Pergamon

Tetrahedron 55 (1999) 14885–14900

TETRAHEDRON

New Synthetic Method to 1,2-Benzisothiazoline-3-one-1,1-dioxides and 1,2-Benzisothiazoline-3-one-1-oxides from *N*-Alkyl(*o*-methyl)arenesulfonamides

Masashi Katohgi[a)], Hideo Togo*[a,b)], Kentaro Yamaguchi[c)], and Masataka Yokoyama[a,b)].

a) Graduate School of Science and Technology, b) Department of Chemistry, Faculty of Science, c) Chemical Analysis Center, Chiba University, Yayoi-cho 1-33, Inage-ku, Chiba 263-8522 Japan

Received 8 September 1999; accepted 28 October 1999

Abstract: Various *N*-alkylsaccharins were easily prepared in moderate to good yields by the reaction of *N*-alkyl(*o*-methyl)arenesulfonamides with (diacetoxyiodo)benzene in the presence of iodine under irradiation with a tungsten lamp (W-hv). On the other hand, irradiation of *N*-alkyl(*o*-methyl)arenesulfonamide derivatives bearing various substituents on the aromatic ring with a high-pressure mercury lamp (Hg-hv), in the presence of (diacetoxyiodo)benzene and iodine gave the corresponding *N*-alkyl-1,2-benzisothiazoline-3-one-1-oxide derivatives in moderate yields, together with *N*-alkyl-1,2-benzisothiazoline-3-one-1,1-dioxide (saccharin) derivatives.

Keywords: 1,2-benzisothiazoline-3-one-1,1-dioxide derivatives, 1,2-benzisothiazoline-3-one-1-oxide derivatives, (diacetoxyiodo)benzene

Introduction

Trivalent iodine compounds have been used for various organic syntheses. For example, oxidation, halogenation, alkylation, and arylation have been studied, and most of these reactions proceed through ionic reaction pathways.[1] On the other hand, the reactions through radical pathways have also been studied extensively as follows. For instance, (diacyloxyiodo)arenes can generate alkyl,[2] alkoxy,[3] aminyl,[4] and aryl cation radicals[5] by the reaction of carboxylic acids, alcohols, amines, and electron-rich aromatics, respectively. Here, the alkyl radicals formed were used for C-C bond formations such as alkylation of π-deficient heteroaromatic compounds, addition to activated olefins having electron-withdrawing groups, and functionalization. Oxygen-centered radicals, such as carbonyloxy radicals and alkoxy radicals, were used for intramolecular cyclization[6] and fragmentation. In the case of nitrogen-centered radicals, the Hofmann-Löffler-Freytag-type reactions by the photolysis of *N*-nitroamine, *N*-cyanamide, and *N*-phosphoramidate derivatives from steroidal compounds, with (diacetoxyiodo)benzene or iodosobenzene,[4] have been studied by Suárez.

Today, it is well-known that many isothiazole derivatives exhibit biological activity in the medical and agrochemical fields.[7] Among them, saccharin derivatives, *i.e.*, α-ethyl[3-oxo-1,2-benzisothiazole-2(3H)]acetamide-1,1-dioxide and 2-{4-[4-(2-pyrimidinyl)piperazinyl]butyl}-3-oxo-1,2-benzisothiazole-2(3H)-1,1-dioxide (Ipsapirone), have potent antibacterial, sedative-hypnotic, anti-anxiety and anti-convulsant activities.[7] Recently, as an orally active bioavailable human leukocyte elastase (HLE)

PII: S0040-4020(99)00974-6

inhibitor, [6-methoxy-4-isopropyl-3-oxo-1,2-benzisothiazole-2(3H)-yl]methyl-2,6-dichloro-3-[2-(4-morpholinyl)ethoxy]benzoate-*S*,*S*-dioxide (WIN) series[8], saccharin-based inhibitors, were found to have potent HLE inhibitory activity. Therefore, extensive studies on the preparation of these skeletons have been carried out, mainly by the *ortho*-lithiation and subsequent sulfonation of benzamide, or the *ortho*-lithiation and subsequent carbonation of benzenesulfonamides.[9]

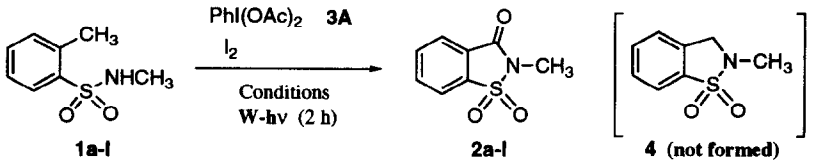
Here, as a part of our study on the synthetic use of sulfonamidyl radicals,[10] we would like to report the direct preparation of various 1,2-benzisothiazoline derivatives, including saccharin derivatives, from various *N*-alkyl(*o*-methyl)arenesulfonamides with (diacetoxyiodo)arenes in the presence of iodine *via* sulfonamidyl radicals.[11]

Results and Discussion

Conversion to the Saccharin (1,2-Benzisothiazoline-3-one-1,1-dioxide) Derivatives.

To carry out the cyclization to *N*-alkyl-1,2-benzosultams *via* a sulfonamidyl radical, *N*-methyl(*o*-methyl)benzenesulfonamide **1a-I** was treated with (diacetoxyiodo)benzene **3A** and iodine in 1,2-dichloroethane under irradiation with a tungsten lamp (**W-hv**, 500 W), and the unexpected cyclization product, *N*-methylsaccharin **2a-I**, was obtained. However, *N*-methyl-1,2-benzosultam **4** was not formed. The reaction also proceeds in ethyl acetate which is a less toxic solvent (entry 8 in Table 1). The reaction was completely inhibited by the addition of a galvinoxyl free radical (entry 7 in Table 1). This result suggests that the reaction proceeds by way of a radical pathway, indirectly. Moreover, as the reaction temperature was elevated, the yields slightly increased. The various conditions to optimize the yield were carried out as shown in Table 1.

Table 1. Direct Formation of Saccharin Skeleton



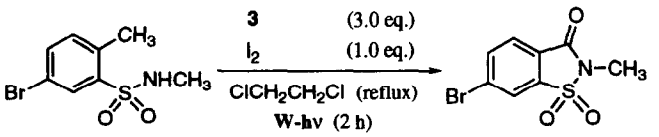
1a-I **2a-I** **4 (not formed)**

entry	Conditions			Yield (%)
	Ratio (**1a-I** / **3A** / I_2)	Temp.	Solvent	**2a-I**
1	1.0 / 1.6 / 1.0	25 ~ 30 °C	$ClCH_2CH_2Cl$	37
2	1.0 / 1.6 / 1.0	55 ~ 60 °C	$ClCH_2CH_2Cl$	51
3	1.0 / 2.4 / 1.0	55 ~ 60 °C	$ClCH_2CH_2Cl$	55
4	1.0 / 3.0 / 1.0	55 ~ 60 °C	$ClCH_2CH_2Cl$	57
5	1.0 / 3.0 / 1.0	reflux	$ClCH_2CH_2Cl$	61
6	1.0 / 3.0 / 2.0	reflux	$ClCH_2CH_2Cl$	22
7	1.0 / 3.0 / 1.0	reflux	$ClCH_2CH_2Cl$	0[a)]
8	1.0 / 3.0 / 1.0	reflux	AcOEt	56

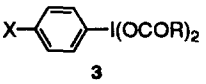
a) Galvinoxyl free radical (1.5 eq.) was added.

The substituent effect of (diacetoxyiodo)arene **3** in the formation of *N*-methyl-6-bromosaccharin **2b-I** from sulfonamide **1b-I** was studied. Here, (diacetoxyiodo)benzene (**3A**) showed the best reactivity (entry 1). However, other (diacetoxyiodo)arenes gave compound **2b-I** in low yields; especially, [bis(trifluoroacetoxy)iodo]benzene (**3E**) gave a complex reaction mixture, without formation of compound **2b-I**.

