667, 1631, 1591, 1555 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=329 (4.33), 500 (4.02) nm. ^1H NMR ($CDCl_3$): 3.69 (s 3H, N-CH_3), 3.85 and 3.86 (d 6H, two OCH_3), 6.81–6.99 (m 2H, 3′,4′-H), 7.01 (s 1H, 3-H), 7.54–7.56 ('d' 1H, 6′-H), 7.63–7.77 (m 2H, 6,7-H), 8.04–8.12 (m 2H, 5,8-H), 8.26 (s 1H, N=CH). Anal. calcd for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.63; H, 5.16; N, 7.85.

3-(2,5-Dimethoxy-phenyl)-1-methyl-1*H*-benzo[*f*]indazole-4,9-dione (12d). 11d (0.35 g, 1 mmol) was dissolved in xylene (50 ml) and stirred 5 days under reflux (TLC control). The solvent was removed, the residue treated with dichloromethane (1 ml) and chromatographed on silica gel (0.06–0.2 mm) with eluent dichloromethane/ethyl acetate (90/10). Yellow needles from methanol. Mp 252°C. MS: *m/z* (%): 348 (51) [M^+],333 (15), 317 (18), 305 (16), 262 (16), 233 (8), 205 (10), 159 (15), 129 (17), 105 (35), 76 (93), 50 (100). IR (KBr): ν=3073, 3000, 2950, 2837, 1676, 1590 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=248 (4.61), 267 (4.25), 276 (4.25), 312 (3.93) nm; ^1H NMR ($CDCl_3$): 3.77 (s 3H, OCH_3), 3.81 (s 3H, OCH_3), 4.39 (s 3H, N-CH_3), 6.98–7.05 (m 3H, 3′,4′,6′-H), 7.72–7.77 (m 2H, 6,7-H), 8.17–8.25 (m 2H, 5,8-H). Anal. calcd for $C_{20}H_{16}N_2O_4$: C, 68.96; H, 4.63; N, 8.04. Found: C, 69.06; H, 4.64; N, 7.79.

2-Acetyl-3-(*N′*-benzylidene-*N*-methyl-hydrazino)-[1,4]-naphthoquinone (14a). To a suspension of 2-acetyl-naphthoquinone **2** (0.20 g, 1 mmol) in methanol (5 ml) was added slowly benzaldehyde methylhydrazone **10a** (0.23 g, 1.7 mmol) in methanol (3 ml) and the mixture was stirred 20 min at 20°C. The red precipitate (0.25 g, 75%) was filtered off, washed with methanol and dried. Mp 172°C (methanol). MS: *m/z* (%): 332 (3) [M^+], 317 (1), 289 (25), 261 (1), 228 (11), 213 (7), 186 (30), 158 (6), 129 (11), 105 (34), 77 (65), 43 (100). IR (KBr): ν=3060, 2923, 1700, 1674, 1689, 1617, 1595, 1561 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=312 (4.31), 491 (3.79) nm. ^1H NMR ($CDCl_3$): 2.53 (s 3H, acetyl), 3.63 (s 3H, N-CH_3), 7.37–7.47 (m 3H), 7.57–7.63 (m 2H) (C_6H_5), 7.67–7.81 (m 3H, 6,7-H, N=CH), 8.04–8.11 (m 2H, 5,8-H). ^{13}C NMR ($CDCl_3$): 200.56 (s, *C*OCH_3), 183.03 (s, C-1), 182.32 (s, C-4), 146.19 (s, C-3), 140.94 (d, N=CH), 134.37 (d, C-6 or C-7), 133.99 (s, C-2), 133.10 (d, C-7 or C-6), 131.60 (s, C-4a or C-C8a), 131.51 (s, C-8a or C-4a), 129.91 (d, phenyl-CH), 128.77 (d, phenyl-CH), 128.13 (s, phenyl-C), 127.44 (d, phenyl-CH), 126.45 (d, C-5 or C-8), 125.74 (d, C-8 or C-5), 37.68 (q, N-*C*H_3), 32.64 (q, CO*C*H_3). Anal. calcd for $C_{20}H_{16}N_2O_3$: C, 72.28; H, 4.85; N, 8.43. Found: C, 71.82; H, 4.79; N, 8.53.

2-Acetyl-3-[*N*-methyl-*N′*-(2-oxo-propylidene)-hydrazino]-[1,4]naphthoquinone (14e). 2-Acetyl-naphthoquinone **2** (1.80 g, 9 mmol) in 10 ml toluene was added slowly to a solution of 1-methyl-hydrazonopropanone **10e** (0.91 g, 9 mmol) in 10 ml toluene with stirring at room temperature.

