Investigation of Interaction of Benzoquinones and Naphthoquinones with Substituted Hydrazides

Alaa A. Hassan,* Yusria R. Ibrahim, and Ahmed M. Shawky

Department of Chemistry, Faculty of Science, Minia University, El-Minia, A. R. Egypt
*E-mail: alaahassan2001@yahoo.com

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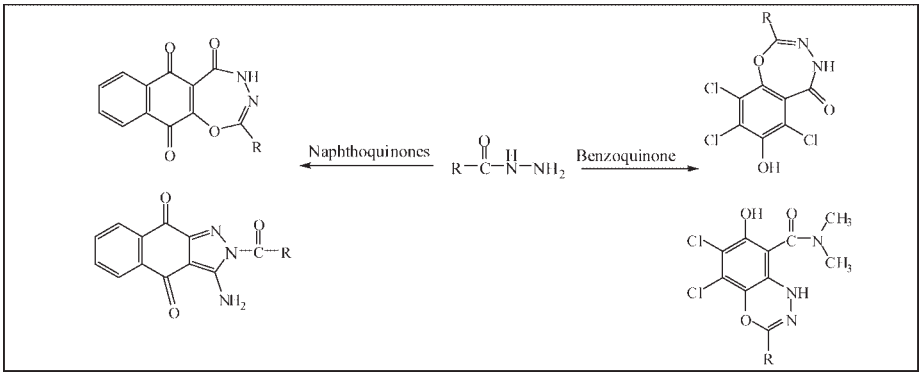

Nucleophilic attack by substituted hydrazides on C-2, C-3 of 2,3,5,6-tetrachloro-1,4-benzoquinone and 2,3-dichloro-1,4-naphthoquinone initiates the formation of benzo[e][1,3,4]oxadiazine and benzo- as well as naphthoxadiazepine derivatives. On the other hand, substituted hydrazides attack 1,4-naphthoquinone-2,3-dicarbonitrile to form benzo[f]indazole-4,9-dione derivatives. A rationale for the conversions observed is presented.

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INTRODUCTION

2,3,5,6-Tetrachloro-1,4-benzoquinone (**2**) and 2,3-dichloro-1,4-naphthoquinone (**3**) undergo nucleophilic substitution of one or two chlorine atoms by primary amines [1,2], amino acids [3,4], and aziridines [5]. Up to four nitrogen residues are introduced into **2** and **3** in their reaction with pyrazole [6], imidazole [7,8], and 1,2,4-triazole [7,9]. Amides and thioamides were added to **3** to produce two related heterocyclic diones series in excellent yields [10–14]. The reaction of **2** and **3** with N^1, N^2-diarylamidines to give benzimidazole and indole derivatives has been reported [15,16]. Heterocyclization of substituted thiosemicarbazides and dithiobiureas during the reaction with benzoquinones and naphthoquinones, different successful approach for the synthesis of oxathiadiazole [17], thiadiazine [17,18], imidazoxadiazole [19], imidazothiadiazole [20], and indazole [21] derivatives. A large variety of quinones, including many fused heterocyclic rings, have been used as synthetic intermediates in medicinal [22–25] and dye chemistry [26–29].

RESULTS AND DISCUSSION

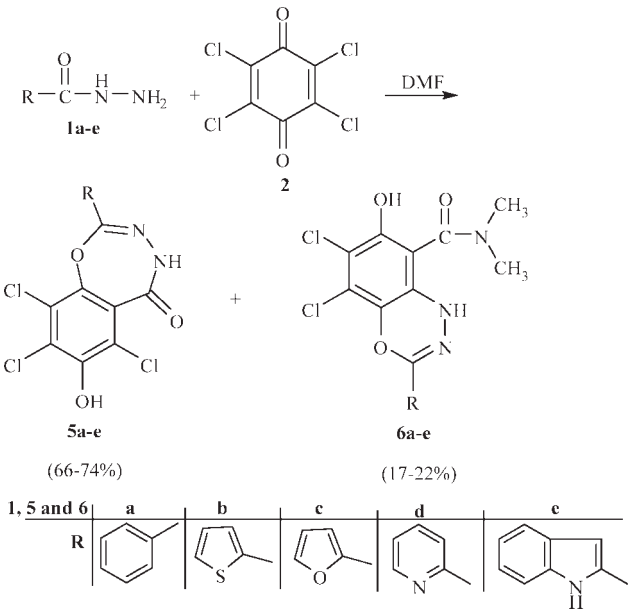
We report herein the results of our recent investigation on the reactions of substituted hydrazides **1a-e** with 2,3,5,6-tetrachloro-1,4-benzoquinone (**2**), 2,3-dichloro-1,4-naphthoquinone (**3**) and 1,4-naphthoquinone-2,3-dicarbonitrile (**4**).

Equimolar solutions of **1a-e** and **2** in DMF upon standing for 48 hours at room temperature formed the derivatives of benzoxadiazepine **5a-e** as major product (66–74%) and benzoxadiazine **6a-e** as minor product (17–22%) (Scheme 1).

The structural assignment of 6,8,9-trichloro-7-hydroxy-2-(substituted)benzo[*f*][1,3,4]oxadiazepine-5(*H*)-one **5a-e** are based on the following spectral data: The IR spectrum showed a broad bands at ν_{max} 3455–3480 and 3280–3335 because of OH and NH, sharp band at 1700–1710 for carbonyl group and 1620–1630 cm^{-1} for C=N.

The ^1H NMR displayed two broad singlets, one at δ = 7.79–7.86 ppm and the other at δ = 9.57–9.62 ppm because of oxadiazepine-NH and phenolic-OH, respectively. The ^{13}C NMR spectrum showed a signal at δ = 152.46–152.75 ppm for aromatic quaternary carbon atom bearing a hydroxyl group [30], the presence of one carbonyl group at δ = 169.73–169.84 ppm and oxadiazepinone-C-2 at δ = 156.66–156.86 ppm. In the ^{13}C NMR the absence of characteristic resonance signals of the carbonyl carbon atoms of chloranil **2** around 182–184 [31] ppm support the structure **5a-e**. The formation of **5b** was further confirmed by mass spectrometry.

