Synthetic Utilization of Polynitroaromatic Compounds. 2. Synthesis of 4,6-Dinitro-1,2-benzisothiazol-3-ones and 4,6-Dinitro-1,2-benzisothiazoles from 2-Benzylthio-4,6-dinitrobenzamides

S. G. Zlotin,* P. G. Kislitsin, A. I. Podgursky, A. V. Samet, and V. V. Semenov

N.D. Zelinsky Institute of Organic Chemistry RAS, Leninsky Pr., 47 Moscow, 117913, Russia

A. C. Buchanan III and Andrei A. Gakh*

Chemical and Analytical Sciences Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee 37831-6197

gakhaa@ornl.gov

Received March 29, 2000

Cyclization of 2-benzylthio-4,6-dinitrobenzamides to 4,6-dinitro-1,2-benzisothiazol-3-ones was achieved using SO_2Cl_2 in CH_2Cl_2 at room temperature. Alkylation of these heterocycles proceeded in a nonregioselective manner to yield a mixture of corresponding O- and N-alkylated products. Oxidation of 4,6-dinitro-1,2-benzisothiazoles (50% H_2O_2 in AcOH) afforded the corresponding *S*-oxides and *S*,*S*-dioxides, depending on oxidation conditions. Unexpectedly, oxidation of a 3-methoxy derivative resulted in ring opening with the formation of the corresponding sulfamide. Chlorination of these 4,6-dinitro-1,2-benzisothiazol-3-ones (PCl_5−$POCl_3$) gave the expected 3-chloroisothiazoles.

Introduction

It is known that 1,2-benzisothiazoles and 1,2-benzisothiazol-3-ones, containing a nitro group in the aromatic ring, possess bactericide,[1−5] fungicide,[6,7] and nematocide[8] properties, and can be used as intermediates for azo dyes.[9,10] These compounds have been synthesized by various methods including amination of 2-(chlorosulfanyl)nitrobenzoyl chlorides[3,11,12] chlorination of 2-(alkylthio)nitrobenzamides[7,13] and 2-(alkylthio)nitrobenzaldoximes,[4,14] reaction of 2-(alkylthio)nitrobenzaldoximes with polyphosphoric acid,[15] reaction of 2-(alkylsulfinyl)-nitrobenzamides with trichloroacetic anhydride[16,17] or bases,[16−18] and reaction of nitro-substituted 2-chlorobenzaldehydes with a mixture of sulfur and ammonia.[9,10,19] In most cases, only 5- and 7-nitro-1,2-benzisothiazoles and isothiazol-3-ones but not 4- and 6-nitro-isomers can be prepared using these methods.

It is expected that 1,2-benzisothiazoles and 1,2-benzisothiazol-3-ones containing two nitro groups in the aromatic ring would have useful biological activities as well. They also may serve as valuable intermediates for synthesis of other functionalized nitro- and dinitro-1,2-benzisothiazoles or isothiazol-3-ones via alkylation, halogenation, oxidation as well as reactions with nucleophilic reagents.

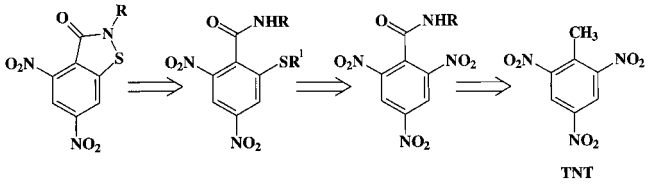
To the best of our knowledge, there is only one literature report of a 1,2-benzisothiazole containing two nitro groups in the aromatic ring. Thus, nitration of 4-chloro-1,2-benzisothiazole gave 4-chloro-5,7-dinitro-1,2-benzisothiazole, patented as an intermediate for synthesis of azo dyes.[10] 4,6-Dinitro-1,2-benzisothiazoles and 4,6-dinitro-1,2-benzisothiazol-3-ones have not yet been reported.

In our previous paper,[20] we proposed to use 2,4,6-trinitroaromatic compounds as possible starting materials for synthesis of various aromatic and heterocyclic intermediates. In the case of benzisothiazoles, a possible synthetic strategy includes transformation of readily available 2,4,6-trinitrotoluene (TNT) to 2,4,6-trinitrobenzamides, followed by substitution of an *o*-nitro group by