Table 2. Substituent Effect of (Diacyloxyiodo)arenes



1b-I **2b-I**



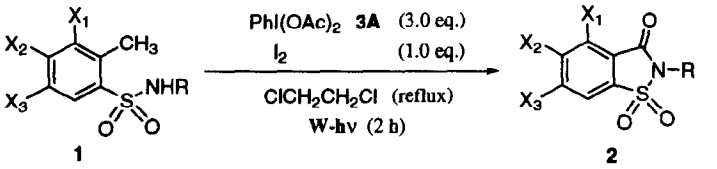
3

entry	3 - X	3 - R		Yield (%) 2b-I
1	- H	- CH_3	**3A**	80
2	- OCH_3	- CH_3	**3B**	29
3	- CH_3	- CH_3	**3C**	28
4	- Cl	- CH_3	**3D**	63
5	- H	- CF_3	**3E**	0
6	- H	- CH_2CH_3	**3F**	29

Next, the substituent effect of *N*-alkyl groups, *N*-methyl (**I**), *N*-ethyl (**II**), *N*-propyl (**III**), *N*-butyl (**IV**), and *N*-benzyl (**V**), with sulfonamide **1c** was investigated. Thus, the substituent effect was clearly observed and the *N*-methyl group (**1c-I**) gave the *N*-methyl-6-methylsaccharin **2c-I** in the best yield among these alkyl groups, while other *N*-alkyl(*o*-methyl)arenesulfonamides did not form the corresponding saccharin derivatives effectively as shown in Table 3 (entries 1~5). Here, in entry 5, using *N*-benzyl(*o*-methyl)arenesulfonamide as the starting material, benzaldehyde was obtained in 20% yield. The same treatment with *o*-toluenesulfonamide, without *N*-alkyl group, did not give the corresponding cyclized product **2** at all (entry 6).

Then, *N*-methyl(*o*-methyl)arenesulfonamides (**1-I**), which bear various substituents on the aromatic rings (**d~h**), were treated with (diacetoxyiodo)benzene and iodine under the best conditions, based on the above results, and the corresponding *N*-methylsaccharins were obtained in moderate to good yields as shown in Table 3. In entry 11, the starting material was recovered in 32% yield together with saccharin derivative **2g-I**. Here, the substituent effect on the aromatic ring is not clear. However, the electron-withdrawing group apparently reduces the reactivity.

Table 3. Conversion of Various Sulfonamides to Saccharin Derivatives



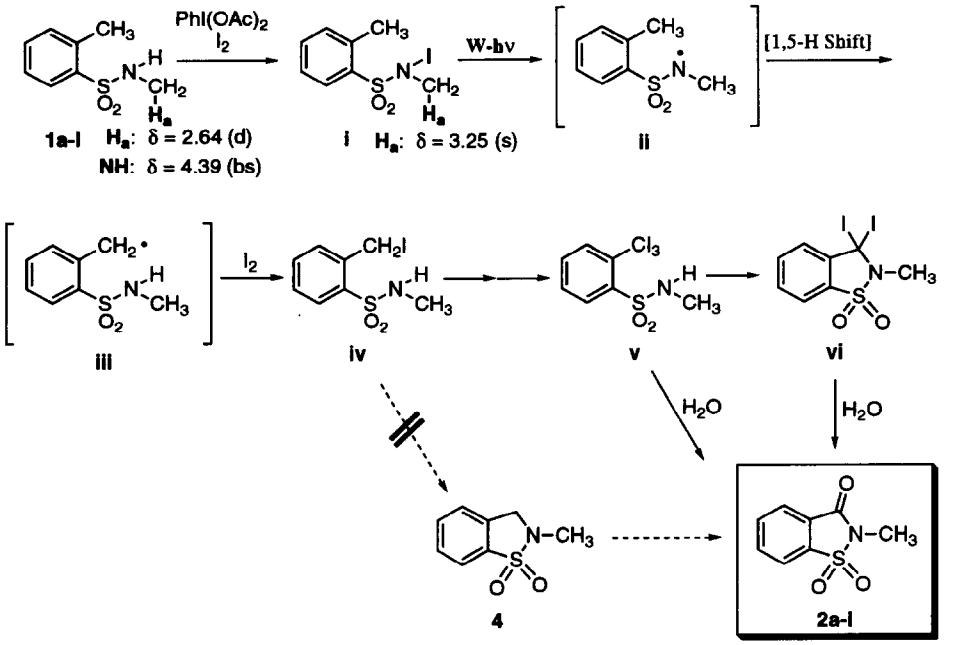
entry	1					Yield (%)
	$-X_1$	$-X_2$	$-X_3$	-R		2
1	-H	-H	$-CH_3$	$-CH_3$	**(1c-I)**	99
2	-H	-H	$-CH_3$	$-CH_2CH_3$	**(1c-II)**	33
3	-H	-H	$-CH_3$	$-(CH_2)_2CH_3$	**(1c-III)**	33
4	-H	-H	$-CH_3$	$-(CH_2)_3CH_3$	**(1c-IV)**	25
5	-H	-H	$-CH_3$	$-CH_2C_6H_5$	**(1c-V)**	0[a]
6	-H	-H	$-CH_3$	-H	**(1c-VI)**	0
7	-H	-H	-Br	$-CH_3$	**(1b-I)**	80
8	-H	$-CH_3$	-H	$-CH_3$	**(1d-I)**	84
9	$-CH_3$	-H	$-C(CH_3)_3$	$-CH_3$	**(1e-I)**	42
10	-H	-H	$-CONEt_2$	$-CH_3$	**(1f-I)**	45
11	-H	-H	$-NO_2$	$-CH_3$	**(1g-I)**	48
12	-H	-H	$-SO_2CH_3$	$-CH_3$	**(1h-I)**	51

a) Benzaldehyde was obtained in 20% yield.

Many types of saccharin derivatives having biological activities have been reported in the medical and agrochemical fields. However, all of the preparation methods of saccharin derivatives usually require butyllithium (BuLi), a powerful nucleophile and base, and therefore, the type of substituents on the aromatic rings is strictly limited. On the other hand, saccharin derivatives having various substituents on the aromatic rings with the present novel preparation method were easily prepared in moderate to good yields. A plausible reaction mechanism for the present reaction is shown in Scheme 1. Here, the formation of *N*-iodo compound **i** could be observed by ^{1}H NMR under dark conditions. Then, irradiation of the solution with a tungsten-lamp showed that *N*-iodo compound **i** was consumed completely, and only a small amount of a saccharin derivative was observed in the reaction solution by ^{1}H-NMR. However, a saccharin skeleton was mainly formed after preparative-TLC (pTLC) treatment of the reaction mixture. Moreover, compound **4** is not an intermediate which is formed *via* the Hofmann-Löffler-Freytag-type reaction pathway as expected previously, because it was not converted to the saccharin **2a-I** under the same conditions by the blank experiment. Compounds **iv~vi**, which could not be isolated due to their chemical instability, are likely to be the intermediates.

In addition, the present reaction does not proceed at all under dark conditions, and also lack of (diacetoxyiodo)benzene or iodine does not give the saccharin derivatives. The same treatment of *N*-

methyl(*o*-methyl)benzamide, instead of *N*-methyl(*o*-methyl)arenesulfonamide, with (diacetoxyiodo)-benzene and iodine was not a clean reaction and gave *N*-methylphthalimide only in 25% yield.



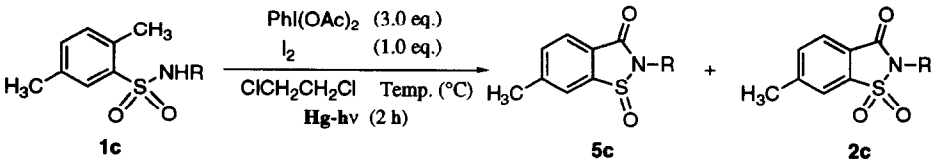
Scheme 1. Plausible Reaction Mechanism (Formation of **2a-I**)

Conversion of *N*-Alkyl(*o*-methyl)arenesulfonamides to 1,2-Benzisothiazoline-3-one-1-oxide Derivatives and 1,2-Benzisothiazoline-3-one-1,1-dioxide Derivatives.

As a further extension for the construction of the saccharin skeleton, we carried out the same reaction with compound **1c** under the irradiation with a high-pressure mercury lamp (**Hg-hv**), instead of a tungsten lamp. However, surprisingly, the unexpected monodeoxygenative cyclized products, 1,2-benzisothiazoline-3-one-1-oxide derivatives **5c**, were obtained in moderate yields, together with 1,2-benzisothiazoline-3-one-1,1-dioxide (saccharin) derivatives **2c**.

