

David M. McKinnon\* and Azza A. Abouzeid

Chemistry Department, University of Manitoba,  
Winnipeg, Canada R3T 2N2  
Received February 28, 1991

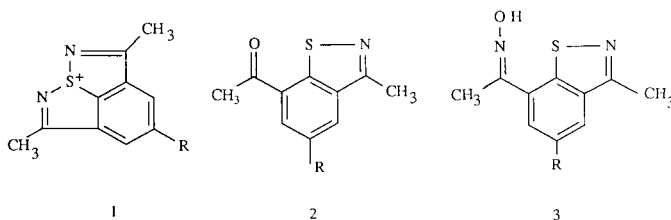
Three 7-acetyl-1,2-benzisothiazoles have been made by cyclisation of the monooximes of 2-methylthio-1,3-diacetylbenzenes. The oximes of these ketones dissolved in acidic media give only protonated forms, and no indication of the formation of stable bridged sulfonium ions.

*J. Heterocyclic Chem.*, **28**, 1193 (1991).

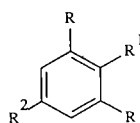
In a number of heterocyclic sulfur compounds, the interaction of some substituent groups with the ring sulfur has been demonstrated. For example, the interaction of an acylmethylene- or thioacylmethylene-group with the ring sulfur in the 1,2-dithioles leads to extra bonding [1,2]. The low, *ca.* 1660  $\text{cm}^{-1}$ , infra red carbonyl stretching frequency in some 7-acetyl-1,2-benzisothiazoles has been attributed to sulfur-oxygen interaction, also leading to extra bonding [3]. A 7-thioacylbenzo-1,2-dithiolium salt demonstrates symmetry as determined by nmr [4]. Whether this is due to a degenerate rearrangement or to resonance has not been established. Diazonium groups in the 7-position of benzothiazoles, 1,2-benzisothiazoles and 1,2,3-benzothiadiazoles interact with the ring sulfur atom, leading to rearranged products [5,6,7,8]. Although in most cases metal ions appear to be involved in the interaction in other cases these are not present and the nature of the interaction may be by a bridged sulfonium ion, allowing the rearrangement. However such sulfonium salts were not detectable by spectroscopy. Because of our interest in isothiazoles, we have investigated whether similarly fused isothiazolo[4,5,1-*hi*]-benzisothiazolium salts of type **1**, made from the oximes of 7-acetyl-1,2-benzisothiazoles **2**, could be made or detected. The cyclisation of *o*-methylthioarylketoximes represents a useful synthesis of 1,2-benzisothiazoles [9], and the oximes **3** appeared suitable precursors for the salts **1**.

7-Acetyl-3-methyl-1,2-benzisothiazole (**2a**) was converted to its oxime **3a**. When this was treated with perchloric acid or hydrobromic acid, salt-like materials were obtained. These were rather poorly soluble but the spectrum of the product from perchloric acid indicated two different methyl groups, and the aromatic protons as an ABC pattern, inconsistent with the symmetrical fused structure **1a**. Likewise the spectrum of the oxime dissolved in a mixture of hexadeuterioacetone and trifluoroacetic anhydride demonstrated two different methyl groups. This spectrum was unchanged over several days. The analysis of the salt from hydrobromic acid was consistent with a protonated form of the oxime, and treatment of the salts with aqueous potassium hydroxide regenerated the starting oxime. No products arising from a Beckmann rearrangement were observed.

With the possibility that the bridged cations might be stabilised by electron releasing groups, compounds with

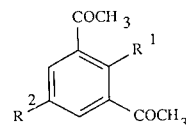


a R = H  
b R = S $\text{CH}_3$   
c R = N(CH $_3$ ) $_2$



4

a R = CO $_2$ H, R $^1$  = Cl, R $^2$  = NO $_2$   
b R = COCH $_3$ , R $^1$  = Cl, R $^2$  = NO $_2$   
c R = COCH $_3$ , R $^1$  = R $^2$  = S $\text{CH}_3$



5

a R $^1$  = Cl, R $^2$  = NH $_2$   
b R $^1$  = Cl, R $^2$  = N(CH $_3$ ) $_2$   
c R $^1$  = S $\text{CH}_3$ , R $^2$  = N(CH $_3$ ) $_2$

