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Synthesis of 1,3-dialkyl-4-[(arylmethylidene)amino]glycolurils

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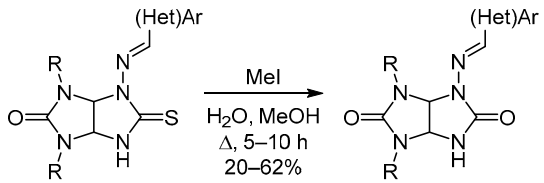


10 examples

A method for the synthesis of 1,3-dialkyl-4-[(arylmethylidene)amino]glycolurils was developed based on nucleophilic substitution of the sulfur atom with the oxygen atom in the corresponding thioglycolurils *via* alkylation of the latter followed by acid hydrolysis of alkylsulfanyl derivatives of thioglycolurils, both with the isolation of alkylsulfanyl intermediates and by the one-pot method. The structure of the synthesized compounds was confirmed by X-ray structural analysis of several examples.

Keywords: 5-[(4-bromobenzyl)sulfanyl]-3,3a,6,6a-tetrahydroimidazo[4,5-*d*]imidazol-2(1*H*)-ones, glycolurils, 5-methylsulfanyl-3,3a,6,6a-tetrahydroimidazo[4,5-*d*]imidazol-2(1*H*)-ones, tetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-diones, thioglycolurils, 5-thioxohexahydroimidazo[4,5-*d*]imidazol-2(1*H*)-ones, *S*-alkylation, hydrolysis.

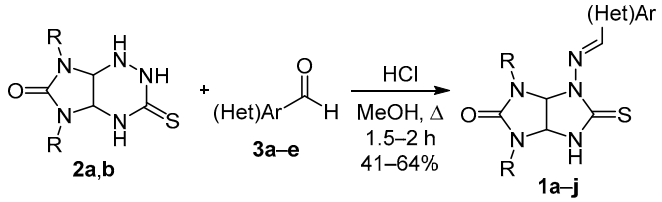
Amides and thioamides, including cyclic ones, are widely used in medicinal chemistry.[1] Depending on the availability of the corresponding amides or thioamides, it becomes necessary to replace the amide oxygen atom with a sulfur atom[1c–e,2] or desulfurize thioamides.[3] Glycolurils (tetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-diones) are an important class of cyclic amides that exhibit a wide spectrum of neurotropic activity.[4] 1,3,4,6-Tetraalkylglycolurils are recommended for the treatment of neuroses.[4a,b] *N*-(Carboxyalkyl)glycolurils showed neuroprotective activity.[4c] Nootropic and anxiolytic effects of *N*-(2-acetylaminoethyl)glycolurils were revealed.[4d] At the same time, substituted *N*-aminothioglycolurils have antiproliferative, fungicidal,[5] and sedative[6] effects, while *N*-aminoglycolurils are practically inaccessible.

The replacement of the thioxo group with the oxo group is based on two main approaches: nucleophilic substitution[3d,e,5b,7] and oxidation.[3a–c] Earlier, we showed by several examples the possibility of synthesizing 1,3-dialkyl-4[(*E*)-((*E*)-3-phenylallylidene)amino]glycolurils by alkylation of the corresponding thioglycolurils with MeI followed by hydrolysis of the resulting methylsulfanyl derivatives; isolation of the methylsulfanyl derivatives afforded higher yields (62–81%) of the target glycolurils as compared to the one-pot process (48–69% yields of glycolurils).[5b] The literature data also confirmed the efficiency of the method of the synthesis of imidazolidin-2-ones *via* hydrolysis of imidazolidine-2-thione alkylsulfanyl derivatives.[7]

In this regard, the aim of this work was to develop a method for the synthesis of 1,3-dialkyl-4-[(arylmethylidene)amino]glycolurils by alkylation of the corresponding thioglycolurils followed by hydrolysis of alkylsulfanyl derivatives.

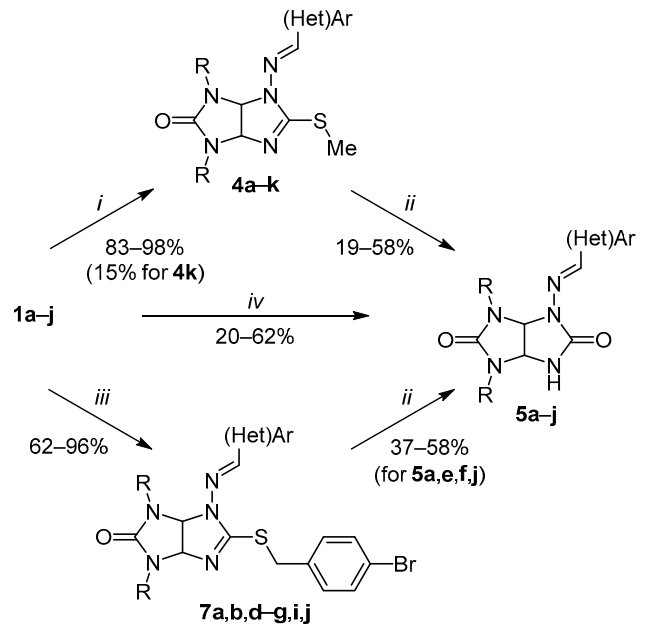
1,3-Dialkyl-4-[(arylmethylidene)amino]thioglycolurils **1a**–**j** were obtained according to a previously developed procedure[8] by the reaction of octahydroimidazo[4,5-*e*]-[1,2,4]triazines **2a**,**b** with (hetero)aromatic aldehydes **3a**–**e** (Scheme 1). 5-Methylsulfanyl derivatives **4a**–**k** were synthesized by alkylation of thioglycolurils **1a**–**j** by the action of MeI in the presence of an equimolar amount of K_2CO_3 similarly to the known procedure.[5] The yields of compounds **4a**–**j** were 83–98%, the yield of product **4k** was 15% (Scheme 2).

Scheme 1



1 a R = Me, Ar = Ph; **b** R = Me, Ar = 2-HOC$_6$H$_4$; **c** R = Me, Ar = 2-HO-5-O$_2$NC$_6$H$_3$; **d** R = Me, Het = furan-2-yl; **e** R = Me, Het = thiophen-2-yl; **f** R = Et, Ar = Ph; **g** R = Et, Ar = 2-HOC$_6$H$_4$ **h** R = Et, Ar = 2-HO-5-O$_2$NC$_6$H$_3$; **i** R = Et, Het = furan-2-yl; **j** R = Et, Het = thiophen-2-yl; **2 a** R = Me, **b** R = Et; **3 a** Ar = Ph, **b** Ar = 2-HOC$_6$H$_4$ **c** Ar = 2-HO-5-O$_2$NC$_6$H$_3$, **d** Het = furan-2-yl, **e** Het = thiophen-2-yl

Scheme 2



i: MeI, K_2CO_3, MeOH, 60°C, 2 h; *ii*: HCl, MeOH, Δ, 1 or 6 h
iii: 4-BrC$_6$H$_4$CH$_2$Br, K_2CO_3, DMSO, rt, 5 h
iv: MeI, H_2O–MeOH, Δ, 5–10 h

1, **5**, **7 a** R = Me, Ar = Ph; **b** R = Me, Ar = 2-HOC$_6$H$_4$ **c** R = Me, Ar = 2-HO-5-O$_2$NC$_6$H$_3$; **d** R = Me, Het = furan-2-yl **e** R = Me, Het = thiophen-2-yl; **f** R = Et, Ar = Ph **g** R = Et, Ar = 2-HO-C$_6$H$_4$; **h** R = Et, Ar = 2-HO-5-O$_2$NC$_6$H$_3$ **i** R = Et, Het = furan-2-yl; **j** R = Et, Het = thiophen-2-yl **4 a** R = Me; Ar = Ph; **b** R = Me, Ar = 2-HOC$_6$H$_4$ **c** R = Me, Ar = 2-KO-5-O$_2$NC$_6$H$_3$; **d** R = Me, Het = furan-2-yl **e** R = Me, Het = thiophen-2-yl; **f** R = Et, Ar = Ph **g** R = Et, Ar = 2-HOC$_6$H$_4$; **h** R = Et, Ar = 2-KO-5-O$_2$NC$_6$H$_3$ **i** R = Et, Het = furan-2-yl; **j** R = Et, Het = thiophen-2-yl **k** R = Et, Ar = 2-HO-5-O$_2$NC$_6$H$_3$

As shown by the data of elemental analysis and NMR spectroscopy, the alkylation of compound **1c** containing hydroxy and nitro groups in the phenyl substituent resulted in the formation of the potassium salt of *S*-methylsulfanylglycoluril **4c** in high yield (93%). The most characteristic feature of the ^{13}C NMR spectrum of salt **4c** is the downfield shift of the signal of the aromatic carbon atom directly bonded to the oxygen atom, which is observed at 178.1 ppm, in contrast to the signal of a similar carbon atom which is observed in compounds **4b**,**g**,**k** at 156.2–161.7 ppm. For comparison, the signal of a similar carbon atom in the spectrum of sodium 4-nitrophenoxide is observed at 178.6 ppm.[9] Alkylation of 1,3-diethyl-substituted thioglycoluril **1h** at a molar ratio of K_2CO_3:**1h** = 1:1 gave a mixture of potassium salt **4h** and hydroxy derivative **4k**, the separation of which by fractional crystallization from EtOH led to a decrease in the total yield of *S*-alkylation products from ~80 to ~41%. An increase in the molar ratio of K_2CO_3:**1h** to 1.2:1 made it possible to obtain potassium salt **4h** in 85% yield.

Alkylation of thioglycoluril **1g** containing a hydroxybenzylidene moiety resulted in the formation of trace amounts of the *O*-methylation product. The ^{1}H NMR spectrum of the reaction mixture showed a minor signal of the methoxy group at 3.85 ppm; in the high-resolution mass spectrum, along with the molecular ion peak $[M+H]^+$ of compound **4g** (*m*/*z* 348.1493), a peak corresponding to the molecular ion $[M+H]^+$ of compound **4l** (*m*/*z* 362.1648), methylated both at the sulfur atom and at the oxygen atom, was present (Fig. 1).

