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Synthesis and some properties of 2*H*-benzimidazole 1,3-dioxides

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Dedicated in memoriam of Professor Alan Katritzky because of his great contribution to heterocyclic chemistry

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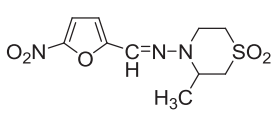
ABSTRACT

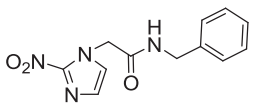
The synthesis of novel 2*H*-benzimidazole 1,3-dioxides on the basis of benzofuroxans interaction with alcohols in acids is described. The formation of a stable secondary carbocation from alcohol is necessary for formation of 2*H*-benzimidazole 1,3-dioxide while substituents in benzofuroxans don't prevent the reaction. Under heating 2*H*-benzimidazole 1,3-dioxides are rearranged to 3*H*-[2,1,4]benzoxadiazine 4-oxides whose stability depends on substituents in the aromatic ring. Under irradiation oxadiazines are converted back to 2*H*-benzimidazole 1,3-dioxides.

1. Introduction

Chagas disease affects an estimated 8 million people in 21 countries and is spread by human migration to a number of non-endemic regions.[1] The two registered drugs for Chagas disease treatment were introduced in the 1960s (Nifurtimox, Bayer) and 1970s (Benznidazole, Roche). Nifurtimox and Benznidazole require prolonged treatment (60 days) and have frequent side-effects.[2]



Nifurtimox



Benznidazole

Cerecetto et al.[3] evaluated a group of *N*-oxide containing heterocycles, as in vitro *anti-Trypanosoma cruzi* (*T. cruzi*) agents revealing that some benzofuroxan (Bfx) derivatives are the best parasite-growth inhibitors. Cytotoxicities, against mammalian fibroblasts, of the most active trypanocidal Bfxs were comparable to that of the reference drug, Nifurtimox. These results allowed the authors to select Bfx as the lead system for further structural modifications.[4]

To search new more active compounds Cerecetto et al. studied in this way for other *N*-oxide containing heterocycles using the Beirut reaction for obtaining different quinoxaline *N*,*N*′-dioxide systems and series of benzimidazole *N*-oxides. 2*H*-Benzimidazole 1,3-dioxides among other explored compounds are the most in vitro active derivatives against *T. cruzi* and *Leishmania* spp. Furthermore, these derivatives possess in vivo activity, which alongside with excellent solubility in water makes them promising candidates for drug development.[5]

Thus an actual task is searching for new active compounds of this class and development of new methods for synthesizing 2*H*-benzimidazole 1,3-dioxides. In the current issue the synthesis of new 2*H*-benzimidazole 1,3-dioxides on the basis of benzofuroxans was examined and the transformations of 2*H*-benzimidazole 1,3-dioxides on heating and on exposure to light were studied. The main synthetic approach for new compounds creation is introducing of functional groups to the second position of the imidazole ring and to the benzene ring of 2*H*-benzimidazole 1,3-

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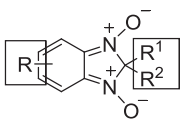
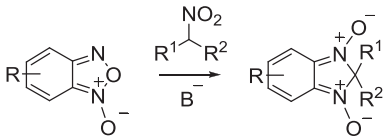
dioxides that can provide the possibility of their further modification.



2. Discussion

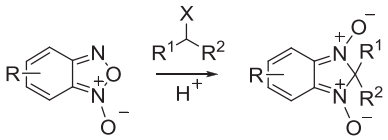
The main approach to the 2*H*-benzimidazole 1,3-dioxides is based on the reaction of the corresponding benzofuroxans with secondary nitroalkanes in basic media at room temperature (Scheme 1).



Scheme 1. The synthesis of 2*H*-benzimidazole 1,3-dioxides via the reaction of the corresponding benzofuroxans with secondary nitroalkanes.

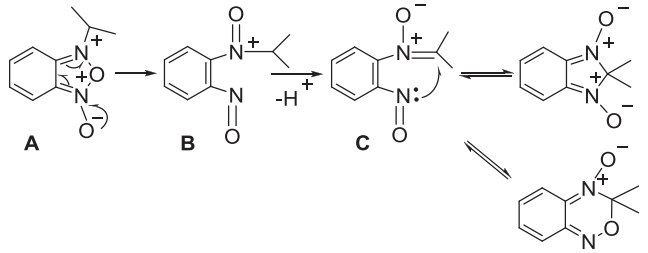
Limitations of such reaction are evident: (i) relatively low availability of nitroalkane, (ii) 2*H*-benzimidazole derivatives are not formed in the presence of electron-withdrawing substituents in the furoxan ring, for example, in the case of 5-nitrobenzofuroxan.[6]

In 1967 Katritsky A. and colleagues published a paper showing the possibility of furoxan ring disclosure under the action of electrophilic agents leading to the formation of benzimidazole derivatives.[7] Recently we have discovered in further study of benzofuroxans a new method for the synthesis of 2*H*-benzimidazole 1,3-dioxides. Benzofuroxans were revealed to react easily with alcohols or haloalkanes in sulfuric or perchloric acids giving rise to 2*H*-benzimidazole 1,3-dioxides (Scheme 2).[8] The method allowed preparation of a large series of 2*H*-benzimidazole 1,3-dioxides, including those inaccessible by other methods.



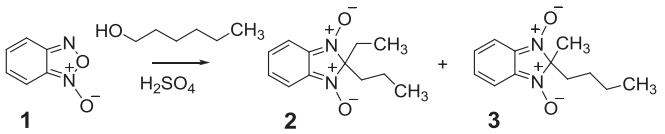
Scheme 2. The synthesis of 2*H*-benzimidazole 1,3-dioxides via the reaction of the corresponding benzofuroxans with alcohols or haloalkanes in sulfuric or perchloric acids.

Benzofuroxans have been supposed earlier to react with alcohols or alkyl halides in the presence of acids via the alcohol transformation to a carbocation, which further reacts with a nitrogen atom of benzofuroxan in the 3 position (Scheme 3).[8] The adduct **A** obtained isomerizes with the disclosure of ring to cation **B**, which loses a proton and turns into nitrosonitron **C**. The ring closure in nitrosonitron leads either to 2*H*-benzimidazole 1,3-dioxide in the case of nucleophilic attack by the nitrogen atom of the nitroso group or to 3*H*-[2,1,4]benzoxadiazine 4-oxide, in the case of nucleophilic attack on the oxygen atom by the nitrone group. Due to its greater stability in acidic medium 2*H*-benzimidazole 1,3-dioxide is the dominant product in the reaction mixture and benzoxadiazine *N*-oxide is formed in trace amounts. Thus, 2*H*-benzimidazole 1,3-dioxide is formed almost quantitatively upon dissolution of 3*H*-[2,1,4]benzoxadiazine 4-oxide in sulfuric acid and pouring in water.



Scheme 3. The mechanism of the formation of 2*H*-benzimidazole 1,3-dioxide.

This fact is confirmed in the present research by study of the interaction of benzofuroxan **1** with 1-hexanol (Scheme 4). Isomeric compounds **2** and **3** with ratio 1:1 are formed and separated. These results are in agreement with the hypothesis that the reaction of benzofuroxans with alcohols in acid occurs through the formation of carbocation from the alcohol, which then react with benzofuroxan.

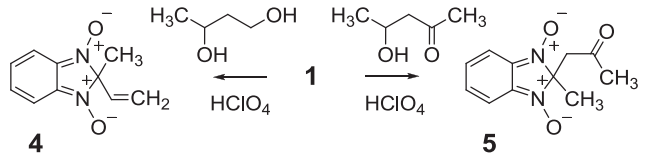


Scheme 4. The interaction of benzofuroxan **1** with 1-hexanol.

The second product is produced due to isomerization of the carbocation formed from hexanol. Thus the formation of the stable secondary carbocation from appropriate reagent is the necessary condition for obtaining 2*H*-benzimidazole 1,3-dioxide from benzofuroxan.

If the initial alcohol yields several carbocations then several products are expected. If the structure of alcohol allows rearrangement of the initially generated carbocation to the more stable tertiary one then 2*H*-benzimidazole 1,3-dioxide is not formed. For example during the interaction of benzofuroxan with cyclohexanol formation of 2*H*-benzimidazole 1,3-dioxide occurs very easily, but the reaction with menthol does not run.

The reaction with 1,3-butanediol in acid results in 2-methyl-2-vinyl-2*H*-benzimidazole 1,3-dioxide **4** instead of expected bis-2*H*-benzimidazole 1,3-dioxide. 2-Methyl-2-(2-oxopropyl)-2*H*-benzoimidazole 1,3-dioxide **5** was obtained on reaction of 4-hydroxypentan-2-one with benzofuroxan (Scheme 5).



Scheme 5. Synthesis of compounds **4** and **5** from benzofuroxan **1**.

Thus the introduction of functional groups to the second position of the molecule of 2*H*-benzimidazole 1,3-dioxide molecule via the interaction of benzofuroxans with alcohols in acids is limited by the possibility to obtaine the stable secondary carbocation from the corresponding alcohol.

In the next step we applied the approach stated above to synthesize compounds **7a**,**b**,**f**, known from literature as highly biological active agents against *T. cruzi*.[9] and also new compounds **7c**,**d**,**e** (Scheme 6).

We also demonstrated that benzofuroxan **8** with nitro-group in the 4th position of the benzene ring reacted readily with isopropyl alcohol resulting in 4-nitro-2*H*-benzimidazole 1,3-dioxide **9** (Scheme 7).

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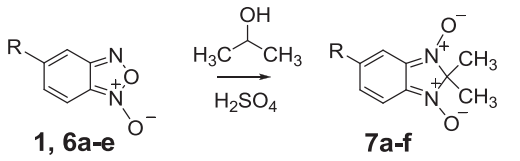
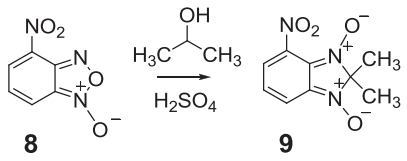


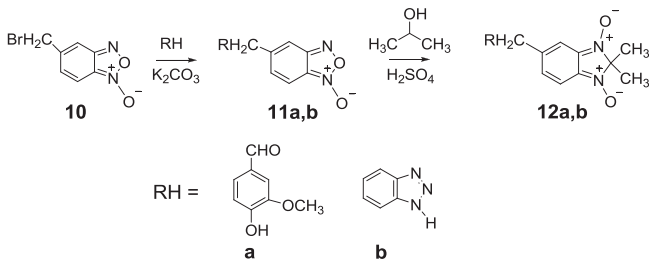
a, R = CH_3; **b**, R = CH=NOH; **c**, R = CHO; **d**, R = CF_3; **e**, R = COOH; **1**, R = H; **f**, R = H

Scheme 6. Synthesis of compounds **7a**–**f**.



Scheme 7. Synthesis of compound **9**.

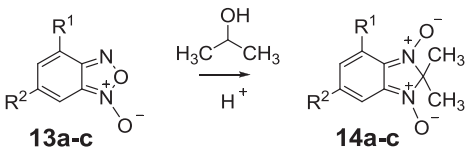
Beside this, the bulky substituents in the 5th position of the benzene ring was revealed not to prevent the formation of substituted 2*H*-benzimidazole 1,3-dioxides. So 5-((4-formyl-2-methoxyphenoxy)methylbenzofuroxan **11a** obtained by alkylation of vanillin (**a**) by 5-(bromomethyl)benzofuroxan **10** reacts with isopropyl alcohol in sulfuric acid giving 5-((4-formyl-2-methoxyphenoxy)methyl)-2,2-dimethyl-2*H*-benzimidazole 1,3-dioxide **12a** (Scheme 8). Similarly the alkylation of benzotriazole (**b**) by bromomethylbenzofuroxan **10** and subsequent treatment of obtained 5-((1*H*-benzo[d][1,2,3]triazol-1-yl)methyl)benzofuroxan **11b** by isopropyl alcohol in sulfuric acid leads to 5-((1*H*-[1,2,3]benzotriazol-1-yl)methyl)-2,2-dimethyl-2*H*-benzimidazole 1,3-dioxide **12b**.