After 20 min the yellow precipitate (2-acetyl-1,4-dihydroxy-naphthalene) was filtered off. The solution was evaporated at room temperature, the residue treated with a mixture of cyclohexane (2 ml)/ethyl acetate (2 ml) and the precipitate **14e** (0.68 g, 25%) was then filtered off and dried. Red crystals. Mp 124°C. MS: *m/z* (%): 299 (1) [M^++1], 256 (5), 228 (3), 213(2), 186 (4), 105 (3), 76 (7), 43 (100). IR (KBr): ν=3067, 3008, 2974, 1712, 1673, 1629, 1595, 1572, 1556 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=298 (4.57), 439 (4.03) nm. ^{1}H NMR ($CDCl_3$): 2.33 (s 3H, CH_3), 2.57 (s 3H, acetyl), 3.43 (s 3H, N-CH_3), 7.08 (s 1H, N=CH), 7.77–7.83 (m 2H, 6,7-H), 8.09–8.12 (m 2H, 5,8-H). ^{13}C NMR ($CDCl_3$): 198.85 (q, *C*OCH_3), 196.59 ('quint', *C*OCH_3), 182.66 (d, C-4), 181.95 (d, C-1), 146.03 (s, C-3), 136.56 (d, N=CH), 134.77 (m, C-7/C-6), 133.96 (m, C-6/C-7), 133.10 (s, C-4a/C-8a), 131.16 (s, C-8a/C-4a), 131.02 (q, C-2), 126.73 (m, C-5/C-8), 126.18 (m, C-8/C-5), 38.66 (q, N*C*H_3), 32.62 (q, CO*C*H_3), 25.35 (q, CO*C*H_3). Anal. calcd for $C_{16}H_{14}N_2O_4$: C, 64.42; H, 4.73; N, 9.39. Found: C, 64.47; H, 4.60; N, 9.36.

1,3-Dimethyl-1*H*-benzo[*f*]indazole-4,9-dione (15). 14a or **14e** (0.10 g) was dissolved in methanol/glacial acetic acid (10 ml, 10%). After 5 h stirring, the colorless solution was evaporated and the residue (85%) was recrystallized from methanol. Mp 140°C (methanol). Lit.[24]: mp 158°C. MS: *m/z* (%): 226 (100) [M^+], 197 (11), 169 (8), 158 (14), 129 (44), 102 (46), 76 (73), 50 (54), 43 (22). IR (KBr): ν=3074, 3032, 1678, 1591. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=266 (4.25), 275 (4.30), 329 (3.89) nm. ^{1}H NMR ($CDCl_3$): 2.65 (s 3H, CH_3), 4.27 (s 3H, N-CH_3), 7.69–7.82 (m 2H, 6,7-H), 8.16–8.25 (m 2H, 5,8-H), ^{13}C NMR ($CDCl_3$): 179.90 (s, C-9), 176.09 (s, C-4), 155.40 (s, C-9a), 148.99 (s, C-3), 137.74 (s, C-4a), 134.18 (d, C-6 or C-7), 133.23 (d, C-7 or C-6), 133.10 (s, C-8a), 126.67 (d, C-5+C-8), 119.66 (s, C-3a), 38.69 (q, N*C*H_3), 12.87 (q, CH_3). Anal. calcd for $C_{13}H_{10}N_2O_2$: C, 69.02; H, 4.46; N, 12.38. Found: C, 68.88; H, 4.47; N, 12.43.