(1) Clarke, K.; Gleadhill, B.; Scrowston, R. M. *J. Chem. Res. Synop.* **1979**, *12*, 395.
(2) Vicini, P.; Mazza, P. *Farmaco* **1989**, *44*(5), 511.
(3) Fischer, R.; Hurni, H. *Arz.-Forshung* **1964**, *14*(12), 1301.
(4) Kagano, H.; Goda, H.; Yoshida, K.; Yamamoto, M.; Sakaue, S. Can. Pat. Appl. CA 2,151,074 (Cl. C07D275/04), 1996; *Chem. Abstr.* **1996**, *124*, 317152h.
(5) Zani, F.; Mingiardi, M. R.; Maggiali, C. A.; Mazza, P. *Farmaco* **1996**, *51*(11), 707.
(6) Hagen, H.; Ziegler, H.; Pommer, E. H.; Ammermann, E. Ger. Offen. DE 3,202,298 (C1. C07D275/04), **1983;** *Chem. Abstr.* **1983**, *99*, 175752t.
(7) Kagano, H.; Itsuda, H.; Sakagami, S. J. P. 07,330,745 [95,330,-745] (C1. C07D275/04), 1995; *Chem. Abstr.* **1996**, *124*, 289523j.
(8) Sutter, M.; Kunz, W. Eur. Pat. Appl. EP 454,621 (Cl. C07D275/04) **1991**; *Chem. Abstr.* **1992**, *116*, 106280v.
(9) Hagen, H.; Markert, J. Ger. Offen. DE 3,018,108 (Cl. C07D275/04), 1981; *Chem. Abstr.* **1982**, *96*, 68980g.
(10) Gruettner-Merten, S.; Grund, C.; Guldner, A.; Hagen, H.; Reichelt, H.; Sens, R. Ger. Offen. DE 4,339,270 (C1. C09B29/09), 1995; *Chem. Abstr.* **1995**, *123*, 259743t.
(11) Hagen, H.; Ziegler, H. Ger. Offen. DE 3,150,629 (Cl. C07D275/04), 1983; *Chem. Abstr.* **1983**, *99*, 175750r.
(12) Ponci, R.; Gialdi, F.; Baruffini, A. *Farmaco* **1964**, *19*(3), 254.
(13) Kagano, H.; Goda, H.; Sakaue, S. Eur. Pat. Appl. EP 657,438 (Cl. C07D275/04), 1995; *Chem. Abstr.* **1995**, *123*, 313964b.
(14) Kagano, H.; Goda, H.; Yamamoto, M.; Sakaue, S.; Toudou, M. PTC Int. Appl. WO 96 17,834 (C1. C07D275/04), 1996; *Chem. Abstr.* **1996**, *125*, 142716m.
(15) Rahman, L. K. A.; Scrowston, R. M. *J. Chem. Soc., Perkin Trans. 1* **1984**, (3), 385.
(16) Wright, S. W.; Abelman, M. M.; Bostrom, L. L.; Corbett, R. L. *Tetrahedron Lett.* **1992**, *33*(2), 153.
(17) Wright, S. W.; Petraitis, J.; Abelman, M. M.; Batt, D. G.; Bostrom, L. L.; Corbett, R. L.; Decicco, C. P.; Di Meo, S. V.; Freimark, B.; Giannaras, J. V.; Green, A. M.; Jetter, J. M.; Nelson, D. J.; Orwat, M. J.; Pinto, D. J.; Pratta, M. A.; Sherk, S. R.; Williams, J. M.; Magolda, R. L.; Arner, E. S. J. *Med. Chem.* **1994**, *37*(19), 3071.
(18) Bamfield, P.; Greenwood, D.; Lotey, H.; Stirling, C. J. M. *J. Chem. Soc., Perkin Trans. 2* **1988**, (5), 691.
(19) Markert, J.; Hagen, H. *Lieb. Ann. Chem.* **1980**, (5), 768.

10.1021/jo000480c CCC: $19.00
Published on Web 11/10/2000

an alkylthio group, and cyclization to the desired 4,6-dinitro-1,2-benzisothiazol-3-ones by chlorinating agents. The retro-synthetic analysis is presented below.



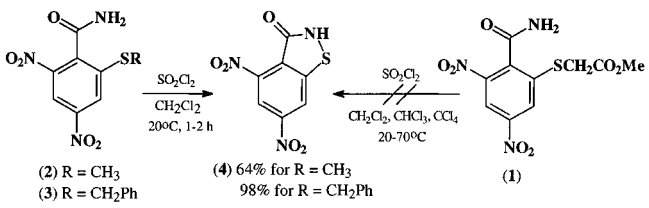
Conversion of TNT to 2,4,6-trinitrobenzoic acid and its amides was described previously, as well as reaction of these amides with alkyl- and arylmercaptans which produced 2-(alkylthio)-4,6-dinitrobenzamides.[20] In this paper, we will describe cyclization of the 2-(alkylthio)-4,6-dinitrobenzamides leading to the desired 4,6-dinitro-l,2-benzisothiazol-3-ones, and some further reactions of these compounds with electrophilic reagents.

Results and Discussion

It is known that *S*-aryl-*S*-benzylsulfides easily react with Cl_2 or SO_2Cl_2 to give arylthiochlorides—possible intermediates for synthesis of 1,2-benzisothiazoles.[21] Examples include conversion of the *N*-phenylamide of 3-(benzylthio)pyridine-2-carboxylic acid to 2-phenylpyridoisothiazol-3-one by reaction with SO_2Cl_2.[17] In addition, synthesis of 1,2-benzisothiazole-3-ones by reactions of 2-(alkylthio)-N-arylbenzamides (alkyl = C_1−C_4) with Cl_2 or SO_2Cl_2 have been reported by Japanese authors in two recent patents.[7,13]

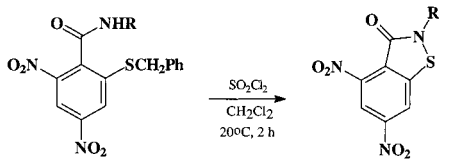
To determine the effect of thioalkyl groups in 2-(alkylthio)-4,6-dinitrobenzamides on the yield of the desired 4,6-dinitro-l,2-benzisothiazol-3-ones, we have investigated reactions of 2-(alkylthio)-4,6-dinitrobenzamides (**1**−**3**)[20] (Scheme 1) with sulfuryl chloride. It appeared that 2-methoxycarbonylmethylthio-4,6-dinitrobenzamide (**1**) did not react with SO_2Cl_2 in chlorohydrocarbons (CH_2Cl_2, $CHCl_3$, CCl_4) at 20−70 °C. On the other hand, treatment of 2-methylthio- and 2-benzylthio-4,6-dinitrobenzamides (**2**) and (**3**) with SO_2Cl_2 in CH_2Cl_2 at 15−20 °C afforded the desired 4,6-dinitro-1,2-benzisothiazol-3-one (**4**) in 64% and 98% yields, respectively (see also ref 23). Based on these results, we selected 2-benzylthio-4,6-dinitrobenzamides as starting compounds for synthesis of 4,6-dinitro-1,2-benzisothiazol-3-ones.