The formation of compounds **5c** depends on the *N*-alkyl group of starting material **1c** (entries 1~6). Thus, among various *N*-alkyl derivatives, the ethyl derivative **1c-II** gave the best yield of **5c**, as shown in Table 4 (entry 2). Again, free sulfonamide **1c-VI** did not give the cyclized products at all (entry 6) Moreover, the same reaction was carried out under various temperatures. Here, the best yield of **5c-II** was obtained at room temperaturer (25~35 °C). As the reaction temperature was elevated , the yield of **5c-II** decreased and the yield of **2c-II** increased. Based on these results, the photodeoxygenative cyclization

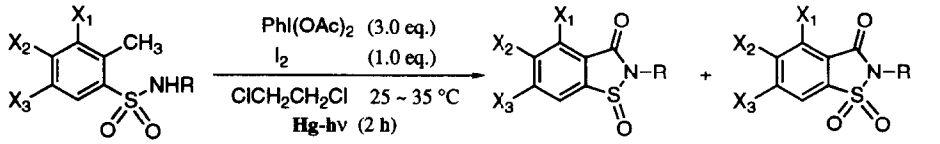
Table 4. Effect of *N*-Alkyl Groups in Sulfonamides and Reaction Temperature.



1c 5c 2c

entry	1c - R		Temp. (°C)	Yields (%) 5c	2c
1	$-CH_3$	**(1c-I)**	25 ~ 35	20	53
2	$-CH_2CH_3$	**(1c-II)**	25 ~ 35	43	40
3	$-(CH_2)_2CH_3$	**(1c-III)**	25 ~ 35	38	47
4	$-(CH_2)_3CH_3$	**(1c-IV)**	25 ~ 35	20	55
5	$-CH_2C_6H_5$	**(1c-V)**	25 ~ 35	23	27
6	-H	**(1c-VI)**	25 ~ 35	0	0
7	$-CH_2CH_3$	**(1c-II)**	10 ~ 15	19	16
8	$-CH_2CH_3$	**(1c-II)**	35 ~ 40	35	40
9	$-CH_2CH_3$	**(1c-II)**	45 ~ 50	38	47
10	$-CH_2CH_3$	**(1c-II)**	55 ~ 60	20	55

Table 5. Conversion of Various Sulfonamides to Benzisothiazoline Compounds



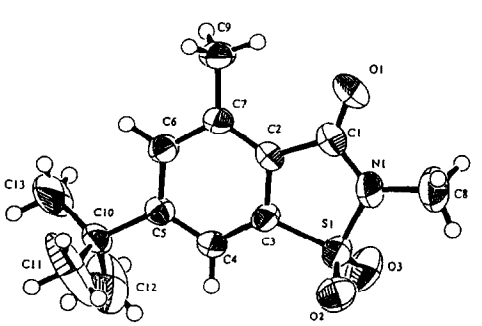
1 5 2

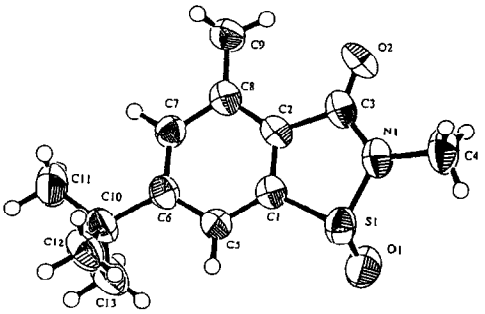
entry	1 -X_1	-X_2	-X_3	-R		Yields (%) 5	2
1	-H	-H	-H	$-CH_2CH_3$	**(1a-II)**	22	41
2	-H	-H	-Br	$-CH_2CH_3$	**(1b-II)**	17	39
3	-H	-H	$-CH_3$	$-CH_2CH_3$	**(1c-II)**	43	40
4	-H	$-CH_3$	-H	$-CH_2CH_3$	**(1d-II)**	40	37
5	$-CH_3$	-H	$-C(CH_3)_3$	$-CH_2CH_3$	**(1e-II)**	43	46
6	-H	-H	$-CONEt_2$	$-CH_2CH_3$	**(1f-II)**	16	37
7	-H	-H	$-NO_2$	$-CH_2CH_3$	**(1g-II)**	trace	51
8	-H	-H	$-SO_2CH_3$	$-CH_2CH_3$	**(1h-II)**	21	53
9	$-CH_3$	$-CH_3$	-H	$-CH_2CH_3$	**(1i-II)**	46	41
10	$-CH_3$	$-CH_3$	$-CH_3$	$-CH_2CH_3$	**(1j-II)**	41	37
11	-H	-Br	$-CH_3$	$-CH_2CH_3$	**(1k-II)**	25	41
12	$-CH_3$	-H	$-C(CH_3)_3$	$-CH_3$	**(1e-I)**	32	50

with various kinds of *N*-ethyl(*o*-methyl)arenesulfonamides **1** was carried out and the results are shown in Table 5. Here, 1,2-benzisothiazoline derivatives were obtained in moderate to good yields. The yield of compound **2** was unchanged with each substrate; however, the yield of compound **5** was drastically decreased when an electron-withdrawing group was introduced onto the aromatic ring of the starting sulfonamide **1**. Nevertheless, to our knowledge, the synthetic methodology of 1,2-benzisothiazoline-3-one-1-oxide derivatives **5** is quite limited.[12] Therefore, the present new reaction should be very useful for the preparation of compound **5** as an analogue of a saccharin skeleton, because the comparison of the biological activities of compounds **2** and **5** is attractive.

The formation of compound **5** does not occur under irradiation with a low-pressure mercury lamp (25W) in a quartz cell or a tungsten lamp. The structures of compounds **2e-I** and **5e-I** were supported by the X-ray crystal structure analysis as shown in Fig. 1.

Fig. 1 X-Ray Crystal Structures of Compounds **2e-I** and **5e-I**





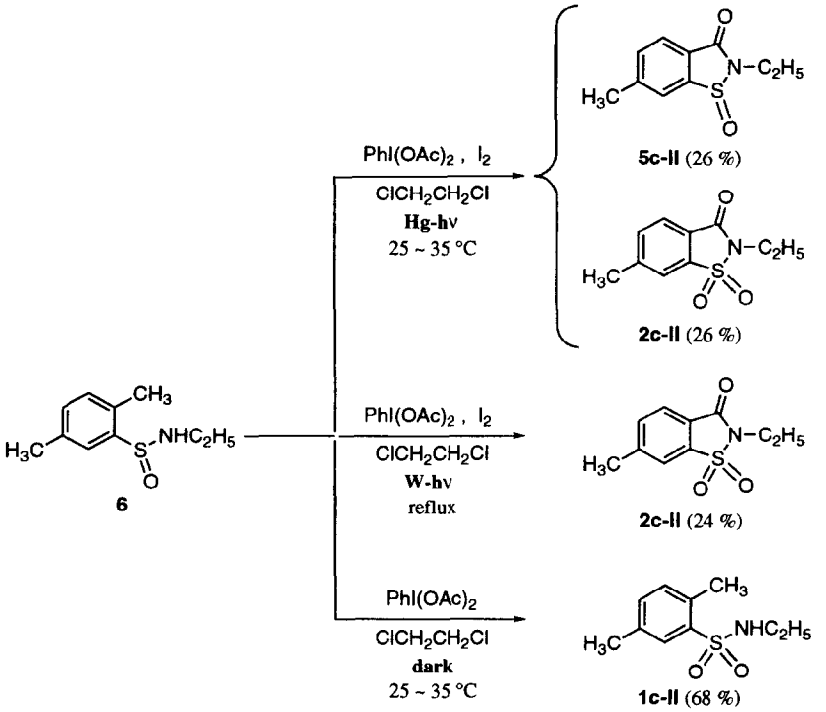
2e-I Bond Lengths (Å)
S(1) - N(1) 1.657
S(1) - C(3) 1.748
S(1) - O(2) 1.412
S(1) - O(3) 1.481

Bond Angles (°)
C(3) - S(1) - N(1) 92.8

5e-I Bond Lengths (Å)
S(1) - N(1) 1.707
S(1) - C(1) 1.755
S(1) - O(1) 1.482

Bond Angles (°)
C(1) - S(1) - N(1) 89.0

Next, to clarify the reaction mechanism, some control experiments were performed. As a result, compound **5c-II** and compound **2c-II** did not interconvert, under the present reaction conditions. Furthermore, the same treatment with *N*-ethyl-2,5-dimethylbenzenesulfinamide **6** was carried out to give compounds **5c-II** and **2c-II** in 26% and 26% yields, respectively.