Scheme 1



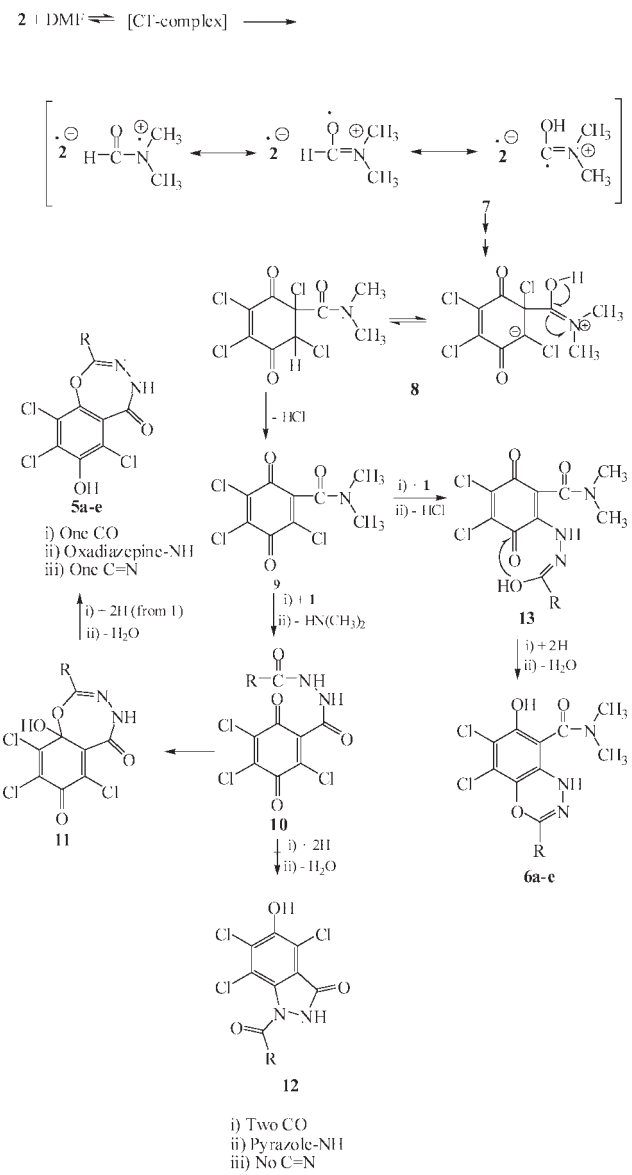
Besides the molecular ion at 362/368, the characteristic fragment ion patterns of trichloro compounds were observed. The EI mass spectrum of **5b** is characterized by loss of 111 a.m.u (most likely thiophene carbonyl group) followed by loss of 28 a.m.u (dinitrogen or carbonyl group). The *a priori* possible isomeric structure **12a-e** (Scheme 2) was ruled out on the basis of IR and ^{13}C NMR spectral data.

The structural assignment of **6a-e** was supported by the following spectral data: In its ^{13}C NMR spectrum, the characteristic absorption signal of two carbonyl carbon atoms of chloranil are replaced by signals at δ = 140.87–141.12 and δ=152.46–153.04 ppm, which are characteristic of aromatic quaternary carbon bearing oxygen [30]. In addition Ph—C—Cl appears at 121.94–122.32 and 123.14–123.46 [31] ppm. The carbonyl group attached to $N(CH_3)_2$ resonates at δ = 171.23–171.42 [31] ppm. The IR spectrum of **6a-e** showed bands at 3470–3490 and 3290–3315 due to OH and NH, and strong absorption at 1680–1690 due to carbonyl group. The ^1H NMR spectrum of **6a-e** showed signals at 3.36–344, 7.69–7.81, and 9.61–9.74 due to $N(CH_3)_2$, oxadiazine–NH and hydroxyl group, respectively. It is worthy to note that the mass spectra of compounds **6a-e** show the loss of O=C—$N(CH_3)_2$, N_2 or CO, as well as RCO from the molecular ions.

Scheme 2 summarizes the reactions responsible for the formation of compounds **5** and **6**. It shows the interaction of **1a-e** with chloranil (**2**) in DMF as a solvent proceeded in an interesting manner because of the participation of DMF in the course of the reaction, as reported in our earlier publications on the reactions of hydrazino-1,2,4-triazinoindole [32], amino- and diamino-1,2,4-triazole derivatives [9] and 3,5-diaminopyrazoles [6] with chloronated benzoquinones and naphthoquinones.

Unstable charge-transfer complexes may be formed during the reaction between chlorinated quinone and DMF, followed by the formation of anionic cationic radicals **7**. Recombination of the radicals afforded the adduct **8**, which gradually split off a molecule of hydrogen chloride to form **9**. The latter interacted with the hydrazide **1** with elimination a molecule of dimethylamine and another of water in presence of hydrogen protons (possibly from **1**) to afford benzoxadiazepine derivatives **5a-e**. On the other hand compound **9** reacted with **1** to give **6a-e** as illustrated in Scheme 2.

Scheme 2



2,3-Dichloro-1,4-naphthoquinone **3** was chosen to compare its reactivity toward the hydrazides **1a-e** with chloranil (**2**).

It has been described in the literature that **3** resembles **2** in most of its substitution reactions, especially with compounds containing nucleophilic nitrogen (amines, amino acids, pyrazoles, imidazoles, etc) [1–7,9]. From this point of view one might expect that **1a-e** should react with **2** similarly like **3**. Earlier, it had been reported that **1a** reacted with **3**, ultimately giving 2,3-di(benzoyl-hydrazinyl)naphthalene-1,4-dione (**14**) (Scheme 3). We report here the results of recent investigations on the reaction of **1a-e** with **3**.

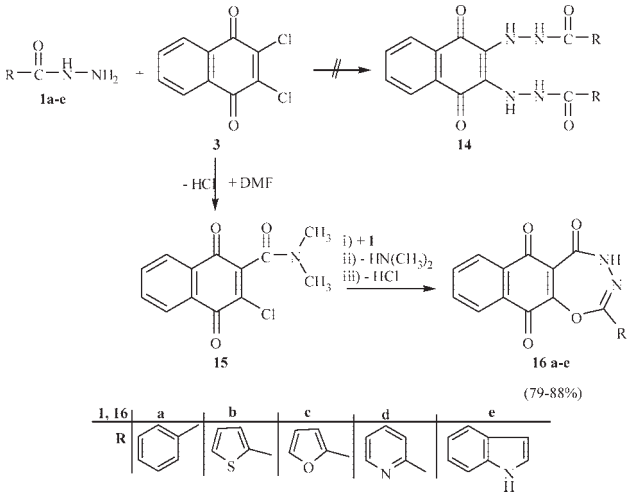
Mixing equimolar amounts of **1a-e** and **3** in DMF for 72 hours led to the formation of 2-substituted naphtho[2,3-*f*][1,3,4]oxadiazepine-5,6,11-(4*H*)-triones **16a-e** (Scheme 3). The IR spectra of **16a-e** (in KBr) showed NH absorption at 3230–3245 cm^{-1}, carbonyl groups at 1705–1725 and 1680–1690, as well as bands characteristic of C—O—C and C=N at 1090 and 1620–1630, respectively. The ^1H NMR spectra of **16a-e** clearly show one broad signal at 7.78–7.84 ppm due to oxadiazepine-NH.