Scheme 1



We investigated the behavior of a series of N-substituted 2-benzylthio-4,6-dinitrobenzamides (**5**−**10**) to explore the scope of the cyclization reaction. Synthesis of the starting benzamides (**5**−**10**) was described previously.[20] We found that **5**−**10** reacted smoothly with SO_2Cl_2 in CH_2Cl_2 at room temperature to afford N−alkyl- and N-aryl-4,6-dinitro-1,2-benzisothiazol-3-ones (**11**−**16**)-in 55−91% yields (Scheme 2).

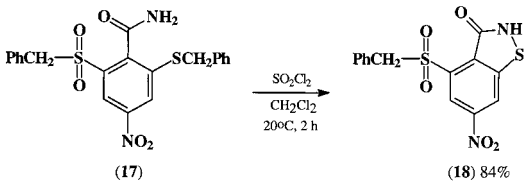
Scheme 2



(**5**),(**11**) R = CH_3; (**6**),(**12**) R = CH_2Ph; (**7**),(**13**) R = Ph; (**8**),(**14**) R = $C_6H_4Br(p)$; (**9**),(**15**) R = C_6H_4-$OCClF_2(p)$; (**10**),(**16**) R = C_6H_4-$OCF_3(p)$

2-Benzylthio-4-nitrobenzamides containing other electron withdrawing groups at the 6- position react similarly. Thus, 2-benzylthio-6-benzylsulfonyl-4-nitrobenzamide (**17**)[20] is easily converted to 4-benzylsulfonyl-6-nitro-l,2-benzisothiazol-3-one (**18**) in 84% yield by treatment with sulfuryl chloride at room temperature (Scheme 3). It is noteworthy that the use of pure *o*-(benzylthio)-benzamides in the cyclization reaction is not required. Compounds **3**, **5**−**10**, and **17**, containing the related *p*-benzylthio isomers,[20] could be used without further purification. In these cases, isolation of analytically pure nitro-1,2-benzisothiazol-3-ones (**4**, **11**−**16**, and **18**) is achieved by simple recrystallization from *i*-PrOH or its mixtures with heptane, $CHCl_3$, or acetone.

Scheme 3



It should be noted that benzyl chloride, a byproduct of the cyclization process, can be easily isolated from the reaction mixture by extraction with petroleum ether or hexane. Hence, it can be reused for synthesis of the starting 2-benzylthio-4,6-dinitrobenzamides. This feature improves the potential for developing an industrial process for production of the target heterocycles.

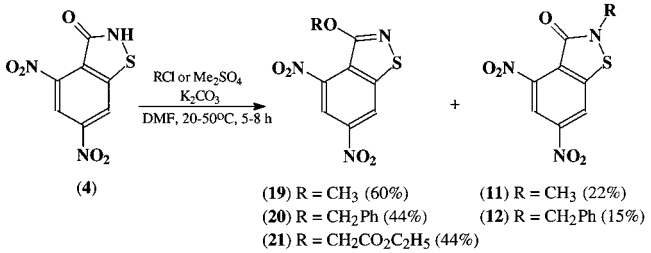
4,6-Dinitro-l,2-benzisothiazol-3-ones (**4**, **11**−**16**) are found to be useful intermediates in the synthesis of other 1,2-benzisothiazol-3-ones and 1,2-benzisothiazoles bearing diverse substituents in isothiazole and benzene rings. Thus, **4** reacts with dimethyl sulfate and benzyl chloride in DMF in the presence of K_2CO_3 to afford mixtures of 3-alkoxy-4,6-dinitro-1,2-benzisothiazoles (**19** and **20**) and 2-alkyl-4,6-dinitro-1,2-benzisothiazol-3-ones (**11** and **12**) in which products of O-alkylation **19** and **20** were the principal components (Scheme 4). Products of O- and N-alkylation were easily separated due to their different solubility in hexane: **19** and **20** are much more soluble

(20) Zlotin, S. G.; Kislitsin, P. G.; Serebryakov, E. A.; Samet, A. V.; Konyushkin, A. L.; Semenov, V. V.; Buchanan, A. C.; Gakh, A. A. *J. Org. Chem.* **2000**, *64*, 8430. Previous communication: Zlotin, S. G.; Serebryakov, E. A.; Kislitsin, P. G.; Konyushkin, L. D.; Semenov, V. V.; Buchanan, A. C. III.; Gakh, A. A. Abstract Paper, The 218th ACS National Meeting, New Orleans, 48-Orgn. Part 2, Aug 22, 1999.

(21) Hogg, D. R. In *Sulfenic acids and their derivatives" in "Comprehensive Organic Chemistry*; Barton, D., Ollis, W. D., Eds.; Pergamon Press Ltd.: New York, 1979; Vol. 3.

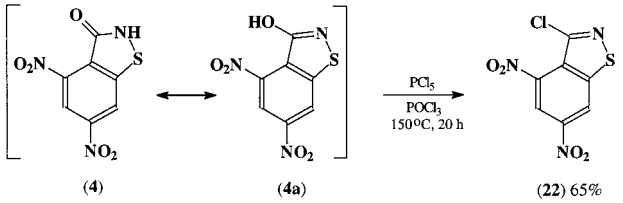
than **11** and **12**. Reaction of **4** with ethylchloroacetate under the same conditions afforded only (4,6-dinitro-1,2-benzisothiazol-3-yl)oxyacetic acid ethyl ester (**21**) in 44% yield.

