1,2-Benzisothiazole 1,1-Dioxides. Synthesis of 3-Alkyl-(or Aryl-)1,2-benzisothiazole 1,1-Dioxides and Related Compounds †

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A synthesis of 3-substituted 1,2-benzisothiazole 1,1-dioxides from saccharin (1,2-benzisothiazolin-3-one 1,1-dioxide) and organolithium compounds is described. The reaction of saccharin and of saccharin *pseudo*-chloride (3-chloro-1,2-benzisothiazole 1,1-dioxide) with Grignard reagents has been investigated systematically. 1,2-Benzisothiazole 1,1-dioxides (1) are formed together with the open-chain tertiary alcohols (8) and, in one case, the 3,3-disubstituted 1,2-benzisothiazoline 1,1-dioxide (2). Intramolecular cyclisation of *N*-acyl-*o*,*N*-dilithiobenzenesulphonamides gives a low yield of 3-substituted 1,2-benzisothiazole 1,1-dioxides.

THERE are many examples of 3-alkylamino-[1-3] and 3-alkoxy-1,2-benzisothiazole 1,1-dioxides [2] but only a few examples of the 3-aryl- and 3-alkyl-derivatives are known, and there is no general method for their preparation. The 3-phenyl-derivative (1d) was obtained as the major product when 3-chloro-1,2-benzisothiazole 1,1-dioxide

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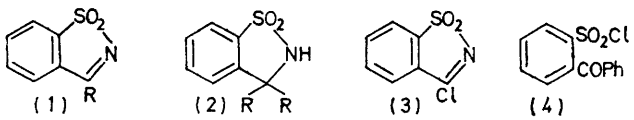
[1] H. Hettler, *Z. analyt. Chem.*, 1966, **220**, 9.

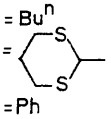
[2] C. H. Grogan, E. E. Reid, and L. M. Rice, *J. Org. Chem.*, 1955, **20**, 1425.

[3] C. W. Whitehead and J. J. Traverso, *J. Org. Chem.*, 1960, **25**, 413.

(saccharin *pseudo*-chloride) (3) was heated in benzene in the presence of anhydrous aluminium chloride,[4] the minor product being 3,3-diphenyl-1,2-benzisothiazoline 1,1-dioxide (2d). The corresponding *p*-dimethylaminophenyl derivatives were prepared similarly. Compound (1d) was also synthesised by treating 2-benzoylbenzenesulphonyl chloride (4) with ammonium hydroxide.[5] 3-Amino-4-aroyl-5-sulphamoylbenzoic acids underwent similar cyclodehydration to the corresponding 3-arylbenzisothiazoles.[6] Treatment of ammonium 2-benzoyl-5-chlorobenzenesulphonate with phosphorus pentachloride yields 3-(4-chlorophenyl)-1,2-benzisothiazole 1,1-dioxide.[7]



(1) (2) (3) (4)

a R = Me
b R = Bu^n
c R = 
d R = Ph
e R = *p*-MeOC$_6$H$_4$
f R = *o*-MeC$_6$H$_4$
g R = 2-Pyridyl
h R = *o*-HO$_2$C·C$_6$H$_4$

A sulphamyl-saccharin derivative (5) and Grignard reagents yield the 3-substituted 1,2-benzisothiazole 1,1-dioxides (6).[8] In contrast, the reaction of saccharin (1,2-benzisothiazolin-3-one 1,1-dioxide) in ether with Grignard reagents (Me, Et, Pr, or Ph) was reported to lead to the tertiary alcohol, 3-alkyl-(or aryl)-1,2-benzisothiazolin-3-ol 1,1-dioxide (7).[9,10] Preliminary experiments[11] indicated that when saccharin was treated with n-butyllithium and pyridine was added, some 3-butyl-1,2-benzisothiazole 1,1-dioxide was formed. Subsequently, it was found that the pyridine was not essential in the reaction.

In view of the above apparent discrepancy, and in the hope of developing a general synthesis of 3-alkyl- or -aryl-substituted 1,2-benzisothiazole-1,1-dioxide derivatives the reaction of Grignard reagents with saccharin was re-investigated in detail. At least 2 equiv. of reagent are needed since saccharin contains an acidic hydrogen atom. The results are summarised in Table 1. Either the 3-substituted 1,2-benzisothiazole 1,1-dioxide (1) and/or the open-chain tertiary alcohol (8) were obtained, the proportion of each depending on the solvent, temperature, and number of equivalents of Grignard reagent added. None of the cyclic tertiary alcohol (7) was detected. At low temperatures, treatment of saccharin with 2 equiv. of Grignard reagent gave the benzisothiazole 1,1-dioxide (1)