Signals around 169.58–169–84 (C-5), 187.39–187.78 (C–6) [31] and 187.33–187.80 (C-11) [31] and 156.78–156.86 (C-2), in ^{13}C NMR spectra lend further support to the structure assigned to **16a-e**. The EI-mass spectra need a brief comment for **16a-e**, m/z = 213 represent the derivative of benzindazolyl fragment formed by release of corresponding RCO from the molecular ion, which undergo loss of 28 a.m.u (dinitrogen or CO group).

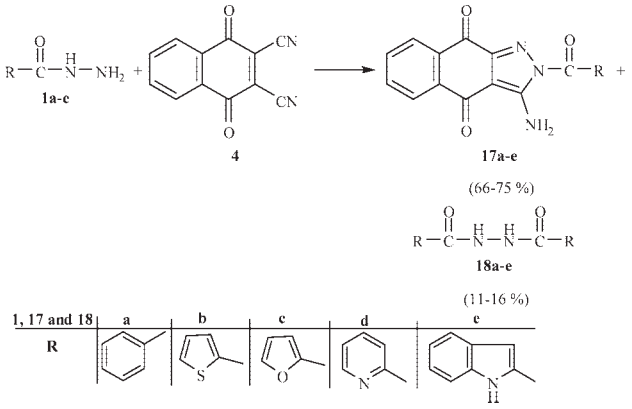
The present investigation also dealt with the study of the chemical behavior of hydrazides **1a-e** toward 1,4-naphthoquinone-2,3-dicarbonitrile (**4**). Substituted benzo[*f*]indazolediones **17a-e** and diacylhydrazines **18a-e** were obtained from the reaction of **1a-e** with (**4**) (Scheme 4).

Compounds **17a-e** exhibited IR absorptions at 3330–3345 (NH_2), 1685–1690 and 1660–1665 (CO). The ^1H NMR spectra of **17a-e** clearly showed one broad signal at 6.67–6.73 ppm because of NH_2, besides the aromatic protons. Signals at 153.29–153.48 (C-3), 100.89–101.46 (C-3a), 139.81–140.11 (C9a), 188.54–188.74 (C-4), 187.75–187.89 (C-9), 165.46–165.73 (CO), 137.86 (indole-C-2) and 99.74 (indole-C-5) in the ^{13}C NMR spectra of **17a-e** lend further supported the structure assigned to **17a-e**. The structure of **17e** was evidently confirmed by mass spectrometrically, besides the molecular ion at m/z = 356 (39%), the characteristic fragment ion pattern of indole-2-carbonyl at 144 (86), $C_6H_4CO^+$ group at 104 (77), benzoyl cation at 91 (89) and 77 (100) as a base peak. A possible reaction process is depicted in Scheme 5.

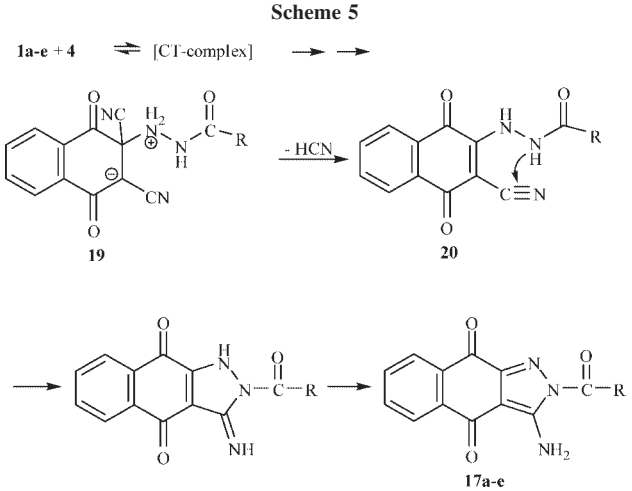
Scheme 3



Scheme 4



Scheme 5



CONCLUSIONS

In a fairly complex and multistep process, benzo[e][1,3,4]oxadiazine, benzo[f]indazole-4,9-dione and benzoxadiazepine as well as naphthoxadiazepine derivatives are formed from **1a-e** and (**2-4**) during the nucleophilic attack by substituted hydrazides on C-2, C-3 of 2,3,5,6-tetrachloro-1,4-benzoquinone and 2,3-dichloro-1,4-naphthoquinone. On the other hand, 1,4-naphthoquinone-2,3-dicarbonitrile (**4**) may act as either as a mediator or as a building block in heterocyclization of substituted hydrazides. The results reported here supplement the rich of substituted hydrazides **1a-e**.

EXPERIMENTAL

Mp's were determined using open glass capillaries on a Gallenkamp melting point apparatus and are uncorrected. The IR spectra were recorded with a Shimadzu 408 instrument using potassium bromide pellets. The ^{1}H NMR (400.13 MHz) and ^{13}C NMR (100.6 MHz) spectra were measured in DMSO-d_6 using a Bruker AM400 with TMS as an internal standard. Chemical shifts are expressed as δ [ppm], s = singlet, m = multiplet and b = broad. Assignments of carbon resonances have been supported by DEPT experiments. Mass spectra have been obtained with Varian MAT CH-7 instrument using electron impact ionization (70 eV). Elemental analyses have been determined by the Microanalytical Center, Cairo University, Egypt. For preparative layer chromatography (plc) 1.0 mm thick air-dried layers of slurry applied silica gel, Merck Pf_{254} on 48 cm wide and 20 cm high glass plates were used, zones were detected by their color and indicator fluorescence quenching upon exposure to 254 nm light and extracted with acetone.