Scheme 2. Control Experiments

Here, the benzisothiazoline compound was not formed under dark conditions and the lack of (diacetoxyiodo)benzene or iodine did not give benzisothiazoline compounds again. However, on treatment of sulfinamide **6** with (diacetoxyiodo)benzene in 1,2-dichloroethane solution under dark conditions at room temperature, *N*-ethyl-2,5-dimethylsulfonamide **1c-II** was obtained in 68% yield. From these results, it was found that compounds **2c-II** and **5c-II** were formed *via* the formation of compound **1c-II** in the above reaction with *N*-ethyl-2,5-dimethylbenzenesulfinamide **6**.

The reaction mechanism for the formation of compound **5** under the irradiation with Hg-hv is still not clear. However, compound **5** may be formed through a radical pathway *via* the corresponding sulfonamidyl radical formed from *N*-iodo compound **i**, in Scheme 1.

In conclusion, the present reactions are very useful for the preparation of various 1,2-benzisothiazoline-3-one-1,1-dioxides and 1,2-benzisothiazoline-3-one-1-oxides, because the starting

sulfonamides are obtained easily by the chlorosulfonation of methylarenes and subsequent amidation with alkylamine, and the experimental operation is simple, giving the products in good yields.

Experimental Section

General: All reactions were carried out under an argon atmosphere. ^{1}H NMR spectra were measured with 400 MHz and 500 MHz spectrometers, and ^{13}C NMR spectra were measured with 100 MHz and 125 MHz spectrometers. Chemical shifts are reported as ppm downfield from tetramethylsilane (TMS) in δ units. *J* Values are given in Hz. Melting points were determined on an electrothermal apparatus in open capillary tubes and are uncorrected. Wakogel C-200 and C-300 were used for column chromatography, Kieselgel 60 F254 (Merck) was used for TLC, and Wakogel B-5F was used for p-TLC.

Materials: (Diacetoxyiodo)benzene and [bis(trifluoroacetoxy)iodo]benzene are commercially available. Other (diacetoxyiodo)arenes were prepared by the oxidation of the corresponding iodoarenes by the literature method.[13] Most *N*-alkyl(*o*-methyl)arenesulfonamides were easily prepared by the chlorosulfonation of methylarenes and subsequent amidation with alkylamine. *N*-Ethyl-2,5-dimethylbenzenesulfinamide was prepared as follows: chlorosulfonation of *p*-xylene, treatment with sodium sulfite (Na_2SO_3), consecutive trimethylsilyl chloride (TMSCl), and subsequent amidation with ethylamine.[14]

Typical Procedure: Conversion of *N*-Alkyl(*o*-methyl)arenesulfonamides to the Saccharin Derivatives: (Diacctoxyiodo)benzene (1.5 mmol) and iodine (0.5 mmol) were added to a solution of *N*-alkyl(*o*-methyl)arenesulfonamide (0.5 mmol) in 1,2-dichloroethane (7 ml). The mixture was irradiated with a tungsten-lamp (500 W) at refluxing temperature for 2 h under an argon atmosphere. After the reaction, the mixture was poured into chloroform and washed with aq. sodium sulfite solution and subsequently with water. The organic layer was dried over sodium sulfate. After removal of the solvent under reduced pressure, the residue was chromatographed by p-TLC on silica gel using a mixture of hexane and ethyl acetate (1:3-10:1) as an eluent.

Typical Procedure: Conversion of *N*-Alkyl(o-methyl)arenesulfonamides to the 1,2-Benzisothiazoline-3-one-1-oxide and 1,2-Benzisothiazoline-3-one-1,1-dioxide (Saccharin) Derivatives: (Diacetoxyiodo)benzene (1.5 mmol) and iodine (0.5 mmol) were added to a solution of *N*-alkyl(*o*-methyl)arenesulfonamide (0.5 mmol) in 1,2-dichloroethane (7 ml). The mixture was irradiated with a high pressure mercury lamp (400 W) under stirring for 2 h under an argon atmosphere at the range of 25-35 °C. After the reaction, the mixture was poured into chloroform and washed with aq. sodium sulfite solution and subsequently with water. The organic layer was dried over sodium sulfate. After removal of the solvent under reduced pressure, the residue was chromatographed on silica gel by p-TLC using the mixture of hexane and ethyl acetate (1:3-10:1) as an eluent.

***N*-Methylsaccharin (2a-I)** : m.p 127.0-128.0 °C; IR (KBr) 1740, 1595, 1470, 1325, 1175 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$) δ 3.28 (s, 3H), 7.82-7.90 (m, 2H), 7.94 (d, *J*=6.8 Hz, 1H), 8.07 (d, *J* =6.8 Hz, 1H); MS (EI) M^+ 197. Anal. Calcd for $C_8H_7NO_3S$: C, 48.72; H, 3.58; N, 7.10. Found: C, 48.72; H, 3.54; N, 6.85.

***N*-Methyl-6-bromosaccharin (2b-I)** : m.p 191.0-192.0 °C; IR (KBr) 1725, 1585, 1470, 1335, 1185 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 3.27 (s, 3H), 7.91 (d, *J*=8.3 Hz, 1H), 7.95 (d, *J*=8.3 Hz, 1H), 8.07 (s, 1H); MS (EI) M^+ 275. Anal. Calcd for $C_8H_6BrNO_3S$: C, 34.80; H, 2.19; N, 5.07. Found: C, 34.96; H, 2.03; N, 5.01.

***N*-Methyl-6-methylsaccharin (2c-I)** : m.p 172.0-173.5 °C; IR (KBr) 1730, 1600, 1490, 1330, 1160 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 2.57 (s, 3H), 3.52 (s, 3H), 7.61 (d, *J*=7.7 Hz, 1H), 7.72 (s, 1H), 7.93 (d, *J*=7.7 Hz, 1H); ^{13}C-NMR (125MHz, $CDCl_3$) δ 22.0 (p), 23.1 (p), 121.2 (t),124.9 (t), 135.0 (t), 137.8 (q), 146.5 (q), 158.8 (q); MS (EI) M^+ 211. Anal. Calcd for $C_9H_9NO_3S$: C, 51.17; H, 4.29; N, 6.63. Found: C, 51.04; H, 4.25; N, 6.57.

***N*-Methyl-5-methylsaccharin (2d-I)** : m.p 128.0-129.0 °C; IR (KBr) 1740, 1600, 1475, 1330, 1185 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 2.55 (s, 3H), 3.26 (s, 3H), 7.64 (d, *J*=7.8 Hz, 1H), 7.81 (d, *J*=7.8 Hz, 1H), 7.86 (s, 1H); MS (EI) M^+ 211. Anal. Calcd for $C_9H_9NO_3S$: C, 51.17; H, 4.29; N, 6.63. Found: C, 51.03; H, 4.19; N, 6.57.

***N*-Methyl-4-methyl-6-*tert*-butylsaccharin (2e-I)** : m.p 128.0-129.0 °C; IR (KBr) 1725, 1605, 1480, 1325, 1155 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.38 (s, 9H), 2.76 (s, 3H), 3.23 (s, 3H), 7.54 (s, 1H), 7.76 (s, 3H); MS (EI) M^+ 267. Anal. Calcd for $C_{13}H_{17}NO_3S$: C, 58.40; H, 6.41; N, 5.24. Found: C, 58.44; H, 6.39; N, 5.20. Crystal data for **2e-I** (296K, Cu-Kα radiation, Rigaku AFC5S diffractometer): $C_{13}H_{17}NO_3S$, FW = 267.34, a = 9.167(3) Å, b = 7.944(2) Å, c = 19.478(2) Å, β = 101.55(1)°, monoclinic, $P2_1/n$, Z = 4, V = 1389.8(5) $Å^3$, D_C = 1.278 g cm^{-3}. R factor = 0.058 for 1627 independent observed reflections ($I > 3.00\sigma(I)$); R_W factor = 0.075; Bond lengths: S-N, 1.657 Å; S-C, 1.748 Å; S-O(1), 1.412 Å; S-O(2), 1,481 Å.