Scheme 8. Synthesis of compounds **11a**,**b**, **12a**,**b**.

Thus, the monosubstituted benzofuroxans can easily form 2*H*-benzimidazole 1,3-dioxides.

4,6-Disubstituted benzofuroxans was established also easily to form 2*H*-benzimidazole 1,3-dioxides via reaction with isopropyl alcohol in sulfuric or perchloric acids (Scheme 9). However, 4,6-dinitrobenzofuroxan does not react this way.

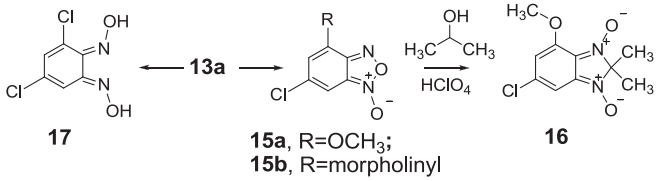


a, $R_1 = R_2 = Cl$; **b**, $R_1 = Cl$, $R_2 = NO_2$; **c**, $R_1 = Br$, $R_2 = NO_2$

Scheme 9. Synthesis of compounds **14a**–**c** from 4,6-disubstituted benzofuroxans.

The use of sulfuric or perchloric acid in each case was determined experimentally, because in some cases the reaction do not occur in the presence of sulfuric acid in the right way, giving the products of sulfonation. Therefore, the main criterion when choosing the acid was the product yield and its purity.

To expand the range of parent benzofuroxans used for formation of novel 2*H*-benzimidazole 1,3-dioxides we have studied the reaction of nucleophilic substitution of the chlorine atoms in 4,6-dichlorobenzofuroxan **13a** (Scheme 10). So 4-morpholinyl-6-chlorobenzofuroxan **15b** is formed in the reaction of 4,6-dichlorbenzofuroxan **13a** with morpholine as the result of chlorine atom substitution in the 4th position as described in literature for another similar compound, 4,6-dichloro-5-nitrobenzofuroxan.[10] As well as the substitution of chlorine in the 4th position of **13a** under the action of sodium methoxide gives 4-methoxy-6-chlorobenzofuroxan **15a**. The structure of compounds **13a**, **15a**,**b** has been confirmed by X-ray analysis (Figs. 1 and 2). The reaction of 4,6-dichlorobenzofuroxan with ethanolamine or benzylamine leads to reduction of benzofuroxan ring with formation of 4,6-dichloro-1,2-benzoquinonedioxime **17**.



Scheme 10. Nucleophilic substitution of the chlorine atoms in 4,6-dichlorobenzofuroxan **13a**.

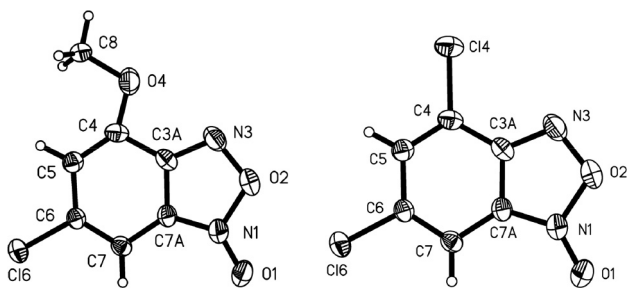


Fig. 1. Molecular structures of 6-chloro-4-methoxybenzofuroxan **15a** (a) and parent 6,4-dichlorobenzofuroxan **13a** (b) mixed in crystal with approximate ratio 30:70.

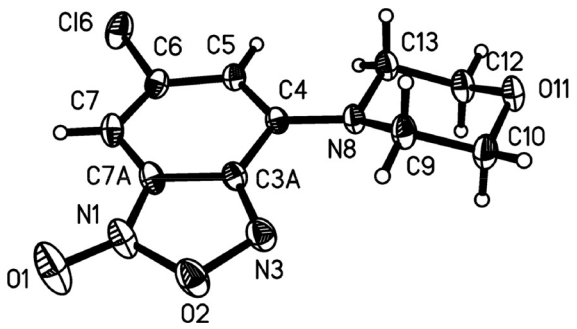


Fig. 2. Molecular structure of 6-chloro-4-morpholinobenzofuroxan **15b**.

4-Methoxy-6-chloro-2,2-dimethyl-2*H*-benzimidazole 1,3-dioxide **16** is smoothly formed in the reaction of 4-methoxy-6-chlorobenzofuroxan **15a** with isopropyl alcohol in the perchloric acid.

A new compound **18** was obtained in the reaction of 4-morpholinyl-6-chlorobenzofuroxan **15b** with isopropyl alcohol in sulfuric acid (Scheme 11). The ^{1}H NMR spectrum of this compound contains the signals of the isopropyl group protons, morpholine ring proton signals and signals of two protons of the benzene ring (see Experimental part). Additionally we observed a broad signal of one proton of NH-group related with intramolecular hydrogen

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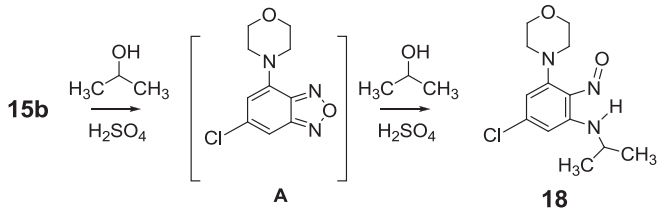
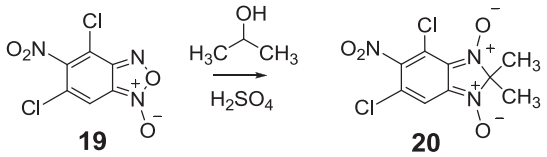


Scheme 11. The reaction of 4-morpholinyl-6-chlorobenzofuroxan **15b** with isopropyl alcohol in sulfuric acid.

bond at 12.14 ppm. These data with the data of ^{13}C NMR and mass spectrum allowed us to suppose structure of the resulting compound: 5-chloro-*N*-isopropyl-3-morpholino-2-nitrosoaniline **18**. Apparently, the first benzofurazan has been formed from benzofuroxan and further reaction of benzofurazan with secondary alcohols in sulfuric acid lead to disclosure of benzofurazan ring and formation of *o*-nitrozoaniline.[11]

Trisubstituted benzofuroxan—4,6-dichloro-5-nitrobenzofuroxan **19** reacts with isopropyl alcohol in sulfuric acid giving 2,2-dimethyl-4,6-dichloro-5-nitro-2*H*-benzimidazole 1,3-dioxide **20** (Scheme 12).

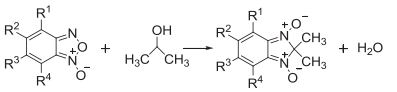


Scheme 12. Synthesis of compound **20**.

Attempts to obtain 2*H*-benzimidazole 1,3-dioxides in reactions of 4,6-dinitrobenzofuroxan, 4,6-dinitro-5,7-dichlorobenzofuroxan and 4,6-dinitro-7-chlorobenzofuroxan with alcohols failed.

To shed light on the reasons that cause the failure of the latter reactions we have estimated with quantum-chemical methods relative energies of products for the model reactions 1–5 (Table 1) of benzofuroxanes with the number of substituents from 2 to 4. Table 1 represents relative energies of the reactions, computed with B3LYP/6-31G* method. Computations show that in all cases products are more energetically favorable independent on number of substituents as well as their positions.

Table 1
Energies and Gibbs free energies of reactions, computed with B3LYP/6-31G* method, kcal/mol

Reaction					Relative energy, kcal/mol	
	R^1	R^2	R^3	R^4	E	G
1	Cl	H	Cl	H	−8	−6
2	Br	H	NO_2	H	−9	−7
3	Cl	NO_2	Cl	H	−9	−8
4	NO_2	Cl	NO_2	Cl	−10	−8
5	NO_2	H	NO_2	Cl	−7	−5

We also attempted to estimate effects from enlarging the basis set, taking dispersion corrections and solvent effects into account on the examples of reactions 1 from Table 1, which takes place and reaction 5 which failed. All methods predict the same tendency as B3LYP/6-31G*: both reactions are energetically favorable (Table 2).

Table 2
Energies and Gibbs free energies of reactions 1 and 5, computed with different methods, kcal/mol

Reaction	B3LYP/ 6-311++G**	B3LYP/ 6-311++G** d3[a]	B3LYP/ 6-311++G** pcm[b]	B97D/ 6-311++G** pcm[b]
1	−18	−23	−22	−25
5	−17	−23	−21	−26

[a] Dispersion-corrected energies were calculated (for B3LYP functional) within the recently developed approach DFT-D3.
[b] Solvent effects were taking into account with the use of the polarized continuum model (PCM).

Thus, we suppose that the presence of two nitro groups in benzofuroxan greatly reduces the electron density on the nitrogen atom, which inhibits the reaction and the reactions with dinitrobenzofuroxans do not proceed.

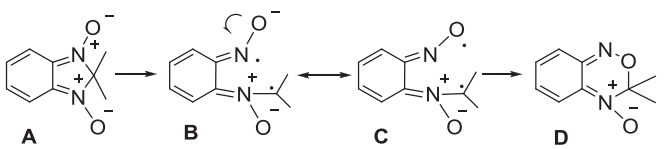
2*H*-Benzimidazole 1,3-dioxides in reactions with nucleophilic and electrophilic agents at elevated temperatures lose very easy one *N*-oxide oxygen atom. Perhaps because of this these compounds are oxidants, for example, they easily oxidize hydroquinone to benzoquinone.[12] Mono-*N*-oxide **21a** and benzaldehyde were isolated with 90% yield in reaction of 2*H*-benzimidazole 1,3-dioxide **14a** with benzylamine in chloroform under heating.

3. Thermal isomerization of 2*H*-benzimidazole 1,3-dioxides and photochromism of obtained 3*H*-[2,1,4]benzoxadiazine 4-oxides

Alongside their high biological activity another interesting property of the systems under study is that they can be involved into thermal reactions. Thermal transformations of 2*H*-benzimidazole 1,3-dioxides are poorly studied and present doubtless interest for chemists. Only few papers describe the heating of 2*H*-benzimidazole 1,3-dioxides leading to formation of benzoxadiazine *N*-oxides easily transforming to the starting dioxide in the light.[12]

Earlier it was shown that heating of 5-nitro-2*H*-benzimidazole 1,3-dioxide results in 3H-[2,1,4]benzoxadiazine 4-oxide and more prolonged heating causes sequential elimination of the *N*-oxide oxygen atom to form 2*H*-benzimidazole mono *N*-oxide, the final product of thermal reaction at moderate temperatures. The reaction runs with the change of colour from violet (2*H*-benzimidazole 1,3-dioxides) to orange (3H-[2,1,4]benzoxadiazine 4-oxide and 2*H*-benzimidazole mono *N*-oxides).[12]

Probably the transformation of 2*H*-benzimidazole 1,3-dioxide under heating to 3*H*-[2,1,4]benzoxadiazine 4-oxides is another example of Cope rearrangement (nitrones under heating become the oxime ethers).[13] Herein we present the proposed mechanism of 2*H*-benzimidazole 1,3-dioxide rearrangement to 3*H*-[2,1,4] benzoxadiazine 4-oxide (Scheme 13):



Scheme 13. Probable scheme of 2*H*-benzimidazole 1,3-dioxide rearrangement to 3*H*-[2,1,4] benzoxadiazine 4-oxide.

