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SYNTHETIC UTILIZATION OF POLYNITRO AROMATIC COMPOUNDS. 5. MULTI-CENTERED REACTIVITY PATTERN IN REACTIONS OF 4,6-DINITRO-1,2-BENZISOTHIAZOLES AND -ISOTHIAZOL-3(*2H*)-ONES WITH C-, N-, O-, S-, AND F-NUCLEOPHILES

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Abstract—Reactions of 4,6-dinitro-1,2-benzisothiazoles, -isothiazol-3(2*H*)-ones, and -isothiazol-3(2*H*)-one-1-oxides with C-, N-, O-, S-, and F-nucleophiles give products of aromatic nucleophilic substitution of one or two nitro groups, "vicarious" substitution of the hydrogen atom H-7, or heterocyclic S-N bond cleavage depending on the structure of the starting compound and the nature of the nucleophile. These reactions provide a new synthetic approach to a family of biologically active benzisothiazol-3(2*H*)-ones based on 2,4,6-trinitrotoluene (TNT).

INTRODUCTION

1,2-Benzoisothiazole derivatives have been intensively studied during the last decade due to their favorable biological activity profile. For example, the compound PD 161374 is capable of removing zinc from HIV nucleocapsid protein (NCp7), thereby inhibiting the viral replication in infected cells.[1a–e] Other compounds act as irreversible inhibitors of serine protease[2] and Human leukocyte elastase.[3a,b] They influence potent, dose-dependent inhibition of an interleukin IL-1β-induced breakdown of proteoglycan in a cartilage organ culture assay and binding of interleukin-5 (IL5) to hIL5Ra and are being considered as nonpeptidic agents for the treatment of arthritic diseases.[4a,b] Some benzisothiazol-3(2*H*)-one-1,1-

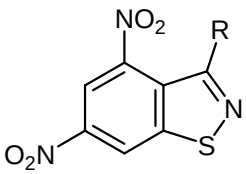
dioxides, in particular BAYx3702 (Repinotan hydrochloride), were recognized as selective high affinity 5-HT_{1A} receptor agonists with neuroprotective, anxiolytic, and antidepressant effects in animal models[5] and inhibitors of apoptosis caused by Serum deprivation in cultured neurons.[6]

A majority of these biologically active 1,2-benzoisothiazol-3-ones does not contain functional groups in the aryl moiety, presumably due to synthesis-related affordability problems. In contrast, introduction of functional groups with diverse electronic and spatial properties may enhance the selectivity of the interaction between 1,2-benzisothiazol-3(2*H*)-ones and thiol receptors and may influence the biological activity profile.[1c]

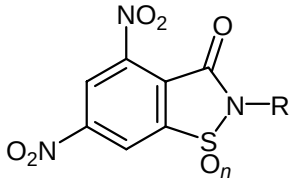
We have recently discovered that 4,6-dinitro-1,2-benzisothiazoles and -isothiazole-3(2*H*)-ones can be synthesized from 2,4,6-trinitrotoluene (TNT).[7a,b,c] Some of these compounds are known to irreversibly inhibit Ca^{2+}-ATPase of sarcoplasmic reticulum (SERCA) influencing the protein transport in living cells.[8] Furthermore, judging from the ability of related nitro derivatives of fused heterocycles to react with nucleophiles via replacement of nitro group(s),[9a–e] we expected that they might serve as intermediates for the synthesis of 1,2-benzisothiazoles (-isothiazol-3(2*H*)-ones) with various functional groups in the aromatic ring. Taking into account that the reported reactions of 1,2-benzisothiazol-3(2*H*)-ones with nucleophiles proceeded with heterocycle ring opening,[10a,b] it was difficult to predict *a priori* whether 4,6-dinitro-1,2-benzisothiazoles (-isothiazol-3(2*H*)-ones) would either undergo the nucleophilic substitution reaction or the S-N bond cleavage.

RESULTS AND DISCUSSION

This paper presents a new synthetic approach to substituted 1,2-benzisothiazoles, -isothiazol-3(2*H*)-ones, and -isothiazol-3(2*H*)-one-1-oxides based on reactions of corresponding 4,6-dinitro derivatives (**1–11**) (Scheme 1) with C-, N-, O-, S-nucleophiles and CsF.



R = Cl (**1**), OCH_3 (**2**), OCH_2CO_2Et (**3**)



n = 0; R = H (**4**), CH_3 (**5**), Ph (**6**);
n = 1; R = H (**7**), CH_3 (**8**), Bn (**9**), CH_2CO_2Me (**10**), Ph (**11**)

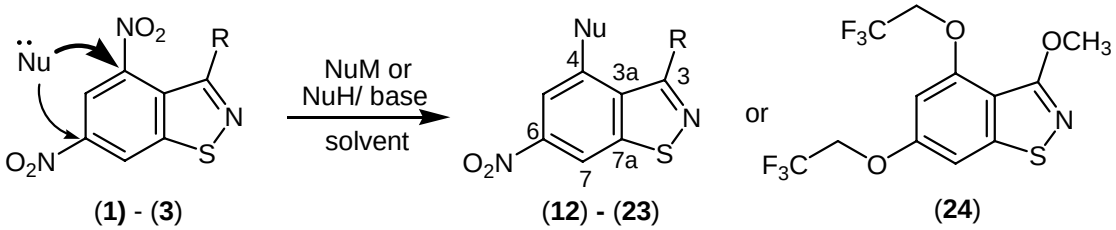
Scheme 1

Aliphatic and aromatic alcohols were used as examples of O-nucleophiles; alkylamines, hydrazine hydrate, sodium azide and hydroxylamine — as N-nucleophiles; S-(Chloromethyl)-S-(*p*-tolyl)sulfone and α-benzylthiol served as examples of C and S-nucleophiles, respectively. Reactions of 4,6-dinitro-1,2-benzisothiazoles (-isothiazol-3(2*H*)-ones) with NaN_3, α-benzylthiol, and phenol were performed in DMF

(in the latter two cases — in the presence of metal carbonates); with alkylamines and hydrazine hydrate — in DMSO or *i*-PrOH; with aliphatic alcohols — in neat alcohol or in DMF in the presence carbonates; with hydroxylamine — in CH_3OH; and with CsF— in CH_3CN.

We have found that 4,6-dinitro-1,2-benzisothiazoles (**1**)–(**3**) react with these nucleophiles with retention of the isothiazole moiety to afford 4-substituted-6-nitro-1,2-benzisothiazoles (**12**)–(**23**) in moderate to high yield (Table 1). Reactions of 3-chloro-1,2-benzisothiazole (**1**) proceed faster and at lower temperature than respective reactions of 3-alkoxy-1,2-benzisothiazoles (**2**), (**3**). In most cases (but not always) the nitro group at C-6 position remains unchanged under these reaction conditions even with excess of nucleophile. As an exception, both nitro groups of the compound (**2**) were substituted with excess of 2,2,2-trifluoroethanol (4 equiv.) to yield the product (**24**).

Table 1. Reactions of 4,6-dinitro-1,2-benzisothiazoles (**1**)–(**3**) with nucleophiles.