5-methylthio- and 5-dimethylamino-groups have been synthesised. 2-Chloro-5-nitrobenzene-1,3-dicarboxylic acid (**4a**) was converted by reaction of its acid chloride with diethyl ethoxymagnesiummalonate and hydrolysis into 1,3-diacetyl-2-chloro-5-nitrobenzene (**4b**). When this was treated with lithium methanethiolate in dimethylformamide both chlorine and nitro substituents were displaced giving 1,3-diacetyl-2,5-bismethylthiobenzene (**4c**). Related displacements of nitro groups by methanethiolate have been reported [10]. The diketone was treated with one equivalent of hydroxylamine and the resulting mixture of monooxime, dioxime and starting material was heated in a mixture of acetic anhydride and pyridine giving 7-acetyl-3-methyl-5-methylthio-1,2-benzisothiazole (**2b**).

The chloronitrodiketone **4b** was reduced with tin in hydrochloric acid giving 5-amino-2-chloro-1,3-diacetylbenzene (**5a**), which reacted with methyl iodide and potassium carbonate giving the dimethylamino-compound **5b**. This was unreactive to lithium methanethiolate at room temperature but at 150° in a pressure bottle it gave 1,3-diacetyl-5-dimethylamino-2-methylthiobenzene (**5c**). Treatment of this with one equivalent of hydroxylamine and reaction of the crude oxime mixture gave 7-acetyl-5-dimethylami-

no-3-methyl-1,2-benzisothiazole (**2c**). These ketones **2b** and **2c** had infra red absorptions at 1662 and 1657  $\text{cm}^{-1}$  respectively, frequencies similar to those observed for other 7-acetyl-1,2-benzisothiazoles [3].

The ketones **2b** and **2c** were converted into their oximes **3b** and **3c** respectively by reaction with hydroxylamine. Compound **1b** reacted with both hydrobromic and perchloric acids to form salts. The bromide was insufficiently soluble for an nmr study, but the perchlorate, dissolved in hexadeuterioacetone, gave a spectrum with three methyl peaks, and two distinct aromatic peaks, consistent with an asymmetrical structure, and therefore assigned to a protonated form of the oxime rather than a bridged ion. Had the latter been formed, as the preferred conformation of the methylthio-group would have been in the plane of the aromatic ring, an asymmetrical structure would have been formed. However in thioanisoles the observed rotational barrier of methylthio-groups are only of the order of 5 KJ.  $\text{Mol}^{-1}$  [11], and thus at room temperature the two C-methyl groups should have become almost equivalent. In trifluoroacetic anhydride two of the methyl groups and the two aromatic protons become more magnetically equivalent but we consider that this is only a solvent effect. The analyses of these salts were consistent with protonated forms of the oximes.

Likewise the oxime of **1c** reacted with hydrobromic and perchloric acid to form salts. Unfortunately these were too insoluble for nmr studies, but the oxime reacted with trifluoroacetic anhydride to give a yellow material that dissolved in a mixture of trifluoroacetic anhydride and hexadeuterioacetone. The nmr of this solution indicated three separate methyl peaks, in the ratios of 1:1:2, assigned to the two C-methyl groups and the *N,N*-dimethyl groups of an asymmetrical structure. The analysis of the product from hydrobromic acid was consistent with a dihydrobromide of the oxime.

The electron impact mass spectrum of the oxime **3b** indicated a major ion at *M*-16. By accurate mass measurement this was assigned to loss of an oxygen atom. This process was also evident, but to a lesser extent, in the mass spectrum of the oxime **3a**. This process may reflect some substituent-sulfur interaction, *ie.* of hydrogen bonding of the oxime proton to the ring sulfur atom. Thus the oxime proton in the parent ion is attached to the heterocyclic ring, allowing the oxygen atom to be lost. This process should be enhanced by the electron-releasing methylthio group in the 5-position. Consistent with this is the appearance of a large (45%), *M*-16 peak in the oxime **3c** which has the strongly electron-releasing dimethylamino group in the 5-position. Mass spectra of the oximes **3a,b,c** and their hydrobromides, using a FAB technique gave in all cases large *M* + 1 ions, corresponding to protonated species. None of these showed any significant amounts of *M*-17 species corresponding to bridged sulfonium ions.