***N*-Methyl-6-(*N'*, *N'*-diethylaminocarbonyl)saccharin (2f-I)** : m.p 186.5-188.0 °C; IR (KBr) 1725, 1630, 1580, 1490, 1340, 1170 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.15 (bt, *J*=7.9 Hz, 3H), 1.29 (bt, *J*=7.9 Hz, 3H), 3.22 (bq, *J*=7.9 Hz, 2H), 3.29 (s, 3H), 3.58 (bq, *J*=7.9 Hz, 2H), 7.79 (d, *J*=7.8 Hz, 1H), 7.92 (s, 1H), 8.09 (d, *J*=7.8 Hz, 1H); MS (EI) M^+ 296 Anal. Calcd for $C_{13}H_{16}N_2O_4S$: C, 52.69; H, 5.44; N, 9.45. Found: C, 52.26; H, 5.43; N, 9.22.

***N*-Methyl-6-nitrosaccharin (2g-I)** : m.p 162.0-163.5 °C; IR (KBr) 1740, 1610, 1540, 1340, 1190 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 3.33 (s, 3H), 8.28 (d, *J*=8.3 Hz, 1H), 8.68 (d, *J*=8.3 Hz, 1H), 8.79 (s, 1H); MS (EI) M^+ 242. Anal. Calcd for $C_8H_6N_2O_5S$: C, 39.67; H, 2.50; N, 11.57. Found: C, 39.41; H, 2.47; N, 11.43.

***N*-Methyl-6-(methanesulfonyl)saccharin (2h-I)** : m.p 186.5-188.0 °C; IR (KBr) 1730, 1560, 1410, 1325, 1160 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 3.17 (s, 3H), 3.32 (s, 3H), 8.28 (d, *J*=8.0 Hz, 1H), 8.40 (d, *J*=8.0 Hz, 1H), 8.52 (s, 1H); MS (EI) M^+ 275. Anal. Calcd for $C_9H_9NO_5S_2$: C, 39.26; H, 3.30; N, 5.09. Found: C, 39.51; H, 3.38; N, 4.95.

***N*-Ethyl-6-bromosaccharin (2b-II)** : m.p 124.5-125.5 °C; IR (KBr) 1725, 1585, 1460, 1340, 1190 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.45 (t, *J*=7.3 Hz, 3H), 3.85 (q, *J*=7.3 Hz, 2H), 7.91 (d, *J*=8.2 Hz, 1H), 7.95 (d, *J*=8.0 Hz, 1H), 8.05 (s, 1H); MS (EI) M^+ 289. Anal. Calcd for $C_9H_8BrNO_3S$: C, 37.26; H, 2.78; N, 4.83. Found: C, 37.50; H, 2.79; N, 4.66.

***N*-Ethyl-6-methylsaccharin (2c-II)** : m.p 106.5-108.0 °C; IR (KBr) 1725, 1605, 1490, 1330, 1160 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.44 (t, *J*=7.3 Hz, 3H), 2.56 (s, 3H), 3.84 (q, *J*=7.3 Hz, 2H), 7.60

(d, J=8.0 Hz, 1H), 7.70 (s, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 14.2 (p), 22.0 (p), 34.4 (s), 121.1 (t), 124.9(t), 125.0 (q), 135.0 (t), 138.0 (q), 146.5 (q), 158.8 (q); MS (EI) M^+ 225. Anal. Calcd for $C_{10}H_{11}NO_3S$: C, 53.32; H, 4.92; N, 6.22. Found: C, 53.31; H, 4.88; N, 6.14.

***N*-Propyl-6-methylsaccharin (2c-III)** : m.p 77.0-78.5 °C; IR (KBr) 1725, 1600, 1485, 1335, 1175 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$) δ 1.10 (t, J=7.5 Hz, 3H), 1.88 (dt, J=7.5 Hz, 2H), 2.56 (s, 3H), 3.72 (t, J=7.5 Hz, 2H), 7.61 (d, J=8.0 Hz, 1H), 7.71 (s, 1H), 7.92 (d, J=8.0 Hz, 1H) ; ^{13}C NMR (125MHz, $CDCl_3$) δ 11.3 (p), 21.9 (p), 22.0 (p), 41.0 (s), 121.1 (t), 124.9, 125.0, 135.0 (t), 138.0 (q), 146.5 (q), 159.2 (q); MS (EI) M^+ 239. Anal. Calcd for $C_{11}H_{13}NO_3S$: C, 55.21; H, 5.48; N, 5.85. Found: C, 55.29; H, 5.56; N, 5.75.

***N*-Butyl-6-methylsaccharin (2c-IV)** : m.p 79.0-80.5 °C; IR (KBr) 1730, 1605, 1485, 1330, 1170 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$) δ 0.98 (t, J=7.5 Hz, 3H), 1.44 (sixt., J=7.5 Hz, 2H), 1.83 (quint., J=7.7 Hz, 2H), 2.56 (s, 3H), 3.76 (t, J=7.5 Hz, 2H), 7.61 (d, J=8.5 Hz, 1H), 7.71 (s, 1H), 7.92 (d, J=7.7 Hz, 1H); MS (EI) M^+ 253. Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.90; H, 5.97; N, 5.53. Found: C, 56.52; H, 5.93; N, 5.44.

***N*-Ethyl-5-methylsaccharin (2d-II)** : m.p 64.5-66.0 °C; IR (KBr) 1730, 1605, 1480, 1330, 1190 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$) δ 1.44 (t, J=7.3 Hz, 3H), 2.55 (s, 3H), 3.84 (q, J=7.3 Hz, 2H), 7.64 (d, J=8.0 Hz, 1H), 7.79 (d, J=7.7 Hz, 1H), 7.84 (s, 1H); MS (EI) M^+ 225. Anal. Calcd for $C_{10}H_{11}NO_3S$: C, 53.32; H, 4.92; N, 6.22. Found: C, 53.34; H, 4.85; N, 6.17.

***N*-Ethyl-4-methyl-6-*tert*-butylsaccharin (2e-II)** : m.p 78.5-80.0 °C; IR (KBr) 1715, 1605, 1510, 1330, 1150 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$) δ 1.38 (s, 9H), 1.43 (t, J=7.3 Hz, 3H), 2.76 (s, 3H), 3.81 (q, J=7.3 Hz, 2H), 7.54 (s, 1H), 7.75 (s, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 14.0 (p), 19.2 (p), 30.1 (p), 34.0 (s), 35.7 (q), 115.4 (t), 121.8 (q), 133.8 (t), 138.5 (q), 139.7 (q), 158.8 (q), 159.5 (q); MS (EI) M^+ 281. Anal. Calcd for $C_{14}H_{19}NO_3S$: C, 59.76; H, 6.81; N, 4.98. Found: C, 59.89; H, 7.00; N, 4.86.

***N*-Ethyl-6-(*N'*,*N'*-diethylaminocarbonyl)saccharin (2f-II)** : oil, IR (neat) 1735, 1640, 1580, 1490, 1335, 1160 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$) δ 1.14 (bt, J=8.0 Hz, 3H), 1.28 (bt, J=8.0 Hz, 3H), 1.46 (t, J=7.3 Hz, 3H), 3.23 (bq, J=8.0 Hz, 2H), 3.57 (bq, J=8.0 Hz, 2H), 3.87 (q, J=7.3 Hz, 2H), 7.79 (d, J=8.0 Hz, 1H), 7.90 (s, 1H), 8.09 (d, J=8.0 Hz, 1H) ; HRMS (FAB) Found: m/z 295.1097 Calcd for $C_{14}H_{19}N_2O_3S$: (M+H) 295.1116.

***N*-Ethyl-6-nitrosaccharin (2g-II)** : IR (KBr) 1740, 1610, 1535, 1340, 1170 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$) δ 1.48 (t, J=7.3 Hz, 3H), 3.91 (q, J=7.3 Hz, 2H), 8.27 (d, J=7.8 Hz, 1H), 8.68 (d, J=8.5 Hz, 1H), 8.76 (s, 1H); HRMS (FAB) Found: m/z 257.0230 Calcd for $C_9H_9N_2O_5S$: (M+H) 257.0232.