Generally, in the ^{1}H NMR spectra of alkylation products **4a**–**k**, in comparison with the spectra of thioglycolurils **1a**–**j**, the signal of the NH proton disappears (singlet in the region of 9.94–10.44 ppm)[8] and the signal of protons of the SCH_3 group emerges (singlet in the region 2.40–2.46 ppm). In the ^{13}C NMR spectra, the signal of the carbon atom of the C=S group disappears in the 178.2–179.7 ppm range[8] and the signals of the carbon atoms of the SCH_3 and N=CS groups appear in the 12.9–13.0 and 166.0–167.2 ppm ranges, respectively.

Compound **4f** was chosen as a model for studying the hydrolysis of alkylsulfanylglycolurils. The reactions were carried out in MeOH in the presence of an equivalent amount of concentrated HCl. The progress of the reactions was monitored by ^{1}H NMR spectroscopy. At room temperature, the hydrochloride of the starting compound **4f**·HCl was formed (Table 1). According to the ^{1}H NMR spectrum of the reaction mixture, the conversion of hydrochloride **4f**·HCl was about 5% after 24 h (entries 1 and 2). When heating to 40°C, the yield of the target compound **5f** reached 50% after 1.5 h, after which its amount did not increase, and the formation of byproducts began 5.5 h after the start of the reaction (entries 3–5).

Upon heating under reflux in MeOH, already 15 min after the start of the reaction, the signals of the target product **5f** were recorded in the ^{1}H NMR spectrum, along with the signals of hydrochloride **4f**·HCl (Table 1, entry 6). After 1 h, about 10% of compound **4f**·HCl remained,

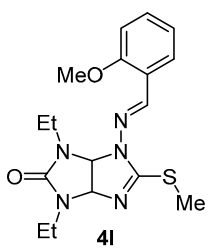
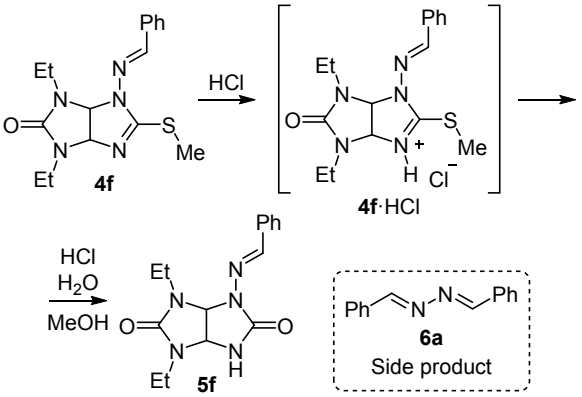


Figure 1. Byproduct **4l** of alkylation of thioglycoluril **1g**.

Table 1. Optimization of the reaction conditions of the hydrolysis of *S*-methyl derivative **4f***



Entry	Amount of HCl, equiv	Temperature, °C	Time, h	Yield,** %	
				4f·HCl	**5f**
1	1	20	1	100	0
2	1	20	24	95	5
3	1	40	0.5	67	33
4	1	40	1.5	50	50
5	1	40	5.5	20	50
6	1	Reflux	0.25	93	6
7	1	Reflux	1	10	60
8	1	Reflux	3	5	43***
9	0.1	Reflux	2	0	0

* Amounts of reagents: glycoluril **4f** (331 mg, 1 mmol), MeOH (30 ml).
** According to ^{1}H NMR spectroscopy data.
*** Yield of isolated product.

while, along with the signals of the target glycoluril **5f** (about 60% yield, entry 7), signals of byproducts, apparently, decomposition products (for example, 1,2-di((*E*)-benzylidene)hydrazine (**6a**), about 15%), emerged. After 3 h, the conversion of compound **4f**·HCl reached 95%; however, along with an increase in the relative integral intensity of the signals from glycoluril **5f**, the intensity of signals from the degradation products also increased. Glycoluril **5f** was isolated in 43% yield (entry 8). When the amount of HCl was decreased to 0.1 equiv, neither glycoluryl **5f** nor hydrochloride **4f**·HCl was formed from methylsulfanyl derivative **4f** (entry 9).

Considering the obtained results, glycolurils **5a**–**j** were synthesized by heating compounds **4a**–**j** with an equivalent amount of HCl under reflux in MeOH for 1 or 6 h (the course of reactions was monitored by ^{1}H NMR spectroscopy) in 19–58% yields (Scheme 2). For the hydrolysis of potassium salts **4c**,**h**, 2 equiv of HCl was used. Since the yields of the target glycolurils **5a**–**j** are far from quantitative, we attempted to obtain them *via* the (4-bromobenzyl)sulfanyl derivatives of thioglycolurils **7a**,**b**,**d**–**g**,**i**,**j**. Compounds **7a**,**b**,**d**–**g**,**i**,**j** were prepared by alkylation of thioglycolurils **1a**,**b**,**d**–**g**,**i**,**j** with 4-bromobenzyl bromide in DMSO in the presence of K_2CO_3 at room temperature for 5 h. Yields of compounds **7a**,**b**,**d**–**g**,**i**,**j** amounted to 62–96% (Scheme 2). Alkylation of compounds **1c**,**h** led to a mixture of *S*- and *O*,*S*-alkylation products, as well as a mixture of potassium salts of the starting thioglycolurils **1c**,**h** and *S*-alkylation products. The

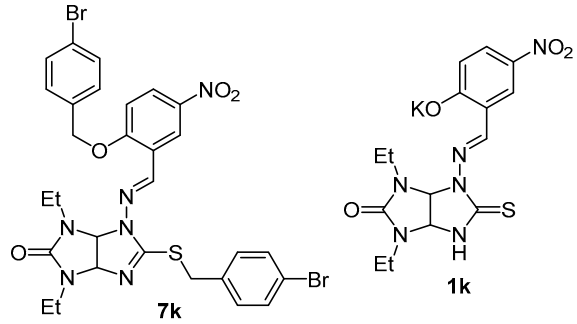


Figure 2. *O*,*S*-Alkylation product **7k** and potassium salt of thioglycoluril **1k** obtained by alkylation of compound **1h**.

O,*S*-alkylation product **7k** and the potassium salt of thioglycoluril **1k** (Fig. 2) were isolated in 2 and 8% yields, respectively, and characterized.

In the ^{1}H NMR spectra of the alkylation products **7a**,**b**,**d**–**g**,**i**,**j**, in comparison with the spectra of thioglycolurils **1a**,**b**,**d**–**g**,**i**,**j**, the NH proton signal disappears (singlet in the 9.94–10.44 ppm region)[8] and proton signals of the SCH_2 group (singlet in the range of 4.25–4.29 ppm) and the 4-bromophenyl fragment (two doublets in the range of 7.38–7.52 ppm) appear. In the ^{13}C NMR spectra of compounds **7a**,**b**,**d**–**g**,**i**,**j**, the signal of the carbon atom of the C=S group disappears in the range of 178.2–179.7 ppm,[8] accompanied with the appearance of signals of the (4-bromobenzyl)sulfanyl group (the most characteristic signals at 33.1–33.2, 131.2–131.3, and 131.3–131.4 ppm) and the N=CS group at 164.9–165.6 ppm.

Hydrolysis of 4-bromobenzyl derivatives **7a**,**b**,**d**–**g**,**i**,**j** was carried out by heating with an equivalent amount of HCl under reflux in MeOH for 1 or 6 h (the progress of the reactions was monitored by ^{1}H NMR spectroscopy). The yields of target glycolurils **5a**,**e**,**f**,**j** were 37–58% (Scheme 2). The hydrolysis of compounds **7b**,**d**,**g**,**i** was more severe with the formation of a mixture of products that was difficult to identify.

Next, the possibility of accessing glycolurils **5a**–**j** by the reaction of *N*-aminothioglycolurils **1a**–**j** with an excess of MeI in a H_2O–MeOH, 1:80 mixture was investigated (Scheme 2). Heating the reaction mixture under reflux for 5 h using a fourfold excess of MeI resulted in a mixture of the starting thioglycoluril **1a**–**j** with a small amount of the target glycoluril **5a**–**j**. An increase in the degree of conversion of the starting thioglycolurils **1a**–**j** to 90–100% (according to ^{1}H NMR spectroscopy) was achieved by increasing the amount of MeI to 7 equiv, and in some cases also by increasing the reaction time to 8–10 h. The yields of glycolurils **5a**–**j** were 20–62%. Due to the low solubility of thioglycolurils **1c**,**h** in MeOH, their reactions with MeI were also carried out in a DMF–H_2O, 10:1 mixture both at room temperature and at 60°C, but this did not lead to a significant increase in the yields of glycolurils **5c**,**h** (20–22%). In general, the moderate yields of glycolurils **5a**–**j** are explained by hydrolysis in an alternative direction leading to the formation, in particular, of the above-mentioned *N*,*N*'-dibenzylidenehydrazines **6**. In addition to ^{1}H NMR spectroscopy data, the structure of compound **6b**

(Ar = 2-HO-5-$O_2NC_6H_3$) was confirmed by mass spectroscopy.

In the ^{1}H NMR spectra of glycolurils **5a**–**j**, an upfield shift of the signal of the NH proton (8.41–8.55 ppm) is observed in comparison with the signal of the same proton in the spectra of thioglycolurils **1a**–**j** (9.94–10.44 ppm). In the ^{13}C NMR spectra of glycolurils **5a**–**j**, the signal of the C=O group at 155.7–156.6 ppm appears instead of the signal of the C=S group in the spectra of thioglycolurils **1a**–**j** at 178.2–179.7 ppm.