## EXPERIMENTAL

Nuclear magnetic resonance spectra were measured on a Bruker model 360 spectrometer, and, unless otherwise stated, in deuteriochloroform solution using tetramethylsilane as an internal standard, infra red spectra on a Perkin-Elmer model 881 spectrometer in liquid paraffin mulls, and mass spectra on a model VG707E spectrometer. Mass spectra obtained by the FAB technique were in 4-nitrophenylmethanol matrices. Solutions were dried over anhydrous magnesium sulfate, and thick layer chromatography was performed on 1 mm thick layers of Camag silica gel type DSF-5 in hexane/ethyl acetate mixtures. Analyses were performed by Guelph Chemical Laboratories, Guelph, Ontario, Canada.

### 7-Acetyl-3-methyl-1,2-benzisothiazole Oxime (**2a**).

A solution of 7-acetyl-3-methyl-1,2-benzisothiazole (0.764 g, 4 mmoles) [3] and hydroxylamine hydrochloride (0.278 g, 4 mmoles) and pyridine (0.32 g, 4 mmoles) in methanol (5 ml) was heated under reflux for 4 hours, then the methanol was evaporated. The residue was triturated with water and the product collected. It recrystallised from benzene as pale yellow prisms, mp 222° (87%);  $^1\text{H}$  nmr (hexadeuterioacetone):  $\delta$  = 2.42 ppm (3H, s, oxime methyl), 2.72 (3H, s, acetyl methyl), 7.60 (1H, t, *J* = 6 Hz, C5-H), 7.98, 8.16 (two 1H, d, *J* = 6 Hz, C4-H, C6-H); ms: Calcd. *M* = 206; Found: (electron impact) 206 (*M*<sup>+</sup>) 191 (*M*<sup>+</sup>-CH<sub>3</sub>, 42%), 190 (*M*<sup>+</sup>-O, 30%), 175 (*M*<sup>+</sup>-O, CH<sub>3</sub>, 52%); by FAB, 207 (*MH*<sup>+</sup>).

*Anal.* Calcd. for C<sub>10</sub>H<sub>10</sub>N<sub>2</sub>SO: C, 58.25; H, 4.85; N, 13.59; S, 15.53. Found: C, 58.16; H, 4.91; N, 13.90; S, 15.62.

### 2-Chloro-1,3-diacetyl-5-nitrobenzene (**4b**).

2-Chloro-5-nitrobenzene-1,3-dicarboxylic acid (5.55 g, 0.02 mole) [12] was converted into its acid chloride by treatment with thionyl chloride (10 ml) in benzene (100 ml) at reflux for 24 hours. The solution was evaporated, the product redissolved in benzene (20 ml) and added to a solution of diethyl ethoxymagnesiummalonate [prepared from magnesium (1.44 g, 0.06 mole), diethyl malonate (9.6 g, 0.06 mole) and ethanol (10 ml), as described for related compounds [3,12] in benzene (50 ml)]. The reaction was left at room temperature for 18 hours, then acidified with dilute sulfuric acid. The benzene layer was separated and evaporated to an oil which was boiled in a mixture of acetic acid (10 ml), water (10 ml), and sulfuric acid (1 ml) for 6 hours. This mixture was cooled and extracted with dichloromethane. This extract was washed with base, and water, dried, and evaporated to a crystalline solid which recrystallised from acetone as buff plates, mp 162° (98%);  $^1\text{H}$  nmr:  $\delta$  = 2.78 ppm (6H, s, acetyl), 8.46 (2H, s, C4-H, C6-H); ir 1720 (C=O)  $\text{cm}^{-1}$ ; ms: Calcd. *M* = 243, 241; Found: 243, 241 (*M*<sup>+</sup>); 228, 226 (*M*<sup>+</sup>-CH<sub>3</sub>).