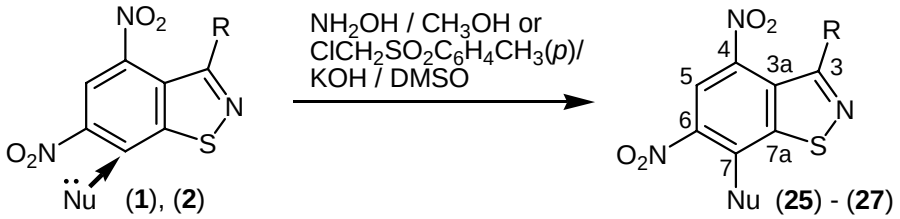


Starting compound	R	Product	NuM or NuH/base	Solvent	Temp. (^oC)	Time, (h)	Yield (%)
1	Cl	**12**	MeONa	MeOH	20	4	49
2	OMe	**13**	MeONa	MeOH	20	6	53
1	Cl	**14**	$PhOH/K_2CO_3$	DMF	20	4	50
2	OMe	**15**	$PhOH/K_2CO_3$	DMF	50	6	76
1	Cl	**16**	$BnSH^b$	DMF	20	12	91
1	Cl	**17**	$BnNH_2{}^b$	DMSO	20	48	16
1	Cl	**18**	NaN_3	DMF	20	1	96
2	OMe	**19**	NaN_3	DMF	50	4	91
2	OMe	**20**[a]	$N_2H_4{}^b$	*i*-PrOH	80	1	45
1	Cl	**21**	CsF	MeCN	50	6	72
2	OMe	**22**	CsF	MeCN	80	16	78
3	OCH_2CO_2Et	**23**	CsF	MeCN	80	16	54
2	OMe	**24**	CF_3CH_2OH/K_2CO_3	DMF	100	12	56

[a] Compound (**20**) was isolated as hydrazone of acetone;
[b] No base was added to the reaction mixture.

Hydroxylamine and S-chloromethyl)-S-(*p*-tolyl)sulfone, bearing good leaving groups (the hydroxy group or the chlorine atom, respectively), react with compounds (**1**) and (**2**) differently to yield products of

"vicarious"[11a,b] substitution of hydrogen atom H-7 (**25**)–(**27**) (Scheme 2). The heterocyclic ring remains intact under these reaction conditions.

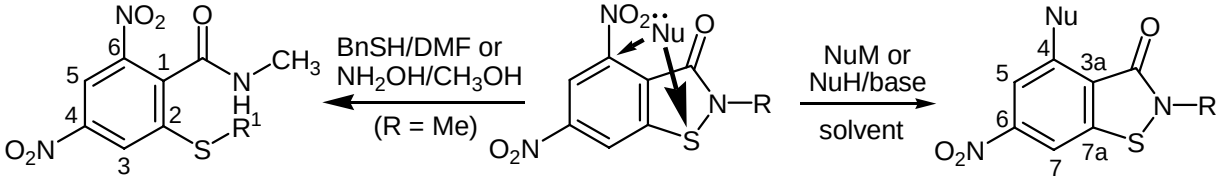


(**25**) Nu = NH_2; R = Cl (66%); (**26**) Nu = NH_2; R = OCH_3 (66%)
(**27**) Nu = $CH_2SO_2C_6H_4CH_3$(-*p*), R = OCH_3 (90%)

Scheme 2

The S-N bond cleavage appeared to be a secondary process in the case of 4,6-dinitro-1,2-benzisothiazol-3(2*H*)-ones (**4**)–(**6**), in which the isothiazol-3(2*H*)-one moiety is expected to be less aromatic than the isothiazole moiety in heterocycles (**1**)–(**3**). Compounds (**4**)–(**6**) react with sodium alcoholates, NaN_3, and CsF yielding substitution products (**28**)–(**33**) (Table 2). Similar reactions with α-benzylthiol or hydroxylamine lead to heterocycle cleavage products (**34**) or (**36**). It is possible that the synthesis of symmetrical disulfide (**36**) proceeds through intermediate formation of the unstable S-hydroxylamino derivative (**35**) undergoing dimerisation with elimination of N_2 and H_2O under the reaction conditions.

Table 2. Reactions of 4,6-dinitro-1,2-benzisothiazol-3(2*H*)-ones (**4**)–(**6**) with nucleophiles.



(**34**) R^1 = SBn
[(**35**) R^1 = NHOH]
(**36**) R^1 = $SC_6H_2(NO_2)_2$-3',5'-C(O)NHMe-1'

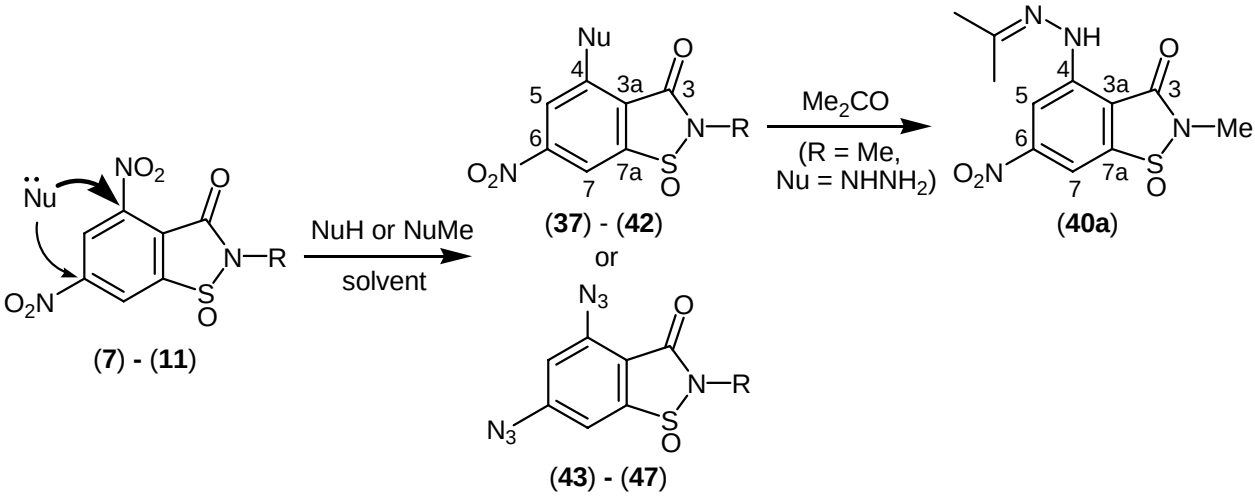
(**4**) - (**6**)

(**28**) - (**33**)

Starting compound	R	Product	NuM or NuH/base	Solvent	Temp. (°C)	Time, (h)	Yield (%)
5	Me	**28**	MeONa	MeOH	20	24	56
5	Me	**29**	PhOH/Na_2CO_3	DMF	100	4	42
4	H	**30**	NaN_3	DMF	40	6	71
5	Me	**31**	NaN_3	DMF	20	24	91
6	Ph	**32**	NaN_3	DMF	20	2	81
5	Me	**33**	CsF	CH_3CN	80	16	44

The heterocycle framework in 4,6-dinitro-1,2-benzisothiazol-3(2*H*)-one-1-oxides (**7**)–(**11**) appears to be more resistant against the action of nucleophiles compared to 4,6-dinitro-1,2-benzisothiazol-3(2*H*)-one analogs (**4**)–(**6**). S-Oxides (**7**)–(**11**) react with akylamines, hydrazine hydrate, and CsF with the retention of the heterocycle ring to yield nucleophilic substitution products (**37**)–(**42**). **4**-Hydrazino-1,2-benzisothiazol-3(2*H*)-one-1-oxide (**40**) was converted to corresponding acetone hydrazone (**40a**) for analytical purposes. Sodium azide (4 equiv.), which is the most active among the studied nucleophiles, replaces both nitro groups in compounds (**7**)–(**11**) to afford diazides (**43**)–(**47**) (Table 3).