The observed rearrangement is a thermal process. It is possible that:

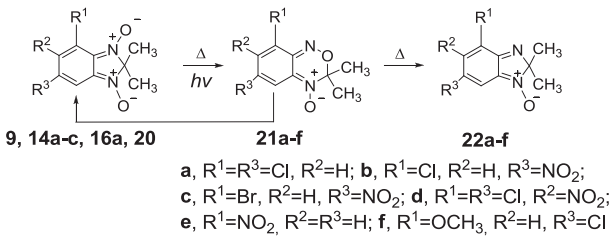
1. Upon heating homolytic bond cleavage occurs with the formation of the biradical **B**.
2. Iminoyl radical isomerizes to the more stable iminoxyl radical forming compound **C**. It is a driving force of rearrangement.

(The arrow shows the movement of the electron from oxygen to nitrogen.)

3. Dimerization of radicals leads to the product of rearrangement **D**.

Such thermo- and photochromic properties of 2*H*-benzimidazole 1,3-dioxides open additional perspectives for photochromic switches design. Molecular photochromic switches are an intriguing class of organic molecules, which allow the control of molecular structures and properties. Consequently, this offers the possibility of effecting dramatic changes to the bulk properties of a system by irradiation. Attractive features of these systems include their short response times, reversibility, clean and tunable energy input, and the ability to convert an optical input into a variety of useful output signals. This is demonstrated by the fact that these molecules have already found commercial application in optical memory devices (including the recordable compact discs, CD-R), light-sensitive sun glasses and ophthalmic lenses. More recently, there has been a growing interest in using these materials in new applications such as molecular electronics, smart surfaces, control of supramolecular organization, and nanomachinery.[14]

Similar behaviour was observed in the present study for 4,6-dichloro-2*H*-benzimidazole 1,3-dioxide **14a**, heating (Scheme 14) of which leads to formation of compound **21a** with high yield 75–80%. The further heating leads to formation of 2*H*-benzimidazole mono-*N*-oxide **22a**.



Scheme 14. Transformation of 2*H*-benzimidazole 1,3-dioxides under heating to 3*H*-[2,1,4]benzoxadiazine 4-oxides.

To find out the influence of substituents in the aromatic ring on the thermal stability of oxadiazines we carried out the investigations with compounds **9**, **14b**,**c**, **16a** and **20**.

Unsubstituted 3*H*-[2,1,4]benzoxadiazine 4-oxide (R^1=R^2=R^3=H) is a less stable compound than other substituted benzoxadiazines,[8] but the introduction of an electron-withdrawing substituent into the aromatic ring increases their stability. For example, benzoxadiazine with a cyano group in the 2-position is stable.[15] So, for formation of 3*H*-[2,1,4]benzoxadiazine 4-oxides **21a** from 4,6-dichloro-2*H*-benzimidazole 1,3-dioxide **14a** boiling temperature of dichloroethane (87°C) is enough while boiling temperature of chlorobenzene (130°C) is necessary for the similar conversion of 5-nitro-2*H*-benzimidazole 1,3-dioxide.[12] 3*H*-[2,1,4] benzoxadiazine 4-oxide **21d** obtained from 4,6-dichloro-5-nitro-2*H*-benzimidazole 1,3-dioxide **20** is stable and easily formed even at room temperature (Fig. 3).

Such behaviour is in agreement with quantum chemical computations predicting compound **21d** to be more stable than compound **20** with energy difference 2.9 kcal/mol. Similar energy differences (2.7 kcal/mol) are predicted between **21a** and corresponding benzimidazole dioxide **14a**. At the same time for unsubstituted benzoxadiazine, described earlier[8] and compound **21e** computations predict almost negligible energy compared to initial dioxides (0.7 and 0.2 kcal/mol respectively). Thus according to computations introducing chlorine atoms makes 3*H*-[2,1,4]benzoxadiazine 4-oxides more stable.

In all cases the reaction occurs with the change of colour. Benzoxadiazine *N*-oxide **21a**–**f** are yellow and orange compounds

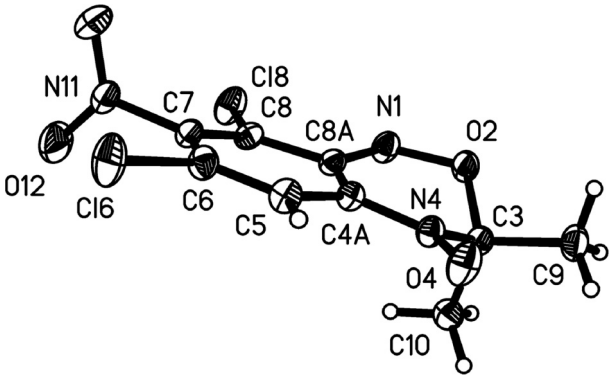


Fig. 3. Molecular structure of 6,8-dichloro-3,3-dimethyl-7-nitro-3*H*-[2,1,4]benzoxadiazine 4-oxide **21d**.

($\lambda_{max.}$=389–495 nm) while 2*H*-benzimidazole di-*N*-oxides **22a**–**f** are strongly colored from dark red to violet compounds ($\lambda_{max.}$=510–560 nm).

UV spectrum of 4,6-dichloro-2*H*-benzimidazole 1,3-dioxide **14a** contains a band at 527 nm (Fig. 4) that corresponds to absorbed yellow-green color and observed violet-purple color of the sample. In the UV spectra of benzoxadiazine **21a** and 2*H*-benzimidazole mono-*N*-oxide **22a**, obtained by heating of compound **14a**, the corresponding band is blue-shifted to 452 nm and 438 nm (Fig. 4) accordingly that corresponds to absorbed violet light and observed red color of the samples.

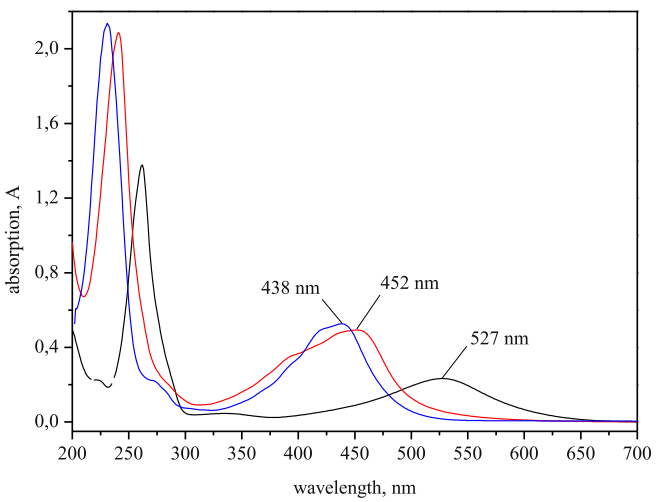


Fig. 4. Experimental UV spectra of compounds **14a** (black), **21a** (red) and **22a** (blue).

The trend represented in Fig. 4 for compounds **14a**, **21a** and **22a** is similar for all compounds **9**, **14a**–**c**, **16a**, **20**, **21a**–**f** and **22a**–**f** and is confirmed computationally: the wavelength of the lowest excitation, assigned to the transition from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO), in all cases decreases in the row dioxide—diazine—monoxide (Table 3). According to computations HOMO and LUMO are partially localized on benzyl moiety of compounds **14a**, **21a** and **22a**, thus, substituents in 4–6 position should affect the wavelength of the first excitation. According to computations introducing of electron-withdrawing NO_2 group leads to bathochromic shift (**0**–**e**, **a**–**d**) of the corresponding band with more pronounced effect in **0**–**e** case compared to **a**–**d**, as in **d** NO_2 group is orthogonal to the benzyl ring. Introduction of Cl atoms also shifts considered band bathochromicaly (**0**–**a**) with less notable effect. Replacement of Cl atom by NO_2 group in 6th position (**a**–**b**)

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Table 3
Comparison of calculated and experimental wavelength (nm) of the low-energy transitions

		[a]R[1]	H	Cl	Cl	Br	Cl	NO_2	OMe
		[a]R[2]	H	H	H	H	NO_2	H	H
		[a]R[3]	H	Cl	NO_2	NO_2	Cl	H	Cl
			(0)	(a)	(b)	(c)	(d)	(e)	(f)
2*H*-benzimidazole 1,3-dioxides	E		525	527	555	561	556	547	512
	C		*564*	*576*	*616*	*619*	*588*	*616*	*542*
3*H*-[2,1,4]benzoxadiazines	E			452	495	482	446	470	459
	C		*453*	*468*	*483*	*483*	*470*	*467*	*464*
2*H*-benzimidazole 1-oxides	E		416	438	457	455		463	433
	C		*428*	*445*	*453*	*454*	*447*	*457*	*436*

[C] Calculated value.
[E] Experimental value.
[a] Substituents is numbering according Scheme 14.

leads to further increasing of the wavelength of the band, whereas replacement of Cl atom in the obtained compounds (**b**) by Br atom (**c**) do not lead to any notable differences in full agreement with experimental results. Introducing an electron donating OMe group in 4th position should lead to hypsochromic shift of the lowest transition that is observed in experiment for oxides. Thus, it is possible to obtain compounds with definite color controlled by light and temperature, further tuning could be achieved by variation of substituents in benzyl ring.

Under heating of 5-substituted 2*H*-benzimidazole 1,3-dioxides two isomeric 3*H*-[2,1,4]benzoxadiazine 4-oxides are formed, further heating leads to two isomeric mono-*N*-oxides of 2*H*-benzimidazole.[12] However in the case of 4-nitro-2,2-dimethyl-2*H*-benzimidazole 1,3-dioxide **9** and compounds **14a**–**c**, **16a** and **20** only one isomeric 3*H*-[2,1,4]benzoxadiazine 4-oxide and one corresponding mono *N*-oxide of 2*H*-benzimidazole are formed under heating.

The position of *N*-oxide oxygen atom in mono-*N*-oxide **22a** is established by X-ray analysis (Fig. 5). These data are in agreement with those published earlier, which confirms that heating of 3*H*-[2,1,4]benzoxadiazine 4-oxides cause loss of an oxygen atom located in oxadiazine ring.[16]

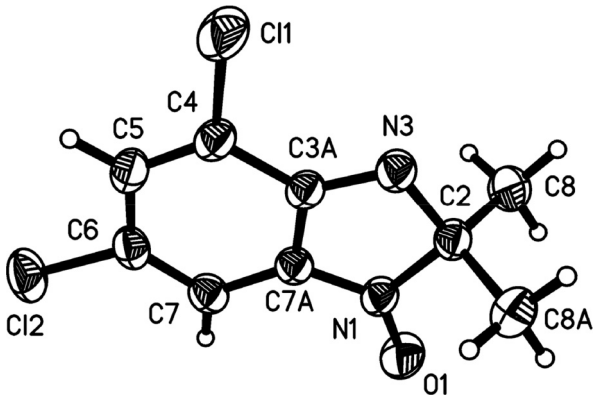

Fig. 5. Molecular structure of 4,6-dichloro-2,2-dimethyl-2*H*-benzimidazole 1-oxide **22a**.

Obtained 3*H*-[2,1,4]benzoxadiazine 4-oxides are easily transformed into initial 2*H*-benzimidazole 1,3-dioxides on exposure to sunlight (Fig. 6). Transition of 3*H*-[2,1,4]benzoxadiazine 4-oxides to 2*H*-benzimidazol-1,3-dioxide under the action of sunlight occurs both in solution and in crystalline form.

4. Conclusion

The interaction of benzofuroxans with alcohols in sulfuric or perchloric acid results in novel 2*H*-benzimidazole 1,3-dioxides.