2-Methoxycarbonyl-1,4-benzoquinone (17). See Ref. 22

4-Acetyl-5,8-dihydroxy-2-methyl-2*H*-phthalazine-1-one (18). 17 (1.00 g, 6 mmol) was dissolved in methanol (10 ml). 1-methylhydrazono-propanone **10e** (1.00 g, 10 mmol) was added and the mixture left at room temperature over night. The precipitate (0.70 g, 50%) was filtered off, washed with methanol and dried. Yellow needles (methanol). Mp 190°C. MS: *m/z* (%): 234 (42) [M^{+1}], 219 (5), 191 (11), 162 (8), 161 (5), 135 (3), 107 (5), 78 (10), 51 (10), 43 (100)]. IR (KBr): ν=3446, 2953, 2802, 1674, 1650, 1613, 1578, 1531 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=238 (4.28), 366 (3.95) nm. ^{1}H NMR ($CDCl_3$): 2.77 (s 3H, CO–CH_3), 3.87 (s 3H, N-CH_3), 7.19, 7.34 (AB, 2H, ^3J=9 Hz 6,7-H), 11.07 (s 1H, 6-OH), 12.04 (s 1H, 8-OH). ^{13}C NMR ($CDCl_3$): 203.54 (s, *C*OCH_3), 163.30 (s, C-1), 154.15 (s, C-8 or C-5), 146.02 (s, C-5 or C-8), 141.61 (s, C-4), 126.81 (d, C-6 or C-7), 121.60 (d, C-7 or C-6), 113.79 (s, C-8a or C-4a), 110.65 (s, C-4a or C-8a), 39.56 (q, N-CH_3), 27.98 (q, $COCH_3$). Anal. calcd for $C_{11}H_{10}N_2O_4$: C, 56.41; H, 4.27; N, 11.96. Found: C, 56.2; H, 4.34; N, 11.93.

4-Acetyl-2-methyl-2*H*-phthalazine-1,5,8-trione (20). 18 (1.00 g, 4.3 mmol) was dissolved in dry acetone and the flask was then flushed with argon. Na_2SO_4 (2 g) and Ag_2O (3.00 g, 13 mmol) were added and the mixture stirred 30–40 min (TLC control). The mixture was filtered off and the solution was evaporated at room temperature. Orange crystals (0.79 g, 80%). Mp:146°C. MS: *m/z* (%): 232 (3) [M^+], 217 (3), 162 (1), 133 (1), 104 (4), 78 (10), 43 (100). IR (KBr): ν=3052, 2931, 1694, 1670, 1640, 1611, 1568 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=241 (4.25), 428 (3.54) nm. ^{1}H NMR ($CDCl_3$): 2.63 (s 3H, acetyl), 3.91 (s 3H, N-CH_3), 6.94 and 7.00 (AB 2H, ^3J=10.2 Hz). Anal. calcd for $C_{11}H_{18}N_2O_4$: C, 56.9; H, 3.47; N, 12.06. Found: C, 56.68; H, 3.45; N, 11.88.

2-(*N'*-Benzylidene-*N*-methyl-hydrazino)-3,6-dioxo-cyclohexa-1,4-dienecarboxylic acid methyl ester (21). 17 (0.33 g, 2 mmol) was suspended in methanol (5 ml) and benzaldehyde methylhydrazone **10a** (0.13 g, 1 mmol) was added slowly under stirring. The mixture was evaporated to dryness, dissolved in dichloromethane (0.5 ml) and chromatographed on silica gel (0.063–0.200 mm) with eluent dichloromethane/ethyl acetate (95/5). Violet crystals (0.09 g, 30%). Mp 148°C. MS: *m/z* (%): 298 (41) [M^+], 267 (88), 239 (83), 197 (11), 162 (56), 136 (44), 113 (41), 104 (21), 82 (100), 77 (74), 54 (43). IR (KBr): ν=3001, 2948, 1730, 1676, 1644, 1603, 1549 cm^{-1}. ^{1}H NMR ($CDCl_3$): 3.58 (s 3H, OCH_3), 3.64 (s 3H, N-CH_3), 6.72 (AB 2H, 5,6-H ^3J=10.2 Hz), 7.34–7.47 (m 3H), 7.60–7.67 (m 2H) (C_6H_5), 7.76 (s 1H, N=CH). Anal. calcd for $C_{16}H_{14}N_2O_4$: C, 64.42; H, 4.73; N, 9.39; Found: C, 64.69; H, 4.81; N, 9.40.

2,5-Bis-(*N'*-benzylidene-hydrazino)-3,6-dioxo-cyclohexa-1,4-dienecarboxylic acid methyl ester (22). 17 (0.33 g, 2 mmol) was suspended in methanol (5 ml) and benzaldehyde methylhydrazone **10a** (0.27 g, 2 mmol) was added slowly under stirring. After 1 h the mixture was cooled to −20°C and the precipitate (0.17 g, 29%) was filtered off, washed with methanol and dried. Brown powder. Mp 166°C. MS: *m/z* (%): 430 (2) [M^+], 399 (1), 369 (20), 323 (7), 292 (27), 266 (8), 223 (12), 191 (74), 118 (13), 104 (62), 82 (100), 77 (52), 51 (30), 42 (17). IR (KBr): ν=3062, 2947, 2911, 1732, 1633, 1596, 1560, 1556 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=310 (4.39), 458 (4.42) nm. ^{1}H NMR (DMSO-d6): 3.52 (s 3H, OCH_3), 3.60 (s 3H, N-CH_3), 3.63 (s 3H, N-CH_3), 6.50 (s 1H, 4-H), 7.45–7.51 (m 6H), 7.68–7.72 (m 2H), 7.78–7.83 (m 2H), (two C_6H_5), 8.11 (s 1H, N=CH), 8.20 (s 1H, N=CH). Anal. calcd for $C_{24}H_{22}N_4O_4$: C, 66.97; H, 5.15; N, 13.02. Found: C, 66.95; H, 4.97; N, 12.94.