*Anal.* Calcd. for C<sub>10</sub>H<sub>8</sub>ClNO<sub>4</sub>: C, 49.69; H, 3.31; Cl, 14.70; N, 5.79. Found: C, 49.63; H, 3.09; Cl, 14.62; N, 5.88.

### 2,5-Bismethylthio-1,3-diacetylbenzene (**4c**).

To a stirred cold solution of 2-chloro-1,3-diacetyl-5-nitrobenzene (4.82 g, 0.02 mole) in dimethyl formamide (30 ml) was added liquid methanethiol (5 ml). The solution rapidly turned darker. It was stirred a further 30 minutes then poured into ice cold dilute (10%) hydrochloric acid and extracted with dichloromethane (2 x 30 ml). The dried extracts gave a yellow oil on evaporation. This was purified by chromatography. Yellow needles, mp 37°, were obtained (90%);  $^1\text{H}$  nmr:  $\delta$  = 2.35 ppm (3H, s, the 5-S-methyl),

2.43 (3H, s, the 2-S-methyl), 2.61 (6H, s, acetyls), 7.20 (two 1H, s, C4-H, C6-H); ir (1715 (C=O)  $\text{cm}^{-1}$ ; ms: Calcd.  $M = 254$ ; Found: 254, ( $M^+$ ), 239 ( $M^+ \cdot \text{CH}_3$ ), 224 ( $M^+ \cdot 2\text{CH}_3$ ).

*Anal.* Calcd. for  $\text{C}_{12}\text{H}_{14}\text{O}_2\text{S}_2$ : C, 56.69; H, 5.51; S, 25.20. Found: C, 56.83; H, 5.46; S, 25.38.

#### 7-Acetyl-3-methyl-5-methylthio-1,2-benzisothiazole (2b).

A mixture of 2,5-bismethylthio-1,3-diacetylbenzene (0.254 g, 1 mmole), hydroxylamine hydrochloride (0.069 g, 1 mmole) and pyridine (0.1 ml) in ethanol (10 ml) was refluxed for 2 hours. The mixture was diluted with dilute hydrochloric acid and extracted with dichloromethane (2 x 30 ml). The extract was dried and evaporated to a yellowish oil which was heated at reflux in a mixture of acetic anhydride (1 ml) and pyridine (1 ml) for 16 hours. The mixture was cooled and diluted with dilute hydrochloric acid and extracted with dichloromethane (2 x 30 ml). The extracts were washed with water, dilute sodium hydroxide solution, dried and evaporated to a yellow oil. This was separated by chromatography into two main bands. The starting diketone was a virtually colorless band at greater Rf, and the desired isothiazole as a more strongly adsorbed pale yellow band. This was removed and the product isolated. It crystallised from ethanol as pale yellow needles, mp 127-128° (43%);  $^1\text{H}$  nmr:  $\delta = 2.70$  ppm (3H, s, tentatively S-CH<sub>3</sub>), 2.82 (6H, s, the acetyl and 3-methyl), 8.01, 8.08 (two 1H, s, C4-H, C6-H); ir: 1662 (C=O)  $\text{cm}^{-1}$ ; ms: Calcd.  $M = 237$ ; Found: 237 ( $M^+$ ), 222 ( $M^+ \cdot \text{CH}_3$ ), 194 ( $M^+ \cdot \text{CH}_3\text{C}=\text{O}$ ).

*Anal.* Calcd. for  $\text{C}_{11}\text{H}_{11}\text{NOS}_2$ : C, 55.70; H, 4.64; N, 5.90; S, 27.00. Found: C, 55.63; H, 4.65; N, 6.09; S, 26.78.

#### 7-Acetyl-3-methyl-5-methylthio-1,2-benzisothiazole Oxime (3b).

A mixture of the ketone (0.474 g, 2 mmoles), hydroxylamine hydrochloride (0.138 g, 2 mmoles) and pyridine (0.154 g, 2 mmoles) in ethanol (10 ml) was refluxed for 4 hours. The mixture was evaporated and the residue triturated with water (5 ml). The product was collected and recrystallised from ethanol as fibrous pale yellow needles, mp 210° (95%);  $^1\text{H}$  nmr (hexadeuterioacetone):  $\delta = 2.37$  ppm (3H, s, tentatively S-CH<sub>3</sub>), 2.56, 2.64 (two 3H, s, the acetyl and oxime methyls), 7.84, 8.03 (two 1H, s, C4-H and C6-H); ms: Calcd.  $M = 252$ ; Found: 252 ( $M^+$ ), 237 ( $M^+ \cdot \text{CH}_3$ , 24%), 236 ( $M^+ \cdot \text{O}$ , 85%), 221 ( $M^+ \cdot \text{O}$ , CH<sub>3</sub>, 57%); ms: by FAB 253 (MH<sup>+</sup>).