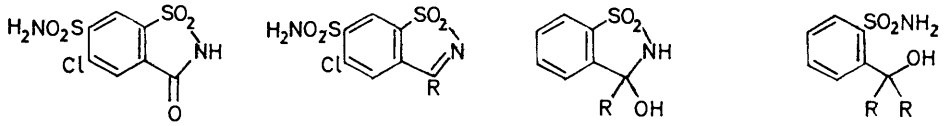
TABLE 1

Reaction of saccharins with Grignard and organolithium reagents

Organometallic reagent (equiv.)		Solvent [a]	Temp. (°C) [b]	Time (h)	Products [yield (%)]
MeMgI	2	E	A	12	(1a) 45, (8a) 15
	4	E	R	12	(1a) 36, (8a) 42
Bu^{n}MgBr	2	E	A	4	(1b), 25 (8b) 25
	2	E	R	18	(1b) 14, (8b) 5
	2	B	R	7	(1b) 2, (8b) 10
	4	B	R	6	(8b) 57
MeLi	2	E	−78	4	(1a) 60
	2	E	A	12	(1a) 25, (8a) 15
Bu^{n}Li	2	T	−78	4	(1b) 75
$C_4H_7S_2Li$ [c]	5	T	−20	4	(1c) 80
PhLi	2	E	−78	4	(1d) 70
	2	E	0	4	(1d) 63, (8d) 20
	4	E	R	8	(1d) 40, (8d) 20
PhMgBr	2	T	A	18	(1d) 80
	4	T	A	18	(1d) 42, (8d) 36
	4	T	R	18	(8d) 65, (2d) 20
PhLi	4	T	0	3	(1d) 64, (8d) 27
p-MeOC$_6$H$_4$Li	5	E	−78	4	(1e) 50
o-MeC$_6$H$_4$Li	2	E	−78	4	(1f) 80
C_5H_4NLi [d]	2	E	−78	4	(1g) 30

[a] E = Et_2O, B = C_6H_6, T = tetrahydrofuran. [b] A = Ambient temperature, R = reflux temperature. [c] $C_4H_7S_2Li$ = 1,3-Dithian-2-yl-lithium. [d] C_5H_4NLi = 2-Pyridyl-lithium.

as the major product and the open-chain tertiary alcohol (8) as the minor one. The alcohol undoubtedly arises by nucleophilic displacement at C(3) in the intermediate (7) initially formed. When saccharin and an excess of Grignard reagent were heated under reflux in benzene or tetrahydrofuran, the open-chain tertiary alcohol (8) was the major product. Treatment of saccharin with an excess of phenylmagnesium bromide in boiling tetrahydrofuran gave the open-chain tertiary alcohol (8d) as the major product together with 3,3-diphenyl-1,2-benzisothiazoline 1,1-dioxide (2d). Formation of the latter may involve nucleophilic addition of the Grignard reagent to any (1d) present. Isolation of the open-chain compound (8) and of the 3,3-disubstituted 1,2-benzisothiazoline 1,1-dioxide (2) was not reported previously.[8,9]

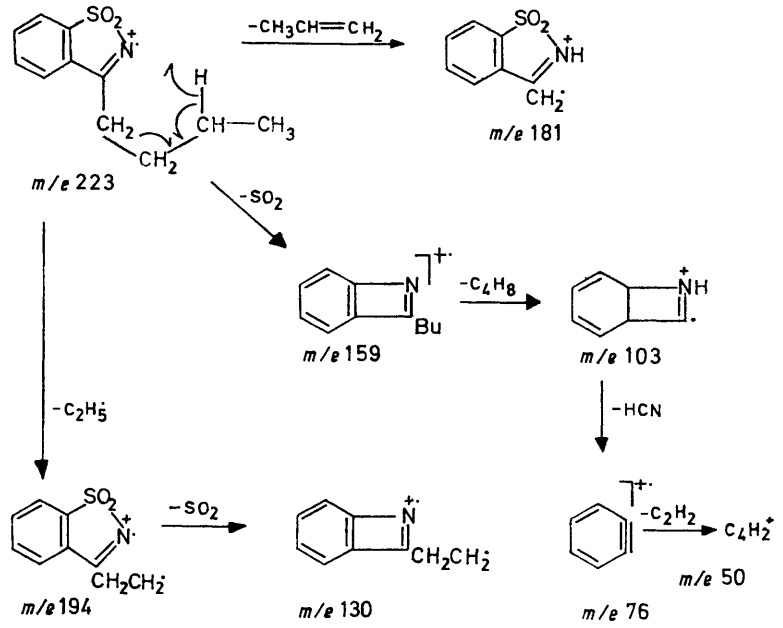


(5) (6) (R = Et or Ph) (7) (R = Me, Et, Pr, or Ph) (8) [R as for (1) and (3)]

The proof of structure of the products is based mainly on microanalytical and spectral data. For example, the i.r. spectrum of 3-butyl-1,2-benzisothiazole 1,1-dioxide (1b) exhibited bands for the aliphatic C–H stretching modes (3000—2850 cm^{-1}), for a C=N group (1605 cm^{-1}), a sulphonamide function (ν_{SO_2} 1330 and 1163 cm^{-1}), and for an *ortho*-disubstituted benzene (775 and 743 cm^{-1}).