Table 3. Reactions of 4,6-dinitro-1,2-benzisothiazol-3(2*H*)-one-1-oxides (**7**)–(**11**) with nucleophiles.



Starting compound	R	Product	NuH or NuM	Solvent	Temp. (°C)	Time, (h)	Yield (%)
8	Me	**37**	$BnNH_2$	*i*-PrOH	82	0.25	54
9	Bn	**38**	$BnNH_2$	*i*-PrOH	82	0.25	61
8	Me	**39**	$O(CH_2CH_2)_2NH$	*i*-PrOH	82	0.25	72
8	Me	**40**	N_2H_4	*i*-PrOH	82	0.1	69
9	Bn	**41**	N_2H_4	*i*-PrOH	82	0.1	71
8	Me	**42**	CsF	CH_3CN	50	2	48
7	H	**43**[a]	NaN_3	DMF	40	5	55
8	Me	**44**	NaN_3	DMF	40	3.5	63
9	Bn	**45**	NaN_3	DMF	40	3.5	90
10	CH_2CO_2Me	**46**	NaN_3	DMF	40	3.5	52
11	Ph	**47**	NaN_3	DMF	40	3	71

[a]The reaction product was isolated as the 1 : 1 complex with DMF.

The structures of 1,2-benzisothiazoles (**12**)–(**27**), -isothiazol-3(2*H*)-ones (**28**)–(**33**) and -isothiazol-3(2*H*)-one-1-oxides (**37**)–(**47**) were elucidated by ^{1}H, ^{13}C, ^{14}N, ^{19}F NMR and mass spectroscopy. In some cases,

^{1}H-^{1}H, and ^{1}H-^{13}C NMR NOE experiments were performed to determine the reaction regioselectivity. The C(4) position of the fluorine atom in compounds (**21**)–(**23**), (**33**), and (**42**) was assigned based on the different values of $^3J_{H(5),F}$ = 9.5 – 10.0 Hz and $^5J_{H(7),F}$ < 1.5 Hz, which are in agreement with the literature data for fluoroaromatic compounds.[12] In case of alternative C(6) position of the fluorine atom the $^3J_{H,F}$ values for protons H(5) and H(7) would be similar (~9-10 Hz). The C(4) position of methoxy group in compounds (**12**), (**13**), and (**28**) was confirmed by the presence of the through-space interaction between OCH_3 and the adjacent proton H(5) in the 2D ^{1}H-^{1}H NMR NOESY experiment.[13] The C(7) position of the amino group in compounds (**25**), (**26**) was determined by the NMR ^{1}H-^{13}C COLOC experiments,[13] which confirmed the presence of a through-space H(N) – C(6) interaction and absence of H(N) – C(4) interaction. Alternative structure with amino group at C(5) was rejected since in this case H(N) – C(NO_2) interaction with both carbons C(4) and C(6) would be observed. The structure of compounds (**14**)–(**20**), (**29**)–(**32**), (**37**)–(**41**) as 4-substituted-6-nitro-1,2-benzisothiazoles (benzisothiazol-3(2*H*)-ones) was assigned on the basis of the difference between adjacent H(5) and remote H(7) ^{1}H NMR upfield shifts (0.68–1.85 and 0.35–0.92 ppm, respectively) caused by replacement of the nitro group in the corresponding dinitro compound and taking into account reported ^{1}H NMR data for similar heterocycles.[9a-e]

We believe that the discovery of facile nitro group substitution with the retention of heterocyclic moiety in 4,6-dinitro-1,2-benzisothiazoles, -isothiazol-3(2*H*)-ones, and -isothiazol-3(2*H*)-one-1-oxides in reaction with C-, N-, O-, S-, and F-nucleophiles is the main synthetic achievement of this research. It allows the synthesis of previously unknown functional derivatives of these heterocycles. The regioselectivity of nucleophilic substitution of the nitrogroup at C-4 in compounds (**1**)–(**11**) is not uncommon. It is consistent with similar regioselectivity of nucleophilic substitution reactions in phthalimide,[9a,b] benzo[*b*]thiophene,[9c] benz[*d*]isoxazole,[9d] and indazole[9e] dinitro derivatives, bearing a 5-member heterocyclic moiety fused with the benzene ring. Yet, it is different from the selectivity of nucleophilic substitution reactions in 1,3-dinitrodibenz[*b,f*][1,4]oxazepin-11(10*H*)-ones, containing a 7-member fused heterocyclic moiety (for a possible explanation please see Ref. 14).

CONCLUSIONS

In summary, a new efficient synthesis of new functionalized 1,2-benzisothiazoles and 1,2-benzisothiazol-3(2*H*)-ones based on reactions of 4,6-dinitro-1,2-benzisothiazoles and 4,6-dinitro-1,2-benzisothiazol-3(2*H*)-ones with O-, S-, N-, C-nucleophiles and CsF has been developed. The method creates new opportunities for the synthesis of functionalized analogs of bio-active benzisothiazol-3(2*H*)-ones. Given the fact that starting heterocyclic nitro derivatives are available from high-tonnage 2,4,6-trinitrotoluene,

the proposed methodology may be useful for the synthetic utilization of polynitroaromatics and their transformation into valuable products.

EXPERIMENTAL

The NMR experiments were performed using a Bruker DRX500 (^{1}H – 500.13 MHz, ^{13}C – 125.76 MHz, ^{19}F – 470.59 MHz) and Bruker AM300 spectrometers (^{1}H – 300.13 MHz, ^{13}C – 75.47 MHz, ^{14}N – 21.67 MHz) in DMSO-d_6. Chemical shifts were measured from the solvent signal and were recalculated to Me_4Si (^{1}H, ^{13}C), to $CFCl_3$ (^{19}F) and to CH_3NO_2 (^{14}N) references. The IR spectra were recorded on a Specord M-80 instrument in KBr pellets. The mass spectra (MS) were obtained on a Finnigan MAT.INCOS 50 instrument (EI, 70 eV) using a direct inlet system. TLC was performed on Silpearl UV-250 silica gel. Solvents were purified by standard methods. Compounds (**1**)–(**6**)[7a] and (**7**)–(**11**)[7b] were synthesized by literature procedures.

3-R-4-methoxy-6-nitro-1,2-benzisothiazoles (12), (13) (General procedure)

Isothiazole (**1**) or (**2**) (3.85 mmol) was added to a MeONa solution (prepared from 0.10 g, 4.35 mmol of Na and 20 mL of MeOH). The reaction mixture was kept at 20°C for 4–6 h (Table 1). The solvent was evaporated *in vacuo*, water (30 mL) was added to the residue, and the resulting suspension was adjusted to pH~6–7 by 10% HCl. The solid was filtered off, washed with water (2 × 20 mL), dried in air, and crystallized from the *i*-PrOH–acetone mixture. The following compounds were obtained:

3-Chloro-4-methoxy-6-nitro-1,2-benzisothiazoles (12)

Yield 0.46 g (49%), yellow crystals, mp 229–231°C. ^{1}H NMR: δ 4.10 (s, 3H, CH_3), 7.67 (s, 1H, H^5), 8.80 (s, 1H, H^7); MS (*m/z*, I): 246 (M^+, Cl^{37}, 44%), 244 (M^+, Cl^{35}, 100%), 200 (14%), 198 (42%), 163 (88%), 148 (32%). *Anal*. Calcd for $C_8H_5N_2O_3ClS$: C, 39.27; H, 2.06; Cl, 14.49; N, 11.45; S, 13.11. Found: C, 39.05; H, 1.98; Cl, 14.64; N, 11.59; S, 13.28.