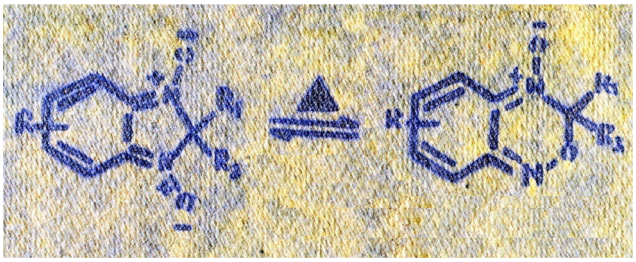

Fig. 6. Photochemical transformation of 3*H*-[2,1,4]benzoxadiazine 4-oxides (yellow color) surfaced on filter paper to 2*H*-benzimidazole 1,3-dioxides (blue color). Image was obtained with help of stencil in sunlight.

Prerequisite for formation of 2*H*-benzimidazole 1,3-dioxide from benzofuroxan and alcohol is the formation of a stable secondary carbocation from alcohol. Substituents in benzofuroxans do not prevent the reaction. Under heating 2*H*-benzimidazole 1,3-dioxides are rearranged to 3*H*-[2,1,4]benzoxadiazine 4-oxide, which under irradiation is converted back to 2*H*-benzimidazole 1,3-dioxides. It is shown that the introduction of electron-withdrawing substituents in the aromatic ring increases the stability of obtained 3*H*-[2,1,4] benzoxadiazine 4-oxides. More prolonged heating causes sequential elimination of an oxygen atom leading to the formation of 2*H*-benzimidazole mono *N*-oxide.

5. Experimental section

5.1. General

The analytic and spectral measurements were carried out in the Chemical Service Center for collective use of the Siberian Division, Russian Academy of Sciences.

The IR spectra were recorded in KBr (sample concentration 0.25%) on a Bruker Vector-22 spectrometer; given are the most intense absorption bands. The UV spectra were measured on a Hewlett–Packard 4853 spectrophotometer from solutions in ethanol. The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AV-400 instrument (400.13 (^{1}H) and 100.61 MHz (^{13}C)) at 25 °C from 10% solutions in $CDCl_3$ or DMSO-d_6; the chemical shifts were determined relative to the residual proton and carbon signals of the solvent ($CHCl_3$, δ 7.24, δ_C 76.90 ppm; DMSO-d_6, δ 2.50, δ_C 39.50 ppm). Signal multiplicities in the ^{13}C NMR spectra were determined using J-modulation (JMOD) technique. The mass spectra (electron impact, 70 eV) were recorded on a Thermo Scientific DFS mass spectrometer with direct sample admission into the ion source (ion source temperature 180 °C); ion peaks with a relative intensity higher than 10% are given. The progress of reactions and the purity of products were monitored by TLC on Sorbfil UV-254 plates (Sorbpolimer, Krasnodar, Russia); the chromatograms were developed under UV light and by treatment with iodine vapor. Column chromatography was performed on silica gel (60-mesh, Merck). The melting points were measured on a Kofler hot stage. The elemental compositions were determined at the Microanalysis Laboratory, Novosibirsk Institute of Organic Chemistry, Siberian Division of the Russian Academy of Sciences.

For the experiments concentrated chemically pure grade sulfuric acid and 65% chemically pure grade perchloric acid were used. All other solvents were purified and dried according to standard procedures.

The following compounds were prepared following the literature procedures indicated: 5-formylbenzofuroxan **6c** and 5-trifluoromethylbenzofuroxan **6d**,[17] 4-chloro-6-nitrobenzofuroxan **13b**,[18] 5-hydroxyiminomethylbenzofuroxan **6b**,[19] 4,6-dichlorobenzofuroxan **13a**,[20] 4-bromo-6-nitrobenzofuroxan**13c**,[21] 4-nitrobenzofuroxan **8**,[22] 5-carboxybenzofuroxan **6e**,[23] 5-

bromomethylbenzofuroxan **10**,[24] 4,6-dichloro-5-nitrobenzofuroxan **19**,[25] 4-hydroxypentan-2- one.[26]

Benzofuroxan **1**, 5-methylbenzofuroxan **6a** and 1,3-butanediol are commercially available research-grade chemicals and were used without further purification.

The X-ray diffraction experiments for compounds **15a**, **15b**, **21d** and **22a** were carried out on a Bruker KAPPA APEX II diffractometer (graphite-monochromated Mo Kα radiation). Reflection intensities were corrected for absorption by SADABS program. The structures was solved by direct methods using the SHELXS-97 program and refined by anisotropic (isotropic for all H atoms) full-matrix least-squares method against F^2 of all reflections using SHELX-97 program.[27] The positions of the hydrogen were calculated geometrically and refined in riding model.

Crystallographic data for the structures of cocrystals of compounds **15a** and **13a**, compounds **15b**, **21d** and **22a** have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 991083-991085 and 1040866 accordingly. Copy of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: +44 122 3336033 or e-mail: deposit@ccdc.cam.ac.uk; internet: www.ccdc.cam.ac.uk).

All quantum-chemical computations were carried out using the Gaussian 09[28] suite of programs. Calculations were performed with Becke's three parameter hybrid exchange functional[29] and the gradient-corrected nonlocal correlation functional of Lee et al.[30] (B3LYP) and B97D functional.[31] Standard 6–31G* and 6–311+G* basis sets were used.[32–37] Dispersion-corrected energies were calculated (for B3LYP functional) within the recently developed approach DFT-D3[38] together with the Becke-Johnson (BJ) damping function.[39] For this purpose the program dftd3 v2.1 Rev1 was used.[40] The obtained values were added to the electronic energies. For simulation of solvent effects the polarized continuum model (PCM) was used.[41,42] All stationary points were characterized as minima by analysis of the Hessian matrices. UV/Vis spectra were calculated with the use of wB97xD[43] functional for structures optimized with PBE[44,45] functional in combination with def2-TZVP basis set.[46]

5.2. Synthesis of mixture 2-ethyl-2-propyl-2*H*-benzimidazole 1,3-dioxide (2) and 2-methyl-2-butyl-2*H*-benzimidazole 1,3-dioxide (3)

To a solution of 1.36 g (0.01 mol) of benzofuroxan **1** in 10 mL of concentrated sulfuric acid was added dropwise 1.2 g (0.012 mol) of 1-hexanol. The reaction mixture was stirred at room temperature for 1.5 h then poured into 100 mL of ice-water. The products were extracted with chloroform (3×20 mL), the extract was washed with water (2×100 mL), dried over magnesium sulfate, and evaporated in vacuo to give the crude products, which were separated by column chromatography (25% hexane–ethyl acetate) to give the 2 pure fractions. The first fraction—*2-ethyl-2-propyl-2H-benzimidazole 1,3-dioxide* (**2**), red powder. Yield (38%). Mp: 101–103 °C. UV, λ_{max} (lg ε) 249 (4.00), 518 (3.40) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 0.62 (3H, t, CH_3, J=7.2 Hz), 0.80 (3H, t, CH_3, J=7.2 Hz), 0.91–1.03 (2H, m, CH_2), 1.99–2.06 (2H, m, CH_2), 2.09 (2H, q, CH_2, J=7.0 Hz, J=7.4 Hz), 6.80–6.86 (2H, m, 2CH), 7.13–7.19 (2H, m, 2CH). ^{13}C NMR ($CDCl_3$), δ (ppm): 5.9, 13.0, 14.9, 30.8, 38.9, 103.3, 114.9, 130.8, 138.6. MS, m/z (I, %) 220 $[M]^+$ (51), 178 (57), 161 (13), 147 (19), 130 (12). HRMS: m/z (M^+) calcd for $C_{12}H_{16}N_2O_2$: 220.1206; found: 220.1212. Anal. Calcd (%) for $C_{12}H_{16}N_2O_2$ (220.2): C, 58.25; H, 4.85; N, 13.59. Found: C, 58.4; H, 4.88; N, 13.64.

The second fraction gives *2-methyl-2-butyl-2H-benzimidazole 1,3-dioxide* (**3**), red powder. Yield (42%). Mp: 95–97 °C. UV, λ_{max} (lg ε) 248 (4.06), 515 (3.40) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 0.78 (3H, t, CH_3 J=5.8 Hz), 0.90–0.99 (2H, m, CH_2), 1.18–1.27 (2H, m, CH_2), 1.63 (3H, s, CH_3), 2.04–2.10 (2H, m, CH_2), 6.80–6.86 (2H, m, 2CH), 7.13–7.19 (2H, m, 2CH). ^{13}C NMR ($CDCl_3$), δ (ppm): 13.4, 24.0, 21.7, 24.5, 36.8, 99.6, 115.2, 130.5, 137.3. MS, m/z (I, %) 220 $[M]^+$ (18), 203 (25), 164 (25), 147 (25), 132 (15), 121 (12), 106.(16). HRMS: m/z (M^+) calcd for $C_{12}H_{16}N_2O_2$: 220.1206; found: 220.1203. Anal. Calcd (%) for $C_{12}H_{16}N_2O_2$ (220.2): C, 58.25; H, 4.85; N, 13.59. Found: C, 58.3; H, 4.88; N, 13.50.

5.3. Synthesis of 2-methyl-2-vinyl-2H-benzimidazole 1,3-dioxide (4)

To a solution of 1.36 g (0.01 mol) of benzofuroxan **1** in 10 mL of 65% perchloric acid was added dropwise 1.8 g (0.02 mol) of 1,3-butanediol. The reaction mixture was stirred at 30 °C for 36 h then poured into 100 mL of ice-water. The product was extracted with chloroform (5×20 mL), the extract was washed with water (2×100 mL), dried over magnesium sulfate, and evaporated in vacuo to give the crude product, which was purified by column chromatography (25% hexane–ethyl acetate), pure fractions were collected, solvents were evaporated in vacuo and the residue was triturated with hexane to give red powder. Yield 0.82 g (43%). Mp: 53–55 °C. UV, λ_{max} (lg ε) 247 (4.34), 515 (3.80) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.75 (3H, s, CH_3), 5.54 (1H, d, CH, J=10.5 Hz), 5.66 (1H, d, CH, J=16.8 Hz), 5.93 (1H, dd, CH, J=10.5 Hz), 6.84 (2H, s, 2CH), 7.16 (2H, s, 2CH). ^{13}C NMR ($CDCl_3$), δ (ppm): 22.8, 97.9, 115.5, 130.8, 131.2, 121.4, 136.9. MS, m/z (I, %) 190 $[M]^+$ (100), 174 (22), 157 (19), 149 (54), 131 (41), 120 (51). HRMS: m/z (M^+) calcd for $C_{10}H_{10}N_2O_2$: 190.0737; found: 190.0736. Anal. Calcd (%) for $C_{10}H_{10}N_2O_2$ (190.2): C 63.15; H 5.30; N 14.73. Found: C, 63.19; H 5.24; N 14.71.

5.4. Synthesis of 2-methyl-2-(2-oxopropyl)-2*H*-benzimidazole 1,3-dioxide (5)

Compound **5** was prepared from 4-hydroxypentan-2-one according to the same procedure as that described for compound **4**. Yield of red powder is 0.28 g (25%). Mp: 76–79 °C. IR (KBr), ν: 1712 (C=O) cm^{-1}. UV, λ_{max} (lg ε) 248 (4.12), 513 (3.26) nm; ^{1}H NMR (DMSO-d_6), δ (ppm): 1.53 (3H, s, CH_3), 2.03 (3H, s, CH_3), 3.43 (2H, s, CH_2), 6.97 (2H, m, 2CH), 7.16 (2H, m, 2CH). ^{13}C NMR (DMSO-d_6), δ (ppm): 25.5, 30.0, 46.7, 95.0, 115.1, 130.9, 137.5, 202.6. MS, m/z (I, %) 220 $[M]^+$ (36), 204 (15), 161 (17),143 (31), 130 (17), 119 (38). HRMS: m/z (M^+) calcd for $C_{11}H_{12}N_2O_3$: 220.0842; found: 220.0845. Anal. Calcd (%) for $C_{11}H_{12}N_2O_3$ (220.2): C 59.99; H 5.49; N 12.72. Found: C 59.90; H 5.38; N 12.49.