The structures of compounds **4j** and **5g**,**h** were confirmed by X-ray structural analysis of their single crystals (Figs. 3–5), which, in the case of compound **5h**, contained one solvate MeOH molecule per one molecule of the target product. According to the data obtained in this way, compounds **4j** and **5g**,**h** have the *E*-configuration of the C=N bond and the molecular geometry expected for this class of compounds,[8,10] including the planar conformation of the heterocyclic rings in the glycoluryl fragment, the angle between which is 60.76(6), 60.77(9), and 59.37(10)°, respectively. In addition, the rings of the thiophene and phenol substituents and the corresponding heterocycle are practically in the same plane as indicated by the angle between their rms planes of 15.07(7)–21.62(6)°. In the case of glycolurils **5g**,**h**, such a planar configuration is additionally stabilized by intramolecular hydrogen bonds O–H···N (distance O···N: 2.6559(18) and 2.5591(13) Å, angle O–H···N: 144.72(10) and 148.96(6)°, respectively) with the hydroxy group of the phenol substituent. On the contrary, the NH group in compounds **5g**,**h**, which is absent in sulfanylglycoluril **4j**, participates in the formation of intermolecular hydrogen bonds N–H···O (distance N···O: 2.8494(19) and 2.8377(13) Å, angle N–H···O: 168.87(10) and 165.27(7)°, respectively) either with the neighboring molecule of the target product, as in glycoluril **5g**, or with the MeOH solvate molecule, as in glycoluril **5h**. In the first case, this leads to the appearance of centrosymmetric dimers in the solid state, or, in the second, infinite chains formed by the O–H···O hydrogen bond (distance O···O: 2.7106(12) Å, angle O–H···O: 171.10(6)°) between the indicated MeOH molecule and the O(2) oxygen atom of the glycoluryl fragment.

The synthesized glycolurils **5f**,**g** and methylsulfanyl derivatives **4i**,**j** were tested for cytotoxicity against human rhabdomyosarcoma (RD), lung carcinoma (A549), and intestinal carcinoma (HCT116) cell lines. It was shown that compounds **5f**,**g** and **4i**,**j** do not possess cytotoxicity, which is a positive result for potential neurotropically active compounds.

To conclude, methods for the synthesis of 1,3-dialkyl-4-[(arylmethylidene)amino]glycolurils were developed based on nucleophilic substitution of the sulfur atom with the oxygen atom in the corresponding thioglycolurils by alkylation of the latter and acid hydrolysis of alkylsulfanyl derivatives of thioglycolurils. The one-pot method involving alkylation of thioglycolurils at the sulfur atom with an excess of MeI followed by hydrolysis of the resulting methylsulfanyl derivatives by the released HI can be considered as a general and convenient approach to the synthesis of the target glycolurils.

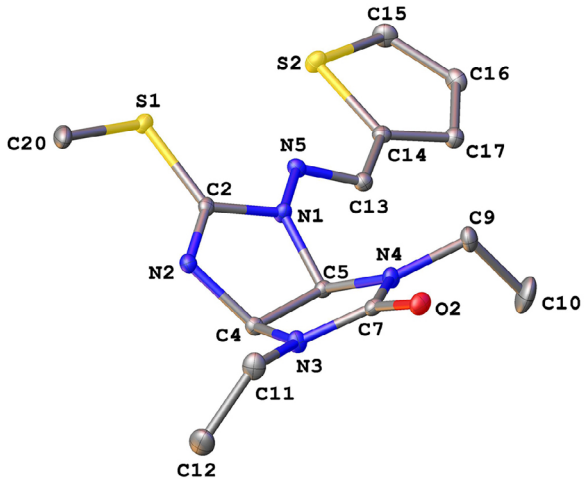


Figure 3. The molecular structure of compound **4j** with atoms represented as thermal vibration ellipsoids of 50% probability. Hydrogen atoms are not shown for clarity.

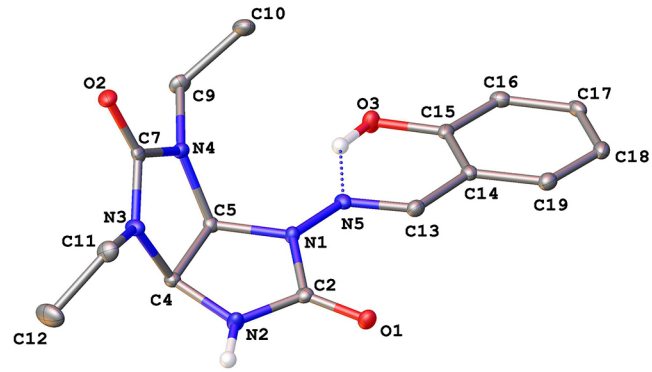


Figure 4. The molecular structure of compound **5g** with atoms represented as thermal vibration ellipsoids of 50% probability. Hydrogen atoms (with the exception of those belonging to the NH and OH groups) are not shown for clarity. The dotted line shows the O–H···N hydrogen bond.

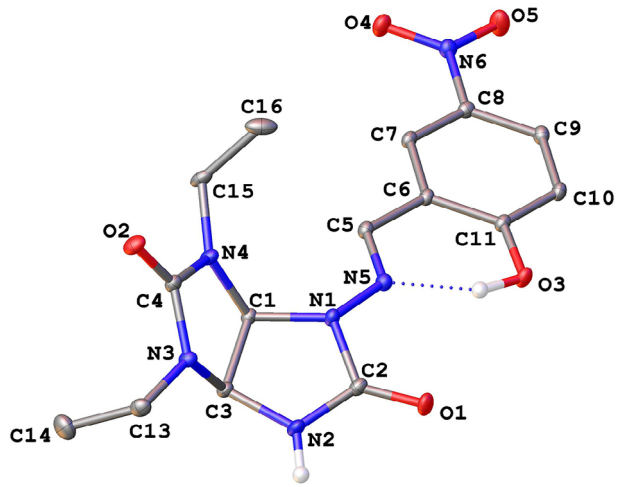


Figure 5. The molecular structure of compound **5h** with atoms represented as thermal vibration ellipsoids of 50% probability. Hydrogen atoms (with the exception of those belonging to the NH and OH groups) and the MeOH solvate molecule are not shown for clarity. The dotted line shows the O–H···N hydrogen bond.

Experimental

IR spectra were registered on a Bruker ALPHA Fourier transform spectrometer in KBr pellets. ^{1}H and ^{13}C NMR spectra (300 and 75 MHz, respectively) were acquired on a Bruker AM-300 spectrometer in DMSO-d_6 with TMS as internal standard. High-resolution mass spectra were recorded on a Bruker micrOTOF II mass spectrometer with electrospray ionization in the positive ion registration mode (capillary voltage 4500 V). Scanning range *m*/*z* 50–3000, external or internal calibration (Fluka Electrospray Calibrant Solution). Syringe injection was used for solutions of compounds in MeCN or MeOH, flow rate 3 μl/min. N_2 was used as spray gas (flow rate 4 l/min), interface temperature 180°C. The mass spectrum of compound **6b** was registered on a Finnigan MAT INCOS-50 mass spectrometer (EI, 70 eV). Elemental analysis was performed on a Perkin Elmer Series II 2400 CHN-analyzer. Melting points were determined on a Boetius heating bench.

Synthesis of thioglycolurils 1a–j (General method). Aldehyde **3a**–**e** (2.05 mmol) and concentrated HCl (2 drops) were added to a suspension of imidazotriazine **2a**,**b** (2.00 mmol) in MeOH (30 ml). The resulting mixture was stirred and heated under reflux for 1.5–2 h, then cooled to room temperature. After 4–48 h, the formed precipitate was filtered off, washed with MeOH (5 ml), and air-dried. Compound **1b** was recrystallized from MeOH.

Yields, melting points, and ^{1}H NMR spectra of thioglycolurils **1a**,**b**,**d**–**g**,**i**,**j** correspond to the previously published.[8]

(*E*)-4-[(2-Hydroxy-5-nitrobenzylidene)amino]-1,3-dimethyl-5-thioxohexahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one (1c). Yield 315 mg (45%), yellowish powder, mp 281–283°C (decomp., MeOH). IR spectrum, ν, cm^{-1}: 3436 (OH), 3139 (NH), 1798, 1693 (C=O), 1625, 1576 (C=N), 1529 (NO_2), 1497, 1477, 1451, 1340 (NO_2), 1275, 1207. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.78 (3H, s, NCH_3); 2.96 (3H, s, NCH_3); 5.51 (1H, d, *J* = 8.3, CH); 6.13 (1H, d, *J* = 8.3, CH); 7.13 (1H, d, *J* = 9.1, H Ar); 8.20 (1H, dd, *J* = 9.1, *J* = 2.9, H Ar); 8.63 (1H, d, *J* = 2.9, H Ar); 8.96 (1H, s, N=CH); 10.44 (1H, s, NH); 12.28 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 28.2; 30.8; 69.0; 72.3; 117.5; 119.0; 125.3; 126.6; 139.9; 143.7; 157.4; 162.4; 179.6. Found, *m*/*z*: 351.0862 $[M+H]^+$. $C_{13}H_{15}N_6O_4S$. Calculated, *m*/*z*: 351.0870.

(*E*)-1,3-Diethyl-4-[(2-hydroxy-5-nitrobenzylidene)-amino]-5-thioxohexahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one (1h). Yield 423 mg (56%), yellowish powder, mp 255–256°C (decomp., MeOH). IR spectrum, ν, cm^{-1}: 3448 (OH), 3231 (NH), 1700, 1688 (C=O), 1624, 1574 (C=N), 1519 (NO_2), 1478, 1452, 1342 (NO_2), 1290, 1254, 1200, 1182. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.01–1.12 (6H, m, $2CH_3$); 3.10–3.52 (4H, m, $2NCH_2$); 5.60 (1H, d, *J* = 8.3, CH); 6.15 (1H, d, *J* = 8.3, CH); 7.14 (1H, d, *J* = 9.1, H Ar); 8.20 (1H, dd, *J* = 9.1, *J* = 2.9, H Ar); 8.62 (1H, d, *J* = 2.9, H Ar); 9.12 (1H, s, N=CH); 10.31 (1H, s, NH); 12.12 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 12.9; 13.7; 36.0; 37.9; 67.0; 72.3; 117.4; 119.5; 124.3; 126.9; 140.0; 144.8; 156.9; 162.5; 179.2. Found, *m*/*z*: 379.1181 $[M+H]^+$. $C_{15}H_{19}N_6O_4S$. Calculated, *m*/*z*: 379.1183.