3,4-Dimethoxy-6-nitro-1,2-benzisothiazole (13)

Yield 0.52 g (53%), yellow crystals, mp 227–228°C. ^{1}H NMR: δ 4.05 (s, 3H, CH_3), 4.13 (s, 3H, CH_3), 7.56 (s, 1H, H^5), 8.50 (s, 1H, H^7). *Anal*. Calcd for $C_9H_8N_2O_4S$: C, 45.00; H, 3.36; N, 11.66; S, 13.35. Found: C, 45.23; H, 3.49; N, 11.45; S, 13.47.

3-R-6-nitro-4-phenoxy-1,2-benzisothiazoles (14), (15) (General procedure)

Powdered K_2CO_3 (0.60 g, 4.35 mmol) was added to a stirred solution of isothiazole (**1**) or (**2**) (3.85 mmol) and phenol (0.40 g, 4.25 mmol) in abs. DMF (20 mL). The reaction mixture was stirred at 20–50°C for 4–6 h (Table 1), poured into water (20 mL), and adjusted to pH~6–7 by 10% HCl. The precipitate was filtered off, washed with water (2 × 20 mL), dried in air, and crystallized from heptane (for **14**) or *i*-PrOH–acetone mixture (for **15**). The following compounds were obtained:

3-Chloro-6-nitro-4-phenoxy-1,2-benzisothiazole (14)

Yield 0.59 g (50%), yellow crystals, mp 132–135°C. ^{1}H NMR: δ 7.22 (d, *J* = 7.5 Hz, 2H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.40 s (1H, H^5), 7.53 (t, *J* = 7.5 Hz, 2H), 8.98 s (1H, H^7); MS (*m/z*, I): 308 (M^+, Cl^{37}, 5%), 306 (M^+, Cl^{35}, 14%), 271 (13%), 225 (27%). *Anal*. Calcd for $C_{13}H_7N_2O_3ClS$: C, 50.91; H, 2.30; Cl, 11.56; N, 9.13; S, 10.45. Found: C, 51.10; H, 2.39; Cl, 11.44; N, 9.29; S, 10.33.

3-Methoxy-6-nitro-4-phenoxy-1,2-benzisothiazole (15)

Yield 0.88 g (76%), yellow crystals, mp 176–179°C. ^{1}H NMR: δ 4.12 (s, 3H, CH_3), 7.18 (d, *J* = 7.4 Hz, 2H), 7.26 (s, 1H, H^5), 7.32 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.4 Hz, 2H), 8.71 (s, 1H, H^7). *Anal*. Calcd for $C_{14}H_{10}N_2O_4S$: C, 55.62; H, 3.33; N, 9.27; S, 10.61. Found: C, 55.80; H, 3.41; N, 9.13; S, 10.76.

4-Benzylthio-3-chloro-6-nitro-1,2-benzisothiazole (16)

α-Benzylthiol (0.63 g, 5.11 mmol) was added to a solution of isothiazole (**1**) (1.00 g, 3.85 mmol) in abs. DMF (5 mL). The reaction mixture was kept at 20°C overnight, poured into cold water (100 mL). The product (**16**) was filtered off, washed with water, dried in air, and crystallized from heptane. Yield 1.18 g (91%), yellow crystals, mp 125–127°C. ^{1}H NMR: δ 4.20 s (2H, CH_2), 7.08 (t, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 2H), 7.32 (d, *J* = 7.5 Hz, 2H), 8.50 (s, 1H, H^5), 8.62 (s, 1H, H^7). ^{13}C NMR: δ 42.6 (CH_2), 109.0 (C^7), 111.6 (C^5), 117.6 (C^4), 124.9 (C^{3a}), 127.5, 128.4, 129.4, 135.9, 148.3 (C^{7a}), 148.7 (C^6), 150.0 (C^3). *Anal*. Calcd for $C_{14}H_9N_2O_2ClS_2$: C, 49.92; H, 2.69; Cl, 10.53; N, 8.32; S, 19.04. Found: C, 50.09; H, 2.78; Cl, 10.38; N, 8.20; S, 18.82.

4-Benzylamino-3-chloro-6-nitro-1,2-benzisothiazole (17)

Benzylamine (0.08 ml, 0.08 g, 0.75 mmol) was added to a solution of isothiazole (**1**) (0.10 g, 0.38 mmol) in abs. DMSO (2 mL). The reaction mixture was kept at 20 °C for 48 h, poured into water (15 mL). Organic materials were extracted with Et_2O (3 x 3 mL). The combined organic extracts were washed with water (3 mL), dried over anhydrous $MgSO_4$. The solvent was evaporated *in vacuo*, the residue was crystallized from heptane. Yield 0.02 g (16%), brown crystals, mp 126-129 °C. ^{1}H NMR: δ 4.63 (d, *J* = 6.6 Hz 2H, CH_2N), 7.10 (s, 1H, H^5), 7.26 (t, *J* = 7.5 Hz, 1H), 7.34 (m, 3H), 7.43 (d, *J* = 7.5 Hz, 2H), 8.21 (s, 1H, H^7). *Anal*. Calcd for $C_{14}H_{10}N_3O_2ClS$: C, 52.59; H, 3.15; Cl, 11.09; N, 13.14; S, 10.03. Found: C, 52.77; H, 3.23; Cl, 10.92; N, 13.30; S, 9.87.

3-R-4-azido-6-nitro-1,2-benzisothiazoles (18), (19) (General procedure)

Powdered NaN_3 (0.50 g, 7.69 mmol) was added to a solution of isothiazole (**1**) or (**2**) (3.85 mmol) in abs. DMF (20 mL). The reaction mixture was stirred at 20–50°C for 1–4 h (Table 1) and poured into water (100 mL). The precipitate was filtered off, dried in air, and crystallized from the *i*-PrOH–acetone mixture. The following compounds were obtained:

3-Chloro-4-azido-6-nitro-1,2-benzisothiazole (18)

Yield 0.95 g (96%), yellow crystals, mp 179–181°C (dec.). IR: γ (cm^{-1}) 2128 (N_3), 1520 (NO_2), 1348 (NO_2), 1276. ^{1}H NMR: δ 8.05 (s, 1H, H^5), 9.02 (s, 1H, H^7); *Anal*. Calcd for $C_7H_2N_5O_2ClS$: C, 32.89; H, 0.79; Cl, 13.87; N, 27.40; S, 12.54. Found: C, 33.16; H, 0.86; Cl, 13.68; N, 27.57; S, 12.42.