5.5. Synthesis of compounds 7a–e

*5.5.1. 5-Formyl-2,2-dimethyl-2H-benzimidazole l,3-dioxide (**7c**).* To a solution of 1.0 g (0.01 mol) of 5-formylbenzofuroxan **6c** in 10 mL of concentrated sulfuric acid was added dropwise 1.0 g (0.016 mol) of isopropyl alcohol. The reaction mixture was stirred at room temperature for 1.5 h then poured into 100 mL of ice-water. The product was extracted with chloroform (3×20 mL), the extract was washed with water (2×100 mL), dried over magnesium sulfate, and evaporated in vacuo to give the crude product, which was purified by column chromatography (25% hexane–ethyl acetate), pure fractions were collected, solvents were evaporated in vacuo and the residue was triturated with hexane to give 0.76 g (68%) of red powder. Mp: 128–130 °C. IR (KBr), ν: 1691 (C=O) cm^{-1}. UV, λ_{max} (lg ε) 255 (4.34), 298 (3.70), 513 (3.65) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.64 (6H, s, $2CH_3$), 7.25 (2H, s, 2CH), 7.64 (1H, s, CH), 9.75 (1H, s, CH). ^{13}C NMR ($CDCl_3$), δ (ppm): 24.2, 116.9, 126.4, 138.0, 189.1, 98.9, 122.6, 136.5, 136.6. HRMS: m/z (M^+) calcd for $C_{10}H_{10}N_2O_3$: 206.0686; found: 206.0684. Anal. Calcd (%) for

$C_{10}H_{10}N_2O_3$ (206.2): C 58.59; H 4.89; N 13.58. Found: C 58.90; H 5.38; N 13.29.

In a similar manner starting from benzofuroxans **6a**,**b**,**d**,**e** and benzofuroxan **1** were prepared:

*5.5.2. 2,2,5-Trimethyl-2*H*-benzimidazole 1,3-dioxide (**7a**).* Yield 25%. Dark red powder. Mp: 116–118 °C. (lit.[9] 116.4–117.7 °C).

*5.5.3. 5-Hydroxyiminomethyl-2,2-dimethyl-2*H*-benzimidazole l,3-dioxide (**7b**).* Dark red powder. Yield 64%. Mp: 177–178 °C. (lit.[9] 177.5–177.6 °C).

*5.5.4. 2,2-Dimethyl-5-(trifluoromethyl)-2H-benzimidazole 1,3-dioxide (**7d**).* Dark blue powder. Yield 67%. Mp: 123–125 °C. IR (KBr), ν: 1593 (C=N) cm^{-1}. UV, λ_{max} (lg ε) 251 (3.80), 525 (3.30) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.66 (6H, s, $2CH_3$), 6.93 (1H, d, CH, J=8.8 Hz), 7.29 (1H, d, CH, J=8.8 Hz), 7.50 (1H, s, CH). ^{13}C NMR ($CDCl_3$), δ (ppm): 24.2, 98.6, 114.5 (CH, q, J=6.0 Hz), 117.3, 126.1 (CH, q, J=3.3 Hz), 122.2 (CF_3, q, J=271.4 Hz), 132.6 (CH, q, J=33.0 Hz), 135.3, 136.0. ^{19}F NMR ($CDCl_3$), δ (ppm): 95.76 (3F, s, CF_3). MS m/z (I, %) 246 $[M]^+$ (100), 231 (28), 188 (27), 158 (30) 145 (23), 138 (18). HRMS: m/z (M^+) calcd for $C_{10}H_9F_3N_2O_2$: 246.0611; found: 246.0605. Anal. Calcd (%) for $C_{10}H_9F_3N_2O_2$ (246.0): C 48.78; H 3.66; F 23.17; N 11.39. Found: C 49.00; H 3.68; F 23.22; N 11.40.

*5.5.5. 5-Carboxy-2,2-dimethyl-2H-benzimidazole 1,3-dioxide (**7e**).* Dark blue powder. Yield 72%. Mp: 168 °C with decomposition. IR (KBr), ν: 1712 (C=O) cm^{-1}. UV, λ_{max} (lg ε) 256 (4.00), 521 (3.80) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.56 (6H, s, $2CH_3$), 7.19 (1H, d, CH, J=9.8 Hz), 7.39 (1H, d, CH, J=9.8 Hz), 7.65 (1H, s, CH), 4.54 (1H, br s, OH). ^{13}C NMR ($CDCl_3$), δ (ppm): 23.8, 97.4, 115.2, 116.7, 130.9, 136.2, 136.4, 136.8, 166.6. MS m/z (I, %) 222 $[M]^+$ (15), 206 (47), 190 (41), 161 (49), 149 (20), 130 (21), 117 (47). HRMS: m/z (M^+) calcd for $C_{10}H_{10}N_2O_4$: 222.0635; found: 220.0636. Anal. Calcd (%) for $C_{10}H_{10}N_2O_4$ (222.2): C 54.05; H 4.54; N 12.61. Found: C 54.18; H 4.48; N 12.59.

*5.5.6. 2,2-Dimethyl-2H-benzimidazole 1,3-dioxide (**7f**).* Dark red powder. Yield 75%. Mp: 122–123 °C. (lit.[9] 122.6–123.4 °C).

5.6. Synthesis of 2,2-dimethyl-4-nitro-2*H*-benzimidazole 1,3-dioxide (9)

Compound **9** was prepared from 4-nitrobenzofuroxan **8** as described above for compound **7c**. Dark blue powder. Yield 72%. Mp: 103–106 °C. IR (KBr), ν: 1595 (C=N), 1357, 1537 (NO_2) cm^{-1}. UV, λ_{max} (lg ε) 254 (3.90), 547 (3.80) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.68 (6H, s, $2CH_3$), 6.84–6.95 (1H, m, CH), 7.29 (1H, d, CH, J=7.4 Hz), 7.40 (1H, d, CH, J=9.4 Hz). ^{13}C NMR ($CDCl_3$), δ (ppm): 24.4, 99.0, 120.2, 126.8, 127.9, 127.1, 137.2, 140.1. MS m/z (I, %) 223 $[M]^+$ (100), 207 (23), 165 (18), 130 (19), 105 (37). HRMS: m/z (M^+) calcd for $C_9H_9N_3O_4$: 223.0588; found: 223.0587. Anal. Calcd (%) for $C_9H_9N_3O_4$ (223.0): C 48.43; H 4.04; N 18.84. Found: C 48.60; H 4.08; N 18.80.

5.7. Synthesis of compounds 11a,b, 12a,b

*5.7.1. 5-((4-Formyl-2-methoxyphenoxy)methyl)benzofuroxan (**11a**).* To a solution of 2.29 g (0.01 mol) of 5-(bromomethyl)benzofuroxan **10** in 100 mL of acetonitrile was added 1.7 g (0.012 mol) of vanillin and 1.5 g (0.01 mol) of potassium carbonate. The reaction mixture was stirred at room temperature for 3 h. Solvent was evaporated under reduced pressure, resulting solid was washed with water, filtered and dried in vacuo (1 h, 0.01 Torr) to give compound **11a** as a white powder. Yield 2 g (88%). Mp: 166–168 °C. IR (KBr), ν: 1690 (C=O) cm^{-1}. UV, λ_{max} (lg ε) 274 (3.40), 310 (3.20), 356 (3.18) nm; ^{1}H NMR (DMSO-d_6), δ (ppm): 3.88 (3H, s, OCH_3), 5.30 (2H, s, OCH_2), 7.22–7.83 (6H, m, 6CH), 9.88 (1H,s, CH). ^{13}C NMR (DMSO-d_6), δ (ppm): 55.8, 68.8, 110.0, 112.9, 125.8, 130.3, 149.5, 152.5, 191.5. Six signals of benzofuroxan carbon atoms are not observed due to their strong broadening owing to tautomerism. Signals of benzofuroxan carbon ring appear during recording the spectrum at 80 °C on account averaging. ^{13}C NMR (DMSO-d_6), 80 °C, δ (ppm): 55.8, 69.1, 111.2, 111.8, 113.7, 115.2, 124.6, 130.5, 131.0, 140.6, 152.4, 190.6. MS m/z (I, %) 300 $[M]^+$ (12), 284 (7), 151 (34), 149 (100), 133 (17), 95 (39). HRMS: m/z (M^+) calcd for $C_{15}H_{12}N_2O_5$: 300.0741; found: 300.0742. Anal. Calcd (%) for $C_{15}H_{12}N_2O_5$ (300.2): C 60.00; H 4.03; N 9.33. Found: C 60.00; H 4.38; N 9.29.

*5.7.2. 5-((1H-[1,2,3]Benzotriazol-1-yl)methyl)benzofuroxan (**11b**).* 5-((1H-[1,2,3]Benzotriazol-1-yl)methyl)benzofuroxan (**11b**) was synthesized as described above for compound **11a** from 11.13 g (0.04 mol) of 5-(bromomethyl)benzofuroxan **10**, 5.76 g (0.04 mol) of 1,2,3-benzotriazole and 9.6 g (0.09 mol) of potassium carbonate. White powder. Yield 10.8 g (97%). Mp: 145–146 °C. IR (KBr), ν: 1603 (C=N) cm^{-1}. ^{1}H NMR (DMSO-d_6), δ (ppm): 5.53 (2H, s, CH_2), 7.15–7.77 (6H, m, 6CH), 7.92 (1H, d, CH, J=8.5 Hz), 8.03 (1H, d, CH, J=8.5 Hz). ^{13}C NMR (DMSO-d_6), δ (ppm): 50.6, 110.9, 119.6, 124.7, 128.2, 133.1, 145.6. The signals of furoxan ring carbon atoms are not observed in the ^{13}C NMR spectrum due to the strong broadening of these signals. MS m/z (I, %) 267 $[M]^+$ (100), 251 (25), 222 (7), 192 (23), 179 (38), 178 (45), 149.(16), 133 (23). HRMS: m/z (M^+) calcd for $C_{13}H_9N_5O_2$: 267.0751; found: 267.0744. Anal. Calcd (%) for $C_{13}H_9N_5O_2$ (267.2): C 58.43; H 3.37; N 26.22. Found: C 58.90; H 3.38; N 26.39.

*5.7.3. 5-((4-Formyl-2-methoxyphenoxy)methyl)-2,2-dimethyl-2H-benzimidazole 1,3-dioxide (**12a**).* 5-((4-Formyl-2-methoxyphenoxy)methyl)-2,2-dimethyl-2H-benzimidazole 1,3-dioxide (**12a**) was synthesized as described above for compound **7c** from compound **11a** as dark red powder. Yield 48%. Mp: 162–164 °C. IR (KBr), ν: 1680 (C=O) cm^{-1}. UV, λ_{max} (lg ε) 270 (3.40), 254 (3.39), 231 (3.30), 309 (3.20) nm; ^{1}H NMR (DMSO-d_6), δ (ppm): 1.53 (6H, s, $2CH_3$), 3.83 (3H, s, OCH_3), 5.07 (2H, s, CH_2), 6.98 (1H, d, CH, J=9.0 Hz), 7.29–7.38 (3H, m, 3CH), 7.41 (1H, s, CH), 7.52 (1H, d, CH, J=9.0 Hz), 9.82 (1H, s, CH). ^{13}C NMR (DMSO-d_6), δ (ppm): 23.7, 55.7, 110.0, 112.8, 112.9, 115.9, 125.7, 130.9, 96.8, 130.2, 135.5, 136.6, 140.1, 149.4, 152.5. MS m/z (I, %) 342 $[M]^+$ (5.8), 326,[29] 191,[15] 175 (100), 159,[35] 151,[35] 144.(59), 133.[43] HRMS: m/z (M^+) calcd for $C_{18}H_{18}N_2O_5$: 342.1210; found: 242.1212. Anal. Calcd (%) for $C_{18}H_{18}N_2O_5$ (342.2): C 63.15; H 5.30; N 8.18. Found: C 63.40; H 5.38; N 8.10.