Starting materials. Substituted hydrazides **1a-e** were prepared according to published procedures, as were 2-thiophene carbohydrazide (**1b**), mp 135–137°C (ref. [33] 134–136°C); furan-2-carbohydrazide (**1c**), mp 77–79 (ref. [34] 78°C); 2-pyridine carbohydrazide (**1d**), mp 136–138°C (ref. [35] 137°C); indole-2-carbohydrazide (**1e**), mp 243–245°C (ref. [36,37] 246°C) and phenyl carbohydrazide (**1a**) (Aldrich), 2,3,5,6-tetrachloro-1,4-benzoquinone (**2**) (Aldrich) and 2,3-dichloro-1,4-naphthoquinone (**3**) (Aldrich) were used as received. 1,4-Naphthoquinone-2,3-dicarbonitrile (**4**) was prepared from 2,3-dichloro-1,4-naphthoquinone (**3**) according to Budni et al [38].

Reaction of substituted hydrazides 1a-e with (2). To a solution of **2** (246 mg, 1 mmol) in dry DMF (15 mL) a solution of **1a-e** (1.0 mmol each) in 5 mL of DMF was added dropwise over 5 min. at room temperature with stirring and admission of air. The stirring was continued for 48 h with admission of air to complete the reaction. The reaction mixture was concentrated to drynes. The residue was taken up several times with cold ethanol (10 mL) and slurry was concentrated again to remove any residual DMF. The residue was dissolved in acetone (5 mL). This solution in each case was applied to 5 plc-plates and developed with toluene/ethyl acetate (5:1) for the run with **1a**, toluene/ethyl acetate (4:1) for the runs with **1b-d** and toluene/ethyl acetate (3:1) for the run with **1e** to give numerous colored zones. The two intense of which were removed and extracted. The fastest migrating one contained substituted benzo[1,3,4]oxadiazepine **5a-e**, the slowest migrating zone contained substituted benzo-[1,3,4]oxadiazinecarboxamide **6a-e**. Extraction of zones with acetone and recrystallized.

6,8,9-Trichloro-7-hydroxy-2-phenylbenzo[*f*][1,3,4]-oxadiazepin-5-(4*H*)-one (5a). Compound **5a** was obtained as reddish brown crystals (0.264 g, 74%), mp 216–217°C (acetonitrile), IR: 3460 (OH), 3310 (NH), 1705 (CO), 1625 (C=N), 1596 (Ar—C=C), 1085 (C—O—C). ^{1}H NMR: δ 7.18–7.53 (m, 5H, Ar—H), 7.84 (br, 1H, oxadiazepine—NH), 9.56 (br, 1H, OH); ^{13}C NMR: δ 120.71 (C-5a), 122.53, 123.74, 124.17 (C-6, 8 and 9), 126.51, 128.26, 130.14 (Ar—CH), 134.72 (Ar—C), 147.38 (C-9a), 152.56 (C-7), 156.86 (C-2), 169.84 (CO); ms m/z: 356/362 (M^+, 42), 322 (26), 286 (34), 250 (21), 194 (26), 158 (11), 105 (67), 77 (100), 65 (49); Anal. Calcd. for $C_{14}H_7Cl_3N_2O_3$ (357.58): C, 47.02; H, 1.97; Cl, 29.74; N, 7.83. Found: C, 46.81; H, 2.11; Cl, 29.51; N, 7.64.

6,8,9-Trichloro-7-hydroxy-2-(thiophen-2-yl)benzo[*f*][1,3,4]-oxadiazepin-5-(4*H*)-one (5b). Compound **5b** was obtained as reddish brown crystals (0.258g, 71%), mp 257–259°C (acetonitrile). IR: 3470 (OH), 3295 (NH), 1700 (CO), 1630 (C=N), 1585 (Ar—C=C), 1090 (C—O—C). ^{1}H NMR: δ 7.05–7.38 (m, 3H, thiophene-H), 7.79 (br, 1H, oxadiazepine-NH), 9.62 (br, 1H, OH); ^{13}C NMR: δ 120.59 (C-5a), 122.42, 123.55, 123.96 (C-6, 8 and 9), 126.27, 127.69, 127.94 (thiophene-CH), 130.16 (thiophene-C), 148.06 (C-9a), 152.61 (C-7), 156.79 (C-2), 169.76 (CO); ms m/z: 362/368 (M^+, 34), 328 (18), 292 (27), 218 (41), 111 (100), 107 (53), 82 (46); Anal. Calcd. for $C_{12}H_5Cl_3N_2O_3S$ (363.60): C, 39.64; H, 1.39; Cl, 29.25; N, 7.70. Found C, 39.41; H, 1.51; Cl, 29.47; N, 7.54.

6,8,9-Trichloro-7-hydroxy-2-(furan-2-yl)benzo[*f*][1,3,4]-oxadiazepin-5-(4*H*)-one (5c). Compound **5c** was obtained as reddish brown crystals (0.229 g, 66%), mp 207–208°C (acetonitrile). IR: 3455 (OH), 3335 (NH), 1710 (CO), 1625 (C=N), 1085 (C—O—C); ^{1}H NMR: δ 7.11–7.46 (m, 3H, furan-H), 7.82 (br, 1H, oxadiazepine-NH), 9.57 (br, 1H, OH); ^{13}C NMR: δ 120.71 (C-5a), 122.19, 123.64, 123.92 (C-6, 8 and 9), 125.98, 126.11 (furan-CH), 141.57, 142.11 (furan-C-2, C-5), 147.96 (C-9a), 152.75 (C-7), 156.68 (C-2), 169.81 (CO); ms m/z: 346/352 (M^+, 38), 312 (25), 276 (16), 220 (31), 184 (27), 95 (100), 67 (71); Anal. Calcd. For $C_{12}H_5Cl_3N_2O_4$ (347.54): C, 41.47; H, 1.45; Cl, 30.60; N, 8.06. Found C, 41.66; H, 1.56; Cl, 30.38; N, 7.87.