4-Azido-3-methoxy-6-nitro-1,2-benzisothiazole (19)

Yield 0.87 g (91%), yellow crystals, mp 149–150°C. ^{1}H NMR: δ 4.15 (s, 3H, CH_3), 7.90 (s, 1H, H^5), 8.80 (s, 1H, H^7). *Anal*. Calcd for $C_8H_5N_5O_3S$: C, 38.25; H, 2.01; N, 27.88; S, 12.76. Found: C, 38.42; H, 2.15; N, 27.69; S, 12.54.

Acetone (3-methoxy-6-nitro-1,2-benzisothiazol-4-yl)hydrazone (20)

Hydrazine hydrate (0.2 mL, 4.04 mmol) was added to a solution of isothiazole (**2**) (0.10 g, 0.39 mmol) in *i*-PrOH (2 mL). The reaction mixture was refluxed for 1 h and cooled to ambient temperature. The precipitated solid was filtered off and crystallized from the *i*-PrOH–acetone mixture (1 : 1). Yield 0.05 g (45%), red crystals, mp 205–207°C. ^{1}H NMR: δ 2.00 (s, 3H, CH_3C), 2.12 (s, 3H, CH_3C), 4.20 (s, 3H, CH_3O), 7.80 (s, 1H, H^5), 8.08 (s, 1H, H^7), 9.00 (s, 1H, NH). *Anal*. Calcd for $C_{11}H_{12}N_4O_3S$: C, 47.13; H, 4.32; N, 19.99; S, 11.44. Found: C, 46.97; H, 4.40; N, 20.15; S, 11.26.

3-R-4-fluoro-6-nitro-1,2-benzisothiazoles (21)–(23) (General procedure)

Freshly dried CsF (1.71 g, 11.3 mmol) was added to a stirred solution of isothiazole (**1**–**3**) (3.85 mmol) in abs. MeCN (40 mL). The reaction mixture was stirred at 50–80°C for 6–16 h (Table 1), the solvent was evaporated *in vacuo*. Water (30 mL) was added to the residue. The precipitate was filtered off, washed with water, dried in air, and crystallized from hexane (heptane). The following compounds were obtained:

3-Chloro-4-fluoro-6-nitro-1,2-benzisothiazole (21)

Yield 0.65 g (72%), yellow crystals, mp 80–83°C. ^{1}H NMR: δ 8.19 (d, $^3J_{H\text{-}F}$ = 9.8 Hz 1H, H^5), 9.17 (s, 1H, H^7). ^{19}F NMR: δ -111.0. MS (*m/z*, I): 234 (M^+, Cl^{37}, 30%), 232 (M^+, Cl^{35}, 70%); 188 (10%); 186 (25%); 151 (100%). *Anal*. Calcd for $C_7H_2N_2O_2ClFS$: C, 36.14; H, 0.87; F, 8.17; N, 12.04; S, 13.78. Found: C, 35.98; H, 0.95; F, 8.03; N, 11.86; S, 13.96.

4-Fluoro-3-methoxy-6-nitro-1,2-benzisothiazole (22)

Yield 0.68 g (78%), yellow crystals, mp 115–118°C. ^{1}H NMR: δ 4.18 (s, 3H, CH_3), 7.90 (d, $^3J_{H\text{-}F}$ = 9.8 Hz 1H, H^5), 8.90 s (1H, H^7). *Anal*. Calcd for $C_8H_5N_2O_3FS$: C, 42.11; H, 2.21; F, 8.33; N, 12.28; S, 14.05. Found: C, 41.94; H, 2.12; F, 8.14; N, 12.37; S, 13.93.

4-Fluoro-6-nitro-1,2-benzisothiazol-3-yl-oxyacetic acid ethyl ester (23)

Yield 0.62 g (54%), yellow crystals, mp 107–110°C. ^{1}H NMR: δ 1.28 (t, J = 7.0 Hz, 3H, CH_3), 4.22 (q, J = 7.0 Hz, 2H, CH_2), 5.10 (s, 2H, CH_2), 7.96 (d, $^3J_{H\text{-}F}$ = 9.8 Hz, 1H, H^5), 8.97 (s, 1H, H^7). *Anal*. Calcd for $C_{11}H_9N_2O_5FS$: C, 44.00; H, 3.02; F, 6.33; N, 9.33; S, 10.68. Found: C, 44.21; H, 3.16; F, 6.18; N, 9.17; S, 10.45.

4,6-Bis-(2,2,2-trifluoroethoxy)-3-methoxy-1,2-benzisothiazole (24)

A mixture of isothiazole (**3**) (0.50 g, 1.96 mmol), 2,2,2-trifluoroethanol (0.84 g, 8.38 mmol), K_2CO_3 (0.82 g, 5.94 mmol), and DMF (10 mL) was stirred at 100°C for 6 h. Then a new portion of 2,2,2-trifluoroethanol (0.84 g, 8.38 mmol) was added, and the reaction mixture was stirred at 100°C for additional 6 h, cooled to ambient temperature and poured into water (100 mL). The solid was filtered off, washed with water, dried in air, and crystallized from *i*-PrOH. Yield 0.40 g (56%), colorless crystals, mp 102–103°C. ^{1}H NMR: δ 4.10 (s, 3H, OCH_3); 4.70 (q, $^3J_{H\text{-}F}$ = 5.0 Hz, 4H, $2CH_2CF_3$); 6.75 (s, 1H, H^5); 7.17 (s, 1H, H^7). ^{13}C NMR: δ 55.8 (CH_3); 64.9 (q, $^2J_{C\text{-}F}$ = 34.4 Hz, $\underline{C}H_2CF_3$); 65.2 (q, $^2J_{C\text{-}F}$ = 34.4 Hz, $\underline{C}H_2CF_3$); 97.7 (C^5); 98.9 (C^7); 110.0 (C^{3a}); 123.7 (q, CF_3, $^1J_{C\text{-}F}$ = 277.9 Hz); 154.3 (C^{7a}); 155.8 (C^4); 158.9 (C^3); 162.4 (C^6). ^{19}F NMR: δ -72.8. *Anal*. Calcd for $C_{12}H_9NO_3F_6S$: C, 39.90; H, 2.51; F, 31.55; N, 3.88; S, 8.88. Found: C, 40.13; H, 2.62; F, 31.39; N, 3.94; S, 9.05.

3-R-7-amino-4,6-dinitro-1,2-benzisothiazoles (25), (26) (General procedure)

A solution of KOH (0.77 g, 13.8 mmol) in MeOH (20 mL) was added to a stirred suspension of isothiazole (**1-2**) (3.85 mmol) and hydroxylamine hydrochloride (1.10 g, 15.8 mmol) in MeOH (30 mL). The reaction mixture was stirred at 15°C for 2 h. The solvent was evaporated *in vacuo*. Water (50 mL) was added to the residue, and the mixture was adjusted to pH~1 by 10% HCl. The precipitate was filtered off, washed with water (20 mL), dried in air, and crystallized from the appropriate solvent. The following compounds were obtained:

7-Amino-3-chloro-4,6-dinitro-1,2-benzisothiazole (25)

Yield 0.70 g (66%), dark crystals, mp 215–218°C (*i*-PrOH–acetone). ^{1}H NMR: δ 8.68 (s, 1H, CH), 9.11 (br.s, 2H, NH_2). *Anal*. Calcd for $C_7H_3N_4O_4ClS$: C, 30.61; H, 1.10; Cl, 12.91; N, 20.40; S, 11.68. Found: C, 30.77; H, 10.19; Cl, 13.03; N, 20.62; S, 11.43.