Scheme 4



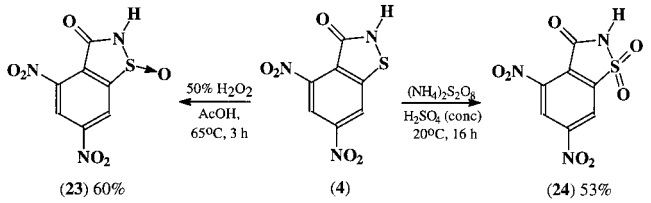
We also found that the carbonyl group in **4** can be replaced with chlorine, probably via tautomer **4a**. Indeed, **4** reacts with a mixture of PCl_5 and $POCl_3$ to give 3-chloro-4,6-dinitro-1,2-benzisothiazole (**22**) in 65% yield (Scheme 5). Prolonged heating (20 h) of the reaction mixture at 150 °C is required for completion of the reaction.

Scheme 5



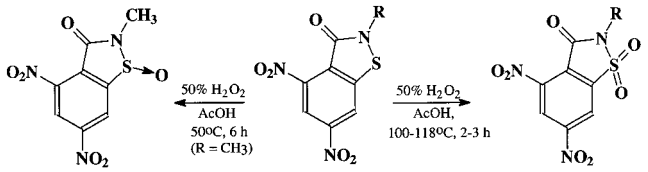
Reaction of **4** with 50% H_2O_2 in glacial acetic acid at 65 °C gave 4,6-dinitro-1,2-benzisothiazol-3-one S-oxide (**23**) in 60% yield. Further oxidation did not take place even if the reaction mixture was heated at 100 °C for several hours. However, we were able to prepare the 4,6-dinitro-1,2-benzisothiazol-3-one *S*,*S*-dioxide (**24**) ("dinitrosaccharine") in 53% yield by reaction of **4** with a stronger oxidizer such as ammonium persulfate in concentrated H_2SO_4 (Scheme 6).

Scheme 6



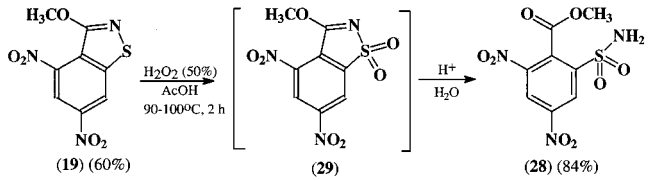
Unlike **4**, 2-methyl-4,6-dinitro-1,2-benzisothiazol-3-one (**11**) reacts with 50% H_2O_2 in glacial acetic acid to afford the S-oxide (**25**) or the S,S-dioxide (**26**), depending on the reaction conditions (Scheme 7). When the reaction was carried out at 50 °C, **25** was formed in 85% yield. On the other hand, 2-methyl-4,6-dinitro-1,2-benzisothiazol-3-one-S,S-dioxide (**26**) was prepared using boiling AcOH (118 °C). 4,6-Dinitro-2-phenyl-1,2-benzisothiazol-3-one (**13**) reacted with 50% H_2O_2 at 100−110 °C to afford the appropriate S,S-dioxide (**27**) in 54% yield.

Scheme 7



1,2-Benzisothiazoles are generally much more resistant toward oxidizers than 1,2-benzisothiazol-3-ones.[22] We found, however, that 4,6-dinitro-3-methoxy-1,2-benzisothiazole (**19**) reacted with 50% H_2O_2 in AcOH at 100 °C to afford 3,5-dinitro-2-(methoxycarbonyl)benzenesulfamide (**28**) in 84% yield. The reaction probably involves formation of 4,6-dinitro-3-methoxy-1,2-benzisothiazole-*S*,*S*-dioxide (**29**) followed by a hydrolytic cleavage of the C=N bond in **29** under the reaction conditions (Scheme 8).

Scheme 8



Conclusions

As a result of our investigations (see also ref 20), new synthetic routes for transformation of polynitroaromatic compounds to 4,6-dinitro-1,2-benzisothiazoles and 4,6-dinitro-1,2-benzisothiazol-3-ones have been developed. The overall strategy includes conversion of TNT to 2,4,6-trinitrobenzamides, nucleophilic substitution of an *o*-nitro group by benzylthio group, cyclization of 2-benzylthio-4,6-dinitrobenzamides to 4,6-dinitro-1,2-benzisothiazol-3-ones and subsequent derivatization (alkylation, chlorination, oxidation). Seventeen new heterocyclic compounds have been synthesized.

Experimental Section

General Methods. Compounds **1**−**3** were synthesized according to known procedures.[20]

Caution: *Polynitroaromatic compounds are potential explosives. Proper protective measures (shields, glasses) should*

(22) Davis, M. Benzisothiazoles. In *Adv. Heterocycl. Chem.*; Katritzky, A. R., Boulton, A. J., Eds.; Academic Press: New York, London, 1972; Vol. 3, p 43.

(23) To the best of our knowledge the mechanism of the formation of 1,2-benzisothiazolones in the reaction of *o*-alkylsulfanylbenzamides with halogenating agents has not been investigated yet. It is well established that S-aryl-S-benzylsulfides easily react with chlorinating agents with C−S bond cleavage to afford arylsulfanyl chlorides.[21] It is also known that 2-bromosulfanylbenzamide, that probably forms in the reaction of *S*,*S*′-bis[2-(aminocarbonyl)phenyl] disulfide with bromine, undergoes termal cyclization to 1,2-benzisothiazolone (A. Reissert, E. Manns, *Chem. Ber.* **1928**, *61*, 1308). These facts as well as literature data[7,13,17] (one step conversion of 2-alkylsulfanylarylamides to isothiazolones under the action of Cl_2 or SO_2Cl_2) suggest that the reaction includes transformation of 2-alkylsulfanyl-benzamides to 2-chlorosulfanylbenzamide followed by intramolecular cyclization of the latter to the appropriate fused isothiazolone. A likely mechanism for reaction of 2-benzylthio-nitrobenzamides with SO_2Cl_2 involves substitution of the benzyl group by chlorine, followed by intramolecular cyclization with the formation of the N−S bond. This mechanism could explain why 2-methoxycarbonylmethylthio-4,6-dinitrobenzamide (**1**) failed to react with SO_2Cl_2 compared to benzylthio derivative **3** since benzyl group is a better leaving group.

be used during experiments with these materials. Scale-up of the reported reactions requires appropriate chemical hazards testing.