2,3-Dimethyl-1,4-benzoquinone (23). 2,3-Dimethyl-1,4-hydroquinone (10.40 g, 75.4 mmol), $KBrO_3$ (5.6 g), sulfuric acid (5 ml) and water (100 ml) were stirred 10 min at 80°C. The mixture was then cooled 3 h with ice. The resulting yellow needles (10.00 g, 98%) were filtered off, washed with ice-water and crystallized from petrolether (60/80). Mp 55°C.[23]

5-(*N'*-Benzylidene-*N*-methyl-hydrazino)-2,3-dimethyl-[1,4]-benzoquinone (24a). Benzaldehyde methylhydrazone **10a** (0.67 g, 5 mmol) was added slowly to a solution of 2,3-dimethyl-benzoquinone **23** (0.68 g, 5 mmol) in methanol (5 ml) under stirring. After 5 min the violet precipitate

(0.40 g, 30 %) was filtered off, washed with methanol and dried. Mp 129°C. MS: *m/z* (%): 268 (18) [M^+], 225 (2), 211 (11), 197 (10), 164 (30), 136 (44), 124 (25), 110 (19), 108 (18), 106 (69), 82 (100), 77 (51), 67 (67), 54 (53), 42 (20). IR (KBr): ν=3183, 3068, 3003, 2946, 2907, 1662, 1646, 1599, 1574, 1507 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=289 (4.33), 314 (4.33), 509 (3.83) nm. ^{1}H NMR ($CDCl_3$): 2.05 (s 6H, two CH_3), 3.55 (s 3H, N-CH_3), 6.70 (s 1H, 3-H), 7.21–7.45 (m 3H), 7.69–7.76 (m 2H) (C_6H_5), 7.78 (s 1H, N=CH). Anal. calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.61; H, 5.97; N, 10.17.

5-[*N′*-(4-Methoxy-benzylidene)-*N*-methyl-hydrazino]-2,3-dimethyl-[1,4]benzoquinone (24c). To a solution of 2,3-dimethylbenzoquinone **23** (0.68 g, 5 mmol) in methanol (3 ml) was added 4-methoxy-benzaldehyde methylhydrazone **10c** (0.82 g, 5 mmol) under stirring. After 5 min the mixture was cooled at −20°C and the precipitate (0.38 g, 39 %) was filtered off, washed with methanol and dried. Mp 170°C (petroleum ether 60/80). MS: *m/z* (%): 298 (40) [M^+], 283 (3), 255 (4), 227 (12), 212 (3), 188 (16), 164 (21), 135 (85), 124 (44), 108 (22), 92 (19), 82 (100), 77 (38), 55 (40), 42 (21). IR (KBr): ν=2997, 2960, 2935, 1646, 1598, 1562, 1513 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=296 (4.47), 312 (4.38), 526 (3.93) nm. ^{1}H NMR ($CDCl_3$): 2.04 (s 6H, two CH_3), 3.53 (s 3H, N-CH_3), 3.88 (s 3H, OCH_3), 6.67 (s 1H, 3-H), 6.89–6.96 ('d' 2H, *AA′*BB′), 7.62–7.70 ('d' 2H, AA′*BB′*) (4-methoxy-phenyl), 7.75 (s 1H, N=CH). Anal. calcd for $C_{17}H_{18}N_2O_3$: C, 68.44; H, 6.08; N, 9.39. Found: C, 68.20; H, 6.26; N, 9.64.