***N*-Ethyl-6-(methanesulfonyl)saccharin (2h-II)** : m.p 171.0-172.5 °C; IR (KBr) 1740, 1590, 1460, 1335, 1150 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$) δ 1.48 (t, J=7.3 Hz, 3H), 3.16 (s, 3H), 3.90 (q, J=7.3 Hz, 2H), 8.27 (d, J=8.0 Hz, 1H), 8.39 (d, J=8.0 Hz, 1H), 8.50 (s, 1H); MS (EI) M^+ 289. Anal. Calcd for $C_{10}H_{11}NO_5S_2$: C, 41.51; H, 3.83; N, 4.84. Found: C, 41.19; H, 3.64; N, 4.75.

***N*-Ethyl-4,5-dimethylsaccharin (2i-II)** : m.p 94.5-96.0 °C; IR (KBr) 1725, 1450, 1320, 1180 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$) δ 1.43 (t, J=7.3 Hz, 3H), 2.43 (s, 3H), 2.74 (s, 3H), 3.81 (q, J=7.3 Hz, 2H), 7.58 (d, J=8.0 Hz, 1H), 7.64 (d, J=8.0 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 13.9 (p), 14.6

(p), 20.1 (p), 34.1 (s), 118.0 (t), 124.2 (q), 135.1 (t), 136.1 (q), 139.2 (q), 145.1 (q), 160.1 (q); MS (EI) M^+ 239. Anal. Calcd for $C_{11}H_{13}NO_3S$: C, 55.21; H, 5.48; N, 5.85. Found: C, 55.22; H, 5.51; N, 5.88.

***N*-Ethyl-4,5,6-trimethylsaccharin (2j-II)** : m.p 112.5-114.0 °C; IR (KBr) 1720, 1595, 1460, 1320, 1185 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.42 (t, *J*=7.3 Hz, 3H), 2.31 (s, 3H), 2.45 (s, 3H), 2.76 (s, 3H), 3.80 (q, *J*=7.3 Hz, 2H), 7.55 (s, 1H), 7.64 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 14.0 (p), 15.0 (p), 15.7 (p), 21.7 (p), 34.0 (s), 119.2 (t), 122.1 (q), 135.5 (q), 138.7 (q), 143.6 (q), 143.8 (q), 160.3 (q); MS (EI) M^+ 253. Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.90; H, 5.97; N, 5.53. Found: C, 57.15; H, 6.07; N, 5.39.

***N*-Ethyl-5-bromo-6-methylsaccharin (2k-II)** : m.p 123.0-124.5 °C; IR (KBr) 1720, 1595, 1465, 1340, 1190 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.44 (t, *J*=7.3 Hz, 3H), 2.60 (s, 3H), 3.83 (q, *J*=7.3 Hz, 2H), 7.76 (s, 1H), 8.20 (s, 1H); MS (EI) M^+ 303. Anal. Calcd for $C_{10}H_{10}{}^{79}BrNO_3S$: C, 39.49; H, 3.31; N, 4.61. Found: C, 39.61; H, 3.25; N, 4.41.

***N*-Ethyl-6-bromo-1,2-benzisothiazoline-3-one-1-oxide (5b-II)** : IR (KBr) 1695, 1585, 1110 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.42 (t., *J*=7.3 Hz, 3H), 3.49-3.89 (m, 1H), 3.96-4.05 (m, 1H), 7.82-7.84 (m, 2H), 8.04 (d, *J*=1.0 Hz, 1H); HRMS (FAB) Found: m/z 275.9518 and 273.9558 Calcd for $C_9H_9{}^{81}BrNO_2S$ and $C_9H_9{}^{79}BrNO_2S$ (M+H) 275.9517 and 273.9537.

***N*-Ethyl-6-methyl-1,2-benzisothiazoline-3-one-1-oxide (5c-II)** : m.p 80.5-82.0 °C; IR (KBr) 1700, 1605, 1505, 1095 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.41 (t, *J*=7.3 Hz, 3H), 2.54 (s, 3H), 3.78-3.87 (m, 1H), 3.96-4.05 (m, 1H), 7.54 (d, *J*=7.7 Hz, 1H), 7.69 (s, 1H), 7.87 (d, *J*=7.7 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 14.6 (p), 21.7 (p), 36.1 (p), 125.2 (t), 125.6 (t), 126.6 (t), 145.4 (q), 145.6 (q), 165.0 (q); MS (EI) M^+ 209. Anal. Calcd for $C_{10}H_{11}NO_2S$: C, 57.39; H, 5.30; N, 6.69. Found: C, 57.12; H, 5.31; N, 6.64.

***N*-Propyl-6-methyl-1,2-benzisothiazoline-3-one-1-oxide (5c-III)** : IR (KBr) 1695, 1605, 1465, 1095 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.00 (t, *J*=7.5 Hz, 3H), 1.83 (dt, *J*=7.5 Hz, 2H), 2.54 (s, 3H), 3.69-3.76 (m, 1H), 3.85-3.93 (m, 1H), 7.54 (d, *J*=7.7 Hz, 1H), 7.69 (s, 1H), 7.87 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 11.3 (p), 21.9 (p), 22.6 (s), 42.8 (s), 125.3 (t), 125.8 (q), 125.8 (t), 133.9 (t), 145.5 (q), 145.9 (q), 165.4 (q); HRMS (FAB) Found: m/z 224.0742 Calcd for $C_{11}H_{14}NO_2S$: (M+H) 224.0745.

***N*-Butyl-6-methyl-1,2-benzisothiazoline-3-one-1-oxide (5c-IV)** : IR (KBr) 1690, 1505, 1465, 1095 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 0.97 (t, *J*=7.5 Hz, 3H), 1.42 (q, *J*=7.5 Hz, 2H), 1.74-1.83 (m, 2H), 2.54 (s, 3H), 3.71-3.79 (m, 1H), 3.89-3.97 (m, 1H), 7.54 (d, *J*=7.7 Hz, 1H), 7.69 (s, 1H), 7.87 (d, *J*=7.7 Hz, 1H); HRMS (FAB) Found: m/z 238.0892 Calcd for $C_{12}H_{16}NO_2S$: (M+H) 238.0902.

***N*-Ethyl-5-methyl-1,2-benzisothiazoline-3-one-1-oxide (5d-II)** : Oil; IR (neat) 1710, 1605, 1450, 1140 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.41 (t, *J*=7.3 Hz, 3H), 2.53 (s, 3H), 3.78-3.87 (m, 1H), 3.96-4.05 (m, 1H), 7.59 (d, *J*=7.7 Hz, 1H), 7.77 (d, *J*=7.7 Hz, 1H), 7.79 (s, 1H); HRMS (FAB) Found: m/z 210.0590 Calcd for $C_{10}H_{12}NO_2S$: (M+H) 210.0589.

2,4-Dimethyl-6-*tert*-butyl-1,2-benzisothiazoline-3-one-1-oxide (5e-I) : m.p 123.5-125.0 °C ; IR (KBr) 1700, 1605, 1480, 1105 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.38 (s, 9H), 2.74 (s, 3H), 3.35

(s, 3H), 7.49 (s, 1H), 7.72 (s, 1H); MS (EI) M^+ 251. Anal. Calcd for $C_{13}H_{17}NO_2S$: C, 62.12; H, 6.82; N, 5.57. Found: C, 61.97; H, 6.90; N, 5.51. Crystal data for **5e-I** (296K, Cu-Kα radiation, Rigaku AFC7S diffractometer): $C_{13}H_{17}NO_2S$, FW=251.34, a=36.22(2) Å, b=11.578(8) Å, c=12.534(6) Å, orthorhomic, Fdd2, Z = 16, V = 5255(11) $Å^3$, D_C = 1.271 g cm^{-3}. R factor = 0.063 for 938 independent observed reflections ($I > 3.00\sigma(I)$) R_W factor = 0.078. Bond lengths: S-N, 1.707 Å; S-C, 1.755 Å; S-O, 1.482 Å.