4,6-Dinitro-1,2-benzisothiazol-3-one (4). Method A. To a stirred suspension of 2-methylthio-4,6-dinitrobenzamide (**2**)[20] (0.50 g, 1.9 mmol) in absolute CH_2Cl_2 (10 mL) was added SO_2Cl_2 (0.30 mL, 0.50 g, 3.7 mmol). The reaction mixture, which turned yellow immediately after the addition, was stirred at 15−20 °C for 2 h. A precipitate was filtered off, washed with CH_2Cl_2 (2 × 3 mL), hexane (2 × 3 mL), and then air-dried to afford 0.30 g (64%) of **4**, bright-yellow crystals: dec ∼270 °C; R_f 0.65 ($CHCl_3$−acetone 5:1); ^{1}H NMR (DMSO-d_6) δ 8.69 (s, 1H), 9.35 (s, 1H), very broad NH signal was not detected. Anal. Calcd for $C_7H_3N_3O_5S$: C, 34.86; H, 1.25; N, 17.42; S, 13.29. Found: C, 35.08; H, 1.34; N, 17.61; S, 13.05.

Method B. To a stirred suspension of 2-benzylthio-4,6-dinitrobenzamide (**3**)[20] (2.6 g, 7.8 mmol) in absolute CH_2Cl_2 (25 mL) was added SO_2Cl_2 (0.75 mL, 1.3 g, 9.3 mmol) at 20 °C. The mixture turned bright yellow immediately. It was stirred for 1 h and diluted with hexane (15 mL). The precipitate was filtered, washed with hexane (2 × 5 mL), and air-dried to yield 1.84 g (98%) of **4**. According to TLC and ^{1}H NMR spectra the compound was identical to **4** prepared by method A.

2-Substituted 4,6-Dinitro-1,2-benzisothiazol-3-ones 11−16. General Procedure. To a stirred suspension of N-substituted 2-benzylthio-4,6-dinitrobenzamide **5**−**10** containing ∼10% of the related 4-(benzylthio)derivative (**5a**−**10a**)[20] (5.8 mmol) in absolute CH_2Cl_2 (30 mL) was added SO_2Cl_2 (0.50 mL, 0.83 g, 6.17 mmol). The reaction mixture was stirred for 2 h at 20 °C during which period a clear brown-yellow solution formed. The solvent was evaporated in vacuo, and hexane (15 mL) was added to the solid residue. The precipitate was filtered, washed with hexane (2 × 5 mL), and air-dried. Recrystallization of the solid from *i*-PrOH (or its mixtures with acetone or heptane) afforded analytically pure 2-substituted 4,6-dinitro-1,2-benzisothiazol-3-one (**11**−**16**).

2-Methyl-4,6-dinitro-1,2-benzisothiazole-3-one (11): yellow crystals; 0.95 g (64%); mp 233−236 °C (*i*-PrOH−acetone); R_f 0.06 (CCl_4−acetone 4:1); ^{1}H NMR (DMSO-d_6): δ 3.42 (s, 3H), 8.55 (s, 1H), 9.25 (s, 1H). Anal. Calcd for $C_8H_5N_3O_5S$: C, 37.65; H, 1.97; N, 16.47; S, 12.56. Found: C, 37.82; H, 2.06; N, 16.29; S, 12.31.

2-Benzyl-4,6-dinitro-1,2-benzisothiazol-3-one (12): yellow crystals; 1.74 g (91%); mp 172−175 °C (*i*-PrOH−$CHCl_3$); R_f 0.28 (CCl_4−acetone 4:1); ^{1}H NMR (DMSO-d_6) δ 5.08 (s, 2H), 7.40 (br.s, 5H), 8.68 (s, 1H), 9.20 (s, 1H). Anal. Calcd for $C_{14}H_9N_3O_5S$: C, 50.76; H, 2.74; N, 12.68; S, 9.68. Found: C, 51.02; H, 2.85; N, 12.50; S, 9.37.

4,6-Dinitro-2-phenyl-1,2-benzisothiazol-3-one (13): yellow crystals; 1.55 g (84%); mp 229−231 °C (*i*-PrOH−acetone); R_f 0.24 (CCl_4−acetone 4:1); ^{1}H NMR (DMSO-d_6) δ 7.45 (t, 1H, J = 7.5 Hz), 7.58 (t, J = 7.5 Hz, 2H), 7.68 (d, J = 7.5 Hz, 2H), 8.77 (s, 1H), 9.29 (s, 1H). Anal. Calcd for $C_{13}H_7N_3O_5S$: C, 49.21; H, 2.22; N, 13.24; S, 10.10. Found: C, 49.02; H, 2.14; N, 13.41; S, 9.89.

2-(*p*-Bromophenyl)-4,6-dinitro-1,2-benzisothiazol-3-one (14): bright yellow crystals; 1.26 g (55%); mp 196−199 °C (*i*-PrOH−acetone); R_f 0.72 (benzene−acetone 4:1); ^{1}H NMR (DMSO-d_6): δ 7.65 (d, J = 7.5 Hz, 2H), 7.71 (d, J = 7.5 Hz, 2H), 8.65 (s, 1H), 9.30 (s, 1H). Anal. Calcd for $C_{13}H_6N_3BrO_5S$: C, 39.41; H, 1.53; N, 10.61; Br, 20.17; S, 8.09. Found: C, 39.18; H, 1.41; N, 10.85; Br, 19.79; S, 7.90.