Synthesis of methylsulfanylglycolurils 4a–k (General method). MeI (125 μl, 2 mmol) was added with stirring to a suspension of thioglycoluril **1a–j** (1 mmol) and K_2CO_3 (138 mg, 1 mmol) (166 mg, 1.2 mmol for the synthesis of salt **4h**) in MeOH (30 ml). The resulting mixture was stirred at 60°C for 2 h, then concentrated under reduced pressure. The residue was triturated with MeOH (for salts **4c**,**h**), H_2O (for compounds **4a**,**d**–**f**,**i**,**j**), or Me_2CO (for compounds **4b**,**g**); the formed precipitate was filtered off, washed with H_2O (5 ml) (2×1 ml for salts **4c**,**h**) and air-dried.

(*E*)-4-Benzylideneamino-1,3-dimethyl-5-methylsulfanyl-3,3a,4,6a-tetrahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one (4a). Yield 288 mg (95%), white powder, mp 189–191°C (MeOH). IR spectrum, ν, cm^{-1}: 1695 (C=O), 1564, 1492, 1449, 1397, 1215, 1089, 1032. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.43 (3H, s, SCH_3); 2.83 (3H, s, NCH_3); 2.92 (3H, s, NCH_3); 5.59 (1H, d, *J* = 7.8, CH); 5.94 (1H, d, *J* = 7.9, CH); 7.38–7.46 (3H, m, H Ph); 7.68 (2H, d, *J* = 7.2, H Ph); 8.10 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 12.9; 28.3; 30.5; 72.2; 80.0; 126.4 (2C); 128.7 (2C); 129.4; 134.4; 138.1; 157.6; 166.8. Found, *m*/*z*: 304.1236 $[M+H]^+$. $C_{14}H_{18}N_5OS$. Calculated, *m*/*z*: 304.1227.

(*E*)-4-[(2-Hydroxybenzylidene)amino]-1,3-dimethyl-5-methylsulfanyl-3,3a,4,6a-tetrahydroimidazo[4,5-*d*]-imidazol-2(1*H*)-one (4b). Yield 313 mg (98%), white powder, mp 157–159°C (Me_2CO). IR spectrum, ν, cm^{-1}: 3401 (OH), 3202, 1704 (C=O), 1670, 1607, 1572, 1499, 1455, 1410, 1260, 1212, 1192, 1169, 1042. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.45 (3H, s, SCH_3); 2.83 (3H, s, NCH_3); 2.92 (3H, s, NCH_3); 5.58 (1H, d, *J* = 7.8, CH); 5.94 (1H, d, *J* = 7.8, CH); 6.86–6.91 (2H, m, H Ar); 7.24 (1H, t, *J* = 7.5, H Ar); 7.58 (1H, d, *J* = 7.6, H Ar); 8.30 (1H, s, N=CH); 10.12 (1H, br. s, OH). ^{13}C NMR spectrum, δ, ppm: 13.0; 28.4; 30.8; 72.7; 80.0; 116.2; 119.4; 119.8; 127.1; 130.8; 137.3; 156.3; 157.7; 166.4. Found, *m*/*z*: 320.1176 $[M+H]^+$. $C_{14}H_{18}N_5O_2S$. Calculated, *m*/*z*: 320.1176.

(*E*)-2-{[(4,6-Dimethyl-2-methylsulfanyl-5-oxo-4,5,6,6a-tetrahydroimidazo[4,5-*d*]imidazol-1(3a*H*)-yl)imino]-methyl}-4-nitrophenol, potassium salt (4c). Yield 374 mg (93%), orange powder, mp >300°C (MeOH). IR spectrum, ν, cm^{-1}: 3449 (br, H_2O), 1707 (C=O), 1597, 1559 (NO_2), 1489, 1444, 1416, 1339 (NO_2), 1283, 1220, 1043. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.41 (3H, s, SCH_3); 2.81 (3H, s, NCH_3); 2.88 (3H, s, NCH_3); 5.52 (1H, d, *J* = 8.0, CH); 5.83 (1H, d, *J* = 8.0, CH); 6.05 (1H, d, *J* = 9.5, H Ar); 7.73 (1H, dd, *J* = 9.5, *J* = 3.1, H Ar); 8.26 (1H, d, *J* = 3.2, H Ar); 8.28 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 12.9; 28.4; 31.2; 73.1; 79.9; 121.0; 121.3; 122.3; 127.3; 128.5; 138.0; 157.9; 167.2; 178.1. Found, *m*/*z*: 365.1019 $[M+H]^+$. $C_{14}H_{17}N_6O_4S$. Calculated, *m*/*z*: 365.1027. Found, %: C 39.47; H 4.03; N 19.51. $C_{14}H_{15}KN_6O_4S\cdot H_2O$. Calculated, %: C 39.99; H 4.08; N 19.99.

(*E*)-4-[(Furan-2-ylmethylidene)amino]-1,3-dimethyl-5-methylsulfanyl-3,3a,4,6a-tetrahydroimidazo[4,5-*d*]-imidazol-2(1*H*)-one (4d). Yield 252 mg (86%), white powder, mp 187–189°C (MeOH). IR spectrum, ν, cm^{-1}: 1719 (C=O), 1563, 1484, 1443, 1412, 1382, 1211, 1040. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.41 (3H, s, SCH_3);

2.82 (3H, s, NCH_3); 2.88 (3H, s, NCH_3); 5.57 (1H, d, *J* = 7.8, CH); 5.90 (1H, d, *J* = 7.8, CH); 6.61 (1H, dd, *J* = 3.3, *J* = 1.8, H Ar); 6.80 (1H, d, *J* = 3.3, H Ar); 7.80 (1H, s, H Ar); 8.00 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 13.0; 28.3; 30.4; 72.2; 79.8; 112.0; 112.5; 128.9; 144.5; 149.4; 157.6; 166.5. Found, *m*/*z*: 294.1023 $[M+H]^+$. $C_{12}H_{16}N_5O_2S$. Calculated, *m*/*z*: 294.1019.

(*E*)-1,3-Dimethyl-5-methylsulfanyl-4-[(thiophen-2-ylmethylidene)amino]-3,3a,4,6a-tetrahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one (4e). Yield 257 mg (83%), white powder, mp 190–193°C (MeOH). IR spectrum, ν, cm^{-1}: 1718, 1697 (C=O), 1564, 1490, 1443, 1392, 1218, 1194, 1042. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.41 (3H, s, SCH_3); 2.82 (3H, s, NCH_3); 2.90 (3H, s, NCH_3); 5.57 (1H, d, *J* = 7.8, CH); 5.88 (1H, d, *J* = 7.9, CH); 7.11 (1H, t, *J* = 4.2, H Ar); 7.41 (1H, d, *J* = 3.2, H Ar); 7.59 (1H, d, *J* = 5.0, H Ar); 8.31 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 13.0; 28.3; 30.4; 72.5; 80.0; 127.8; 127.9; 129.6; 133.9; 139.4; 157.6; 166.5. Found, *m*/*z*: 310.0795 $[M+H]^+$. $C_{12}H_{16}N_5OS_2$. Calculated, *m*/*z*: 310.0791.

(*E*)-4-(Benzylideneamino)-1,3-diethyl-5-methylsulfanyl-3,3a,4,6a-tetrahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one (4f). Yield 321 mg (97%), white powder, mp 136–138°C (MeOH). IR spectrum, ν, cm^{-1}: 1693 (C=O), 1581, 1570, 1473, 1450, 1405, 1357, 1319, 1230, 1195, 1064. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.00 (3H, t, *J* = 7.0, CH_3); 1.14 (3H, t, *J* = 7.2, CH_3); 2.42 (3H, s, SCH_3); 3.17–3.52 (4H, m, $2NCH_2$); 5.70 (1H, d, *J* = 7.9, CH); 6.00 (1H, d, *J* = 7.9, CH); 7.39–7.47 (3H, m, H Ph); 7.67 (2H, d, *J* = 7.0, H Ph); 7.95 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 12.9; 13.3; 13.9; 36.1; 37.6; 70.7; 78.5; 126.4 (2C); 128.8 (2C); 129.4; 134.3; 137.6; 157.0; 166.3. Found, *m*/*z*: 332.1535 $[M+H]^+$. $C_{16}H_{22}N_5OS$. Calculated, *m*/*z*: 332.1540.

(*E*)-1,3-Diethyl-4-[(2-hydroxybenzylidene)amino]-5-methylsulfanyl-3,3a,4,6a-tetrahydroimidazo[4,5-*d*]-imidazol-2(1*H*)-one (4g). Yield 313 mg (90%), white powder, mp 94–96°C (Me_2CO). IR spectrum, ν, cm^{-1}: 3401 (OH), 3174, 1696 (C=O), 1575, 1470, 1388, 1299, 1245, 1193, 1064. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.02–1.17 (6H, m, $2CH_3$); 2.44 (3H, s, SCH_3); 3.18–3.53 (4H, m, $2NCH_2$); 5.68 (1H, d, *J* = 7.8, CH); 6.00 (1H, d, *J* = 7.8, CH); 6.85–6.91 (2H, m, H Ar); 7.23 (1H, t, *J* = 7.5, H Ar); 7.59 (1H, d, *J* = 7.4, H Ar); 8.18 (1H, s, N=CH); 10.20 (1H, br. s, OH). ^{13}C NMR spectrum, δ, ppm: 13.0; 13.3; 13.7; 36.2; 37.6; 70.8; 78.6; 116.1; 119.4; 119.8; 126.6; 130.8; 136.2; 156.2; 156.9; 166.1. Found, *m*/*z*: 348.1493 $[M+H]^+$. $C_{16}H_{22}N_5O_2S$. Calculated, *m*/*z*: 348.1489.