6,8,9-Trichloro-7-hydroxy-2-(pyridin-2-yl)benzo[*f*][1,3,4]-oxadiazepin-5-(4*H*)-one (5d). Compound **5d** was obtained as reddish brown crystals (0.247g, 69%), mp 226–228°C (ethanol). IR: 3480 (OH), 3315 (NH), 1705 (CO), 1620 (C=N), 1590 (Ar—C=C), 1080 (C—O—C); ^{1}H NMR: δ 7.48–8.41 (m, 5H, pyridine-H and oxadiazepine-NH), 9.57 (br, 1H, OH); ^{13}C NMR: δ 121.07 (C-5a), 122.31, 123.62, 123.89 (C-6, 8 and 9), 127.89, 128.75, 130.14 (pyridine-CH), 146.35, 147.11 (pyridine C-2, C-6), 148.22 (C-9a), 152.57 (C-7), 156.85 (C-2), 169.73 (CO); ms m/z: 357/363 (M^+, 21), 323 (18), 287 (34), 195 (47), 106 (83), 78 (100); Anal. Calcd. for $C_{13}H_6Cl_3N_3O_3$ (358.56): C, 43.55; H, 1.69; Cl, 29.66; N, 11.72. Found C, 43.33; H, 1.78; Cl, 29.43; N, 11.87.

2-(1*H*-Indole-2-yl)-6,8,9-trichloro-7-hydroxy-benzo[*f*][1,3,4]-oxadiazepin-5-(4*H*)-one (5e). Compound **5e** was obtained as reddish brown crystals (0.265g, 67%), mp 271–273°C (methanol). IR: 3475–3280 (OH, NH's), 1710 (CO), 1630 (C=N), 1595 (Ar—C=C), 1090 (C—O—C); ^{1}H NMR: δ 6.64 (s, 1H,

indole-CH), 7.12–7.68 (m, 4H, Ar—H), 7.86 (br, 1H, oxadiazepine-NH), 9.58 (br, 1H, OH), 11.62 (br, 1H, indole-NH); ^{13}C NMR: δ 99.71(indole-CH), 121.98 (C-5a), 121.87, 123.35, 123.92 (C-6, 8 and 9), 127.14, 127.96 (Ar—CH), 130.55 (indole-C3a), 134.66, 137.12 (indole C-2 and C-7a), 152.46 (C-7), 156.81 (C-2), 169.80 (CO); MS m/z: 395/361 (M^+, 29), 331 (26), 295 (38), 242 (21), 186 (12), 144 (62), 116 (76), 92 (100), 77 (83), 65 (41); Anal. Calcd. for $C_{16}H_8Cl_3N_3O_3$ (396.61): C, 48.45; H, 2.03; Cl, 26.82; N, 10.59. Found C, 48.64; H, 1.91; Cl, 27.03; N, 10.77.

5,6-Dichloro-7-hydroxy-*N,N′*-dimethyl-3-phenyl-1*H*-benzo[*e*][1,3,4]oxadiazine-8-carboxamide (6a). Compound **6a** was obtained as deep red brown crystals (0.062g, 17%), mp 248–250°C (acetonitrile). IR: 3485 (OH), 3290 (NH), 1690 (CO), 1625 (C=N), 1585 (Ar—C=C), 1080 (C—O—C); ^{1}H NMR: δ 3.44 (s, 6H, $N(CH_3)_2$), 7.24–7.79 (m, 6H, Ar—H and oxadiazine-NH), 9.67 (br, 1H, OH); ^{13}C: δ 36.29 (CH_3), 106.83 (C-8), 122.27, 123.14 (C-5 and C-6), 127.21, 128.54, 130.16 (Ar-CH), 134.27 (Ar-C), 138.44 (C-8a), 141.11 (C-4a), 152.51 (C-7), 156.76 (C-3), 171.41 (CO); MS m/z: 365/369 (M^+, 41), 329 (18), 257 (44), 193 (29), 105 (81), 77 (100), 65 (74); Anal. Calcd. for $C_{16}H_{13}Cl_2N_3O_3$ (366.20): C, 52.48; H, 3.58; Cl, 19.36; N, 11.47. Found C, 52.66; H, 3.45; Cl, 19.59; N, 11.65.

5,6-Dichloro-7-hydroxy-*N,N′*-dimethyl-3-(thio-phen-2-yl-1*H*-benzo[*e*][1,3,4]oxadiazine-8-carbox-amide (6b). Compound **6b** was obtained as reddish brown crystals (0.067g, 18%), mp 276–278°C (ethanol). IR: 3470 (OH), 3310 (NH), 1685 (CO), 1630 (C=N), 1590 (Ar—C=C), 1085 (C—O—C); ^{1}H NMR: δ 3.36 (s, 6H, $N(CH_3)_2$), 7.11–7.39 (m, 3H, thiophene-H), 7.71 (br, 1H, oxadiazine-NH), 9.70 (br, 1H, OH); ^{13}C: δ 36.41 (CH_3), 107.12 (C-8), 121.94, 123.32 (C-5 and C-6), 126.22, 127.56, 127.84 (thiophene-CH), 130.12 (thiophene-C), 138.51 (C-8a), 140.97 (C-4a), 152.46 (C-7), 156.81 (C-3), 171.23 (CO); ms m/z: 371/375 (M^+, 26), 336 (29), 300 (12), 264 (21), 153 (8), 111 (100), 83 (76); Anal. Calcd. for $C_{14}H_{11}Cl_2N_3O_3S$ (372.23): C, 45.17; H, 2.98; Cl, 19.05; N, 11.29; S, 8.61. Found C, 44.94; H, 3.10; Cl, 18.88; N, 11.41; S, 8.83.

5,6-Dichloro-7-hydroxy-*N,N′*-dimethyl-3-(thio-phen-2-yl-1*H*-benzo[*e*][1,3,4]oxadiazine-8-carbox-amide (6c). Compound **6c** was obtained as brown crystals (0.078g, 22%), mp 235–237°C (ethanol). IR: 3480 (OH), 3300 (NH), 1680 (CO), 1625 (C=N), 1590 (Ar—C=C), 1085 (C—O—C); ^{1}Hnmr: δ 3.40 (s, 6H, $N(CH_3)_2$), 6.95–7.35 (m, 3H, furan-H), 7.69 (br, 1H, oxadiazine-NH), 9.67 (br, 1H, OH); ^{13}C: δ 36.38 (CH_3), 106.91 (C-8), 122.18, 123.27 (C-5 and C-6), 125.96, 126.47 (furan-CH), 138.36 (C-8a), 141.12 (C-4a), 142.76, 143.63 (furan-C-2 and C-5), 152.64 (C-7), 156.77 (C-3), 171.34 (CO); MS m/z: 355/359 (M^+, 27), 320 (42), 284 (18), 212 (37), 117 (52), 95 (100), 67 (68); Anal. Calcd. for $C_{14}H_{11}Cl_2N_3O_4$ (356.16): C, 47.21; H, 3.11; Cl, 19.91; N, 11.80. Found C, 47.44; H, 2.98; Cl, 20.08; N, 12.02.