7-Amino-4,6-dinitro-3-methoxy-1,2-benzisothiazole (26)

Yield 0.70 g (66%), dark crystals, mp 226–230°C (benzene). ^{1}H NMR: δ 4.11 (s, 3H, CH_3), 8.50 (s, 1H, H^5), 8.84 (br.s, 2H, NH_2); ^{13}C NMR: δ 56.9 (CH_3), 118.2 (C^{3a}), 121.1 (C^5), 125.2 (C^6), 133.2 (C^4), 141.8 (C^7), 146.4 (C^{7a}), 161.4 (C^3); ^{14}N NMR: δ -13.50 ($\delta\gamma_{1/2}$ = 200 Hz). *Anal*. Calcd for $C_8H_6N_4O_5S$: C, 35.56; H, 2.24; N, 20.73; S, 11.87. Found: C, 35.78; H, 2.39; N, 20.51; S, 11.69.

3-Methoxy-4,6-dinitro-7-*p*-toluylsulfonylmethyl-1,2-benzisothiazole (27)

Isothiazole (**2**) (0.12 g, 0.47 mmol) was added to a stirred suspension of KOH (0.27 g, 4.81 mmol) and S-(*p*-tolyl)-S-(chloromethyl)sulfone (0.10 g, 0.49 mmol) in abs. DMSO (2 mL). The reaction mixture was stirred at 15°C for 1 h and poured into ice-cold 5% HCl (20 mL). The precipitate was filtered off, washed with water (2 × 5 mL), dried in air, and crystallized from *i*-PrOH. Yield 0.18 g (90%), yellow crystals, mp 205–209°C. ^{1}H NMR: δ 2.48 (s, 3H, CCH_3); 4.20 (s, 3H, OCH_3); 5.29 (s, 2H, CH_2); 7.40 (d, *J* = 8.5 Hz, 2H); 7.68 (d, *J* = 8.5 Hz, 2H); 8.52 (s, 1H, H^5). MS (*m/z*, I): 423 (M^+, 10%); 269 (20%); 154

(25%); 139 (30%); 91 (100%). *Anal*. Calcd for $C_{16}H_{13}N_3O_7S_2$: C, 45.39; H, 3.09; N, 9.92; S, 15.15. Found: C, 45.62; H, 3.24; N, 9.75; S, 14.93.

4-Methoxy-2-methyl-6-nitro-1,2-benzisothiazol-3(2*H*)-one (28)

Isothiazol-3-one (**5**) (1.00 g, 3.92 mmol) was added to a stirred MeONa solution, prepared from Na (0.20 g, 8.70 mmol) and abs. MeOH (20 mL). The reaction mixture was stirred at 20°C for 24 h. The solvent was evaporated *in vacuo*. Water (20 mL) was added to the residue. The mixture was adjusted to pH~2 by 10% HCl, the precipitate was filtered off, washed with water, dried in air, and crystallized from *i*-PrOH. Yield 0.53 g (56%), yellow crystals, mp 221–224°C. ^{1}H NMR: δ 3.32 (s, 3H, NCH_3), 4.03 (s, 3H, OCH_3), 7.54 (s, 1H, H^5), 8.41 (s, 1H, H^7). *Anal*. Calcd for $C_9H_8N_2O_4S$: C, 45.00; H, 3.36; N, 11.66; S, 13.35. Found: C, 45.17; H, 3.49; N, 11.43; S, 13.24.

2-Methyl-6-nitro-4-phenoxy-1,2-benzisothiazol-3(2*H*)-one (29)

A mixture of isothiazol-3-one (**5**) (1.00 g, 3.92 mmol), phenol (0.80 g, 8.51 mmol), Na_2CO_3 (0.90 g, 8.49 mmol), and abs. DMF (20 mL) was stirred at 100°C for 4 h, cooled to ambient temperature, diluted with water (100 mL) and adjusted to pH~2 by 10% HCl. The precipitate was filtered off, washed with water (2 × 20 mL), dried in air, and crystallized from the *i*-PrOH–acetone mixture. Yield 0.50 g (42%), yellow crystals, mp 220–223°C. ^{1}H NMR: δ 3.37 (s, 3H, CH_3), 7.12 (d, J = 8.5 Hz, 2H), 7.28 (t, J = 8.5 Hz, 1H), 7.30 (s, 1H, H^5), 7.49 (t, J = 8.5 Hz, 2H), 8.65 (s, 1H, H^7). *Anal*. Calcd for $C_{14}H_{10}N_2O_4S$: C, 55.62; H, 3.33; N, 9.27; S, 10.61. Found: C, 55.86; H, 3.50; N, 9.13; S, 10.47.

2-R-4-Azido-6-nitro-1,2-benzisothiazol-3(2*H*)-ones (30)–(32) (General procedure)

Powdered NaN_3 (0.76 g, 11.7 mmol) was added to a solution of isothiazol-3-one (**4**)–(**6**) (3.92 mmol) in abs. DMF (20 mL). The reaction mixture was stirred at 20–40°C for 2–24 h (Table 2), diluted with water (80 mL). The precipitate was filtered off, washed with water (2 × 10 mL), dried in air, and crystallized from the *i*-PrOH–acetone mixture. The following compounds were obtained:

4-Azido-6-nitro-1,2-benzisothiazol-3(2*H*)-one (30)

Yield 0.66 g (71%), yellow crystals, mp > 300°C. ^{1}H NMR: δ 7.83 (s, 1H, H^5), 8.75 (s, 1H, H^7); 12.3 (br.s., 1H, NH). *Anal*. Calcd for $C_7H_3N_5O_3S$: C, 35.45; H, 1.27; N, 29.53; S, 13.52. Found: C, 35.67; H, 1.34; N, 29.33; S, 13.36.

4-Azido-2-methyl-6-nitro-1,2-benzisothiazol-3(2*H*)-one (31)

Yield 0.90 g (91%), yellow crystals, mp 196–198°C. ^{1}H NMR: δ 3.36 (s, 3H, CH_3), 7.78 (s, 1H, H^5), 8.71 (s, 1H, H^7). *Anal*. Calcd for $C_8H_5N_5O_3S$: C, 38.25; H, 2.01; N, 27.88; S, 12.76. Found: C, 38.43; H, 2.13; N, 27.64; S, 12.83.

4-Azido-6-nitro-2-phenyl-1,2-benzisothiazol-3(2*H*)-one (32)

Yield 0.99 g (81%), yellow crystals, mp 174–177°C (dec.). ^{1}H NMR: δ 7.38 (t, *J* =7.5 Hz, 1H), 7.52 (t, *J* =7.5 Hz, 2H), 7.65 (d, *J* =7.5 Hz, 2H), 7.83 (s, 1H, H^5), 8.77 (s, 1H, H^7). *Anal*. Calcd for $C_{13}H_7N_5O_3S$: C, 49.84; H, 2.25; N, 22.35; S, 10.23. Found: C, 50.02; H, 2.36; N, 22.17; S, 10.06.