(*E*)-2-{[(4,6-Diethyl-2-methylsulfanyl-5-oxo-4,5,6,6a-tetrahydroimidazo[4,5-*d*]imidazol-1(3a*H*)-yl)imino]methyl}-4-nitrophenol, potassium salt (4h). Yield 366 mg (85%), orange powder, mp >255°C (decomp., MeOH). IR spectrum, ν, cm^{-1}: 1699 (C=O), 1571 (NO_2), 1474, 1441, 1318 (NO_2), 1290, 1241, 1193, 1069. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.01 (3H, t, *J* = 7.0, CH_3); 1.13 (3H, t, *J* = 7.1, CH_3); 2.40 (3H, s, SCH_3); 3.10–3.48 (4H, m, $2NCH_2$); 5.62 (1H, d, *J* = 8.0, CH); 5.89 (1H, d, *J* = 8.0, CH); 6.07 (1H, d, *J* = 9.5, H Ar); 7.73 (1H, dd, *J* = 9.5, *J* = 3.2, H Ar); 8.19 (1H, s, N=CH); 8.27 (1H, d, *J* = 3.2, H Ar). ^{13}C NMR spectrum, δ, ppm: 13.0; 13.3; 13.8; 36.2; 37.7; 71.2; 78.5; 121.0; 121.4; 122.3; 127.4; 128.7; 137.6; 157.2; 166.9; 178.2. Found, *m*/*z*: 393.1336 $[M+H]^+$. $C_{16}H_{21}N_6O_4S$. Calculated, *m*/*z*: 393.1340.

(*E*)-1,3-Diethyl-4-[(furan-2-ylmethylidene)amino]-5-methylsulfanyl-3,3a,4,6a-tetrahydroimidazo[4,5-*d*]-imidazol-2(1*H*)-one (4i). Yield 270 mg (84%), white powder, mp 133–135°C (MeOH). IR spectrum, ν, cm^{-1}: 1694 (C=O), 1582, 1486, 1475, 1439, 1396, 1377, 1292, 1244, 1233, 1211, 1197, 1185, 1064. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.98 (3H, t, *J* = 6.9, CH_3); 1.13 (3H, t, *J* = 7.0, CH_3); 2.40 (3H, s, SCH_3); 3.17–3.46 (4H, m, $2NCH_2$); 5.68 (1H, d, *J* = 7.7, CH); 5.96 (1H, d, *J* = 7.8, CH); 6.61 (1H, s, H Ar); 6.81 (1H, d, *J* = 3.0, H Ar); 7.80 (1H, s, H Ar); 7.85 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 13.0; 13.3; 13.8; 36.1; 37.6; 70.7; 78.5; 112.0; 112.3; 128.4; 144.6; 149.3; 157.0; 166.1. Found, *m*/*z*: 322.1321 $[M+H]^+$. $C_{14}H_{20}N_5O_2S$. Calculated, *m*/*z*: 322.1332.

(*E*)-1,3-Diethyl-5-methylsulfanyl-4-[(thiophen-2-ylmethylidene)amino]-3,3a,4,6a-tetrahydroimidazo[4,5-*d*]-imidazol-2(1*H*)-one (4j). Yield 304 mg (90%), white powder, mp 150–157°C (MeOH). IR spectrum, ν, cm^{-1}: 1686 (C=O), 1573, 1471, 1453, 1439, 1386, 1360, 1313, 1248, 1224, 1197, 1180, 1064. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.99 (3H, t, *J* = 7.0, CH_3); 1.14 (3H, t, *J* = 7.1, CH_3); 2.41 (3H, s, SCH_3); 3.17–3.49 (4H, m, $2NCH_2$); 5.68 (1H, d, *J* = 7.8, CH); 5.94 (1H, d, *J* = 7.8, CH); 7.11 (1H, dd, *J* = 4.8, *J* = 3.6, H Ar); 7.41 (1H, d, *J* = 3.4, H Ar); 7.59 (1H, d, *J* = 4.9, H Ar); 8.18 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 12.9; 13.3; 13.9; 36.1; 37.6; 71.1; 78.5; 127.8; 127.9; 129.5; 133.4; 139.2; 156.9; 166.0. Found, *m*/*z*: 338.1100 $[M+H]^+$. $C_{14}H_{20}N_5OS_2$. Calculated, *m*/*z*: 338.1104.

(*E*)-1,3-Diethyl-4-[(2-hydroxy-5-nitrobenzylidene)-amino]-5-methylsulfanyl-3,3a,4,6a-tetrahydroimidazo-[4,5-*d*]imidazol-2(1*H*)-one (4k). Yield 59 mg (15%), beige powder, mp 200–202°C (EtOH). IR spectrum, ν, cm^{-1}: 1703 (C=O), 1592, 1569 (NO_2), 1470, 1436, 1341, 1325 (NO_2), 1295, 1285, 1244, 1185. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.05 (3H, t, *J* = 6.6, CH_3); 1.15 (3H, t, *J* = 6.9, CH_3); 2.46 (3H, s, SCH_3); 3.16–3.54 (4H, m, $2NCH_2$); 5.69 (1H, d, *J* = 7.8, CH); 6.03 (1H, d, *J* = 7.8, CH); 7.07 (1H, d, *J* = 9.0, H Ar); 8.11–8.14 (2H, m, H Ar, N=CH); 8.48 (1H, d, *J* = 2.5, H Ar). ^{13}C NMR spectrum, δ, ppm: 13.0; 13.3; 13.7; 36.2; 37.7; 70.8; 78.6; 116.7; 121.1; 121.2; 126.0; 132.3; 139.9; 156.9; 161.7; 166.0. Found, *m*/*z*: 415.1167 $[M+Na]^+$. $C_{16}H_{20}N_6NaO_4S$. Calculated, *m*/*z*: 415.1159.

(*E*)-1,3-Diethyl-4-[(2-methoxybenzylidene)amino]-5-methylsulfanyl-3,3a,4,6a-tetrahydroimidazo[4,5-*d*]-imidazol-2(1*H*)-one (4l). Found, *m*/*z*: 362.1648 $[M+H]^+$. $C_{17}H_{24}N_5O_2S$. Calculated, *m*/*z*: 362.1645.

Synthesis of 5-[(4-bromobenzyl)sulfanyl]glycolurils 7a,b,d–g,i,j,k and potassium salt 1k (General method). 4-Bromobenzyl bromide (255 mg, 1.02 mmol) was added with stirring to a solution of thioglycoluril **1a**,**b**,**d**–**g**,**i**,**j** (1.00 mmol) and K_2CO_3 (152 mg, 1.1 mmol) in DMSO (5 ml). The resulting mixture was stirred at room temperature for 5 h, then poured into ice-cold H_2O (50 ml) and kept in the refrigerator overnight. The precipitate that formed was filtered off, washed with H_2O (5 ml), and air-dried. The product was recrystallized from MeOH.

Compounds **7k** and **1k** were obtained by fractional crystallization from MeOH of the precipitate isolated during the alkylation of thioglycoluril **1h**.

(*E*)-4-Benzylideneamino-5-[(4-bromobenzyl)sulfanyl]-1,3-dimethyl-3,3a,4,6a-tetrahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one (7a). Yield 422 mg (92%), white powder, mp 178–179°C. IR spectrum, ν, cm^{-1}: 1696 (C=O), 1582, 1568, 1489, 1448, 1412, 1398, 1285, 1206, 1040. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.84 (3H, s, NCH_3); 2.90 (3H, s, NCH_3); 4.27 (2H, s, SCH_2); 5.63 (1H, d, *J* = 7.7, CH); 5.94 (1H, d, *J* = 7.7, CH); 7.38–7.42 (5H, m, H Ar); 7.52 (2H, d, *J* = 8.1, H Ar); 7.66 (2H, d, *J* = 7.0, H Ar); 8.09 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 28.3; 30.5; 33.1; 72.1; 80.1; 120.4; 126.5 (2C); 128.8 (2C); 129.5; 131.2 (2C); 131.4 (2C); 134.4; 137.3; 138.3; 157.6; 165.6. Found, *m*/*z*: 458.0635 $[M+H]^+$. $C_{20}H_{21}BrN_5OS$. Calculated, *m*/*z*: 458.0645.

(*E*)-5-[(4-Bromobenzyl)sulfanyl]-4-[(2-hydroxybenzylidene)amino]-1,3-dimethyl-3,3a,4,6a-tetrahydroimidazo-[4,5-*d*]imidazol-2(1*H*)-one (7b). Yield 294 mg (62%), white powder, mp 203–205°C. IR spectrum, ν, cm^{-1}: 1695 (C=O), 1610, 1579, 1489, 1412, 1399, 1285, 1268, 1199, 1041. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.84 (3H, s, NCH_3); 2.91 (3H, s, NCH_3); 4.29 (2H, s, SCH_2); 5.62 (1H, d, *J* = 7.3, CH); 5.94 (1H, d, *J* = 7.3, CH); 6.85–6.90 (2H, m, H Ar); 7.23 (1H, t, *J* = 7.4, H Ar); 7.43–7.52 (5H, m, H Ar); 8.26 (1H, s, N=CH); 10.07 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 28.3; 30.9; 33.1; 72.6; 80.1; 116.2; 119.5; 119.8; 120.4; 126.9; 130.9; 131.2 (2C); 131.4 (2C); 137.1; 137.2; 156.2; 157.6; 165.3. Found, *m*/*z*: 474.0602 $[M+H]^+$. $C_{20}H_{21}BrN_5O_2S$. Calculated, *m*/*z*: 474.0594.