*5.7.4. 5-((1H-[1,2,3]Benzotriazol-1-yl)methyl)-2,2-dimethyl-2H-benzimidazole 1,3-dioxide (**12b**).* 5-((1H-[1,2,3]Benzotriazol-1-yl)methyl)-2,2-dimethyl-2H-benzimidazole 1,3-dioxide (**12b**) was synthesized as described above for compound **7c** from compound **11b**. Red powder. Yield 36%. Mp: 126–129 °C with decomposition. IR (KBr), ν: 1598 (C=N) cm^{-1}. UV, λ_{max} (lg ε) 255 (4.25), 515 (3.60) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.64 (6H, s, $2CH_3$), 5.62 (2H, s, CH_2), 6.75 (1H, d, CH, J=9.0 Hz), 7.09 (1H, s, CH), 7.15 (1H, d, CH, J=9.0 Hz), 7.49–7.37 (3H, m, 3CH), 8.07 (1H, d, CH, J=9.0 Hz). ^{13}C NMR ($CDCl_3$), δ (ppm): 23.7, 50.3, 97.4, 110.7, 113.5, 116.5, 119.5, 124.8, 128.3, 131.5, 132.9, 135.7, 135.9, 139.7, 145.3. MS m/z (I, %) 309 $[M]^+$ (11), 293 (100), 277 (27), 264 (40), 248 (30), 234 (55), 159 (32), 149 (70), 144 (54), 119 (72). HRMS: m/z (M^+) calcd for $C_{16}H_{15}N_5O_2$: 309.1220; found: 309.1214. Anal. Calcd (%) for $C_{16}H_{15}N_5O_2$ (309.3): C 62.12; H 4.89; N 22.64. Found: C 62.00; H 5.08; N 22.62.

5.8. Synthesis of compounds 14a–c

Compounds **14a**–c were prepared as described above for compound **7c**.

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*5.8.1. 4,6-Dichloro-2,2-dimethyl-2H-benzimidazole 1,3-dioxide (**14a**).* Dark blue powder. Yield 85%. Mp: 147–148 °C with decomposition. UV, λ_{max} (lg ε) 262 (4.34), 336 (3.00) 527 (3.80) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.67 (6H, s, $2CH_3$), 6.76 (1H, d, CH, J=1.5 Hz), 7.15 (1H, d, CH, J=1.5 Hz). ^{13}C NMR ($CDCl_3$), δ (ppm): 24.4, 98.7, 113.0, 131.6, 124.0, 131.9, 135.9, 136.6. MS m/z (I, %) 246 $[M]^+$,[42] 188 (53), 158 (100). HRMS: m/z (M^+) calcd for $C_9H_8{}^{35}Cl_2N_2O_2$: 246.9957; found: 246.9956. Anal. Calcd (%) for $C_9H_8Cl_2N_2O_2$ (247.0): C 43.73; H 3.24; Cl 28.75; N 11.34. Found: C 43.60; H 3.38; Cl 28.39; N 11.36.

*5.8.2. 4-Chloro-2,2-dimethyl-6-nitro-2H-benzimidazole 1,3-dioxide (**14b**).* Dark blue powder. Yield 68%. Mp: 119–121 °C with decomposition. IR (KBr), ν: 1334, 1527 (NO_2) cm^{-1}. UV, λ_{max} (lg ε) 264 (4.11), 337 (3.70), 555 (3.42) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.70 (6H, s, $2CH_3$), 7.51 (1H, d, CH, J=1.2 Hz), 8.05 (1H, d, CH, J=1.2 Hz). ^{13}C NMR ($CDCl_3$), δ (ppm): 24.6, 100.4, 111.7, 123.2, 125.9, 132.9, 136.3, 147.9. MS m/z (I, %) 259 $[M]^+$, 257 $[M]^+$ (43), 243 (21), 241 (62), 226 (22), 199 (32), 164 (49), 150 (15), 141 (16), 130 (26). HRMS: m/z (M^+) calcd for $C_9H_8{}^{35}ClN_3O_4$: 257.0198; found: 257.0203. Anal. Calcd (%) for $C_9H_8ClN_3O_4$ (257.5): C 41.95; H 3.11; Cl 13.79; N 16.31. Found: C 42.10, H 3.15, Cl 14.00, N 16.20.

*5.8.3. 4-Bromo-2,2-dimethyl-6-nitro-2H-benzimidazole 1,3-dioxide (**14c**).* Dark blue powder. Yield 64%. Mp: 119–121 °C with decomposition. IR (KBr), ν: 1332, 1525 (NO_2) cm^{-1}. UV, λ_{max} (lg ε) 263 (4.11), 342 (3.80), 561 (3.40) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.71 (6H, s, $2CH_3$), 7.75 (1H, d, CH, J=1.2 Hz), 8.11 (1H, d, CH, J=1.2 Hz). ^{13}C NMR ($CDCl_3$), δ (ppm): 24.7, 100.3, 112.2, 126.9, 111.3, 133.4, 136.3, 148.3. HRMS: m/z (M^+) calcd for $C_9H_8{}^{79}BrN_3O_4$: 300.9693; found: 300.9690. Anal. Calcd (%) for $C_9H_8BrN_3O_4$ (302.1): C 35.75; H 2.65; Br 26.49; N 13.91. Found C 36.01; H 2.65; Br 26.20; N 14.10.

5.9. Synthesis of 6-chloro-4-methoxybenzofuroxan (15a)

To a solution of 1.0 g (0.004 mol) of benzofuroxan **13a** in 10 mL of methanol 1.0 g (0.018 mol) of sodium methylate was added. The reaction mixture was boiled with reflux condenser for 4 h then cooled. The resulting residue was filtered, washed with water, and dried in vacuo (1 h, 0.01 Torr) to give 0.79 g (79%) of yellow powder of compound **15a**. Mp: 90–81 °C. IR (KBr), ν: 1624 (C=N) cm^{-1}. UV, λ_{max} (lg ε) 373 (3.63) nm; ^{1}H NMR (DMSO-d_6), δ (ppm): 3.88 (3H, s, OCH_3), 6.73 (1H, s, CH), 7.08 (1H, s, CH). Doubled set of signals was observed in the spectrum ^{13}C NMR due to isomerism of benzofuroxan. The spectrum of the dominant isomer in the mixture is described. ^{13}C NMR (DMSO-d_6), δ (ppm): 57.4, 102.9, 110.3, 115.1, 136.0, 147.2, 149.4. MS m/z (I, %) 200 $[M]^+$ (42), 181 (48), 169 (25), 131 (48), 119 (34), 110 (48). HRMS: m/z (M^+) calcd for $C_7H_5{}^{35}ClN_2O_3$: 199.9983; found: 199.9979. Anal. Calcd (%) for $C_7H_5ClN_2O_3$ (200.5): C 41.90; H 2.50; Cl 17.71; N 13.97. Found: C 41.92; H 2.48; Cl 17.60; N 13.92.

Crystallographic data for cocrystals of compounds **15a** with **13a**: mixed crystal of 6-chloro-4-methoxybenzofuroxan **15a** ($C_7H_5N_2O_3Cl$, M=200.59) and 6,4-dichlorobenzofuroxan **13a** ($C_6H_2N_2O_2Cl_2$, M=204.00), monoclinic, $P2_1/c$, a 15.413(1), b 13.945(1), c 7.2214(6) Å, β 91.320(4)°, V 1551.7(2) Å^3, Z 8, D_{calcd} 1.746 g cm^{-3}, μ(Mo-$K\alpha$) 0.708 mm^{-1}, F(000) 816, (θ 1.32–26.08°, completeness 99.8%), T 296(2) K, yellow plate, (0.40×0.40×0.04) mm^3, transmission 0.7326–0.8620, 22,803 measured reflections in index range −19≤h≤19, −17≤k≤16, −8≤l≤8, 3068 independent (R_{int} 0.0536), 255 parameters, R_1 0.0513 (for 2139 observed $I>2\sigma(I)$), wR_2=0.1133 (all data), GOOF 1.096, largest diff. peak and hole 0.199 and −0.255 e.A^{-3}. The atom positions of methoxy group and one of the chlorine atoms are disordered due to cocrystallization of compounds **15a** and **13a** in the same position with ratio 70:30 in both independent molecules.

5.10. Synthesis of 6-chloro-4-morpholinobenzofuroxan (15b)

8 mL of morpholine were added to the solution of 3.0 g (0.015 mol) of benzofuroxan **13a**. The reaction mixture was stirred at room temperature for 24 h. The resulting crystal mass was washed with water, residue filtered, and dried in vacuo (1 h, 0.01 Torr) to give orange powder of compound **15b** with yield 2.82 g (67%). Mp: 179–180 °C. IR (KBr), ν: 1608 (C=N) cm^{-1}. UV, λ_{max} (lg ε) 236 (3.93), 417 (3.60) nm; ^{1}H NMR (DMSO-d_6), δ (ppm): 3.53–3.59 (4H, m, $2CH_2$), 3.76–3.80 (4H, m, $2CH_2$), 6.48 (1H, d, CH, J=1.1 Hz), 7.04 (1H, CH, d, J=1.1 Hz). ^{13}C NMR (DMSO-d_6), δ (ppm): 49.2, 65.9, 100.1, 111.2, 116.0, 136.2, 140.9, 148.4. MS m/z (I, %) 255 $[M]^+$ (39), 239 (17), 208 (28), 197 (100), 181 (18), 151 (28). HRMS: m/z (M^+) calcd for $C_{10}H_{10}{}^{35}ClN_3O_3$: 255.0400; found: 255.0397. Anal. Calcd (%) for $C_{10}H_{10}ClN_3O_3$ (255.5): C 46.97; H 3.92; Cl 13.90; N 16.44. Found: C 47.02; H 3.76; Cl 13.80; N 16.47.

Crystallographic data for comp **15b**: $C_9H_7N_3O_4Cl_2$, M=292.08, monoclinic, $C2/c$, a 21.788(2), b 5.0093(4), c 21.317(2) Å, β 92.140(4), V 2324.9(3) Å^3, Z 8, D_{calcd}=1.669 g cm^{-3}, μ(Mo-$K\alpha$)=0.569 mm^{-1}, F(000)=1184, (θ 1.87–26.47°, completeness 99.6%), T 296(2) K, yellow alongated plate, (0.60×0.20×0.04) mm^3, transmission 0.6763–0.7454, 28,815 measured reflections in index range −26≤h≤26, −6≤k≤6, −26≤l≤26, 2391 independent (R_{int}=0.0374), 165 parameters, R_1=0.0339 (for 2391 observed $I>2\sigma(I)$, wR_2=0.0883 (all data), GOOF 1.064, largest diff. peak and hole 0.375 and −0.395 e.A^{-3}.

5.11. Synthesis of 6-chloro-4-methoxy-2,2-dimethyl-2*H*-benzimidazole 1,3-dioxide (16)

Compound **16** was prepared as described above for compound **7c** from compound **15a** in 10 mL of 65% perchloric acid. Dark blue powder. Yield 55%. Mp: 122–123 °C. IR (KBr), ν: 1579 (C=N) cm^{-1}. UV, λ_{max} (lg ε) 255 (4.07), 512 (3.71) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.68 (6H, s, $2CH_3$), 3.89 (3H, s, OCH_3), 6.01 (1H, s, CH), 6.52 (1H, s, CH). ^{13}C NMR ($CDCl_3$), δ (ppm): 24.2, 56.6, 98.2, 106.3, 107.9, 129.1, 136.4, 137.7, 150.4. MS m/z (I, %) 244 $[M]^+$ (35), 242 $[M]^+$ (100), 226 (23), 184 (45), 168 (10), 154 (26), 127 (47). HRMS: m/z (M^+) calcd for $C_{10}H_{11}{}^{35}ClN_2O_3$: 242.0453; found: 242.0455. Anal. Calcd (%) for $C_{10}H_{11}ClN_2O_3$ (242.5): C 49.49; H 4.54; Cl 14.64; N 11.55. Found: C 49.40; H 4.38; Cl 14.52; N 11.39.