4-Fluoro-2-methyl-6-nitro-1,2-benzisothiazol-3(2*H*)-one (33)

A mixture of isothiazol-3-one (**5**) (0.10 g, 0.39 mmol), freshly dried CsF (0.20 g, 1.31 mmol), and dry MeCN (10 mL) was refluxed for 16 h. The solvent was evaporated *in vacuo*. Water (5 mL) was added to the residue. The precipitate was filtered off, dried in air, and crystallized from the *i*-PrOH–acetone mixture. Yield 0.04 g (44%), yellow crystals, mp 155–157°C. ^{1}H NMR: δ 3.38 (s, 3H, CH_3), 7.87 (d, $^3J_{H\text{-}F}$ = 9.5 Hz, 1H, H^5), 8.81 (s, 1H, H^7). *Anal*. Calcd for $C_8H_5N_2O_3FS$: C, 42.11; H, 2.21; F, 8.33; N, 12.28; S, 14.05. Found: C, 42.30; H, 2.35; F, 8.15; N, 12.41; S, 13.92.

***N*-methyl-2-(benzyldithio)-4,6-dinitrobenzamide (34)**

α-Benzylthiol (0.05 g, 0.42 mmol) and powdered K_2CO_3 (0.05 g, 0.36 mmol) were added successively to a solution of isothiazol-3-one (**5**) (0.10 g, 0.39 mmol) in abs. DMF (2 mL). The reaction mixture was stirred at 15°C for 2 h and diluted with water (10 mL). The precipitate was filtered off, washed with water (2 × 5 mL), dried in air, and crystallized from the *i*-PrOH–acetone mixture. Yield 0.06 g (40%), yellow crystals, mp 151–153°C. ^{1}H NMR: δ 2.81 (d, *J* = 5.0 Hz, 3H, CH_3); 4.11 (s, 2H, CH_2); 7.18 (t, *J* = 8.0 Hz, 1H); 7.21 (t, *J* = 8.0 Hz, 2H); 7.31 (d, *J* = 8.0 Hz, 2H); 8.52 (s, 2H, H^3 and H^5); 8.77 (q, *J* = 5.0 Hz, 1H, NH). MS (*m/z*, I): 255 (M$^+$- BnSH, 20%); 227 (15%); 225 (25%); 197 (5%); 196 (7%); 179 (10%); 168 (5%); 124 (60%); 91 (100%). *Anal*. Calcd for $C_{15}H_{13}N_3O_5S_2$: C, 47.48; H, 3.45; N, 11.08; S, 16.90. Found: C, 47.31; H, 3.33; N, 11.22; S, 17.08.

S,S'-Bis[2-(methylaminocarbonyl)-3,5-dinitrophen-1-yl]-disulfide (36)

A solution of KOH (0.09 g, 1.60 mmol) in MeOH (2 mL) was added to a stirred suspension of isothiazol-3-one (**5**) (0.10 g, 0.39 mmol) and hydroxylamine hydrochloride (0.10 g, 1.44 mmol) in MeOH (3 mL). The reaction mixture was stirred at 15°C for 2 h. The solvent was evaporated, and water (5 mL) was added to the residue. The mixture was adjusted to pH~1 by 10% HCl. The precipitate was filtered off, washed with water (2 mL), dried in air, and crystallized from AcOH. Yield 0.06 g (59%), colorless crystals, mp 246–250°C. ^{1}H NMR: δ 2.90 (d, *J* = 5.0 Hz, 3H, CH_3), 8.62 (s, 1H, H^4, or H^6), 8.70 (q, *J* = 5.0 Hz, 1H, NH), 8.78 (s, 1H, H^6, or H^4). ^{13}C NMR: δ 26.1 (CH_3), 118.9 (C^4), 127.7 (C^6), 136.7 (C^2), 138.6 (C^1), 146.1 (C^3), 147.6 (C^5), 162.3 (C=O). MS (*m/z*, I): 255 (1/2M$^+$-2H, 65%); 240 (6%); 227 (12%); 209 (16%); 196 (100%). *Anal*. Calcd for $C_{16}H_{12}N_6O_{10}S_2$: C, 37.50; H, 2.36; N, 16.40; S, 12.51. Found: C, 37.67; H, 2.44; N, 16.25; S, 12.67.

4-Alkylamino-6-nitro- and 4-hydrazino-6-nitrobenzisothiazol-3(2*H*)-one-1-oxides (37)–(41) (General procedure)

Hydrazine hydrate (2.50 mmol) or amine (4.00 mmol) was added slowly to a stirred refluxing solution of isothiazol-3(*2H*)-one-1-oxide (**8**) or (**9**) (2.00 mmol) in *i*-PrOH (2 mL). The reaction mixture was refluxed for 6–15 min. (Table 3) and cooled to ambient temperature. The precipitate was filtered off, washed with *i*-PrOH, dried in air, and crystallized from the *i*-PrOH–MeCN mixture. The following compounds were obtained:

4-Benzylamino-2-methyl-6-nitro-1,2-benzisothiazol-3(2*H*)-one-1-oxide (37)

Yield 0.36 g (54%), dark crystals, mp 140–142°C. ^{1}H NMR: δ 3.30 (s, 3H, CH_3); 4.68 (d, J = 8.0 Hz, 2H, CH_2); 7.20–7.48 (m, 5H, Ph); 7.61 (s, 1H, H^5); 8.00 (b.s., 2H, H^7, and NH). MS (*m/z*, I): 331 (M^+, 25%); 314 (3%); 300 (25%); 284 (3%); 256 (35%), 105 (50%); 91 (100%). *Anal*. Calcd for $C_{15}H_{13}N_3O_4S$: C, 54.37; H, 3.95; N, 12.68; S, 9.68. Found: C, 54.56; H, 4.04; N, 12.53; S, 9.51.

2-Benzyl-4-benzylamino-6-nitro-1,2-benzisothiazol-3(2*H*)-one-1-oxide (38)

0.50 g (61%), dark crystals, mp 123–125°C. ^{1}H NMR: δ 4.68 (d, ^3J = 7.0 Hz, 2H, C<u>H</u>$_2$NH); 4.81 (d, ^2J = 16.0 Hz, 1H, CH_2N); 5.11 (d, ^2J = 16.0 Hz, 1H, CH_2N); 7.20–7.49 (m, 10H, 2Ph); 7.62 (s, 1H, H^5); 8.03 (br.s., 2H, NH, and H^7). *Anal*. Calcd for $C_{21}H_{17}N_3O_4S$: C, 61.90; H, 4.21; N, 10.31; S, 7.87. Found: C, 62.09; H, 4.33; N, 10.26; S, 7.71.

2-Methyl-4-morpholinyl-6-nitro-1,2-benzisothiazol-3(2*H*)-one-1-oxide (39)

Yield 0.45 g (72%); dark crystals, mp 171–175°C. ^{1}H NMR: δ 3.33 (s, 3H, CH_3); 4.02 (m, 8H, 4CH_2); 7.96 (s, 1H, H^5); 8.18 (s, 1H, H^7). *Anal*. Calcd for $C_{12}H_{13}N_3O_5S$: C, 46.30; H, 4.21; N, 13.50; S, 10.30. Found: C, 46.48; H, 4.34; N, 13.43; S, 10.17.