[4] P. Fritsch, *Ber.*, 1896, **29**, 2290.
[5] I. Remsen and A. P. Saunders, *Amer. Chem. J.*, 1895, **17**, 347.
[6] O. B. T. Nielsen, C. K. Nielsen, and P. W. Feit, *J. Medicin. Chem.*, 1973, **16**, 1170.
[7] (*a*) Z. Horii, Jap. P. 10,131/1964 (*Chem. Abs.*, 1964, **61**, 12,008*f*); (*b*) Jap. P. 8832/1964 (*Chem. Abs.*, 1964, **61**, 12,008*g*).
[8] J. B. Bicking and F. C. Novello, U.S.P. 3,255,198/1966 (*Chem. Abs.*, 1966, **65**, 15,386*f*).
[9] B. Oddo and Q. Mingoia, *Gazzetta*, 1927, **57**, 465.
[10] W. Asker, A. Mustafa, M. K. Hilmy, and M. A. Allam, *J. Org. Chem.*, 1958, **23**, 2002.
[11] G. M. Singer, Ph.D. Thesis, University of Saskatchewan, 1970.

Its n.m.r. spectrum ($CDCl_3$) contained signals at δ 7·92 (4H, m, Ar*H*), 2·95 [2H, t, *J* 3 Hz, :C(Ar)C*H*$_2$CH$_2$], 1·95 [2H, m, :C(Ar)CH$_2$C*H*$_2$], 1·50 [2H, m, :C(Ar)CH$_2$CHC*H*$_2$-CH$_3$], and 0·97 (3H, m, CH$_3$). The mass spectrum showed *m/e* 223 (M^+, 0·7%), 194 [$(M - 29)^+$, 24], 181 [$(M - 42)^+$, 100], 159 ($M - SO_2$, 6), 130 (5), 103 (14), 76 (18), and 50 (16). This spectrum could be accounted for as in Scheme 1.



SCHEME 1

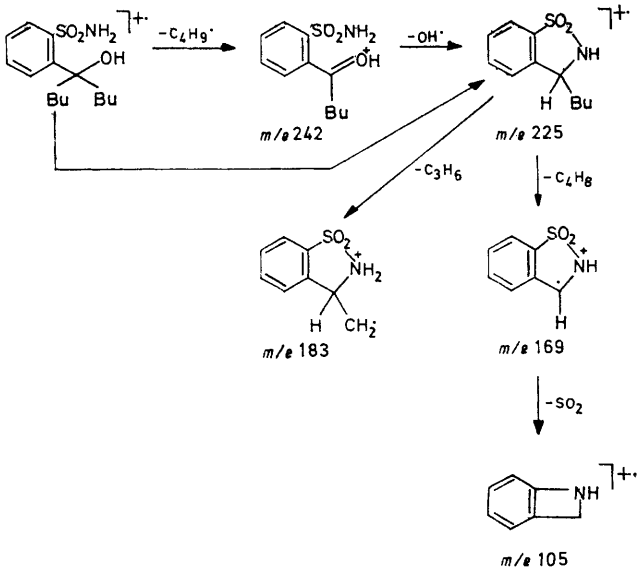
The spectral properties of the carbinols (8) are consistent with the proposed structure and will be illustrated with *o*-(1-butyl-1-hydroxypentyl)benzenesulphonamide (8b). Its i.r. spectrum showed the presence of a hydroxy- (3495 cm^{-1}) and a primary amino-group (3360 and 3255 cm^{-1}), aliphatic C–H (2980—2840 cm^{-1}), a sulphonamide group (ν_{SO_2} 1312 and 1155 cm^{-1}), and an *ortho*-disubstituted benzene (780 and 755 cm^{-1}). The n.m.r. spectrum had signals at δ 8·64 (1H, d, 6-H), 8·10—7·68 (3H, m, ArH), 6·28 (1H, s, OH) and 4·88 (2H, s, NH$_2$) (both D_2O exchangeable, 2·50—2·28 [4H, m, C*H*$_2$·C(OH)·C*H*$_2$], 1·90—1·70 (8H, m), and 1·30 (6H, t, 2 × Me). Not unexpectedly for a tertiary benzylic alcohol, the mass spectrum showed no parent ion peak. Fragment ions were observed at *m/e* 242 (11%), 225 (100), 183 (12), 169 (2), and 105 (11), among others, and can be rationalised as in Scheme 2.