(*E*)-5-[(4-Bromobenzyl)sulfanyl]-4-[(furan-2-ylmethylidene)amino]-1,3-dimethyl-3,3a,4,6a-tetrahydroimidazo-[4,5-*d*]imidazol-2(1*H*)-one (7d). Yield 291 mg (65%), white powder, mp 192–193°C. IR spectrum, ν, cm^{-1}: 1695 (C=O), 1577, 1488, 1413, 1397, 1286, 1205, 1177, 1042. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.83 (3H, s, NCH_3); 2.87 (3H, s, NCH_3); 4.25 (2H, s, SCH_2); 5.60 (1H, d, *J* = 7.8, CH); 5.89 (1H, d, *J* = 7.9, CH); 6.59 (1H, dd, *J* = 3.0, *J* = 1.8, H Fur); 6.79 (1H, d, *J* = 3.0, H Fur); 7.37 (2H, d, *J* = 8.3, H Ar); 7.51 (2H, d, *J* = 8.3, H Ar); 7.78 (1H, s, H Fur); 7.98 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 28.3; 30.5; 33.1; 72.1; 80.0; 112.1; 112.7; 120.3; 129.0; 131.2 (2C); 131.4 (2C); 137.3; 144.6; 149.3; 157.5; 165.4. Found, *m*/*z*: 448.0438 $[M+H]^+$. $C_{18}H_{19}BrN_5O_2S$. Calculated, *m*/*z*: 448.0437.

(*E*)-5-[(4-Bromobenzyl)sulfanyl]-1,3-dimethyl-4-[(thiophen-2-ylmethylidene)amino]-3,3a,4,6a-tetrahydroimidazo-[4,5-*d*]imidazol-2(1*H*)-one (7e). Yield 446 mg (96%), white powder, mp 188–190°C. IR spectrum, ν, cm^{-1}: 1695 (C=O), 1576, 1488, 1442, 1412, 1397, 1380, 1285, 1202, 1174, 1040. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.83 (3H, s, NCH_3); 2.88 (3H, s, NCH_3); 4.25 (2H, s, SCH_2); 5.61 (1H, d, *J* = 7.7, CH); 5.88 (1H, d, *J* = 7.7, CH); 7.10 (1H, t, *J* = 4.0, H Th); 7.40–7.42 (3H, m, H Ar, H Th); 7.51 (2H, d, *J* = 8.2, H Ar); 7.58 (1H, d, *J* = 4.7, H Th); 8.31 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 28.3; 30.5; 33.1; 72.5; 80.0; 120.4; 127.8; 128.0; 129.8; 131.2 (2C); 131.4 (2C); 134.1; 137.3; 139.3; 157.5; 165.3. Found, *m*/*z*: 464.0204 $[M+H]^+$. $C_{18}H_{19}BrN_5OS_2$. Calculated, *m*/*z*: 464.0209.

(*E*)-4-Benzylideneamino-5-[(4-bromobenzyl)sulfanyl]-1,3-diethyl-3,3a,4,6a-tetrahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one (7f). Yield 355 mg (73%), white powder, mp 129–131°C. IR spectrum, ν, cm^{-1}: 1694 (C=O), 1576, 1460, 1388, 1300, 1246, 1229, 1191, 1064. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.00 (3H, t, *J* = 6.2, CH_3); 1.16 (3H, t, *J* = 6.8, CH_3); 3.18–3.52 (4H, m, $2NCH_2$); 4.28 (2H, s, SCH_2); 5.73 (1H, d, *J* = 7.6, CH); 5.99 (1H, d, *J* = 7.6, CH); 7.38–7.44 (5H, m, H Ar); 7.52 (2H, d, *J* = 7.8, H Ar); 7.65 (2H, d, *J* = 6.5, H Ar); 7.94 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 13.3; 13.9; 33.1; 36.3; 37.7; 70.6; 78.8; 120.3; 126.4 (2C); 128.8 (2C); 129.5; 131.2 (2C); 131.3 (2C); 134.3; 137.2; 137.8; 157.0; 165.2. Found, *m*/*z*: 486.0954 $[M+H]^+$. $C_{22}H_{25}BrN_5OS$. Calculated, *m*/*z*: 486.0958.

(*E*)-5-[(4-Bromobenzyl)sulfanyl]-1,3-diethyl-4-[(2-hydroxybenzylidene)amino]-3,3a,4,6a-tetrahydroimidazo-[4,5-*d*]imidazol-2(1*H*)-one (7g). Yield 337 mg (67%), white powder, mp 198–201°C. IR spectrum, ν, cm^{-1}: 1684 (C=O), 1568, 1483, 1455, 1298, 1249, 1224, 1193, 1067. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.04 (3H, t, *J* = 7.0, CH_3); 1.15 (3H, t, *J* = 7.2, CH_3); 3.13–3.52 (4H, m, $2NCH_2$); 4.29 (2H, s, SCH_2); 5.70 (1H, d, *J* = 7.9, CH); 6.00 (1H, d, *J* = 7.9, CH); 6.83–6.89 (2H, m, H Ar); 7.22 (1H, t, *J* = 7.7, H Ar); 7.40 (2H, d, *J* = 8.4, H Ar); 7.51 (2H, d, *J* = 8.4, H Ar); 7.57 (1H, d, *J* = 7.7, H Ar); 8.16 (1H, s, N=CH); 10.06 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 13.4; 13.8; 33.2; 36.4; 37.7; 70.7; 78.9; 116.2; 119.5; 119.9; 120.4; 126.4; 130.9; 131.3 (2C); 131.4 (2C); 136.1; 137.2; 156.2; 157.0; 165.1. Found, *m*/*z*: 502.0893 $[M+H]^+$. $C_{22}H_{25}BrN_5O_2S$. Calculated, *m*/*z*: 502.0907.

(*E*)-5-[(4-Bromobenzyl)sulfanyl]-1,3-diethyl-4-[(furan-2-ylmethylidene)amino]-3,3a,4,6a-tetrahydroimidazo-[4,5-*d*]imidazol-2(1*H*)-one (7i). Yield 381 mg (80%), white powder, mp 136–138°C. IR spectrum, ν, cm^{-1}: 1710 (C=O), 1580, 1556, 1485, 1470, 1433, 1376, 1293, 1237, 1188, 1065. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.97 (3H, t, *J* = 6.1, CH_3); 1.15 (3H, t, *J* = 6.6, CH_3); 3.16–3.49 (4H, m, $2NCH_2$); 4.25 (2H, s, SCH_2); 5.70 (1H, d, *J* = 7.1, CH); 5.95 (1H, d, *J* = 7.1, CH); 6.60 (1H, br. s, H Fur); 6.81 (1H, br. s, H Fur); 7.39 (2H, d, *J* = 7.8, H Ar); 7.50 (2H, d, *J* = 7.8, H Ar); 7.79 (1H, s, H Fur); 7.84 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 13.3; 13.9; 33.1; 36.3; 37.6; 70.7; 78.7; 112.1; 112.5; 120.3; 128.5; 131.2 (2C); 131.3 (2C); 137.3; 144.7; 149.2; 157.0; 165.0. Found, *m*/*z*: 476.0760 $[M+H]^+$. $C_{20}H_{23}BrN_5O_2S$. Calculated, *m*/*z*: 476.0750.

(*E*)-5-[(4-Bromobenzyl)sulfanyl]-1,3-diethyl-4-[(thiophen-2-ylmethylidene)amino]-3,3a,4,6a-tetrahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one (7j). Yield 345 mg (70%), white powder, mp 222–223°C. IR spectrum, ν, cm^{-1}: 1711 (C=O), 1575, 1470, 1438, 1383, 1291, 1244, 1223, 1188, 1065. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.98 (3H, t, *J* = 6.8, CH_3); 1.15 (3H, t, *J* = 6.8, CH_3); 3.18–3.48 (4H, m, $2NCH_2$); 4.25 (2H, s, SCH_2); 5.71 (1H, d, *J* = 7.8, CH); 5.94 (1H, d, *J* = 7.8, CH); 7.10 (1H, t, *J* = 4.1, H Th); 7.38–7.41 (3H, m, H Ar, H Th); 7.50 (2H, d, *J* = 8.1, H Ar); 7.58 (1H, d, *J* = 4.9, H Th); 8.17 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 13.4; 13.9; 33.1; 36.3; 37.7; 71.0; 78.8; 120.4; 127.8; 128.1; 129.7; 131.2 (2C); 131.3 (2C); 133.7;

137.3; 139.2; 157.0; 164.9. Found, *m*/*z*: 492.0524 $[M+H]^+$. $C_{20}H_{23}BrN_5OS_2$. Calculated, *m*/*z*: 492.0522.

(*E*)-4-({2-[(4-Bromobenzyl)oxy]-5-nitrobenzylidene}-amino)-5-[(4-bromobenzyl)sulfanyl]-1,3-diethyl-3,3a,4,6a-tetrahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one (7k). Yield 12 mg (2%), white powder, mp 200–202°C (MeOH). IR spectrum, ν, cm^{-1}: 1729, 1702 (C=O), 1584, 1567 (NO_2), 1488, 1466, 1340 (NO_2), 1284, 1270, 1134, 1073. ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.68 (3H, br. s, CH_3); 1.13 (3H, br. s, CH_3); 2.90–3.01 (1H, m) and 3.20–3.49 (3H, m, $2NCH_2$); 4.29 (2H, s, SCH_2); 5.31 (2H, s, OCH_2); 5.69 (1H, d, *J* = 7.4, CH); 5.93 (1H, d, *J* = 7.4, CH); 7.42–7.64 (9H, m, H Ar); 7.99 (1H, s, H Ar); 8.26 (1H, d, *J* = 3.2, H Ar); 8.46 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 13.2 (2C); 33.1; 36.3; 37.7; 70.2; 70.8; 78.9; 113.6; 120.1; 120.3; 121.8; 123.3; 126.0; 130.6; 130.7 (2C); 131.2 (2C); 131.3 (2C); 131.5 (2C); 134.9; 137.3; 141.2; 156.9; 160.6; 165.0. Found, *m*/*z*: 715.0332 $[M+H]^+$. $C_{29}H_{29}Br_2N_6O_4S$. Calculated, *m*/*z*: 715.0332.