4-Hydrazino-2-methyl-6-nitro-1,2-benzisothiazol-3(2*H*)-one-1-oxide (40)

Yield 0.35 g (69%), dark crystals, mp 238–241°C. ^{1}H NMR: δ 3.30 (s, 3H, CH_3); 4.71 (s, 1H, NH_2); 7.91 (s, 1H, H^5); 8.15 (s, 1H, NH); 8.35 (s, 1H, H^7). MS (*m/z*, I): 256 (M^+, 100%); 240 (20%); 226 (5%); 210 (5%); 197 (30%); 194 (10%); 181 (10%); 165 (10%); 151 (30%). *Anal*. Calcd for $C_8H_8N_4O_4S$: C, 37.50; H, 3.15; N, 21.87; S, 12.51. Found: C, 37.67; H, 3.24; N, 21.92; S, 12.43. [**2-Methyl-4-[2'-(1''-methylethylidene)hydrazino]-6-nitro-1,2-benzisothiazol-3(2*H*)-one-1-oxide (40a)**, mp 187–193°C (*i*-PrOH). ^{1}H NMR: δ 1.91 (s, 3H, CCH_3); 2.08 (s, 3H, CCH_3); 3.28 (s, 3H, NCH_3); 8.18 (b.s., 2H, H^5, and H^7); 9.88 (s, 1H, NH). MS (*m/z*, I): 296 (M^+, 100%); 280 (5%); 240 (55%); 224 (5%); 212 (10%); 194 (20%); 56 (45%); 41 (65%). *Anal*. Calcd for $C_{11}H_{12}N_4O_4S$: C, 44.59; H, 4.08; N, 18.91; S, 10.82. Found: C, 44.80; H, 4.24; N, 18.76; S, 10.65].

2-Benzyl-4-hydrazino-6-nitro-1,2-benzisothiazol-3(2*H*)-one-1-oxide (41)

Yield 0.47 g (71%), dark crystals, mp 218–220°C. ^{1}H NMR: δ 4.68 (s, 2H, NH_2); 4.79 (d, ^2J = 16.0 Hz, 1H, CH_2); 5.11 (d, ^2J = 16.0 Hz, 1H, CH_2); 7.33–7.45 (m, 5H, Ph); 7.98 (s, 1H, H^5); 8.17 (s, 1H, NH);

8.40 (s, 1H, H^7). *Anal*. Calcd for $C_{14}H_{12}N_4O_4S$: C, 50.60; H, 3.64; N, 16.86; S, 9.65. Found: C, 50.46; H, 3.45; N, 16.73; S, 9.82.

4-Fluoro-2-methyl-6-nitro-1,2-benzisothiazol-3(2*H*)-one-1-oxide (42)

Isothiazol-3-one-1-oxide (**8**) (0.36 g, 1.33 mmol) was added to a stirred suspension of freshly dried CsF (0.43 g, 2.80 mmol) in abs. MeCN (5 mL). The reaction mixture was stirred at 50°C for 2 h (TLC-monitoring). The solvent was evaporated *in vacuo*, and water (5 mL) was added to the residue. The precipitate was filtered off, dried in air, and crystallized from *i*-PrOH. Yield 0.16 g (48%), yellow crystals, mp 179–184°C. ^{1}H NMR: δ 3.28 (s, 3H, CH_3); 8.57 (d, $^3J_{H\text{-}F}$ = 10.0 Hz, 1H, H^5); 9.02 (s, 1H, H^7). MS (*m/z*, I): 244 (M^+, 35%); 228 (4%); 215 (6%); 184 (100%). *Anal*. Calcd for $C_8H_5N_2O_4FS$: C, 39.35; H, 2.06; F, 7.78; N, 11.47; S, 13.13. Found: C, 39.49; H, 2.19; F, 7.67; N, 11.55; S, 12.98.

4,6-Diazido-1,2-benzisothiazol-3(2*H*)-one-1-oxides (43)–(47) (General procedure)

Powdered NaN_3 (0.42 g, 6.46 mmol) was added to a solution of isothiazol-3-one-1-oxide (**7**)–(**11**) (2.00 mmol) in DMF (8 mL). The reaction mixture was stirred at 40°C for 3–5 h (Table 3), poured into water, and then adjusted to pH~2 by 10% HCl. The precipitate was filtered off, dried in air, and crystallized from *i*-PrOH. The following compounds were obtained:

4,6-Diazido-1,2-benzisothiazol-3(2*H*)-one-1-oxide – DMF 1 : 1 complex (43)

Yield 0.35 g (55%); dark crystals, mp 181–183°C. ^{1}H NMR: δ 2.73 (s, 3H, CH_3-DMF); 2.88 (s, 3H, CH_3-DMF); 7.94 (s, 1H, CH-DMF); 8.27 (s, 1H, H^5); 8.73 (s, 1H, H^7). MS (*m/z*, I): 249 (M^+ - DMF, 5%); 221 (5%). Anal. Calcd for $C_{10}H_{10}N_8O_3S$: C, 37.27; H, 3.13; N, 34.77; S, 9.95. Found: C, 37.49; H, 3.22; N, 34.58; S, 9.86.

4,6-Diazido-2-methyl-1,2-benzisothiazol-3(2*H*)-one-1-oxide (44)

Yield 0.33 g (63%), dark crystals, mp 144–147°C. ^{1}H NMR: δ 3.34 (s, 3H, CH_3); 7.29 (s, 1H, H^5); 7.82 (s, 1H, H^7). MS (*m/z*, I): 263 (M^+, 25%); 235 (5%). Anal. Calcd for $C_8H_5N_7O_2S$: C, 36.50; H, 1.91; N, 37.25; S, 12.18. Found: C, 36.38; H, 1.83; N, 37.39; S, 12.09.

2-Benzyl-4,6-diazido-1,2-benzisothiazol-3(2*H*)-one-1-oxide (45)

Yield 0.61 g (90%), dark crystals, mp 108–110°C. ^{1}H NMR: δ 4.78 (d, ^2J = 17.0 Hz, 1H, CH_2); 5.08 (d, ^2J = 17.0 Hz, 1H, CH_2); 7.26 (s, 1H, H^5); 7.30–7.42 (m, 5H, Ph); 7.81 (s, 1H, H^7). Anal. Calcd for $C_{14}H_9N_7O_2S$: C, 49.55; H, 2.67; N, 28.89; S, 9.45. Found: C, 49.77; H, 2.75; N, 28.73; S, 9.34.

4,6-Diazido-2-methoxycarbonylmethyl-1,2-benzisothiazol-3(2*H*)-one-1-oxide (46)

Yield 0.33 g (52%); dark crystals, mp 143–146°C. ^{1}H NMR: δ 3.71 (s, 3H, CH_3); 4.56 (d, 1H, CH_2, ^2J = 12.5Hz); 4.80 (d, 1H, CH_2, ^2J = 12.5 Hz); 7.27 (s, 1H, H^5); 7.77 (s, 1H, H^7). Anal. Calcd for $C_{10}H_7N_7O_4S$: C, 37.38; H, 2.20; N, 30.52; S, 9.98. Found: C, 37.55; H, 2.33; N, 30.36; S, 10.08.

4,6-Diazido-2-phenyl-1,2-benzisothiazol-3(2*H*)-one-1-oxide (47)

Yield 0.46 g (71%), dark crystals, mp 153–156°C. ^{1}H NMR: δ 7.37 (s, 1H, H^5); 7.42–7.65 (m, 5H, Ph); 7.90 (s, 1H, H^7). Anal. Calcd for $C_{13}H_7N_7O_2S$: C, 48.00; H, 2.17; N, 30.14; S, 9.86. Found: C, 48.19; H, 2.26; N, 29.98; S, 9.69.

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