The structure of benzisothiazolines (2) followed from their spectral properties and from their synthesis from (8). The secondary NH (3250 cm^{-1}) and sulphonamide group (ν_{SO_2} 1340 and 1135 cm^{-1}) were evident from the i.r. spectra of the compounds. The n.m.r. spectrum of (3d) in $CDCl_3$ exhibited only aromatic protons and an exchangeable singlet due to NH.

The open-chain alcohols (8b and d) were readily dehydrated in concentrated sulphuric acid to give the 1,2-benzisothiazoline 1,1-dioxide (2) in good yield.

The reaction of saccharin with organolithium compounds was found to give the desired 3-alkyl-(or aryl)-1,2-benzisothiazole 1,1-dioxide (1) exclusively at —78°, as shown in Table 1. Thus, a general method for the preparation of (1) is available.

3-Chloro-1,2-benzisothiazole-1,1-dioxide (3) was examined briefly as a possible precursor to (1). It is known [12] to react with Grignard reagents to yield the 3,3-dialkyl-(or diaryl)-1,2-benzisothiazoline 1,1-dioxide (2).



SCHEME 2

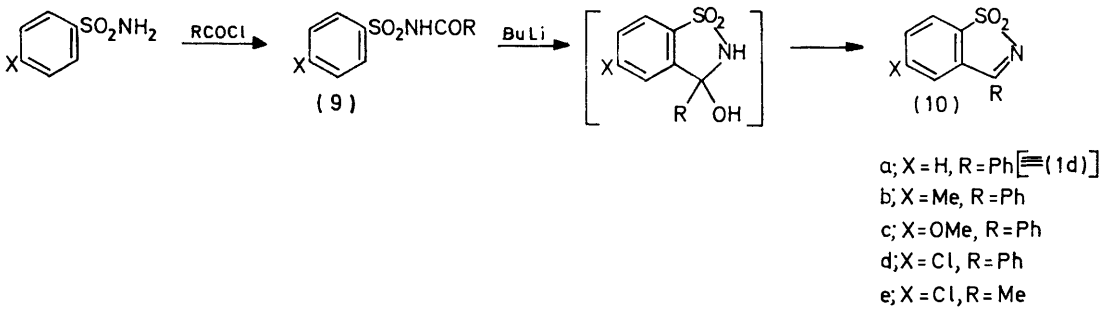
When compound (2) in tetrahydrofuran was treated with n-butyl-lithium at —78°, 3,3-dibutyl-1,2-benzisothiazoline 1,1-dioxide (2b) was isolated as the major product,

[12] A. Mustafa and M. K. Hilmy, *J. Chem. Soc.*, 1952, 1339.

together with a small amount of (1b). A minor amount of another compound was also isolated whose structure is under investigation.

3-(*o*-Tolyl)-1,2-benzisothiazole 1,1-dioxide (1f) was oxidised with potassium permanganate in pyridine to yield 3-(*o*-carboxyphenyl)-1,2-benzisothiazole 1,1-dioxide (1h). All attempts to date to hydrolyse the dithian derivative (1c) to the corresponding aldehyde failed.

An alternative approach to 3-substituted 1,2-benzisothiazole 1,1-dioxides (10) bearing substituents in the benzene ring was sought and the intramolecular cyclisation of *N*-acylbenzenesulphonamides (9) (Scheme 3) was investigated. Attempts to cyclise *N*-benzoylbenzenesulphonamides (9) with concentrated sulphuric acid or polyphosphoric acid failed.

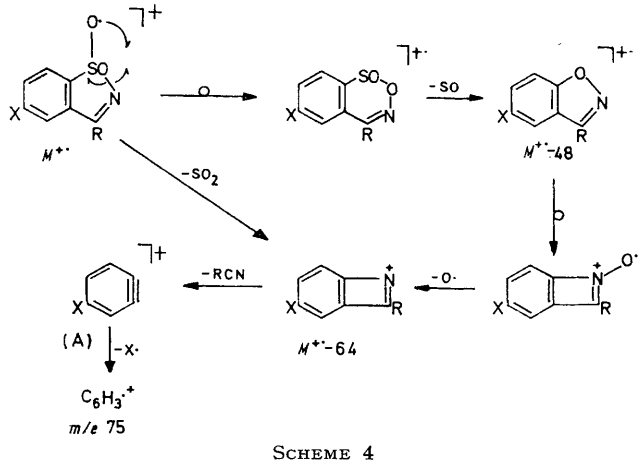


SCHEME 3

TABLE 2

Fragmentation pattern for the mass spectrum of 3,5-disubstituted 1,2-benzisothiazole 1,1-dioxides (10)
m/e (% relative intensity)