*Anal.* Calcd. for  $\text{C}_{11}\text{H}_{12}\text{N}_2\text{OS}_2$ : C, 52.38; H, 4.76; N, 11.11; S, 25.40. Found: C, 52.30; H, 4.88; N, 11.06; S, 25.58.

#### 5-Amino-2-chloro-1,3-diacetylbenzene (5a).

To a mixture of 2-chloro-1,3-diacetyl-5-nitrobenzene (2.41 g, 0.01 mole) and granulated tin [(2 g) amalgamated with mercury(II) chloride (0.1 g)] was added 50% hydrochloric acid (30 ml) and the mixture was heated on a steam bath for 4 hours. The mixture was made alkaline with sodium hydroxide solution and extracted with chloroform. It was necessary to filter off the tin oxides. The chloroform layer was reextracted with concentrated hydrochloric acid, which was then basified and reextracted with chloroform. This was dried and evaporated to give the amine. It was recrystallised from benzene as a pale yellow prisms mp 96-97, (95%);  $^1\text{H}$  nmr:  $\delta = 2.66$  ppm (6H, s, acetyl), 4.10 (2H, bs, amino), 6.90 (2H, s, C4-H, C6-H); ir 1713 (C=O)  $\text{cm}^{-1}$ ; Calcd.  $M = 213$ , 211; Found: 213, 211 ( $M^+$ ); 198, 196 ( $M^+ \cdot \text{CH}_3$ ).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_{10}\text{ClNO}_2$ : C, 56.73; H, 4.73; Cl, 16.78; N, 6.62. Found: C, 56.88; H, 4.77; Cl, 16.59; N, 6.43.

#### 2-Chloro-1,3-diacetyl-5-dimethylaminobenzene (5b).

A mixture of 5-amino-2-chloro-1,3-diacetylbenzene (4.22 g, 0.02 mole), methyl iodide (5 g) and anhydrous potassium carbonate (5 g) in acetone (30 ml), was boiled gently for 16 hours. The mixture was cooled, filtered and evaporated to give a yellowish solid that was recrystallised from methanol as yellow prisms, mp 86-87° (92%);  $^1\text{H}$  nmr:  $\delta = 2.66$  ppm (6H, s, acetyl), 3.03 (6H, s, N-methyls), 6.83 (2H, s, C4-H, C6-H); ir: 1685 (C=O)  $\text{cm}^{-1}$ ; ms: Calcd. = 241, 239; Found: 241, 239 ( $M^+$ ), 198, 196, ( $M^+ \cdot \text{CH}_3$ ).

*Anal.* Calcd. for  $\text{C}_{12}\text{H}_{14}\text{ClNO}_2$ : C, 60.12; H, 5.85; Cl, 14.82; N, 5.85. Found: C, 60.20; H, 5.88; Cl, 14.99; N, 5.76.

#### 1,3-Diacetyl-5-dimethylamino-2-methylthiobenzene (5c).

A solution of 2-chloro-1,3-diacetyl-5-dimethylaminobenzene (4.82 g, 0.02 mole) in dimethylformamide (15 ml) with finely powdered lithium hydroxide monohydrate (2 g) and liquid methanethiol (3 ml) was heated in a pressure bottle at 150° for 1 hour. The mixture turned reddish with the formation of a gelatinous precipitate. The mixture was acidified and extracted with dichloromethane (2 x 30 ml). The extracts evaporated to an oil which was diluted with water, precipitating the desired amine. This was collected and recrystallised from ethanol as pale yellow plates mp 98° (82%);  $^1\text{H}$  nmr:  $\delta = 2.32$  ppm (3H, s, S-methyl), 2.70 (6H, s, acetyl methyls), 3.05 (6H, s, N-methyls), 6.61 (2H, s, C4-H, C6-H); ir: 1700 (C=O)  $\text{cm}^{-1}$ ; ms: Calcd. = 251; Found: 251 ( $M^+$ ), 236 ( $M^+ \cdot \text{CH}_3$ ); ir: 1700 (C=O)  $\text{cm}^{-1}$ .

