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SYNTHESIS AND REACTION OF 3-(ALKYLTHIO)-1,2-BENZISOTHIAZOLE 1,1-DIOXIDES AS AN ODORLESS CRYSTALLINE EQUIVALENT OF THIOLS

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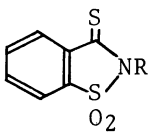
It was found that sodium salt of 1,2-benzisothiazol-3(2H)-thione 1,1-dioxide (thiosaccharin) readily reacted with alkyl halide affording 3-(alkylthio)-1,2-benzisothiazole 1,1-dioxide, which very smoothly produced the corresponding alkanethiol by the reaction with piperidine in almost quantitative yield.

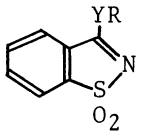
The first report regarding the alkylation of thiosaccharin (1a) has been described by Mannessier,[1] who obtained a methyl derivative of 1a in poor yield in a reaction with dimethyl sulfate and proposed N-methylthiosaccharin (1b) as the structure of the methyl derivative. Meadow and Cavagnol have then reinvestigated the reaction and elucidated that the structure of the methyl derivative was not 1b but 3-(methylthio)-1,2-benzisothiazole 1,1-dioxide (3, R=CH_3, Y=S).[2]

Recently the herbicidal and fungicidal properties of 3-substituted 1,2-benzisothiazole 1,1-dioxides (3) have been noted,[3,4] and the preparation of such compounds was achieved by the reaction of 2 with an alcohol or a thiol in the presence of base.[4] Since almost all thiols have unpleasant odor, it would be better if a synthetic route employing a thiol could be avoided. In cases where there is no alternative than to use a thiol, the development of a new method to produce the thiol quantitatively in situ, especially in an aprotic solvent, will relieve us of the unpleasant odor.



1a, R=H; 1b, R=CH_3

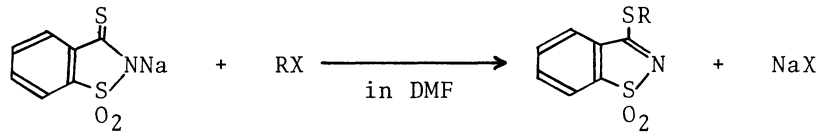
2



3, Y=O or S

From these points of view, we tried to prepare 3-(alkylthio)-1,2-benzisothiazole 1,1-dioxides (6) from sodium salt (4) of 1a and alkyl halides as follows: to a solution of 4 (663 mg, 3 mmol) in DMF (2 ml) was added a solution of benzyl bromide (5a, 564mg, 3.3 mmol) in DMF (2 ml) at room temperature under nitrogen. After stirring for

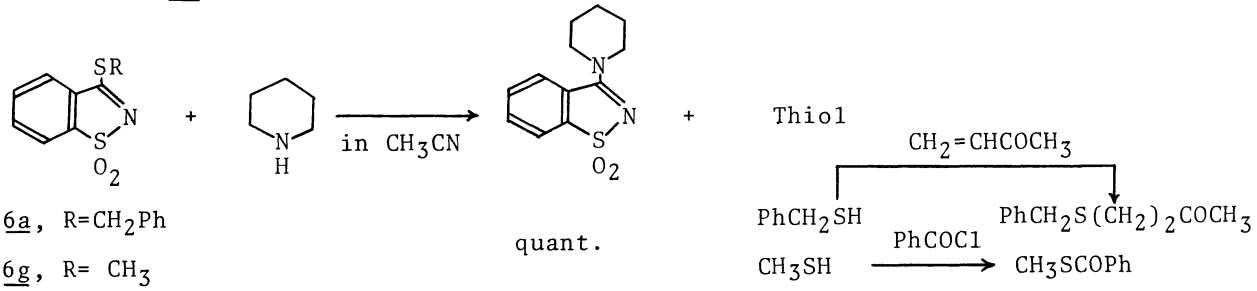
3 h, water was added to reaction mixture to precipitate the product. The precipitate was recrystallized from ethanol and dichloromethane to give 6a (791 mg, 93%). Its structure was found to be consistent with 3-(benzylthio)-1,2-benzisothiazole 1,1-dioxide prepared by the reaction of 2 and benzenemethanethiol in the presence of triethylamine in acetonitrile. In a similar way, other 3-(alkylthio)-1,2-benzisothiazole 1,1-dioxides (6b-g) were prepared in excellent yields as shown in Table. All 6 prepared in such a way were odorless crystalline compounds and reacted smoothly with secondary amines stoichiometrically. For example, the reaction of 6a with piperidine in acetonitrile proceeded completely within 10 min at room temperature (monitored by TLC) producing benzenemethanethiol, which was successfully trapped with 3-buten-2-one without isolation as shown in the following scheme. In a case of 6g the reaction also took place in the same manner.



4 5a-g 6a-g

RX 5a-g	Condition	Yield (%) 6a-g[a]	Mp (°C)
5a, $C_6H_5CH_2Br$	r.t., 3h	93	141.0-142.0
5b, $C_6H_5CH_2CH_2Br$	50°C, 11h	82	144.5-145.5
5c, $C_6H_5CH=CHCH_2Cl$	50°C, 3.5h	84	129.5-130.5
5d, $CH_2=CHCH_2Br$	r.t., 3h	87	114.o-115.0
5e, $CH\equiv CCH_2Br$	r.t., 4h	80	168.0-169.0
5f, $N\equiv CCH_2Cl$	r.t., 3.5h	85	234.5-235.5
5g, CH_3I	r.t., 3h	89	227.5-228.5

a) All new compounds(excepy 6g) have been fully characterized by spectral means and elemental analysis.



6a, R=CH_2Ph

6g, R= CH_3

quant.

From these results, it is clear that readily available 6 is a useful equivalent of the corresponding thiol. The related work is now in progress.

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