***N*-Ethyl-4-methyl-6-*tert*-butyl-1,2-benzisothiazoline-3-one-1-oxide (5e-II)** : m.p 78.5-80.0 °C; IR (KBr) 1710, 1605, 1510, 1095 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.37 (s, 9H), 1.39 (t, *J*=7.3 Hz, 3H), 2.74 (s, 3H), 3.76-3.85 (m, 1H), 3.93-4.02 (m, 1H), 7.49 (s, 1H), 7.72 (s, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 14.5 (p), 17.7 (p), 30.8 (p), 35.3 (q), 35.9 (s), 122.0 (q), 132.5 (t), 139.6 (q), 146.2 (q), 157.6 (q), 165.6 (q); MS (EI) M^+ 265. Anal. Calcd for $C_{14}H_{19}NO_2S$: C, 63.36; H, 7.22; N, 5.28. Found: C, 63.19; H, 7.24; N, 5.23.

***N*-Ethyl-6-(*N'*,*N'*-diethylaminocarbonyl)-1,2-benzisothiazoline-3-one-1-oxide (5f-II)** : oil, IR (neat) 1710, 1620, 1490, 1100 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.13 (bt, *J*=8.0 Hz, 3H), 1.26 (bt, *J*=8.0 Hz, 3H), 1.43 (t, *J*=7.3 Hz, 3H), 3.24 (bq, *J*=8.0 Hz, 2H), 3.56 (bq, *J*=8.0 Hz, 2H), 3.82-3.91 (m, 1H), 3.97-4.07 (m, 1H), 7.73 (d, *J*=7.7 Hz, 1H), 7.89 (s, 1H), 8.03 (d, *J*=7.7 Hz, 1H); HRMS (FAB) Found: m/z 311.1060 Calcd for $C_{14}H_{19}N_2O_4S$: (M+H) 311.1066.

***N*-Ethyl-6-(methanesulfonyl)-1,2-benzisothiazoline-3-one-1-oxide (5h-II)** : IR (KBr) 1715, 1590, 1470, 1340, 1175, 1100 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.45 (t, *J*=7.3 Hz, 3H), 3.25 (s, 3H), 3.87-3.93 (m, 1H), 4.03-4.10 (m, 1H), 8.20 (d, *J*=8.0 Hz, 1H), 8.33 (d, *J*=7.7 Hz, 1H), 8.50 (s, 1H); HRMS (FAB) Found: m/z 274.0203 Calcd for $C_{10}H_{12}NO_4S_2$: (M+H) 274.0208.

***N*-Ethyl-4,5-dimethyl-1,2-benzisothiazoline-3-one-1-oxide (5i-II)** : m.p 102.5-104.0 °C ; IR (KBr) 1710, 1595, 1455, 1090 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.40 (t, *J*=7.3 Hz, 3H), 2.42 (s, 3H), 2.72 (s, 3H), 3.76-3.85 (m, 1H), 3.93-4.02 (m, 1H), 7.53 (d, *J*=7.7 Hz, 1H), 7.61 (d, *J*=7.7 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 13.2 (p), 14.7 (p), 122.3 (t), 124.5 (q), 134.5 (t), 139.3 (q), 143.7 (q), 143.7 (q), 143.8 (q), 166.2 (q); MS (EI) M^+ 223. Anal. Calcd for $C_{11}H_{13}NO_2S$: C, 59.17; H, 5.87; N, 6.27. Found: C, 59.11; H, 5.94; N, 6.16.

***N*-Ethyl-4,5,6-trimethyl-1,2-benzisothiazoline-3-one-1-oxide (5j-II)** : m.p 93.0-94.0 °C; IR (KBr) 1690, 1590, 1460, 1105 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.39 (t, *J*=7.3 Hz, 3H), 2.30 (s, 3H), 2.44 (s, 3H), 2.74 (s, 3H) 3.75-3.84 (m, 1H), 3.92-4.01 (m, 1H), 7.51 (s, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 13.6 (p), 14.8 (p), 15.5 (p), 21.6 (p), 36.2 (s), 122.4(q), 123.8 (t), 139.0 (q), 142.2 (q), 143.1 (q), 143.5 (q), 166.6 (q); MS (EI) M^+ 237. Anal. Calcd for $C_{12}H_{15}NO_2S$: C, 60.73; H, 6.37; N, 5.90. Found: C, 60.52; H, 6.31; N, 6.09.

***N*-Ethyl-5-bromo-6-methyl-1,2-benzisothiazoline-3-one-1-oxide (5k-II)** : IR (KBr) 1720, 1600, 1485, 1160 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.40 (t, *J*=7.3 Hz, 3H), 2.58 (s, 3H), 3.78-3.87 (m, 1H), 3.94-4.03 (m, 1H), 7.75 (s, 1H), 8.14 (s, 1H); HRMS (FAB) Found: m/z 289.9672 and 287.9669 Calcd for $C_{10}H_{11}{}^{81}BrNO_2S$ and $C_{10}H_{11}{}^{79}BrNO_2S$: (M+H) 289.9673 and 287.9694.

***N*-Ethyl-2,5-dimethylbenzenesulfinamide (6)** : IR (KBr) 1630, 1490, 1075 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 1.14 (t, *J*=7.3 Hz, 3H), 2.37 (s, 3H), 2.38 (s, 3H), 2.89-2.99 (m, 1H), 3.12-3.23

(m, 1H), 3.89 (bs, 1H), 7.08 (d, J=7.5 Hz, 1H), 7.17 (d, J=7.5 Hz, 1H), 7.77 (s, 1H); HRMS (FAB) Found: m/z 198.0947 Calcd for $C_{10}H_{16}NOS$: (M+H) 198.0953.

Acknowledgment: H.T. is grateful for financial support from a Grant-in-Aid for Scientific Reseach (No. 08554031) from the Ministry of Education, Science, Sports and Culture, Japan. We thank Ms. Ritsuko Hara for the measurements of MS, and Dr. Hiroko Seki and Ms. Yukiko Hiramoto for the measurements of elemental analysis, in the Chemical Analysis Center of Chiba University.