2-[4′-(Chlorodifluoromethoxy)phenyl]-4,6-dinitro-1,2-benzisothiazol-3-one (15): yellow crystals; 1.83 g (76%); mp 128−131 °C (*i*-PrOH−heptane); R_f 0.70 (benzene−acetone 4:1); ^{1}H NMR (DMSO-d_6) δ 7.48 (d, J = 8.5 Hz, 2H), 7.83 (d, J = 8.5 Hz, 2H), 8.64 (s, 1H), 9.33 (s, 1H). Anal. Calcd for $C_{14}H_6N_3ClF_2O_6S$: C, 40.25; H, 1.45; N, 10.06; S, 7.67. Found: C, 40.03; H, 1.39; N, 10.28; S, 7.42.

2-(4′-Trifluoromethoxyphenyl)-4,6-dinitro-1,2-benzisothiazol-3-one (16): yellow crystals; 1.69 g (76%); mp 150−153 °C (*i*-PrOH−heptane); R_f 0.80 (benzene−acetone 4:1); ^{1}H NMR (DMSO-d_6) δ 7.58 (d, J = 8.5 Hz, 2H), 7.83 (d, J = 8.5 Hz, 2H), 8.77 (s, 1H), 9.29 (s, 1H). Anal. Calcd for $C_{14}H_6N_3F_3O_6S$: C, 41.91; H, 1.51; N, 10.47; S, 7.99. Found: C, 41.69; H, 1.45; N, 10.71; S, 7.70.

4-Benzylsulfonyl-6-nitro-1,2-benzisothiazol-3-one (18). To a solution of the mixture of 2-benzylsulfonyl-6-benzylthio-4-nitrobenzamide (**17**) and 2-benzylsulfonyl-4-benzylthio-6-nitrobenzamide (**17a**) (1:1), prepared as described previously[20] (1.8 g, 4.1 mmol), in CH_2Cl_2 (20 mL) was added SO_2Cl_2 (0.70 g, 0.40 mL, 5.2 mmol). The reaction mixture was stirred at 20 °C for 2 h. A yellow precipitate formed that was filtered, washed successively with CH_2Cl_2 (2 × 5 mL), hexane (2 × 5 mL), and air-dried to afford 0.60 g (84% calculated based on **17**) of **18**: mp 271−275 °C; R_f 0.32 (benzene−acetone 4:1); ^{1}H NMR (DMSO-d_6) δ 5.12 (s, 2H), 7.30 (br.s, 5H), 8.47 (s, 1H), 9.40 (s, 1H), very broad NH signal was not detected. Anal. Calcd for $C_{14}H_{10}N_2O_5S_2$: C, 47.99; H, 2.88; N, 8.00; S, 18.30. Found: C, 48.25; H, 3.01; N, 8.23; S, 18.08.

3-Methoxy-4,6-dinitro-1,2-benzisothiazole (19). To a solution of 4,6-dinitro-1,2-benzisothiazol-3-one (**4**) (1.0 g, 4.2 mmol) in absolute DMF (15 mL) were added successively with stirring K_2CO_3 (0.60 g, 4.4 mmol) and dimethylsulfate (0.40 mL, 0.53 g, 4.2 mmol). The reaction mixture was stirred at 20 °C for 6 h, and then poured into water (100 mL). The water suspension was neutralized to pH∼6−7 using 10% HCl. A precipitate was filtered, washed with water (2 × 10 mL), and dried in air. The solid was extracted with boiling heptane (5 × 10 mL). On cooling, a precipitate formed that was collected by filtration to yield 0.64 g (60%) of **19**: mp 135−138 °C (acetone−*i*-PrOH); R_f 0.53 (CCl_4−acetone 4:1); ^{1}H NMR (DMSO-d_6) δ 4.15 (s, 3H), 8.65 (s, 1H), 9.43 (s, 1H). Anal. Calcd for $C_8H_5N_3O_5S$: C, 37.65; H, 1.97; N, 16.47; S, 12.56. Found: C, 37.84; H, 2.00; N, 16.32; S, 12.39.

A residue insoluble in boiling heptane was recrystallized from $CHCl_3$−*i*-PrOH mixture to yield 0.24 g (22%) of 2-methyl-4,6-dinitro-1,2-benzisothiazol-3-one (**11**), yellow crystals: mp 231−235 °C. According to TLC and NMR ^{1}H spectra, the compound was identical to **11** prepared by reaction of *N*-methyl-2-benzylthio-4,6-dinitrobenzamide (**5**) with SO_2Cl_2.

3-Benzyloxy-4,6-dinitro-1,2-benzisothiazole (20). To a solution of 4,6-dinitro-1,2-benzoisothiazol-3-one (**4**) (1.0 g, 4.2 mmol) in absolute DMF (15 mL) were added with stirring K_2CO_3 (0.70 g, 5.1 mmol) and then benzyl chloride (0.60 mL, 0.66 g, 5.2 mmol). The reaction mixture was stirred at 45−50 °C for 5 h and poured into water (100 mL). The organic materials were extracted with ether (3 × 3 mL), and the combined organic layers were washed with water (2 mL) and then dried over anhydrous $MgSO_4$. The solvent was evaporated, and the residue was extracted with boiling hexane (5 × 10 mL). The hexane solution was cooled, and the precipitate was collected by filtration to yield 0.60 g (44%) of **20**: mp 135−136 °C; R_f 0.75 ($CHCl_3$); ^{1}H NMR (DMSO-d_6) δ 5.60 (s, 2H), 7.35−7.50 (m, 5H), 8.80 (s, 1H), 9.45 (s, 1H). Anal. Calcd for $C_{14}H_9N_3O_5S$: C, 50.76; H, 2.74; N, 12.68; S, 9.68. Found: C, 50.91; H, 2.80; N, 12.83; S, 9.44.