(*E*)-2-{[(4,6-Diethyl-5-oxo-2-thioxohexahydroimidazo-[4,5-*d*]imidazol-1(2*H*)-yl)imino]methyl}-4-nitrophenol, potassium salt (1k). Yield 33 mg (8%), orange powder, mp 208–210°C (MeOH). IR spectrum, ν, cm^{-1}: 1711 (C=O), 1594, 1535 (NO_2), 1483, 1431, 1358 (NO_2), 1307, 1281, 1241. ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.00–1.09 (6H, m, $2CH_3$); 3.10–3.19 (2H, m, NCH_2); 3.26–3.34 (2H, m, NCH_2); 5.45 (1H, d, *J* = 8.4, CH); 5.94 (1H, d, *J* = 8.4, CH); 6.07 (1H, d, *J* = 9.6, H Ar); 7.75 (1H, dd, *J* = 9.6, *J* = 3.2, H Ar); 8.42 (1H, d, *J* = 3.2, H Ar); 9.05 (1H, s, N=CH); 9.66 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 12.8; 13.4; 35.8; 37.2; 66.1; 74.5; 120.3; 121.7; 123.8; 127.9; 128.5; 155.0; 156.9; 178.4; 178.7. Found, *m*/*z*: 379.1182 $[M+H]^+$. $C_{15}H_{19}N_6O_4S$. Calculated, *m*/*z*: 379.1183.

Synthesis of glycolurils 5a–j. Method I. Concentrated HCl (34.31%, *d* 1.1706 g/cm^3) (91 μl, 1 mmol) (182 μl, 2 mmol for salts **4c**,**h**) was added with stirring to a solution of methylsulfanylglycoluril **4a–j** (1 mmol) in MeOH (30 ml). The resulting solution was heated under reflux for 1 h (for compounds **4a**,**f**), 3 h (for compounds **4b**,**d**,**e**,**g**), or 6 h (for compounds **4c**,**h**–**j**), then cooled to room temperature (for compounds **5a**,**c**,**e**–**h**,**j**). The formed precipitate of compounds **5a**,**e**,**f**,**g**,**j** was filtered off, washed with a H_2O–MeOH, 1:1 mixture (5 ml), and air-dried. Glycolurils **5g**,**j** were recrystallized from Me_2CO. For compounds **5c**,**h**, the precipitate of KCl was filtered, washed with MeOH (5 ml) and Me_2CO (5 ml). The solvent from the filtrate was evaporated under reduced pressure, the residue was recrystallized from a H_2O–MeOH, 3:7 mixture. To obtain compounds **5b**,**d**,**i**, the solvent from the reaction mixture was evaporated to dryness under reduced pressure. Product **5b** was recrystallized from Me_2CO. Glycolurils **5d**,**i** were precipitated with H_2O, filtered off, washed with Et_2O (5 ml) and Me_2CO (2 ml).

Method II. Concentrated HCl (34.31%, *d* 1.1706 g/cm^3) (91 μl, 1 mmol) was added with stirring to a solution of *S*-(4-bromobenzyl) derivative **7a**,**e**,**f**,**j** (1 mmol) in MeOH (30 ml). The resulting solution was heated under reflux for 1 h (for compounds **7a**,**e**,**j**) or 6 h (for compound **7f**), then cooled to room temperature. The formed precipitate of compounds **5a**,**e**,**f**,**j** was filtered off, washed with a H_2O–MeOH, 1:1 mixture (5 ml), and air-dried.

Method III. MeI (435 μl, 7 mmol) and H_2O (0.5 ml) were added dropwise with stirring to a suspension of thioglycoluril **1a–j** (1 mmol) in MeOH (40 ml). The resulting mixture was stirred and heated under reflux for 5–10 h, then concentrated under reduced pressure to half the initial volume, and cooled to room temperature. The formed precipitate of glycoluril **5a–j** was filtered off and air-dried. Compounds **5c**,**h** were recrystallized from Me_2CO. First, hydrazine **6b** precipitates, followed by glycoluril **5c**,**h**.

(*E*)-4-(Benzylideneamino)-1,3-diethyl-5-methylsulfanyl-3,3a,4,6a-tetrahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one hydrochloride (4f·HCl). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.97 (3H, t, *J* = 6.9, CH_3); 1.15 (3H, t, *J* = 7.0, CH_3); 2.80 (3H, s, SCH_3); 3.15–3.62 (4H, m, $2NCH_2$); 6.03 (1H, d, *J* = 8.2, CH); 6.63 (1H, d, *J* = 8.2, CH); 7.52–7.54 (3H, m, H Ph); 7.80–7.83 (2H, m, H Ph); 8.62 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 13.0; 14.1; 14.2; 36.5; 48.6; 72.2; 72.4; 127.7 (2C); 129.3 (2C); 131.7; 132.5; 148.9; 156.8; 172.4.

(*E*)-4-(Benzylideneamino)-1,3-dimethyltetrahydroimid-azo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (5a). Yield 112 mg (41%, method I), 101 mg (37%, method II), 169 mg (62%, method III, 10 h), white powder, mp 252–254°C (MeOH). IR spectrum, ν, cm^{-1}: 3246 (NH), 1725, 1690 (C=O), 1417, 1404, 1390, 1375, 1367, 1227, 1187, 1042. ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.71 (3H, s, NCH_3); 2.85 (3H, s, NCH_3); 5.24 (1H, d, *J* = 8.2, CH); 5.61 (1H, d, *J* = 8.2, CH); 7.42–7.47 (3H, m, H Ph); 7.68–7.71 (2H, m, H Ph); 8.42 (1H, s, NH); 8.98 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 27.8; 29.2; 64.3; 72.6; 126.7 (2C); 128.7 (2C); 129.9; 134.8; 148.4; 156.0; 157.8. Found, *m*/*z*: 296.1123 $[M+Na]^+$. $C_{13}H_{15}N_5NaO_2$. Calculated, *m*/*z*: 296.1118.

(*E*)-4-[(2-Hydroxybenzylidene)amino]-1,3-dimethyl-tetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (5b). Yield 168 mg (58%, method I), 90 mg (31%, method III, 5 h), beige powder, mp 188–189°C (MeOH). IR spectrum, ν, cm^{-1}: 3433 (OH), 3246 (NH), 1738, 1715 (C=O), 1620, 1495, 1454, 1402, 1377, 1275, 1218, 1038. ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.71 (3H, s, NCH_3); 2.85 (3H, s, NCH_3); 5.25 (1H, d, *J* = 8.2, CH); 5.68 (1H, d, *J* = 8.2, CH); 6.87–6.92 (2H, m, H Ar); 7.27 (1H, t, *J* = 7.6, H Ar); 7.58 (1H, d, *J* = 7.6, H Ar); 8.47 (1H, s, NH); 9.02 (1H, s, N=CH); 10.49 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 27.9; 29.4; 64.5; 72.1; 116.2; 119.3; 119.6; 128.1; 131.2; 148.0; 156.0; 156.8; 157.8. Found, *m*/*z*: 290.1241 $[M+H]^+$. $C_{13}H_{16}N_5O_3$. Calculated, *m*/*z*: 290.1248.

(*E*)-4-[(2-Hydroxy-5-nitrobenzylidene)amino]-1,3-di-methyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (5c). Yield 170 mg (51%, method I), 100 mg (30%, method III, 10 h), beige powder, mp 273–276°C (Me_2CO). IR spectrum, ν, cm^{-1}: 3492 (OH), 3266 (NH), 1725, 1682 (C=O), 1604, 1514 (NO_2), 1443, 1405, 1341 (NO_2), 1290, 1220, 1041. ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.72 (3H, s, NCH_3); 2.87 (3H, s, NCH_3); 5.27 (1H, d, *J* = 8.2, CH); 5.70 (1H, d, *J* = 8.2, CH); 7.10 (1H, d, *J* = 9.1, H Ar); 8.15 (1H, dd, *J* = 9.0, *J* = 2.7, H Ar); 8.53–8.55 (2H, m, H Ar, NH); 9.14 (1H, s, N=CH); 11.81 (1H, s, OH). ^{13}C NMR

spectrum, δ, ppm: 27.9; 29.5; 64.5; 72.0; 116.9; 121.2; 121.9; 126.3; 139.9; 142.3; 155.7; 157.7; 162.2. Found, *m*/*z*: 335.1094 $[M+H]^+$. $C_{13}H_{15}N_6O_5$. Calculated, *m*/*z*: 335.1098.

(*E*)-4-[(Furan-2-ylmethylidene)amino]-1,3-dimethyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (5d). Yield 66 mg (25%, method I), 76 mg (29%, method III, 5 h), white powder, mp 202–204°C (MeOH). IR spectrum, ν, cm^{-1}: 1738, 1692 (C=O), 1508, 1480, 1455, 1420, 1384, 1229, 1176, 1042. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.70 (3H, s, NCH_3); 2.81 (3H, s, NCH_3); 5.22 (1H, d, *J* = 7.9, CH); 5.55 (1H, d, *J* = 8.0, CH); 6.62 (1H, dd, *J* = 3.3, *J* = 1.8, H Ar); 6.88 (1H, d, *J* = 3.4, H Ar); 7.80 (1H, s, H Ar); 8.42 (1H, s, NH); 8.87 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 28.4; 29.6; 64.8; 73.2; 112.5; 114.1; 139.3; 145.4; 150.1; 156.6; 158.3. Found, *m*/*z*: 264.1097 $[M+H]^+$. $C_{11}H_{14}N_5O_3$. Calculated, *m*/*z*: 264.1091.