	$M^{+\cdot}$		$M^{+\cdot} - 48$		$M^{+\cdot} - 64$		(A)		*m/e* 75
(10e)	215	(59)	167	(73)	151	(40)	110	(100)	(83)
	217	(22)	169	(24)	153	(18)	112	(35)	
(10b)	257	(32)	209	(26)	193	(100)	90	(40)	(9)
(10c)	273	(81)	225	(24)	209	(33)	106	(76)	(17)
(10d)	277	(50)	229	(26)	213	(100)	110	(39)	(69)
	279	(20)	231	(91)	215	(34)	112	(13)	



SCHEME 4

Several examples are known in which *NN*-disubstituted or *N*-substituted benzenesulphonamides are treated with butyl-lithium to give the *o*-lithio- or the *o*,*N*-dilithio-derivative, respectively, which, on treatment with an aldehyde, ketone, or carbon dioxide yield the desired alcohol or acid.[13-15] Intramolecular cyclisation of *N*-acylbenzenesulphonamides (9) in the presence of n-butyl-lithium gave low yields of the desired 3-alkyl- or 3-aryl-1,2-benzisothiazole 1,1-dioxides (10). The corresponding *N*-acylbenzenesulphonamide and/or benzenesulphonamide were also isolated. The low yields make this an unsatisfactory method of synthesis of benzisothiazole 1,1-dioxides.

The mass spectral fragmentation pattern of the 3,5-disubstituted 1,2-benzisothiazole 1,1-dioxides is summarised in Table 2 and can readily be accounted for on the basis of Scheme 4.

EXPERIMENTAL

All reactions were carried out under a dry nitrogen atmosphere. Ether and tetrahydrofuran (THF) were distilled from lithium aluminium hydride immediately before use. Benzene was distilled from sodium.

Reaction of Saccharin with Organolithium Reagents.—In a typical example, the solution of the organolithium reagent (0·02 mol) was added to a solution of saccharin (1·83 g, 0·01 mol) in anhydrous ether (or THF) (200 ml) at the specified temperature. The reaction mixture was stirred for 4—12 h and then hydrolysed with ice–water (100 ml). The aqueous solution was adjusted to pH 9 with dilute hydrochloric acid and extracted with ether (4 × 50 ml). Evaporation of the dried (Na_2SO_4) ether extract gave a residue which was purified by recrystallisation, column, or preparative layer chromatography (p.l.c.) to yield the products shown in Table 1. Elemental analyses and m.p.s are given in Table 3.

[13] H. Watanabe, R. P. Schwarz, C. R. Hauser, J. Lewis, and D. W. Slocum, *Canad. J. Chem.*, 1969, **47**, 1543.
[14] H. Watanabe, R. L. Gray, and C. R. Hauser, *J. Org. Chem.*, 1968, **33**, 900.
[15] J. C. Lombardino, *J. Org. Chem.*, 1971, **36**, 1843.

The aqueous phase was then acidified to pH 1 with dilute hydrochloric acid and extracted with ether (3 × 25 ml) to give unchanged saccharin.

TABLE 3

3-Substituted 1,2-benzisothiazole 1,1-dioxides (1)

	M.p. (°C) [a]	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
(1a)	217	$C_8H_7NO_2S$	52·9	3·9	53·0	3·9
(1b)	94	$C_{11}H_{13}NO_2S$	59·1	5·9	59·2	5·9
(1c)	175—177	$C_{11}H_{11}NO_2S_3$	46·5	4·0	46·3	3·9
(1d)	168 [b]					
(1e)	201	$C_{14}H_{11}NO_3S$	61·4	4·1	61·5	4·0
(1f)	118	$C_{14}H_{11}NO_2S$	65·4	4·5	65·4	4·3
(1g)	166—168	$C_{12}H_8N_2O_2S$	59·1	3·5	59·1	3·3
(1h)	200—205	$C_{14}H_9NO_4S$	58·8	3·2	58·5	1·3

[a] From absolute ethanol. [b] Lit.,[4] 164°.

Reactions of Saccharin with Grignard Reagents.—General procedure. To a solution of saccharin (1·83 g, 0·01 mol) in dry ether (or THF) (200 ml) was added a solution of the Grignard reagent (0·02 mol) over 15 min. The resulting solution was stirred for 4—12 h at the specified temperature and hydrolysed with ice–water (150 ml). The aqueous phase was acidified to pH 1 and extracted with ether (4 × 50 ml). The combined ether extracts were washed with 10% sodium hydrogen carbonate solution (3 × 50 ml) to remove unchanged saccharin. Evaporation of the dried (Na_2SO_4) ether solution gave a mixture which was resolved by column or preparative layer chromatography to give the products described in Table 1 and whose elemental analyses and m.p.s are given in Tables 3 and 4.

