A Novel Route to 2-Substituted 1,2-Benzisothiazol-3(2*H*)-ones

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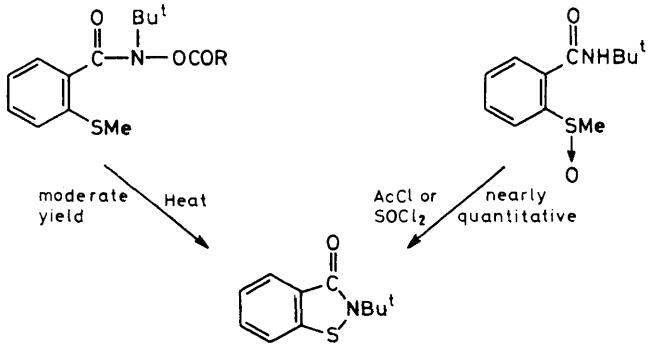
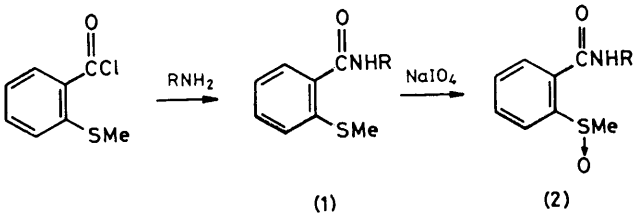
Summary 2-Alkyl- and 2-aryl-1,2-benzisothiazol-3(2*H*)-ones were synthesized in high yields by the cyclization of 2-(methylsulphinyl)benzamides with thionyl chloride.

2-SUBSTITUTED 1,2-benzisothiazol-3(2*H*)-ones have received much attention in recent years, owing to their antibacterial and antifungal properties, and there are many reports of their synthesis.[1–3] Recently, we studied the thermal decomposition of *O*-acyl-*N*-[2-(methylthio)-benzoyl]-*N*-t-butylhydroxylamines and found 2-t-butyl-1,2-benzisothiazol-3(2*H*)-one as one of the major products. During our studies of the mechanism of the thermolysis, to be published in detail elsewhere[4], we found that *N*-t-butyl-2-(methylsulphinyl)benzamide was also converted



smoothly into the same product by reaction with acid halides. We report here that the reaction of sulphinylbenzamides with thionyl chloride is a novel and convenient method for preparing 2-substituted 1,2-benzisothiazol-3(2*H*)-ones.



(1) (2)

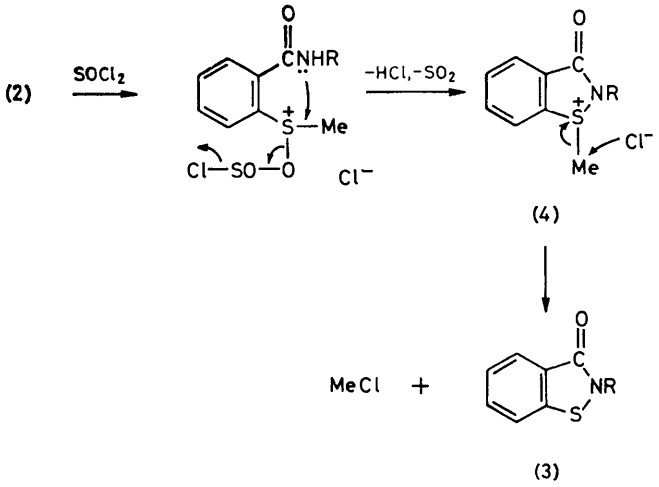
The 2-(methylsulphinyl)benzamides (**2a**—**g**) were prepared (81—94%) by the oxidation of the corresponding sulphides (**1a**—**g**) which were synthesized from the appropriate amines and 2-(methylthio)benzoyl chloride. The cyclizations of (**2a**—**g**) with thionyl chloride were performed in dry dichloromethane. A typical procedure is as follows. Thionyl chloride (1·50 g) was added to a stirred suspension of (**2f**) (2·43 g) in dry dichloromethane (20 ml). The reaction mixture was refluxed for 10 min, then the solvent and the excess of thionyl chloride were removed by distillation under reduced pressure. The residue was chromatographed on alumina with dichloromethane as the eluant to give (**3f**) (2·34 g, 98%) which was recrystallized from carbon tetrachloride–dichloromethane.

TABLE. Preparation of 2-substituted 1,2-benzoisothiazol-3(2*H*)-ones.

Compound	R	m.p. (b.p.)/°C	Yield[a] (%)
(**3a**)	Et	(132 at 2·5 mmHg)	96
(**3b**)	Pr^i	(128 at 2 mmHg)	97
(**3c**)	Bu^t	57—58	77[b]
(**3d**)	C_6H_{11}[c]	87—88[d]	98
(**3e**)	$PhCH_2$	87·5—88·5[e]	98
(**3f**)	Ph	140·5—141·5[f]	98
(**3g**)	*p*-MeC_6H_4	135·5—136·5[g]	98

[a] Isolated yield following chromatographic separation. [b] Isolated yield following distillation;[4] b.p. 166 °C at 2·5 mmHg (lit.,[1] 142 °C at 0·5 mmHg). [c] C_6H_{11} = cyclohexyl. [d] Lit.,[3] m.p. 87—88 °C. [e] Lit.,[3] m.p. 88 °C. [f] Lit.,[3] m.p. 140—141 °C. [g] Lit.,[3] m.p. 136—137 °C.

The other 2-(methylsulphinyl)benzamides (**2a**—**e** and **g**) were smoothly converted into the corresponding compounds (**3**) in nearly quantitative yields by reaction with thionyl chloride under the same conditions (Table). All the compounds synthesized were characterized by spectral and elemental analyses.



(4)

(3)

The formation of another product, chloromethane, derived from the *S*-methyl moiety of the starting material, was confirmed by spectral evidence. Thus, an excess of thionyl chloride was added to (**3e**) in CCl_4–$CDCl_3$ (1 : 1) at room temperature. After about 20 min, the n.m.r. spectrum of the mixture showed completion of the reaction, with singlets at δ 3·00 (3H, MeCl) and 5·13 (2H) and a multiplet at *ca.* δ 7·3—8·3 (9H). A probable mechanism for the cyclization may involve the formation of the acylaminosulphonium salt (**4**) as an intermediate, followed by attack of chloride ion on the *S*-methyl carbon to afford (**3**) and chloromethane.[4,5]

The procedure described here is a convenient method for the general preparation of the title compounds as shown in the Table.

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