7-Hydroxy-1,5,6-trimethyl-3-phenyl-1*H*-benzo[1,3,4]oxadiazine (26a). 24a (1.00 g, 3.7 mmol) were dissolved in methanol (50 ml) and boiled 5 min under stirring. The solvent was evaporated at room temperature and the residue was recrystallized from petroleum ether 60/80. White–yellow wool-like crystals (3.50 g, 95%). Mp 129°C. MS: *m/z* (%): 268 (88) [M^+], 234 (1), 192 (21), 164 (29), 150 (5), 136 (25), 124 (100), 108 (11), 82 (39), 67 (15), 42 (25). IR (KBr): ν=3274, 2999, 2960, 2992, 2623, 1590, 1500. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=254 (5.03), 318 (4.27), 366 (4.32) nm. ^{1}H NMR (DMSO-d6)): 1.97 (s 3H, CH_3), 2.15 (s 3H, CH_3), 3.03 (s 3H, N-CH_3), 6.10 (s 1H, 8-H), 7.44–7.50 (m 3H), 7.76 −7.85 (m 2H) (C_6H_5), 9.07 (s 1H, OH). Anal. calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.69; H, 5.87; N, 10.31.

7-Hydroxy-3-(4-methoxy-phenyl)-1,5,6-trimethyl-1*H*-benzo[1,3,4]oxadiazine (26c). 24c (1.00 g, 3.4 mmol) was dissolved in methanol (50 ml) and boiled 10 min under stirring. The mixture was evaporated and the residue was recrystallized from petroleum ether 68/80. White wool-like crystals (0.90 g, 90%). Mp 143°C. MS: *m/z* (%): 298 (40) [M^+], 283 (1), 269 (1), 216 (1), 164 (23), 136 (20), 124 (100), 108 (10), 96 (10), 82 (37), 67 (16), 42 (56). IR (KBr): ν=3418, 2961, 2924, 1623, 1610, 1577[1], 1514 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=261 (4.55), 349 (3.83) nm. ^{1}H NMR (DMSO-d6): 1.97 (s 3H, CH_3), 2.14 (s 3H, CH_3), 3.00 (s 3H, N-CH_3), 3.80 (s 3H, OCH_3), 6.07 (s 1H, 8-H), 6.97–7.05 ('d' 2H, *AA′*BB′), 7.71–7.78 ('d' 2H, AA′*BB′*) (4-methoxy-phenyl), 9.03 (s 1H, OH). Anal. calcd for $C_{17}H_{18}N_2O_3$: C, 68.44; H, 6.08; N, 9.39. Found: C, 68.48; H, 6.21; N, 9.04.

Acetic acid 1,5,6-trimethyl-3-phenyl-1*H*-benzo[1,3,4]oxadiazin-7-yl ester (27a). 26a (0.10 g) was dissolved in 20 ml $(CH_3CO)_2O$, 2 drops of pyridine were added and the mixture was stirred 1 h at room temperature. The solvent was removed and the residue was recrystallized from petroleum ether 60/80 to give yellow needles (0.10 g 90%). Mp: 105°C. MS: *m/z* (%): 310 (60) [M^+], 268 (88), 239 (1), 206 (1), 164 (36), 136 (21), 124 (100), 108 (9), 82 (73), 67 (22), 42 (45). IR (KBr): ν=3430, 2923, 1760, 1623, 1598, 1576 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=248 (4.49), 309 (3.71), 361 (3.73) nm. ^{1}H NMR ($CDCl_3$): 1,98 (s 3H, CH_3), 2,23 (s 3H, CH_3), 2,31(s 3H, CH_3), 3,10 (s 3H, N-CH_3), 6,08 (s 1H, 8-H), 7,36–7,42 (m 3H), 7,83–7,88 (m 2H) (C_6H_5). Anal. calcd for $C_{18}H_{18}N_2O_3$: C, 69,66; H, 5,85; N, 9,03. Found: C, 69,41; H, 5,82; N, 9,24.

Acetic acid 3-(4-methoxy-phenyl)-1,5,6-trimethyl-1*H*-benzo[1,3,4]oxadiazin-7-yl ester (27c). 26c (0.10 g) was dissolved in 20 ml $(CH_3CO)_2O$, 2 drops of pyridine were added and the mixture was stirred 30 min at room temperature. The solvent was removed and the residue was recrystallized from petroleum ether 60/80 to give yellow needles (0.10 g, 80%). Mp: 167°C. MS: *m/z* (%): 340 [M^+], 324 (1), 298 (48), 256 (1), 226 (1), 215 (1), 164 (41), 136 (19), 124 (100), 82 (62), 67 (20), 55 (11), 42 (55). IR (KBr): ν=3446, 2996, 2968, 2934, 1759, 1622, 1607, 1513 cm^{-1}. UV/VIS (CH_2Cl_2): λ_{max}(log ϵ)=258 (4.18), 330 (3.50) nm. ^{1}H NMR ($CDCl_3$): 1.98 (s 3H, CH_3), 2.22 (s 3H, CH_3), 2.31 (s 3H, CH_3 acetyl), 3.08 (s 3H, N-CH_3), 3.84 (s 3H, OCH_3), 6.10 (s 1H, 8-H), 6.86–6.94 ('d' 2H, *AA′*BB′), 7.76–7.84 ('d' 2H, AA′*BB′*) (4-methoxy-phenyl). Anal. calcd for $C_{19}H_{20}N_2O_4$: C, 67.05; H, 5.92; N, 8.23. Found: C, 67.19; H, 5.83; N, 8.19.