5.12. Synthesis of 3,5-dichlorocyclohexa-3,5-diene-1,2-dione dioxime (17)

5 mL of benzyl amine were added to 0.5 g (0.0025 mol) of compound **13a**. The reaction mixture was stirred at room temperature for 24 h then 20 mL of water were added and a few drops of 5% hydrochloric acid until pH=3. The resulting crystal mass was filtered, washed with water and dried in vacuo (1 h, 0.01 Torr) to give yellow powder. Yield 0.44 g (86%). Mp: 154–156 °C with decomposition. IR (KBr), ν: 1604 (C=N) cm^{-1}. UV, λ_{max} (lg ε) 389 (3.30). nm; ^{1}H NMR (DMSO-d_6), δ (ppm): 6.92 1H, s, CH), 7.21 (1H, s, CH), 13.08 (1H, br s, OH), 14.25 (1H, br s, OH). ^{13}C NMR (DMSO-d_6), δ (ppm): 114.4, 126.4, 133.4, 134.3, 140.8, 146.8. Anal. Calcd (%) for $C_6H_4Cl_2N_2O_2$ (206.1): C 34.94; H 1.95; Cl 33.97; N 13.59. Found: C 34.82; H 1.79; Cl 33.80; N 13.57.

5.13. Synthesis of 3-chloro-*N*-isopropyl-5-morpholino-6- nitrosoaniline (18)

Compound **18** was prepared as described above for compound **7c** from compound **15b**. Dark blue oil. Yield 42%, oil. UV, λ_{max} (lg ε) 379 (3.33), 506 (3.32) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.27 (6H, d, 2 CH_3, J=6.0 Hz), 3.39–3.45 (4H, m, $2CH_2$), 3.67–3.83 (4H, m, 2 CH_2), 6.08 (1H, s, CH), 6.27 (1H, s, CH), 12.14 (1H, br s, NH). ^{13}C

NMR ($CDCl_3$), δ (ppm): 22.2, 43.6, 53.2, 68.8, 103.7, 104.0, 137.4, 146.4, 148.4, 157.3. Anal. Calcd (%) for $C_{13}H_{18}ClN_3O_2$: C 54.26; H 6.26; Cl 12.35; N 14.61. Found: C 54.22; H 6.46; Cl 12.45; N 14.57.

5.14. Synthesis of 4,6-dichloro-2,2-dimethyl-5-nitro-2*H*-benzimidazole 1,3-dioxide (20)

Compound **20** was prepared as described above for compound **7c**. Dark blue powder. Yield 62%. Mp: 116–118 °C. UV, λ_{max} (lg ε) 268, 556 nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.74 (6H, s, $2CH_3$), 7.45 (1H, s, CH). Anal. Calcd (%) for $C_9H_7Cl_2N_3O_4$ (291.1): C 37.10; H 2.41; Cl 24.05; N 14.43. Found: C 37.45; H 2.02; Cl 23.97; N 14.66.

5.15. Thermolysis of 4,6-dichloro-2,2-dimethyl-2*H*-benzimidazole 1,3-dioxide (14a)

A solution of 0.5 g 4,6-dichloro-2,2-dimethyl-2*H*-benzimidazole 1,3-dioxide (**14a**) in dichloroethane (20 mL) was boiled with reflux condenser for 4 h. The solvent was evaporated in vacuo, the residue was subjected to chromatography on SiO_2 (hexane–ethyl acetate (3:1)) to obtain *6,8-dichloro-3,3-dimethyl-3H-[2,1,4]benzoxadiazine 4-oxide* (**21a**) as an orange powder with yield 0.4 g (80%). Mp: 129–131 °C. IR (KBr), ν: 1598 (C=N) cm^{-1}. UV, λ_{max} (lg ε) 241 (4.02), 452 (3.40) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.63 (6H, s, $2CH_3$), 6.80 (1H, d, CH, *J*=1.5 Hz), 7.19 (1H, d, CH, *J*=1.5 Hz). ^{13}C NMR ($CDCl_3$), δ (ppm): 20.5, 96.2, 115.7, 130.5, 129.0, 130.3, 133.5, 146.8. MS *m*/*z* (*I*, %) 246 $[M]^+$ (13), 204 (100), 188 (60), 158 (18), 144 (67), 111 (88). HRMS: *m*/*z* (M^+) calcd for $C_9H_8{}^{35}Cl_2N_2O_2$: 245.9957; found: 245.9961. Anal. Calcd (%) for $C_9H_8Cl_2N_2O_2$ (246.1): C 43.89; H 3.25; Cl 28.465; N 11.38. Found: C 43.69; H 3.38; Cl 28.80; N 11.29.

5.16. Exposure of 6,8-dichloro-3,3-dimethyl-3*H*-[2,1,4]benzoxadiazine 4-oxide (21a) to the light

The solution of compound **21a** (0.5 g) in chloroform (10 mL) was exposed to the scattered sunlight (March, 55 latitude). The starting orange solution rapidly turned dark and the starting compound **21a** disappeared within ~2 h (TLC data). The solvent was evaporated, the residue was triturated with small amount of pentane and filtered to obtain a dark blue compound **14a** with yield 0.49 g (98%), mp 147–148 °C. The IR spectrum of the compound was identical to that of compound **14a** synthesized earlier.

5.17. Thermolysis of compounds 14b, 14c, 20, 9 and 16

*5.17.1. 8-Chloro-3,3-dimethyl-6-nitro-3H-[2,1,4]-benzoxadiazine 4-oxide (**21b**). 8-Chloro-3,3-dimethyl-6-nitro-3H-[2,1,4]-benzoxadiazine 4-oxide* (**21b**) was prepared as described above for compound **21a** from compound **14b**. Dark red powder. Yield 63%. Mp: 157–159 °C with decomposition. IR (KBr), ν: 1334, 1517 (C–NO_2), 1608 (C=N) cm^{-1}. UV, λ_{max} (lg ε) 262 (4.12), 332 (3.70), 495 (3.12) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.68 (6H, s, $2CH_3$), 7.58 (1H, d, CH, *J*=1.2 Hz), 8.13 (1H, d, CH, *J*=1.2 Hz). ^{13}C NMR ($CDCl_3$), δ (ppm): 20.3, 97.4, 115.5, 121.9, 128.3, 131.6, 145.6, 147.4. MS *m*/*z* (*I*, %) 259 $[M]^+$ (8), 257 $[M]^+$ (21), 201 (100), 199 (26), 141 (10). HRMS: *m*/*z* (M^+) calcd for $C_9H_8{}^{35}ClN_3O_4$: 257.0198; found: 257.0195. Anal. Calcd (%) for $C_9H_8ClN_3O_4$ (257.5): C 41.95; H 3.11; Cl 13.79; N 16.31. Found: C 42.10; H 3.15; Cl 14.00; N 16.20.

*5.17.2. 8-Bromo-3,3-dimethyl-6-nitro-3H-[2,1,4]benzoxadiazine 4-oxide (**21c**). 8-Bromo-3,3-dimethyl-6-nitro-3H-[2,1,4]benzoxadiazine 4-oxide* (**21c**) was prepared as described above for compound **21a** from compound **14c**. Dark red powder. Yield 41%. Mp: 164–165 °C with decomposition. IR (KBr), ν: 1330, 1512 (C–NO_2), 1604 (C=N) cm^{-1}. UV, λ_{max} (lg ε) 265 (4.02), 337 (3.72), 482 (3.18) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.68 (6H, s, $2CH_3$), 7.82 (1H, d, CH, *J*=2.1 Hz), 8.19 (1H, d, CH, *J*=2.1 Hz). ^{13}C NMR ($CDCl_3$), δ (ppm): 20.3, 97.4, 116.3, 120.7, 125.7, 128.7, 145.9, 147.9. MS *m*/*z* (*I*, %) 303 $[M]^+$ (20), 301 $[M]^+$ (20), 245 (33), 243 (35), 185 (11), 157 (11), 155 (13). HRMS: *m*/*z* (M^+) calcd for $C_9H_8{}^{79}BrN_3O_4$: 300.9693; found: 300.9690. Anal. Calcd (%) for $C_9H_8BrN_3O_4$ (302.0): C 35.77; H 2.65; Br 26.49; N 13.91. Found: C 35.69; H 2.38; Br 26.65; N 14.09.

*5.17.3. 6,8-Dichloro-3,3-dimethyl-7-nitro-3H-[2,1,4]benzoxadiazine 4-oxide (**21d**). 6,8-Dichloro-3,3-dimethyl-7-nitro-3H-[2,1,4]benzoxadiazine 4-oxide* (**21d**) was prepared as described above for compound **21a** from compound **20**. Dark red powder. Yield 68%. Mp: 83–86 °C. (KBr), ν: 1336, 1512 (C–NO_2), 1604 (C=N) cm^{-1}. UV, λ_{max} (lg ε) 236, 398, 446 nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.72 (6H, s, $2CH_3$), 7.45 (1H, s, CH). Anal. Calcd (%) for $C_9H_7Cl_2N_3O_4$: C 37.01; H 2.42; Cl 24.28; N 14.39. Found: C 37.01; H 2.38; Cl 24.15; N 14.55.

Crystallographic data for comp **21d**: $C_{10}H_{10}N_3O_3Cl$, *M* 255.66, monoclinic, $P2_1/n$, *a* 9.0703(8), *b* 7.5061(8), *c* 16.580(2) Å, β 103.646(4)°, *V* 1097.0(2) Å^3, *Z* 4, D_{calcd} 1.548 g cm^{-3}, μ(Mo-*Kα*) 0.348 mm^{-1}, F(000) 528, (θ 2.36–28.59°, completeness 98.9%), T 296(2) K, yellow plate, (0.60×0.60×0.04) mm^3, transmission 0.8278–0.9281, 16,671 measured reflections in index range $-12\le h\le 12$, $-10\le k\le 10$, $-21\le l\le 22$, 2772 independent (R_{int} 0.0375), 154 parameters, R_1=0.0466 (for 1994 observed $I>2\sigma(I)$), wR_2=0.1469 (all data), GOOF 1.087, largest diff. peak and hole 0.313 and −0.510 e.A^{-3}.

*5.17.4. 3,3-Dimethyl-8-nitro-3H-[2,1,4]benzoxadiazine 4-oxide (**21e**). 3,3-Dimethyl-8-nitro-3H-[2,1,4]benzoxadiazine 4-oxide* (**21e**) was prepared as described above for compound **21a** from compound **9**. Dark red powder. Yield 63%. Mp: 55–57 °C. IR (KBr), ν: 1344, 1529 (C–NO_2) cm^{-1}. UV, λ_{max} (lg ε) 230 (4.09), 404 (3.30), 472 (3.00) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.59 (6H, s, $2CH_3$), 6.78 (1H, m, CH), 7.38 (1H, m, CH), 7.53 (1H, m, CH). ^{13}C NMR ($CDCl_3$), δ (ppm): 19.9, 96.0, 123.9, 124.4, 128.3, 129.4, 143.2, 143.8. MS *m*/*z* (*I*, %) 223 $[M]^+$ (45), 208 (22), 181 (31), 165 (29), 149 (54), 105 (58). HRMS: *m*/*z* (M^+) calcd for $C_9H_9N_3O_4$: 223.0588; found: 223.0584. Anal. Calcd (%) for $C_9H_9N_3O_4$ (223.1): C 48.41; H 4.04; N 18.83. Found: C 48.52; H 4.00; N 18.88.