TABLE 4

Benzenesulphonamides (8)

	M.p. (°C) [a]	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
(8a)	121	$C_9H_{13}NO_3S$	50·3	6·2	50·2	6·1
(8b)	128—130	$C_{15}H_{25}NO_3S$	60·4	8·5	60·2	8·6
(8d)	196	$C_{19}H_{17}NO_3S$	67·3	5·3	67·2	5·1

[a] From absolute ethanol.

3-(1,3-*Dithian*-2-*yl*)-1,2-*benzisothiazole* 1,1-*Dioxide* (1c).—A solution of saccharin (3·66 g, 0·02 mol) in anhydrous THF (100 ml) was added to a solution of 2-lithio-1,3-dithian (0·05 mol) in THF (100 ml) at −20° to give a blue solution which was stirred for 4 h. The reaction mixture was treated as described in the general method to give (1c) as a *yellow solid* (4·56 g, 80%), m.p. 175—177° (from absolute EtOH), $\nu_{max.}$ (KBr) 2960, 2900 (C–H), 1590—1600 (C=N), and 1350 and 1170 cm^{-1} (SO_2); owing to high insolubility in all common n.m.r. solvents, the spectrum was not recorded; *m/e* 285 (60·1%, $M^{+\cdot}$), 252 (32), 220 (12), 193 (16), 192 (20), 188 (26), 162 (64), 148 (26), 147 (14), 146 (24), 136 (10), 135 (14), 119 (28), 103 (100), 86 (60), 76 (54), and 73 (38).

3-(*o-Carboxyphenyl*)-1,2-*benzisothiazole* 1,1-*Dioxide* (1h).—To a solution of 3-(*o*-tolyl)-1,2-benzisothiazole 1,1-dioxide (1f) (2·50 g, 0·01 mol) in pyridine (25 ml) was added a solution of potassium permanganate (8·0 g, 0·05 mol) in water (150 ml) in portions and the solution was stirred at room temperature for 12 h. The excess of permanganate was destroyed with sulphur dioxide and the solution filtered to remove the precipitated manganese dioxide. The aqueous solution was made strongly alkaline with sodium hydroxide pellets (2·0 g) and then extracted with chloroform using a liquid–liquid extractor to remove unchanged (1f) (0·3 g, 12%). The aqueous solution was acidified and extracted in a liquid–liquid extractor with chloroform. Evaporation of the dried (Na_2SO_4) chloroform extract *in vacuo* gave an oil which, on trituration with absolute ethanol, gave (1h) as a *white solid* (1·40 g, 48%), m.p. 200—205° (from absolute ethanol), $\nu_{max.}$ (KBr) 3500—3400 (OH), 3080 (aromatic CH), 3000—2500 (OH), 1670 (C=O), 1340, 1310, and 1180 cm^{-1} (SO_2), δ (CH_3OD) 7·04—7·54 (5H, m), 7·90—8·04 (2H, m), 8·50 (1H, t), and 8·68—8·72 (1H, d), *m/e* 270 (20%), 243 (30), 180 (40), 179 (90), 178 (15), 177 (10), 153 (40), 152 (20), 104 (15), 102 (12), 77 (28), and 76 (100).

3,3-*Di-n-butyl*-1,2-*benzisothiazoline* 1,1-*Dioxide* (2b).—*o*-(1-Butyl-1-hydroxypentyl)benzenesulphonamide (8b) (0·20 g) was dissolved in conc. sulphuric acid (5 ml) at room temperature and the solution kept for 12 h. It was then diluted with water (60 ml) to give a white precipitate which was extracted with ether (2 × 30 ml). The dried ($MgSO_4$) ether extract was evaporated to give (2b) as a white solid (0·166 g), m.p. 64—65° (lit.,[12] 72°), δ ($CDCl_3$) 8·20—8·61 (4H, m), 5·52 (1H, s, exchangeable), 2·71 (4H, m), 2·11 (8H, m), and 1·67 (6H, m).

3,3-Diphenyl-1,2-benzisothiazole 1,1-dioxide (2d) (87%), m.p. 210—212° (lit.,[12] 210°), was similarly prepared from diphenyl-*o*-sulphonamidophenylmethanol.