5,6-Dichloro-7-hydroxy-*N,N′*-dimethyl-3-(pyridin-2-yl-1*H*-benzo[*e*][1,3,4]oxadiazine-8-carboxamide (6d). Compound **6d** was obtained as brown crystals (0.062g, 17%), mp 261–263°C (acetonitrile). IR: 3490 (OH), 3315 (NH), 1690 (CO), 1630 (C=N), 1585 (Ar—C=C), 1080 (C—O—C); ^{1}H: δ 3.38 (s, 6H, $N(CH_3)_2$), 7.36—8.48 (m, 5H, pyridine-H and oxadiazine-NH), 9.74 (br, 1H, OH); ^{13}C: δ 36.44 (CH_3), 107.09 (C-8), 122.28, 123.46 (C-5 and C-6), 127.16, 128.91, 130.28 (pyridine-CH), 138.42 (C-8a), 140.87 (C-4a), 146.42, 147.83 (pyridine-C-2 and C-6), 152.71 (C-7), 156.84 (C-3), 171.42 (CO); MS m/z: 366/370 (M^+, 35), 332 (19), 296 (27), 224 (41), 196 (23), 106 (74), 78 (100); Anal. Calcd. for $C_{15}H_{12}Cl_2N_4O_3$ (367.19): C, 49.07; H, 3.29; Cl, 19.31; N, 15.26. Found C, 48.84; H, 3.41; Cl, 19.07; N, 15.43.

5,6-Dichloro-7-hydroxy-*N,N′*-dimethyl-3-(pyridin-2-yl-1*H*-benzo[*e*][1,3,4]oxadiazine-8-carboxamide (6e). Compound **6e** was obtained as brown crystals (0.073g, 18%), mp 301–303°C (methanol). IR: 3485 (OH), 3340-3295 (NH's), 1690 (CO), 1630 (C=N), 1600 (Ar-C=C), 1085 (C—O—C); ^{1}H NMR: δ 3.41 (s, 6H, $N(CH_3)_2$), 6.64 (s, 1H, indole-CH), 7.26–7.81 (m, 5H, Ar—H and oxadiazine-NH), 9.62 (br, 1H, OH), 11.71 (br, 1H, indole-NH); ^{13}C NMR: δ 36.45 (CH_3), 98.95 (indole-CH), 106.88 (C-8), 122.32, 123.41 (C-5 and C-6), 126.37, 127.74 (Ar-CH), 130.71 (indole-C-3a), 135.07, 137.36 (indole-C-2 and C-7a), 138.53 (C-8a), 141.07 (C-4a), 153.04 (C-7), 156.91 (C-3), 171.26 (CO); MS m/z: 404/408 (M^+, 25), 370 (32), 334 (12), 262 (46), 234 (19), 144 (56), 91 (76), 77 (100), 65 (85); Anal. Calcd. for $C_{18}H_{14}Cl_2N_4O_3$ (405.23): C, 53.35; H, 3.48; Cl, 17.50; N, 13.83. Found C, 53.17; H, 3.61; Cl, 17.72; N, 14.05.

Reaction of substituted hydrazides 1a-e with (3). A solution of **1a-e** (1.0 mmol) in 15 mL of dry DMF was added dropwise with stirring to a solution of **3** (1.0 mmol) in 10 mL of dry DMF. The reaction mixture was stirring for 72 h, during which time it turned from faint orange into deep red. The precipitate of substituted naphtho[2,3-*f*][1,3,4]oxadiazepine-5,6,11-(4*H*)-trione **16** was filtered and washed several times with cold ethanol, and crystallized from suitable solvent.

2-Phenylnaphtho[2,3-*f*][1,3,4]oxadiazepine-5,6,11-(4*H*)-trione (16a). Compound **16a** was obtained as reddish brown crystals (0.280g, 88%), mp 289–291°C (acetonitrile). IR: 3230 (NH), 1710, 1685 (CO), 1620 (C=N), 1585 (Ar—C=C), 1090 (C—O—C); ^{1}H NMR: δ 7.14–7.76 (m, 5H, Ar—H), 7.84 (br, 1H, oxadiazepine-NH), 8.04–8.21 (m, 4H, Ar—H); ^{13}C NMR: δ 126.49, 128.84, 129.12, 134.61, 136.66 (Ar—CH), 131.45, 132.45, 132.17, 141.36 (Ar—C), 156.86 (C-2), 169.64 (oxadiazepine-CO), 187.44, 187.78 (C-6 and C-11); ms m/z: 318 (M^+, 46), 213 (26), 185 (61), 105 (81), 104 (76), 77 (100), 65 (67); Anal. Calcd. for $C_{18}H_{10}N_2O_4$ (318.28): C, 67.92; H, 3.17; N, 8.80. Found C, 68.14; H, 3.06; N, 9.04.

2-(Thiophen-2-yl)naphtho[2,3-*f*][1,3,4]oxadiaz-epine-5,6,11-(4*H*)-trione (16b). Compound **16b** was obtained as brown crystals (0.272 g, 84%), mp 307–309°C (ethanol). IR: 3245 (NH), 1715, 1680 (CO), 1625 (C=N), 1585 (Ar-C=C), 1080 (C-O-C); ^{1}H NMR: δ 7.08–7.46 (m, 3H, thiophene-H), 7.80 (br, 1H, oxadiazepine-NH), 8.05–8.19 (m, 4H, Ar—H); ^{13}C NMR: δ 126.23, 127.76, 128.33, (thiophene-CH), 129.36, 136.94 (Ar-CH), 131.64, 131.16, 141.19 (Ar—C), 156.80 (C-2), 169.58 (oxadiazepine-CO), 187.39, 187.68 (C-6 and C-11); ms m/z: 324 (M^+, 23), 213 (34), 185 (48), 111 (100), 104 (56), 77 (86), 65 (61); Anal. Calcd. for $C_{16}H_8N_2O_4S$ (324.31): C, 59.26; H, 2.49; N, 8.64; S, 9.89. Found C, 59.09; H, 2.61; N, 8.43; S, 10.04.