A residue insoluble in boiling hexane was recrystallized from a $CHCl_3$ − *i*-PrOH mixture to yield 0.20 g (15%) of 2-benzyl-4,6-dinitro-1,2-benzisothiazol-3-one (**12**), yellow crystals: mp 172−175 °C. According to TLC and ^{1}H NMR, the compound was identical to **12** prepared by reaction of *N*-benzyl-2-benzylthio-4,6-dinitrobenzamide (**6**) with SO_2Cl_2.

(4,6-Dinitro-1,2-benzisothiazol-3-yl)oxyacetic Acid Ethyl Ester (21). A mixture of 4,6-dinitro-1,2-benzisothiazol-3-one (**4**) (1.0 g, 4.2 mmol), ethyl chloroacetate (0.50 mL, 0.58 g, 4.7 mmol), K_2CO_3 (0.58 g, 4.2 mmol), and dry DMF (15 mL) was stirred at 40−45 °C for 8 h and then kept at 12 °C overnight. The mixture was poured into water (100 mL) and extracted with ether (5 × 30 mL). The combined ether extracts were dried over anhydrous $MgSO_4$, the solvent was evaporated in vacuo, and the residue was extracted with boiling hexane (5 × 20 mL). A precipitate formed on cooling, which was filtered, washed with hexane, and air-dried to afford 0.60 g (44%) of **21**: yellow crystals; mp 117−120 °C; R_f 0.42 (benzene); ^{1}H NMR (DMSO-d_6) δ 1.25 (t, J = 7.0 Hz, 3H), 4.20 (q, J = 7.0 Hz, 2H), 5.10 (s, 2H), 8.70 (s, 1H), 9.47 (s, 1H). Anal. Calcd for $C_{11}H_9N_3O_7S$: C, 40.37; H, 2.77; N, 12.84; S, 9.80. Found: C, 40.56; H, 2.84; N, 13.01; S, 9.67.

3-Chloro-4,6-dinitro-1,2-benzisothiazole (22). A mixture of 4,6-dinitro-1,2-benzisothiazol-3-one (**4**) (1.0 g, 4.2 mmol), PCl_5 (5.0 g, 24 mmol), and $POCl_3$ (1 mL) was heated at 150 °C for 20 h. Excess quantities of PCl_5 and $POCl_3$ were destroyed by addition of ice (~100 g). Organic materials were extracted with $CHCl_3$ (2 × 50 mL). The combined organic extracts were washed with water (2 × 20 mL), dried over anhydrous $MgSO_4$, and filtered. Evaporation of the solvent and crystallization of the residue from *i*-PrOH afforded 0.70 g (65%) of **22**: mp 127−129 °C; R_f 0.41 (CCl_4−acetone 4:1); ^{1}H NMR (DMSO-d_6) δ 8.94 (s, 1H), 9.62 (s, 1H). Anal. Calcd for $C_7H_2N_3ClO_4S$: C, 32.38; H, 0.78; N, 16.19; C1, 13.66; S, 12.35. Found: C, 32.17; H, 0.82; N, 15.99; Cl, 13.84; S, 12.17. After the submission of the manuscript a compound described as 3-chloro-4,6-dinitrobenzo[*d*]isothiazole (from 2,4,6-trinitrobenzonitrile) was reported elsewhere (Dalinger, I. L.; Cherkasova, T. I.; Khutoretskii, V. M.; Shevelev, S. A. *Mendeleev Comm*. **2000**, 72). However, mp and ^{1}H NMR of this compound are significantly different compared to our data.

4,6-Dinitro-1,2-benzisothiazol-3-one *S*-Oxide (23). To a stirred suspension of 4,6-dinitro-1,2-benzisothiazol-3-one (**4**) (0.20 g, 0.83 mmol) in glacial acetic acid (1 mL) was added 50% H_2O_2 (1 mL). The reaction mixture was stirred at 65 °C for 3 h. After cooling, a precipitate was filtered, washed with water, and air-dried to yield 0.13 g (60%) of **23**: pale-yellow solid; mp 262−263 °C; R_f 0.26 ($CHCl_3$−acetone 5:1); ^{1}H NMR (DMSO-d_6) δ 9.13 (s, 1H), 9.35 (s, 1H); MS (*m*/*z*, I) 257 (M^+, 10), 211 ($M^+ - NO_2$, 13), 194 (M^+ − HNSO, 38), 148 (M^+ − HNSO − NO_2, 18), 74 (S−N=C=O, 100). Anal. Calcd for $C_7H_3N_3O_6S$: C, 32.69; H, 1.18; N, 16.34; S, 12.47. Found: C, 32.84; H, 1.13; N, 16.18; S, 12.30.

4,6-Dinitro-1,2-benzisothiazol-3-one *S*,*S*-Dioxide (24). A suspension of 4,6-dinitro-l,2-benzisothiazol-3-one (**4**) (0.15 g, 0.62 mmol) and $(NH_4)_2S_2O_8$ (0.57 g, 2.5 mmol) in 95% H_2SO_4 (2 mL) was stirred at 20 °C for 16 h. The reaction mixture was poured on ice (~20 g) and extracted with ethyl acetate (5 × 5 mL), and the combined organic layers were washed with water (3 × 2 mL) and dried over anhydrous $MgSO_4$. Evaporation of the solvent and recrystallization of the residue from an *i*-PrOH−hexane mixture afforded 0.09 g (53%) of **24**: colorless crystals; mp 267−270 °C dec; R_f 0.13 ($CHCl_3$−acetone 5:1); ^{1}H (DMSO-d_6) δ 8.70 (s, 1H), 8.92 (s, 1H); MS (*m*/*z*, I) 273 (M^+, 20), 209 ($M^+ - SO_2$, 28), 74 (S−N=C=O, 100). Anal. Calcd for $C_7H_3N_3O_7S$: C, 30.78; H, 1.11; N, 15.38; S, 11.74. Found: C, 30.59; H, 1.06; N, 15.52; S, 11.57.