Reaction of Saccharin pseudo-*Chloride with n-Butyl-lithium.*—(a) *In dilute solution.* A solution of saccharin *pseudo*-chloride [16] (2·10 g, 0·01 mol) in dry THF (200 ml) at −78° was treated with *n*-butyl-lithium (0·01 mol) over 20 min. The red solution was stirred for 3·5 h at −78°, and the mixture was then decomposed with water (30 ml). The excess of THF was evaporated off *in vacuo*, and the aqueous solution was acidified with dilute hydrochloric acid and extracted with chloroform (3 × 100 ml). The dried ($MgSO_4$) chloroform solution was evaporated *in vacuo* to yield a yellow oil (2·42 g). This was dissolved in chloroform (100 ml) and extracted with 5% Na_2CO_3 solution (3 × 20 ml). The dried ($MgSO_4$) chloroform solution was evaporated *in vacuo* to give a yellow oil (1·95 g). Trituration of the oil with ether (10 ml) gave (1b) as a white solid (0·22 g, 10%), m.p. 81—83°. The remaining oil was separated by p.l.c. on silica gel using chloroform as eluant to give a light orange-brown oil (0·097 g), R_F 0·2, which was not further investigated; (2b) (0·66 g, 24%), R_F 0·66, m.p. 63—64° (identical with the sample obtained previously) (lit.,[12] 72°); and (1b) (0·39 g, 17·5%), R_F 0·4, m.p. 79—81°. The red basic solution was acidified with dilute hydrochloric acid and then extracted with chloroform (3 × 40 ml). Evaporation of the dried ($MgSO_4$) extract gave saccharin (0·27 g, 6·7%).

(b) *In concentrated solution.* Saccharin *pseudo*-chloride (2·10 g, 0·01 mol) in dry THF (75 ml) gave a yellow oil (2·02 g) which, on trituration with ether, gave a yellow solid (0·29 g), m.p. 211—212° (from acetone–ether); $\nu_{max.}$ (KBr) 3080w, 3000—2850w, 1605w, 1557m, 1453m, 1376m, 1340s, 1280m, 1258m, 1222m, 1175s, 1131w, 1121w, 1040w, 906w, 897w, 820m, 772s, 748m, 704w, and 680w cm^{-1}. The yellow oil remaining on evaporation of the ether was separated by p.l.c. on silica gel using benzene–ethyl acetate (9 : 1 v/v) as eluant to give a yellow-orange oil (0·030 g), R_F 0·33, which was not further investigated, (3b) (0·76 g, 27%), m.p. 64—65°, and (1b) (0·14 g, 6·5%), m.p. 50—55°, which were identified by comparison of their spectral properties with those of authentic samples.

[16] E. Stephen and H. Stephen, *J. Chem. Soc.*, 1957, 490.

Reaction of Saccharin pseudo-*Chloride with n-Butylmagnesium Bromide at* −8°.—n-Butylmagnesium bromide (0·1 mol) was added to saccharin *pseudo*-chloride (2·02 g, 0·01 mol) in anhydrous ether (100 ml) at −8° to give a red suspension which was stirred at −8 to −5° for 2 h and then at room temperature for 4 h. The mixture was hydrolysed with ice–water, and then acidified to pH 1 with 10% sulphuric acid. An insoluble light yellow solid (0·050 g), m.p. 215—218°, was filtered off and had an i.r. spectrum identical with that of the compound obtained with Bu^nLi. The acidic solution was extracted with ether (3 × 50 ml) and the combined ether extracts were extracted with 5% sodium hydrogen carbonate solution. The dried ($MgSO_4$) ether solution was evaporated to give a yellow oil (0·50 g) which, on p.l.c. on silica gel using chloroform as eluant, gave (1b) (0·12 g), and (2b) (0·097 g), identified by comparison of their i.r. spectra with those of authentic asmples.

p-*Substituted* N-*Benzoyl- and* N-*Acetyl-benzenesulphonamides* (9).—The *p*-substituted benzenesulphonamide (0·10 mol), benzoyl chloride (0·22 mol), and pyridine (90 ml) were mixed and kept at 0—10° for 24 h. Ethanol (40 ml) was added to the mixture which was then poured into 4N-hydrochloric acid (1 l). The acidic solution was extracted with chloroform (3 × 200 ml), the combined extracts were extracted with 10% sodium hydroxide solution, and the basic solution was acidified and extracted with chloroform (3 × 100 ml). The dried ($MgSO_4$) extract was evaporated *in vacuo* to give the benzenesulphonamide as a white crystalline solid: *N*-benzoylbenzenesulphonamide (9a) (72·5%), m.p. 149—151° (lit.,[11] 146—147°); *N*-benzoyltoluene-*p*-sulphonamide (9b) (72·5%), m.p. 135—136° (from absolute ethanol) (lit.,[17] 147—150°); *N*-benzoyl-*p*-methoxybenzenesulphonamide (9c) (67·5%), m.p. 146° (from absolute ethanol) (lit.,[18] 146—147°); *N*-benzoyl-*p*-chlorobenzenesulphonamide (9d) (65%), m.p. 169—170° (lit.,[19] 182°).

N-Acetyl-*p*-chlorobenzenesulphonamide (9e) (96·0%) was prepared from *p*-chlorobenzenesulphonamide (9·60 g, 0·05 mol) and acetic anhydride (7 ml), m.p. 187—188° (lit.,[19,20] 191—192°).