References

1. (a) Umemoto, T. *Yuki Gosei Kagaku Kyokaishi* **1983**, *41*, 251. (b) Varvoglis, A. *Synthesis* **1984**, 709. (c) Ochiai, M.; Nagao, Y. *Yuki Gosei Kagaku Kyokaishi* **1986**, *44*, 660. (d) Moriarty, R. M.; Vaid, R. K. *Synthesis* **1990**, 431. (e) Moriarty, R. M.; Vaid, R. K.; Koser, G. F. *Synlett* **1990**, 365. (f) Prakash, O.; Saini, N.; Sharma, P. K. *Synlett* **1994**, 221. (g) Kitamura, T *Yuki Gosei Kagaku Kyokaishi* **1995**, *53*, 893. (h) Kita, Y.; Takada, T.; Tohma, H. *Pure Appl Chem.* **1996**, *68*, 627. (i) Muraki, T.; Togo, H.; Yokoyama, M. *Rev. Heteroatom Chem.* **1997**, *17*, 213. (j) Zhdankin, V. V. *Rev. Heteroatom Chem.* **1997**, *17*, 133.
2. (a) Concepción, J. I.; Francisco, C. G.; Freire, R.; Hernández, R.; Salazar, J. A.; Suárez, E.; *J. Org.Chem.* **1986**, *51*, 402. (b) Singh, R.; Just, G.; *Synth. Commun.* **1988**, *18*, 1327. (c) Minisci, F. ; Vismara, E.; Fontana, F.; Barbosa, M. C. N. *Tetrahedron Lett.* **1989**, *30*, 4569. (d) Togo, H.; Aoki, M.; Yokoyama, M. *Tetrahedron Lett.* **1991**, *32*, 6559. (e) Togo, H.; Aoki, M.; Yokoyama, M. *Chem. Lett.* **1991**, 1691. (f) Togo, H.; Aoki, M.; Yokoyama, M. *Chem. Lett.* **1992**, 2169. (g) Togo, H.; Aoki, M.; Yokoyama, M. *Tetrahedron* **1993**, *49*, 8241. (h) Togo, H.; Aoki, M.; Kuramochi, T.; Yokoyama, M. *J. Chem. Soc., Perkin Trans.1* **1993**, 2417. (i) Togo, H.; Taguchi, R.; Yamaguchi, K.; Yokoyama, M. *J. Chem. Soc., Perkin Trans.1* **1995**, 2135. (j) Togo, H.; Muraki, T.; Yokoyama, M. *Synthesis* **1995**, 155.
3. (a) Concepción, J. I.; Francisco, C. G.; Hernández, R.; Salazar, J. A.; Suárez, E.; *Tetrahedron Lett.* **1984**, *25*, 1953. (b) Francisco, C. G.; Freire, R.; Rodrigues, M. S.; Suárez, E. *Tetrahedron Lett.* **1987**, *28*, 3397. (c) Freire, R.; Hernández, R.; Rodrigues, M. S.; Suárez, E. *Tetrahedron Lett.* **1987**, *28*, 981. (d) Furuta, K.; Nagata, T.; Yamamoto, H. *Tetrahedron Lett.* **1988**, *29*, 2215. (e) Hernández, R.; Marrero, J. J.; Suárez, E. *Tetrahedron Lett.* **1988**, *29*, 5982. (f) de Armas, P.; Concepción, J. I.; Francisco, C. G.; Hernández, R.; Salazar, J. A.; Suárez, E. *J. Chem. Soc., Perkin Trans.1* **1989**, 405. (g) Brimble, M. A.; Williams, G. M.; Baker, R.; James, M. *Tetrahedron Lett.* **1990**, *31*, 3043. (h) Ellwood, C. W.; Pattenden, G. *Tetrahedron Lett.* **1991**, *32*, 1591. (i) de Armas, P.; Francisco, C. G.; Suárez, E. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 72. (j) de Armas, P.; Francisco, C. G.; Suárez, E. *J. Am. Chem. Soc.* **1993**, *115*, 8865. (k) de Armas, P.; Francisco, C. G.; Suárez, E. *Tetrahedron Lett.* **1993**, *34*, 7731. (l) Boto, A.; Betancor, C.; Suárez, E. *Tetrahedron Lett.* **1994**, *35*, 5509. (m) Boto, A.; Betancor, C.; Suárez, E. *Tetrahedron Lett.* **1994**, *35*, 6993. (n) Arencibia, T.; Salazar, J. A.; Suárez, E. *Tetrahedron Lett.* **1994**, *35*, 7463. (o) Francisco, C. G.; Gonzárez, C. C.; Suárez, E. *Tetrahedron Lett.* **1996**, *37*, 1687.

4. (a) de Armas, P.; Carrau, R.; Concepción, J. I.; Francisco, C. G.; Hernández, R.; Suárez, E. *Tetrahedron Lett.* **1985**, *26*, 2493. (b) Hernández, R.; Medina, M. C.; Salazar, J. A.; Suárez, E. *Tetrahedron Lett.* **1987**, *28*, 2533. (c) Carrau, R.; Hernández, R.; Suárez, E. *J. Chem. Soc., Perkin Trans. 1* **1987**, 937. (d) de Armas, P.; Francisco, C. G.; Hernández, R.; Salazar, J. A.; Suárez, E. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3255. (e) Dorta, R. L.; Francisco, C. G.; Suárez, E. *J. Chem. Soc., Chem. Commun.* **1989**, 1168.

5. (a) Kita, Y.; Tohma, H.; Hatanaka, K.; Takada, T.; Fujita, S.; Mitoh, S.; Sakurai, H.; Oka, S. *J. Am. Chem. Soc.* **1994**, 116, 3684. (b) Kita, Y.; Takada, T.; Mihara, S.; Whelan, B. A.; Tohma, H. *J. Org. Chem.* **1995**, 60, 7144. (c) Kita, Y.; Arisawa, M.; Gyoten, M.; Nakajima, M.; Hamada, R.; Tohma, H.; Takada, T. *J. Org. Chem.* **1998**, 63, 6625.

6. (a) Togo, H.; Muraki, T.; Yokoyama, M. *Tetrahedron Lett.* **1995**, *36*, 7089. (b) Muraki, T.; Togo, H.; Yokoyama, M. *Tetrahedron Lett.* **1996**, *37*, 2441. (c) Togo, H.; Muraki, T.; Hoshina, Y.; Yamaguchi, K.; Yokoyama, M. *J. Chem. Soc., Perkin Trans.1* **1997**, 787.

7. (a) Lombardino, J. G.; Wiseman, E. H.; McLamore, W. M. *J. Med. Chem.* **1971**, *14*, 1171. (b) Svahn C. M.; Jönsson, N. Å. *Acta Chem. Scand.*, (B) **1978**, *32*, 137. (c) Davis, M. "Organic Compounds of Sulfur, Selenium, and Tellurium", vol. 5, Chap 10, Ed by The Chemical Society, London (**1979**). (d) Pain, D. L.; Peart, B. J.; Wooldridge, K. R. H. "Comprehensive Heterocyclic Chemistry" , Eds Katrizky A R.; Rees, C. W., Vol.6, Pergamon Press, Oxford (**1984**). (e) Drug of the future, **1986**, *11*, 565. (f) Sunkel, C. E.; de Casa-Junna, M. F.; Cillero, F. J.; Piego, J. G.; Ortega, M. P. *J. Med. Chem.* **1988**, *31*, 1886. (g) Choi, S.-Y.; Lee, S.-G.; Yoon, Y.-J.; Kim, K.-W. *J. Heterocyclic Chem.* **1989**, *26*, 1073. (h) Nagasawa, H. T.; Kawle, S. P.; Elberling, J. A.; DeMaster, E. G.; Fukuto, J. M. *J. Med. Chem.* **1995**, *38*, 1865. (i) Yeung, K.-S.; Meanwell, N. A.; *Tetrahedron Lett.* **1998**, *39*, 5309.

8. (a) Desai, R. C.; Farrell, R. P.; Kuo, G. -H.; Hlasta, D. J. *Synlett* **1994**, 933. (b) Court, J. J.; Lessen, T. A.; Hlasta, D. J. *Synlett* **1995**, 423. (c) Hlasta, D. J.; Subramanyam, C.; Bell, M. R.; Carabateas, P. M.; Court, J. J.; Desai, R. C.; Drozd, M. L.; Eickhoff, W. M.; Ferguson, E. W.; Gordon, R. J.; Johnson, J. A.; Kumar, V.; Maycock, A. L.; Mueller, K. R.; Pagani, E. D.; Robinson, D. T.; Saindane, M. T.; Silver, P. J.; Subramanian, S. *J. Med. Chem.* **1995**, *38*, 739.

9. (a) Watanabe, H.; Gay, R. L.; Hauser, C. R *J. Org. Chem.* **1968**, *33*, 900. (b) Lombardino, J. G. *J. Org. Chem.* **1971**, *36*, 1843. (c) Saari, W. S.; Schwering, J. E. *J. Heterocyclic Chem.* **1986**, *23*, 1253. (d) Hlasta, D. J.; Court, J. J.; Desai, R. C. *Tetrahedron Lett.* **1991**, *32*, 7179. (e) Desai, R. C.; Hlasta, D. J.; Monsour, G.; Saindane, M. T. *J. Org. Chem.* **1994**, *59*, 7161. (f) Yeung, Kap. -S.; Meanwell, N. A.; Li, Y.; Gao, G. *Tetrahedron Lett.* **1998**, *39*, 1483.

10. Togo, H.; Hoshina, Y.; Muraki, T.; Nakayama, H.; Yamaguchi, K.; Yokoyama, M. *J. Org. Chem.* **1998**, *63*, 5193.

11. As a preliminary report : Togo, H.; Katohgi, M.; Yokoyama, M. *Synlett* **1998**, 131.

12. (a) Klyuev, V. N.; Korzhenevskii, A. B. *Khim. Khim. Tekhnol.* **1978**, *21*, 31. (b) Szabo, J.; Szucs, E.; Fodor, L.; Katocs, A.; Bernath, G. *Tetrahedron* **1988**,*44*, 2985.

13. (a) Schmeisser, M.; Dahmen, K.; Sartori, P. *Chem. Ber.* **1967**, *100*, 1633. (b) Mckillop, A.; Kemp, D. *Tetrahedron* **1989**, *45*, 3299.

14. Oae, S. ; Togo, H.; Numata, T.; Fujimori, K. *Chem. Lett.*, **1980**, 1193.