2-(Furan-2-yl)naphtho[2,3-*f*][1,3,4]oxadiazepine-5,6,11-(4*H*)-trione (16c). Compound **16c** was obtained as brown crystals (0.253 g, 82%), mp 274–276°C (ethanol). IR: 3235 (NH), 1710, 1690 (CO), 1620 (C=N), 1590 (Ar—C=C), 1085 (C—O—C); ^{1}H: δ 6.97–7.38 (m, 3H, furan-H), 7.78 (br, 1H, oxadiazepine-NH), 8.00–8.22 (m, 4H, Ar—H); ^{13}C NMR: δ

126.08, 126.26 (furan-CH), 129.54, 136.89 (Ar—CH), 131.55, 131.96, 140.87 (Ar—C), 141.62, 142.26 (furan-C-2 and C-5), 156.85 (C-2), 169.84 (oxadiazepine-CO), 187.46, 187.72 (C-6 and C-11); ms m/z: 308 (M^+, 32), 213 (28), 185 (57), 157 (21), 104 (71), 95 (63), 77 (100), 65 (84); Anal. Calcd. for $C_{16}H_8N_2O_5$ (308.25): C, 62.34; H, 2.62; N, 9.09. Found C, 62.51; H, 2.77; N, 8.83.

2-(Pyridin-2-yl)naphtho[2,3-*f*][1,3,4]oxadiazepine-5,6,11-(4*H*)-trione (16d). Compound **16d** was obtained as brown crystals (0.255 g, 80%), mp 297-299°C (acetonitrile). IR: 3245 (NH), 1705, 1690 (CO), 1625 (C=N), 1585 (Ar—C=C), 1090 (C—O—C); ^{1}H NMR: δ 7.36–8.49 (m, 9H, Ar—H, pyridine-H and oxadiazepine-NH); ^{13}C NMR: δ 126.54, 128.73 (pyridine-CH), 129.49, 130.37, 136.94 (Ar-CH and pyridine-CH), 131.57 (Ar-C), 146.39, 147.81 (pyridine-C-2 and C-6), 156.82 (C-2), 169.64 (oxadiazepine-CO), 187.51, 187.80 (C-6 and C-11); ms m/z: 319 (M^+, 28), 213 (41), 185 (64), 157 (22), 106 (88), 104 (73), 77 (100), 65 (56); Anal. Calcd. for $C_{17}H_9N_3O_4$ (319.27): C, 63.95; H, 2.84; N, 13.16. Found C, 64.16; H, 2.71; N, 12.98.

2-(1*H*-Indol-2-yl)naphtho[2,3-*f*][1,3,4]oxadiaz-epine-5,6,11-(4*H*)-trione (16e). Compound **16e** was obtained as reddish brown crystals (0.282 g, 79%), mp 331–333°C (methanol). IR: 3330-3240 (NH's), 1710, 1685 (CO), 1630 (C=N), 1600 (Ar—C=C), 1085 (C—O—C); ^{1}H NMR: δ 6.61 (s, 1H, indole-CH), 7.16–7.64 (m, 4H, Ar—H), 7.82 (br, 1H, oxadiazepine-NH), 8.05–8.27 (m, 4H, Ar—H), 11.71 (br, 1H, indole-NH); ^{13}C NMR: δ 99.63 (indole-CH), 127.26, 129.41, 136.22, 137.38 (Ar—CH), 130.26, 131.66, 134.27, 139.26 (Ar—C and indole-C-2), 156.78 (C-2), 169.75 (oxadiazepine-CO), 187.48, 187.73 (C-6 and C-11); ms m/z: 357 (M^+, 34), 213 (26), 185 (54), 144 (62), 104 (57), 91 (74), 77 (100), 65 (63); Anal. Calcd. for $C_{20}H_{11}N_3O_4$ (357.32): C, 67.23; H, 3.10; N, 11.76. Found C, 67.06; H, 2.97; N, 11.89.

Reactions of substituted hydrazides 1a-e with (4). A solution of **1a-e** (1.0 mmol) in 15 mL of dry DMF was added dropwise with stirring to a solution of 1,4-naphthoquinone-2,3-dicarbonitrile (**4**) (208 mg, 1.0 mmol) in 10 mL of dry DMF. The reaction colour changed gradually from green to purple and latter turns into brown colour. The stirring was continued for 72 h with admission of air to complete the reaction. The reaction mixture was concentrated and the residue was then separated by plc using toluene/ethyl acetate (5:1) for the runs with (**1a-d**) and toluene/ethyl acetate (3:1) for the run with (**1e**) to give numerous zones, two intense of which were removed and extracted. The fastest migrating one which quenched all indicator fluorescence upon exposure to 254nm UV-light contained diacylhydrazines **18a-e**. The slowest migrating zone (which is always characterized by deep yellow colour) contained substituted benzo[*f*]- indazolediones **17a-e**.

3-Amino-2-benzoyl-2*H*-benzo[*f*]indazole-4,9-dione (17a). Compound **17a** was obtained as deep yellow crystals (0.222 g, 70 %), mp 271–273°C (ethanol). IR: 3345 (NH_2), 1685, 1660 (CO), 1620 (C=N), 1585 (Ar-C=C); ^{1}H NMR: δ 6.71 (br, 2H, NH_2), 7.28–7.77 (m, 5H, Ar—H), 8.06–8.22 (m, 4H, Ar—H); ^{13}C NMR: δ 101.16 (C-3a), 126.52, 128.32, 129.26, 133.12, 136.51 (Ar—CH), 130.76, 131.44 (Ar-C), 139.86 (C-9a), 153.46 (C-3), 165.55 (CO), 187.82 (C-9), 188.68 (C-4); ms m/z: 317 (M^+, 52), 212 (41), 184 (26), 105 (100), 104 (76), 77 (81), 65 (72); Anal. Calcd. for $C_{18}H_{11}N_3O_3$ (317.30): C, 68.14; H, 3.49; N, 13.24. Found C, 67.88; H, 3.61; N, 13.40.