Reaction of N-*Acylbenzenesulphonamides with n-Butyllithium.—General method.* The *N*-acylbenzenesulphonamide (0·01 mol) in anhydrous THF (75 ml) was treated with n-butyl-lithium (0·02 mol) at −78° for 4 h. The mixture was decomposed with water (30 ml), and the THF was removed *in vacuo*. The aqueous solution was extracted with chloroform, and the dried ($MgSO_4$) extract was evaporated *in vacuo* to give the desired product. The aqueous solution was acidified with dilute hydrochloric acid, and the aqueous solution was extracted with chloroform and the dried ($MgSO_4$) extract was evaporated *in vacuo* to give a mixture of sulphonamides.

3-Phenyl-1,2-benzisothiazole 1,1-dioxide (1d) was obtained as white crystals (0·214 g, 8·8%), m.p. 166—168° (from ethanol) (lit.,[4] 164°). From the acidified solution was obtained a white solid (0·701 g) which was a mixture of benzenesulphonamide, *N*-benzoylbenzenesulphonamide, and valerophenone (32%).

5-Methyl-3-phenyl-1,2-benzisothiazole 1,1-*dioxide* (10b). *N*-Benzoyltoluene-*p*-sulphonamide (2·774 g, 0·01 mol) was treated with n-butyl-lithium (0·02 mol) for 14 h at −78° as previously described, to yield an oily solid (1·267 g) which was separated by t.l.c. on silica gel using benzene as eluant, to give crude n-butyl phenyl ketone, R_F 0·5, as a pale yellow oil (0·663 g), and (10b), R_F 0·3 (0·0912 g, 3·5%), as *crystals*, m.p. 176—177° [from chloroform–light petroleum (b.p. 30—60°)] (Found: C, 65·5; H, 4·4. $C_{14}H_{11}NO_2S$ requires C, 65·4; H, 4·3%), $\nu_{max.}$ (KBr) 1590 (C=N), 1329, and 1183 cm^{-1} (SO_2), δ ($CDCl_3$) 2·52 (3H, s, ArMe) and 8·10—7·40 (8H, m, ArH).

From the acidified solution was isolated a white solid (1·615 g) whose i.r. spectrum indicated it to be a mixture of toluene-*p*-sulphonamide and *N*-benzoyltoluene-*p*-sulphonamide.

5-Methoxy-3-phenyl-1,2-benzisothiazole 1,1-*dioxide* (10c). *N*-Benzoyl-*p*-methoxybenzenesulphonamide (2·73 g, 0·0094 mol) was treated with n-butyl-lithium (0·02 mol) for 4 h at −78° as previously outlined to yield a yellow oil (0·507 g) which, on trituration with light petroleum (b.p. 30—60°), gave a white solid (0·157 g, 3·9%). This was purified by t.l.c. on silica gel using chloroform as eluant and recrystallised from chloroform–light petroleum (b.p. 30—60°) to give *compound* (10c) (0·071 g, 1·8%), m.p. 115—116° (Found: C, 61·4; H, 4·3. $C_{14}H_{11}NO_3S$ requires C, 61·5; H, 4·1%), $\nu_{max.}$ (KBr) 1580 (C=N) and 1323 and 1170 cm^{-1} (SO_2), δ ($CDCl_3$) 3·92 (3H, s, ArOMe) and 8·20—7·00 (8H, m, ArH). Evaporation of the light petroleum mother liquors gave n-butyl phenyl ketone. *N*-Benzoyl-*p*-methoxybenzenesulphonamide (2·361 g) was recovered from the aqueous layer.

5-Chloro-3-phenyl-1,2-benzisothiazole 1,1-*dioxide* (10d). T.l.c. of the products on silica gel using chloroform as eluant gave a fraction (R_F 0·1—0·2) as a white solid (0·023 g) which was not further investigated, and *compound* (10d), R_F 0·7 (0·096 g), m.p. 153—154° [from chloroform–light petroleum (b.p. 30—60°)] (Found: C, 56·3; H, 3·1. $C_{13}H_8ClNO_2S$ requires C, 56·2; H, 2·9%), $\nu_{max.}$ (KBr) 1594 (C=N), and 1325 and 1171 cm^{-1} (SO_2), δ ($CDCl_3$) 7·50—8·15 (m, ArH). Starting material (2·507 g) was also recovered.

5-Chloro-3-methyl-1,2-benzisothiazole 1,1-*dioxide* (10e) was obtained as a pale yellow solid (0·032 g), m.p. 211—213° (Found: C, 44·3; H, 2·8. $C_8H_6ClNO_2S$ requires C, 44·5; H, 2·8%), $\nu_{max.}$ (KBr) 1580 (C=N), and 1332 and 1175 cm^{-1} (SO_2), δ ($CDCl_3$) 2·69 (3H, s, ArMe) and 7·60—7·90 (3H, m, ArH). *N*-Acetyl-*p*-chlorobenzenesulphonamide (1·908 g) was recovered.

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