*5.17.5. 8-Chloro-6-methoxy-3,3-dimethyl-3H-[2,1,4]benzoxadiazine 4-oxide (**21f**). 8-Chloro-6-methoxy-3,3-dimethyl-3H-[2,1,4]benzoxadiazine 4-oxide* (**21f**) was prepared as described above for compound **21a** from compound **16**. Yellow powder. Yield 52%. Mp: 142–144 °C. IR (KBr), ν: 1606 (C=N) cm^{-1}. UV, λ_{max} (lg ε) 240 (3.82), 459 (3.40) nm; ^{1}H NMR ($CDCl_3$), δ (ppm): 1.63 (6H, s, $2CH_3$), 3.85 (3H, s, OCH_3), 5.86 (1H, d, CH, *J*=1.5 Hz), 6.90 (1H, d, CH, *J*=1.5 Hz). ^{13}C NMR ($CDCl_3$), δ (ppm): 20.6, 50.4, 96.6, 105.8, 108.6, 128.8, 135.3, 144.6, 153.2. MS *m*/*z* (*I*, %) 244 $[M]^+$ (18), 242 $[M]^+$ (53), 186 (25), 184 (82), 154 (34), 127 (24), 113 (22), 111 (39). HRMS: *m*/*z* (M^+) calcd for $C_{10}H_{11}{}^{35}ClN_2O_3$: 242.0453; found: 242.0455. Anal. Calcd (%) for $C_{10}H_{11}ClN_2O_3$ (242.5): C 49.49; H 4.54; Cl 14.64; N 11.55. Found: C 49.24; H 4.58; Cl 14.50; N 11.49.

5.18. Synthesis of 2*H*-benzimidazole mono-*N*-oxides 22a–f

a) A solution of 0.5 g 4,6-dichloro-2,2-dimethyl-2*H*-benzimidazole 1,3-dioxide (**14a**) in chlorobenzene (10 mL) was boiled with reflux condenser for 1 h until disappearance of the starting compound (control by TLC). The solvent was evaporated in vacuo, the residue was subjected to chromatography on SiO_2 (hexane–ethyl acetate (3:1)) to obtain 72% of *4,6-dichloro-2,2-dimethyl-2H-benzimidazole 1-oxide* (**22a**) as a orange powder.

b) A solution of 0.5 g 6,8-dichloro-3,3-dimethyl-3*H*-[2,1,4]benzoxadiazine 4-oxide (**21a**) in chlorobenzene (10 mL) was boiled with reflux condenser for 1 h until disappearance of the starting compound (control by TLC). The solvent was evaporated in vacuo,

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the residue was subjected to chromatography on SiO_2 (hexane–ethyl acetate (3:1)) to obtain 84% of *4,6-dichloro-2,2-dimethyl-2H-benzimidazole 1-oxide* (**22a**) as a orange powder.

c) 0.5 g of benzylamine were added to 1.0 g of compound **14a** in chloroform (20 mL). The mixture was boiled with reflux condenser for 2 h until disappearance of the starting compound (control by TLC). The solvent was evaporated in vacuo, the residue was subjected to chromatography on SiO_2 (hexane–ethyl acetate (3:1)). The first fraction gives benzaldehyde with yield 89%. IR spectrum is identical for spectrum of benzaldehyde. The second fraction gives compound **22a** with yield 89%.

Mp: 138–140 °C. IR (KBr), ν: 1593 (C=N) cm^{-1}. UV, λ_{max} (lg ε) 231 (4.12), 438 (3.40) nm; ^1H NMR ($CDCl_3$), δ (ppm): 1.53 (6H, s, $2CH_3$), 7.13 (2H, s, 2CH). ^{13}C NMR ($CDCl_3$), δ (ppm): 23.5, 104.3, 113.8, 135.4, 131.2, 133.9, 134.7, 157.9. MS *m/z* (*I*, %) 232 $[M]^+$ (60), 230 $[M]^+$ (100), 217 (18), 215 (34), 187 (24), 185 (23), 166 (28), 165 (83), 164 (80). HRMS: *m/z* (M^+) calcd for $C_9H_8{}^{35}Cl_2N_2O$: 230.0008; found: 230.0003. Anal. Calcd (%) for $C_9H_8Cl_2N_2O$ (230.1): C 46.94; H 3.48; Cl 30.43; N 12.17. Found: C 46.68; H 3.38; Cl 31.04; N 12.23.

Crystallographic data for comp **22a**: $C_9H_8Cl_2N_2O$, *M* 231.07, monoclinic, $P2_1/m$, *a* 8.5840(3), *b* 6.9731(3), *c* 8.5885(4) Å, β 104.761(3)°, *V* 497.12(4) $Å^3$, *Z* 2, D_{calcd} 1.544 g cm^{-3}, μ(Mo-*Kα*) 0.618 mm^{-1}, F(000) 236, (θ 2.45–26.98°, completeness 99.9%), T 293(2) K, orange prism, (0.57×0.49×0.39) mm^3, transmission 0.6658–0.7455, 4530 measured reflections in index range $-10\le h\le 10$, $-8\le k\le 8$, $-10\le l\le 10$, 1169 independent (R_{int} 0.0194), 83 parameters, R_1=0.0319 (for 1063 observed $I>2\sigma(I)$), wR_2=0.0830 (all data), GOOF 1.051, largest diff. peak and hole 0.304 and −0.283 $e.A^{-3}$.

*5.18.1. 4-Chloro-2,2-dimethyl-6-nitro-2H-benzimidazole 1-oxide (**22b**). 4-Chloro-2,2-dimethyl-6-nitro-2H-benzimidazole 1-oxide* (**22b**) was prepared as described above for compound **22a** from compound **14b**. Dark red powder. Yield 71%. Mp: 149–151 °C. IR (KBr), ν: 1317, 1514 (C–NO_2) cm^{-1}. UV, λ_{max} (lg ε) 262 (4.01), 327 (3.40), 457 (3.42) nm; ^1H NMR ($CDCl_3$), δ (ppm): 1.61 (6H, s, $2CH_3$), 7.97 (1H, d, CH, *J*=1.2 Hz), 8.14 (1H, d, CH, *J*=1.2 Hz). ^{13}C NMR ($CDCl_3$), δ (ppm): 23.8, 107.3, 113.8, 126.9, 132.3, 133.8, 145.7, 158.3. MS *m/z* (*I*, %) 241 $[M]^+$ (100), 226 (32), 224 (20), 195 (9), 166 (31), 165 (20), 164 (86), 150 (26), 130 (23). HRMS: *m/z* (M^+) calcd for $C_9H_8{}^{35}ClN_3O_3$: 241.0249; found: 241.0250. Anal. Calcd (%) for $C_9H_8ClN_3O_3$ (241.5): C 44.72; H 3.32; Cl 14.70; N 17.40. Found: C 44.79; H 3.15; Cl 14.70; N 17.36.

*5.18.2. 4-Bromo-2,2-dimethyl-6-nitro-2H-benzimidazole 1-oxide (**22c**). 4-Bromo-2,2-dimethyl-6-nitro-2H-benzimidazole 1-oxide* (**22c**) was prepared as described above for compound **22a** from compound **14c**. Dark red powder. Yield 44%. Mp: 151–153 °C. IR (KBr), ν: 1317, 1508 (C–NO_2) cm^{-1}. UV, λ_{max} (lg ε) 265 (4.00), 337 (3.65), 482 (3.43) nm; ^1H NMR ($CDCl_3$), δ (ppm): 1.56 (6H, s, $2CH_3$), 8.12 (1H, d, CH, *J*=1.9 Hz), 8.14 (1H, d, CH, *J*=1.9 Hz). ^{13}C NMR ($CDCl_3$), δ (ppm): 23.8, 107.0, 114.2, 130.5, 122.0, 133,5, 145.9, 158.9. MS *m/z* (*I*, %) 287 $[M]^+$ (100), 285 $[M]^+$ (91), 272 (18), 270 (19), 210 (11), 130 (13). HRMS: *m/z* (M^+) calcd for $C_9H_8{}^{79}BrN_3O_3$: 284.9744; found: 284.9745. Anal. Calcd (%) for $C_9H_8BrN_3O_3$ (286.0): C 37.77, H 2.80, Br 27.98, N 14.69. Found: C 37.62, H 2.80, Br 28.20, N 14.72.

*5.18.3. 4,6-Dichloro-2,2-dimethyl-5-nitro-2H-benzimidazole 1-oxide (**22d**). 4,6-Dichloro-2,2-dimethyl-5-nitro-2H-benzimidazole 1-oxide* (**22d**) was prepared as described above for compound **22a** from compound **20**. Orange powder. Yield 51%. Mp: 95–97 °C. (KBr), ν: 1332, 1517 (C–NO_2), 1607 (C=N) cm^{-1}. ^1H NMR ($CDCl_3$), δ (ppm): 1.69 (6H, s, $2CH_3$), 7.10 (1H, s, CH). Anal. Calcd (%) for $C_9H_7Cl_2N_3O_3$ (275.0): C 39.28; H 2.55; Cl 25.46; N 15.28. Found: C 39.34; H 2.47; Cl 25.33; N 15.05.

*5.18.4. 2,2-Dimethyl-4-nitro-2H-benzimidazole 1-oxide (**22e**). 2,2-Dimethyl-4-nitro-2H-benzimidazole 1-oxide* (**22e**) was prepared as described above for compound **22a** from compound **9**. Dark red powder. Yield 61%. Mp: 148 °C. IR (KBr), ν: 1344, 1529 (C–NO_2) cm^{-1}. UV, λ_{max} (lg ε) 314 (3.11), 382 (3.40), 463 (3.00) nm; ^1H NMR ($CDCl_3$), δ (ppm): 1.58 (6H, s, $2CH_3$), 6.89 (1H, dd CH, J_1=7.2 Hz, J_2=7.2 Hz), 7.52 (1H, d, CH, *J*=9.0 Hz), 8.15 (1H, d, CH, *J*=7.0 Hz). ^{13}C NMR ($CDCl_3$), δ (ppm): 23.7, 105.2, 123.9, 124.9, 135.5, 136.6, 142,2, 153.8. MS *m/z* (*I*, %) 207 $[M]^+$ (100), 190 (15), 149 (35), 130 (88), 118 (18). HRMS: *m/z* (M^+) calcd for $C_9H_9N_3O_3$: 207.0638; found: 207.0635. Anal. Calcd (%) for $C_9H_9N_3O_3$ (207.1): C 52.17; H 4.38; N 20.28. Found: C 52.22; H 4.40; N 20.17.

*5.18.5. 4-Chloro-6-methoxy-2,2-dimethyl-2H-benzimidazole 1-oxide (**22f**). 4-Chloro-6-methoxy-2,2-dimethyl-2H-benzimidazole 1-oxide* (**22f**) was prepared as described above for compound **22a** from compound **16**. Yellow powder. Yield 55%. Mp: 103–105 °C. IR (KBr), ν: 1606 (C=N) cm^{-1}. UV, λ_{max} (lg ε) 233(4.06), 433 (3.32) nm; ^1H NMR ($CDCl_3$), δ (ppm): 1.49 (6H, s, $2CH_3$), 3.90 (3H, s, OCH_3), 6.12 (1H, s, CH), 6.79 (1H, s, CH). ^{13}C NMR ($CDCl_3$), δ (ppm): 23.5, 56.2, 103.4, 107.3, 110.5, 134.8, 136.3, 153.3, 156.7. MS *m/z* (*I*, %) 228 $[M]^+$ (32), 226 $[M]^+$ (100), 225 (16), 211 (24), 209 (19), 161 (41), 146 (54), 132 (15), 118 (41). HRMS: *m/z* (M^+) calcd for $C_{10}H_{11}{}^{35}ClN_2O_2$: 226.0504; found: 226.0499. Anal. Calcd (%) for $C_{10}H_{11}ClN_2O_2$ (226.5): C 52.98; H 4.86; Cl 15.64; N 12.37. Found: C 53.28; H 4.98; Cl 15.62; N 12.39.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2015.03.096.

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