References

1. Inouye, H.; Leistner, E. Biochemistry of quinones. In *The Chemistry of the Quinoid Compounds*, Patai, S., Ed.; Wiley: New York, 1974; Vol. 1, Part 2, pp 683–735.
2. Bentley, R.; Campbell, I. M. Biological reactions of quinones. In *The Chemistry of the Quinoid Compounds*, Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, NY, 1988; Vol. 2, Part 2, pp 1293–1349.
3. Lown, J. W. Anthracycline and anthracenedione based anticancer agents. In *Bioactive Molecules*, Lown, J. W., Ed.; Elsevier: Amsterdam, 1988; Vol. 6.
4. Ditrich, K.; Hamprecht, G.; Wuerzer, B.; Meyer, N.; Westphalen, K. O.; Laatsch, H. (BASF A.-G.); *Preparation of naphthindazole-4,9-quinones as herbicides*; Ger. Offen. DE 3,831,332 (Cl. C07D231/54); 29. Mar. 1990 Appl. 15. Sep. 1988; *Chem. Abstr.* **1990**, 113, 152403y.
5. Personal information; Hamprecht, G., BASF A.-G.; Ludwigshafen, Germany.
6. Engel, S. *Aminochinone als Synthone der Nenitzescu-Reaktion*. Dissertation, Heinrich-Heine-Universität Düsseldorf, 1998.
7. Kuckländer, U.; Pitzler, H.; Kuna, K. *Arch. Pharm. (Weinheim)* **1994**, *327*, 137–142.
8. Lassaletta, J. M.; Diez, E.; Fernandez, R., et al., *J. Org. Chem* **1997**, *62*, 5144–5155.
9. Lassaletta, J. M.; Enders, D.; Syrig, R., et al., *Synthesis* **1996**, 48–52.

10. Lassaletta, J. M.; Fernandez, R. *Tetrahedron Lett.* **1992**, *33*, 3691–3694.
11. Brehme, R.; Nikolajewski, H.-E. *Tetrahedron Lett.* **1982**, *23*, 1131–1134.
12. Zimmermann, G. *Acetylnaphthochinone als Heterodiene einer Diels–Alder-Reaktion*. Dissertation, Heinrich-Heine-Universität Düsseldorf, 1996.
13. Granik, V. G.; Lyubchanskaya, V. M.; Alekseeva, L. M. *Tetrahedron* **1997**, *53*, 15005–15010.
14. Baldwin, J. E. *J. Chem. Soc. Chem. Commun.* **1976**, 734–738.
15. Green, I. R. *J. Chem. Ed.* **1982**, *52*, 689–699.
16. Read, G.; Ruiz, V. M. *J. Chem. Soc., Perkin Trans. 1* **1973**, 235–243.
17. Hoyo, M.; Kamitori, Y., et al., *J. Org. Chem.* **1988**, *53*, 129–135.
18. Todd, D. *J. Am. Chem. Soc.* **1949**, *71*, 1353–1355.
19. Gillis, B. T.; LaMontagne, M. P. *J. Org. Chem.* **1968**, *33*, 762–766.
20. Sucrow, W.; Slopianka, M.; Neophytou, A. *Chem. Ber.* **1972**, *105*, 2143–2155.
21. Begtrup, M.; Nytoft, H. P. *J. Chem. Soc., Perkin Trans. 1* **1985**, 81–86.
22. Cason, J. *Org. React.* **1948**, *4*, 354–355.
23. Teuber, H.-J. *Chem. Ber.* **1953**, *86*, 1036–1047.
24. Eistert, B.; Fink, H.; Schulz, T.; Riedinger, J. *Liebigs Ann. Chem.* **1971**, *750*, 1–11.