2-Methyl-4,6-dinitro-1,2-benzisothiazol-3-one *S*-Oxide (25). To a stirred suspension of 2-methyl-4,6-dinitro-1,2-benzisothiazole-3-one (**11**) (0.43 g, 1.69 mmol) in glacial acetic acid (9 mL) was added 50% H_2O_2 (0.6 mL). The reaction mixture was stirred at 50 °C for 6 h. After cooling, a precipitate was filtered, washed with AcOH (2 × 2 mL), water (2 mL), dried in the air, and recrystallized from an acetone−*i*-PrOH mixture to yield 0.39 g (85%) of **25**: pale yellow solid; mp 205−206 °C; R_f 0.09 (CCl_4−acetone 4:1); ^{1}H NMR (DMSO-d_6) δ 3.32 (s, 3H), 9.18 (s, 1H), 9.41 (s, 1H); MS (*m*/*z*, I) 271 (M^+, 24), 194 ($M^+ - CH_3$−N=S=O, 100), 148 ($M^+ - CH_3N$=S=O − NO_2, 31), 120 ($M^+ - CH_3N$=S=O − NO_2 −CO, 50); IR spectra (ν, cm^{-1}) 3090, 3000, 2940, 2890 (CH), 1705 (C=O), 1610, 1545 (NO_2), 1360 (NO_2), 1320, 1140 (S−O). Anal. Calcd for $C_8H_5N_3O_6S$: C, 35.43; H, 1.86; N, 15.49; S, 11.82. Found: C, 35.60; H, 1.94; N, 15.63; S, 11.62.

2-Methyl-4,6-dinitro-1,2-benzisothiazol-3-one *S*,*S*-Dioxide (26). A mixture of 2-methyl-4,6-dinitro-1,2-benzisothiazol-3-one (**11**) (0.47 g, 1.8 mmol), 50% H_2O_2 (1.0 mL), and glacial acetic acid (6 mL) was refluxed for 3 h. The solvent was evaporated *in vacuo*, water (5 mL) was added to a residue, a precipitate was filtered and washed with water (2 mL), dried in the air, and recrystallized from acetone−*i*-PrOH mixture to yield 0.15 g (28%) of **26**: colorless solid; mp 240−243 °C; R_f 0.28 (CCl_4−acetone 4:1); ^{1}H NMR (DMSO-d_6) δ 3.25 (s, 3H), 9.22 (s, 1H), 9.50 (s, 1H). Anal. Calcd for $C_8H_5N_3O_7S$: C, 33.46; H, 1.75; N, 14.63; S, 11.16. Found: C, 33.68; H, 1.83; N, 14.48; S, 10.97.

4,6-Dinitro-2-phenyl-1,2-benzisothiazol-3-one *S*,*S*-Dioxide (27). A mixture of 4,6-dinitro-2-phenyl-1,2-benzisothiazol-3-one (**13**) (0.50 g, 1.6 mmol), 50% H_2O_2 (2.0 mL) and glacial AcOH (10 mL) was heated at 100 °C for 2 h. The starting compound (**13**) was dissolved completely followed by formation of a colorless precipitate. The reaction mixture was cooled to 20 °C for 12 h. The resulting precipitate was filtered, washed with water (2 × 5 mL), and air-dried to yield 0.30 g (54%) of **27**: dec 250 °C; R_f 0.41(benzene); ^{1}H NMR (DMSO-d_6) δ 7.60 (m, 2H),7.68 (m, 3H), 9.35 (s, 1H), 9.68 (s, 1H); MS (*m*/*z*, I) 349 (M^+, 42), 119 (PhNCO, 35), 91 (PhN, 100), 74 (C_6H_2, 93), 64 (SO_2, 66). Anal. Calcd for $C_{13}H_7N_3O_7S$: C, 44.70; H, 2.02; N, 12.03; S, 9.18. Found: C, 44.89; H, 1.97; N, 11.92; S, 8.98.

3,5-Dinitro-2-(methoxycarbonyl)benzenesulfamide (28). A mixture of 3-methoxy-4,6-dinitro-1,2-benzisothiazole (**19**) (0.20 g, 0.80 mmol), 50% H_2O_2 (2.0 mL), and glacial acetic acid (10 mL) was heated at 90−100 °C for 2 h. The solvent was evaporated in vacuo, water (3 mL) was added to the residue, and the precipitate was filtered, washed with water (2 × 5 mL), and air-dried to yield 0.20 g (84%) of **28**: mp 170−174 °C; ^{1}H NMR (DMSO-d_6) δ 3.96 (s, 3H), 8.00 (s, 2H), 9.00 (s, 1H), 9.10 (s, 1H); MS (*m*/*z*, I) 305 (M^+, 3), 289 (M^+ − O, 17), 275 (M^+ − O − CH_2, 21), 274 (M^+ − O − NH, 100), 228 (M^+ − O − NH − NO_2, 26). Anal. Calcd for $C_8H_7N_3O_8S$: C, 31.48; H, 2.31; N, 13.77; S, 10.50. Found: C, 31.71; H, 2.39; N, 13.63; S, 10.35.

Acknowledgment. The research was sponsored by the IPP program, U.S. Department of Energy under contract DE-AC05-00OR22725 with Oak Ridge National Laboratory, managed and operated by UT-Battelle, LLC.

JO000480C