3-Amino-2-(thiophen-2-carbonyl)-2*H*-benzo[*f*]-indazole-4,9-dione (17b). Compound **17b** was obtained as yellow crystals (0.242 g, 75%), mp 295–297°C (acetonitrile). IR: 3335 (NH_2), 1690, 1660 (CO), 1625 (C=N), 1590 (Ar-C=C); ^{1}H NMR: δ 6.67 (br, 2H, NH_2), 7.14–7.52 (m, 3H, thiophene-H), 8.05–8.19 (m, 4H, Ar—H); ^{13}C NMR: δ 100.89 (C-3a), 126.72, 129.33, 129.78, 130.12, 136.44 (Ar—CH and thiophene-CH), 131.58, 132.29 (Ar—C and thiophene-C), 140.08 (C-9a), 153.36 (C-3), 165.46 (CO), 187.76 (C-9), 188.54 (C-4); ms m/z: 323 (M^+, 41), 212 (56), 184 (44), 111 (100), 104 (62), 77 (83), 65 (74); Anal. Calcd. for $C_{16}H_9N_3O_3S$ (323.33): C, 59.44; H, 2.81; N, 13.00; S, 9.92. Found C, 59.26; H, 2.94; N, 12.82; S, 10. 13.

3-Amino-2-(furan-2-carbonyl)-2*H*-benzo[*f*]-indazole-4,9-dione (17c). Compound **17c** was obtained as yellow crystals (0.209 g, 68%), mp 259–261°C (ethanol). IR: 3330 (NH_2), 1685, 1665 (CO), 1620 (C=N), 1590 (Ar—C=C), 1080 (C-O-C); ^{1}H NMR: δ 6.69 (br, 2H, NH_2), 7.08–7.46 (m, 3H, furan-H), 8.08-8.24 (m, 4H, Ar—H); ^{13}C NMR: δ 101.14 (C-3a), 126.13, 126.76, 129.41, 136.28 (Ar—CH and furan-CH), 131.64 (Ar—C), 139.90 (C-9a), 147.42, 148.51 (furan-C-2 and C-5), 153.29 (C-3), 165.65 (CO), 187.89 (C-9), 188.74 (C-4). ms m/z: 307 (M^+, 59), 212 (38), 184 (61), 104 (72), 95 (86), 77 (100), 65 (76); Anal. Calcd. for $C_{16}H_9N_3O_4$ (307.26): C, 62.54; H, 2.95; N, 13.68. Found C, 62.37; H, 3.10; N, 13.87.

3-Amino-2-picolinoyl-2*H*-benzo[*f*]indazole-4,9-dione (17d). Compound **17d** was obtained as yellow crystals (0.229 g, 72%), mp 276-278°C (acetonitrile). IR: 3335 (NH_2), 1685, 1660 (CO), 1620 (C=N), 1585 (Ar—C=C). ^{1}H NMR: δ 6.68 (br, 2H, NH_2), 7.56–8.48 (m, 8H, Ar—H and pyridine-H). ^{13}C NMR: δ 100.96 (C-3a), 126.43, 128.51, 129.55, 130.12, 136.34 (Ar—CH and pyridine-CH), 131.59 (Ar—C), 139.81 (C-9a), 147.86, 148.62 (pyridine-C-2, C-6), 153.37 (C-3), 165.55 (CO), 187.75 (C-9), 188.64 (C-4). ms m/z: 318 (M^+, 62), 212 (53), 184 (67), 106 (100), 104 (76), 77 (83), 65 (64). $C_{17}H_{10}N_4O_3$ (318.29): C, 64.15; H, 3.17; N, 17.60. Found C, 63.96; H, 3.28; N, 17.76.

3-Amino-2-(1*H*-indole-2-carbonyl)-2*H*-benzo[*f*]-indazole-4,9-dione (17e). Compound **17e** was obtained as yellowish brown crystals (0.235 g, 66%), mp 324–326°C (acetonitrile). IR: 3340, 3270 (NH_2, NH), 1690, 1665 (CO), 1625 (C=N), 1590 (Ar-C=C); ^{1}H NMR: δ 6.59 (s, 1H, indole-CH), 6.73 (br, 2H, NH_2), 7.28–7.83 (m, 4H, Ar—H), 8.05–8.26 (m, 4H, Ar—H), 11.69 (br, 1H, indole-NH); ^{13}C NMR: δ 99.74 (indole-C-3), 101.46 (C-3a), 126.46, 127.29, 129.41, 130.29, 136.36 (Ar—CH), 130.52, 131.64 (Ar—C), 137.86 (indole-C-2), 138.68 (indole-C-7a), 140.11 (C-9a), 153.48 (C-3), 165.73 (CO), 187.75 (C-9), 188.65 (C-4); ms m/z: 356 (M^+, 39), 212 (26), 184 (55), 144 (86), 104 (77), 91 (89), 77 (100), 65 (62); Anal. Calcd. for $C_{20}H_{12}N_4O_3$ (356.33): C, 67.41; H, 3.39; N, 15.72. Found C, 67.22; H, 3.27; N, 15.89.

***N*′-Benzoylbenzohydrazide (18a).** Yield (0.038g, 16%), mp 239–241°C (ref. [39,40] 237–238°C). ^{1}H NMR: δ 7.26–7.40 (m, 3H, Ar—H), 7.44–7.64 (m, 4H, Ar—H), 7.78–7.83 (m, 3H, Ar—H), 10.68 (br, 2H, NH).

***N*′-(Thiophene-2-carbonyl)thiophen-2-hydrazide (18b).** Yield (0.035g, 14%), mp 276–278°C (ref. [41,42] 274–277°C). ^{1}H NMR: δ 7.19–7.58 (m, 6H, thiophene-H), 10.62 (br, 2H, NH).

***N′*-(Furan-2-carbonyl)furan-2-hydrazide (18c).** Yield (0.026g, 12%), mp 240–242°C (ref. [44] 238–239°C). ^{1}H NMR: δ 7.05–7.52 (m, 6H, furan-H), 10.66 (br, 2H, NH).

***N′*-Picolinoylpicolinohydrazide (18d).** Yield (0.036mg, 15%), mp 224–226°C (ref. [44] 224–225°C). ^{1}H NMR: δ 7.52–8.37 (m, 8H, pyridine-H), 10.65 (br, 2H, NH).

***N′*-(1*H*-Indole-2-carbonyl)-1*H*-indole-2-hydrazide (18e).** Yield (0.035g, 11%), mp 355–357°C (ref. [44] 356.5–357.5°C). ^{1}H NMR: δ 6.62 (s, 2H, indole-CH), 7.30–7.84 (m, 8H, Ar—H), 10.66 (br, 2H, NH), 11.67 (br, 2H, indole-NH).

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