(*E*)-1,3-Dimethyl-4-[(thiophen-2-ylmethylidene)amino]-tetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (5e). Yield 61 mg (22%, method I), 128 mg (46%, method II), 117 mg (42%, method III, 10 h), white powder, mp 251–253°C (MeOH). IR spectrum, ν, cm^{-1}: 1717, 1678 (C=O), 1506, 1438, 1409, 1242, 1214, 1189, 1037. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.70 (3H, s, NCH_3); 2.82 (3H, s, NCH_3); 5.21 (1H, d, *J* = 8.2, CH); 5.54 (1H, d, *J* = 8.2, CH); 7.12 (1H, t, *J* = 4.3, H Ar); 7.45 (1H, d, *J* = 3.1, H Ar); 7.62 (1H, d, *J* = 4.9, H Ar); 8.44 (1H, s, NH); 9.16 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 27.8; 29.1; 64.3; 72.7; 127.9; 128.4; 130.6; 139.8; 144.1; 156.0; 157.8. Found, *m*/*z*: 280.0869 $[M+H]^+$. $C_{11}H_{14}N_5O_2S$. Calculated, *m*/*z*: 280.0863.

(*E*)-4-(Benzylideneamino)-1,3-diethyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (5f). Yield 133 mg (44%, method I), 175 mg (58%, method II), 157 mg (52%, method III, 5 h), white powder, mp 194–196°C (MeOH). IR spectrum, ν, cm^{-1}: 3217 (NH), 1728, 1684 (C=O), 1486, 1470, 1398, 1388, 1336, 1240, 1196. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.05–1.11 (6H, m, $2CH_3$); 3.11–3.38 (4H, m, $2NCH_2$); 5.36 (1H, dd, *J* = 8.3, *J* = 1.6, CH); 5.69 (1H, d, *J* = 8.3, CH); 7.42–7.47 (3H, m, H Ph); 7.67–7.71 (2H, m, H Ph); 8.41 (1H, s, NH); 9.03 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 12.9; 13.2; 35.7; 36.5; 62.6; 71.6; 126.6 (2C); 128.8 (2C); 129.9; 134.7; 149.3; 156.0; 157.1. Found, *m*/*z*: 324.1431 $[M+Na]^+$. $C_{15}H_{19}N_5NaO_2$. Calculated, *m*/*z*: 324.1431.

(*E*)-1,3-Diethyl-4-[(2-hydroxybenzylidene)amino]tetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (5g). Yield 60 mg (19%, method I), 159 mg (50%, method III, 5 h), white crystals, mp 215–217°C (MeOH). IR spectrum, ν, cm^{-1}: 3245 (NH), 1731, 1712 (C=O), 1617, 1601, 1487, 1470, 1415, 1406, 1362, 1268, 1242, 1198. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.07 (6H, t, *J* = 7.0, $2CH_3$); 3.09–3.40 (4H, m, $2NCH_2$); 5.37 (1H, d, *J* = 8.3, CH); 5.75 (1H, d, *J* = 8.3, CH); 6.86–6.92 (2H, m, H Ar); 7.27 (1H, t, *J* = 7.6, H Ar); 7.59 (1H, d, *J* = 7.6, H Ar); 8.45 (1H, s, NH); 9.08 (1H, s, N=CH); 10.38 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 12.9; 13.3; 35.8; 36.6; 62.8; 71.4; 116.3; 119.4; 119.7; 127.8; 131.3; 149.2; 156.2; 156.9; 157.1 Found, *m*/*z*: 340.1381 $[M+Na]^+$. $C_{15}H_{19}N_5NaO_3$. Calculated, *m*/*z*: 340.1380.

(*E*)-1,3-Diethyl-4-[(2-hydroxy-5-nitrobenzylidene)amino]-tetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (5h). Yield 69 mg (19%, method I), 72 mg (20%, method III, 10 h), beige powder, mp 144–146°C (Me_2CO). IR spectrum, ν, cm^{-1}: 3467 (OH), 3229 (NH), 1742, 1681 (C=O), 1618, 1521 (NO_2), 1482, 1460, 1396, 1342 (NO_2), 1289, 1242, 1199, 1128, 1068. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.05–1.12 (6H, m, $2CH_3$); 3.08–3.43 (4H, m, $2NCH_2$); 5.38 (1H, d, *J* = 8.4, CH); 5.78 (1H, d, *J* = 8.4, CH); 7.09 (1H, d, *J* = 9.1, H Ar); 8.14 (1H, dd, *J* = 9.1, *J* = 2.9, H Ar); 8.53 (2H, br. s, H Ar, NH); 9.22 (1H, s, N=CH); 11.74 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 12.9; 13.3; 35.7; 36.6; 62.7; 71.1; 116.9; 121.3; 121.7; 126.4; 140.0; 143.1; 155.8; 157.0; 162.0. Found, *m*/*z*: 363.1412 $[M+H]^+$. $C_{15}H_{19}N_6O_5$. Calculated, *m*/*z*: 363.1411.

(*E*)-1,3-Diethyl-4-[(furan-2-ylmethylidene)amino]-tetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (5i). Yield 105 mg (36%, method I), 93 mg (32%, method III, 5 h), white powder, mp 134–136°C (MeOH). IR spectrum, ν, cm^{-1}: 3249 (NH), 1716, 1690 (C=O), 1484, 1456, 1448, 1399, 1342, 1243, 1199, 1074. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.03–1.10 (6H, m, $2CH_3$); 3.08–3.45 (4H, m, $2NCH_2$); 5.34 (1H, d, *J* = 8.3, CH); 5.63 (1H, d, *J* = 8.3, CH); 6.62 (1H, dd, *J* = 3.3, *J* = 1.8, H Ar); 6.88 (1H, d, *J* = 3.3, H Ar); 7.81 (1H, d, *J* = 1.8, H Ar); 8.42 (1H, s, NH); 8.90 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 13.0; 13.4; 35.7; 36.5; 62.6; 71.8; 112.1; 113.7; 139.5; 145.0; 149.6; 156.2; 157.1. Found, *m*/*z*: 292.1400 $[M+H]^+$. $C_{13}H_{18}N_5O_3$. Calculated, *m*/*z*: 292.1404.

(*E*)-1,3-Diethyl-4-[(thiophen-2-ylmethylidene)amino]-tetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (5j). Yield 77 mg (25%, method I), 148 mg (48%, method II), 187 mg (61%, method III, 8 h), white powder, mp 183–185°C (MeOH). IR spectrum, ν, cm^{-1}: 1715, 1688 (C=O), 1487, 1456, 1447, 1397, 1338, 1253, 1241, 1225, 1201, 1185, 1072. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.03–1.11 (6H, m, $2CH_3$); 3.06–3.33 (4H, m, $2NCH_2$); 5.33 (1H, d, *J* = 8.1, CH); 5.62 (1H, d, *J* = 8.1, CH); 7.12 (1H, t, *J* = 4.2, H Ar); 7.45 (1H, d, *J* = 2.7, H Ar); 7.62 (1H, d, *J* = 4.7, H Ar); 8.42 (1H, s, NH); 9.20 (1H, s, N=CH). ^{13}C NMR spectrum, δ, ppm: 12.9; 13.2; 35.7; 36.5; 62.6; 71.6; 127.9; 128.5; 130.6; 139.8; 144.7; 156.1; 157.1. Found, *m*/*z*: 330.0985 $[M+Na]^+$. $C_{13}H_{17}N_5NaO_2S$. Calculated, *m*/*z*: 330.0995.

1,2-Di((*E*)-benzylidene)hydrazine (6a). ^{1}H NMR spectrum, δ, ppm: 7.49–7.52 (6H, m, H Ph); 7.87–7.90 (4H, m, H Ph); 8.72 (2H, s, 2N=CH).

2,2'-[(1*E*,1'*E*)-Hydrazine-1,2-diylidenebis(methanylylidene)]bis(4-nitrophenol) (6b). Yield 38 mg (23%, from compound **1c**), 48 mg (29%, from compound **1h**), beige powder, mp >320°C (MeOH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.15 (2H, d, *J* = 9.1, H Ar); 8.24 (2H, dd, *J* = 9.1, *J* = 2.4, H Ar); 8.67 (2H, d, *J* = 2.4, H Ar); 9.06 (2H, s, 2N=CH); 12.04 (2H, br. s, 2OH). Mass spectrum, *m*/*z* (I_{rel}, %): 330 $[M]^+$ (100).

X-ray structural analysis of compounds 4j and 5g,**h** was performed at 120K on a Bruker Apex II diffractometer (CCD-detector, MoKα radiation, λ 0.71073 Å, graphite monochromator). The structures were solved using the SHELXT[11] program and refined by the full-matrix least-squares technique using the OLEX2[12] program in the anisotropic approximation for non-hydrogen atoms. Hydrogen atoms of NH and OH groups were localized

from differential Fourier syntheses of electron density, the positions of the remaining hydrogen atoms were calculated geometrically, the positions of all hydrogen atoms were refined in the isotropic approximation according to the rider model. The full sets of X-ray structural data for compounds **4j** and **5g**,**h** were deposited at the Cambridge Crystallographic Data Center (deposits CCDC 2062628, CCDC 2062629, CCDC 2062630, respectively).

The study of the cytotoxicity of compounds 4i,j and 5f,g was performed *in vitro* using the MTT assay against human rhabdomyosarcoma (RD), lung carcinoma (A549), and intestinal carcinoma (HCT116) cell lines according to the described method.[5b,c]

Supplementary information file containing ^{1}H and ^{13}C NMR spectra of compounds **1c**,**h**,**k**, **4a–k**, **4f**·HCl, **7a**,**b**,**d–g**,**i–k**, **5a–j**, ^{1}H NMR spectrum of compound **6b**, as well as X-ray structural analysis data for compounds **4j** and **5g**,**h** is available at the journal website at http://link.springer.com/journal/10593.

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