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{17}\text{NO}_2\text{S}$ : C, 62.15; H, 6.77; N, 5.58; S, 12.75. Found: C, 62.36; H, 6.83; N, 5.33; S, 12.89.

#### 7-Acetyl-5-dimethylamino-3-methyl-1,2-benzisothiazole (2c).

1,3-Diacetyl-4-dimethylamino-2-methylthiobenzene (5c) (0.251 g, 1 mmole), with hydroxylamine hydrochloride (0.069 g, 1 mmole) and pyridine (0.79 g, 1 mmole) in ethanol (10 ml) was heated under reflux for 3 hours. The solution was diluted with water (20 ml) and extracted with dichloromethane (2 x 30 ml). The dried extracts were evaporated and the oxime mixture heated under reflux for 16 hours with a mixture of pyridine (4 ml) and acetic anhydride (1 ml). This was poured into dilute hydrochloric acid and extracted with dichloromethane, (5 x 10 ml). The dried extract was treated with charcoal and evaporated to a dark yellow oil. Chromatography indicated an intense yellow band of the desired compound, with a faster running pale yellow band of the starting diketone. The isothiazole was isolated and crystallised from benzene as fibrous yellow needles, mp 127-128° (38%). The compound has an intense blue fluorescence in dilute solution;  $^1\text{H}$  nmr:  $\delta = 3.76, 3.78$  ppm (two 3H, s, acetyl- and 3-methyls), 3.15 (6H, s, N-methyls), 7.35 (1H, d, J = 3 Hz, C4-H), 7.70 (1H, d, J = 3 Hz, C6-H); ir: 1657 (C=O)  $\text{cm}^{-1}$ ; ms: Calcd. = 234; Found: 234, ( $M^+$ ) 219 ( $M^+ \cdot \text{CH}_3$ ).

*Anal.* Calcd. for  $\text{C}_{12}\text{H}_{14}\text{N}_2\text{OS}$ : C, 61.54; H, 5.98; N, 11.97; S, 13.67. Found: C, 61.38; H, 5.81; N, 11.48; S, 13.52.

#### 7-Acetyl-5-dimethylamino-3-methyl-1,2-benzisothiazole Oxime (3c).

This was prepared as for the oximes 3a and 3b above. It crystallised from ethanol as yellow prisms, mp 280-283° (82%);  $^1\text{H}$  nmr (hexadeuterioacetone):  $\delta = 2.38$  ppm (3H, s, acetyl), 2.63 (3H, s, oxime methyl), 2.77 (1H, bs, oxime proton), 3.08 (6H, s, amino methyls), 7.19, 7.38 (two 1H, s, C4-H, C6-H); ms: Calcd.  $M = 249$ ; Found: (electron impact), 249 ( $M^+$ ), 233 ( $M^+ \cdot \text{O}$ , 45%), 218 ( $M^+ \cdot \text{CH}_3$ , O, 30%); by FAB 250 (MH<sup>+</sup>).

*Anal.* Calcd. for  $\text{C}_{12}\text{H}_{15}\text{N}_3\text{OS}$ : C, 57.83; H, 6.02; N, 16.87; S,

12.85. Found: C, 58.08; H, 6.31; N, 16.56; S, 12.77.

Protonation Studies on Oximes.

7-Acetyl-3-methyl-1,2-benzisothiazole Oxime.

The oxime (100 mg) was dissolved in acetic acid (5 ml) with warming. To the solution was added 48% hydrobromic acid (~0.1 ml). There was a rapid color change and a pale yellow precipitate formed. The solution was allowed to cool for 5 minutes then the precipitate was collected and washed with ether. The product was obtained as pale yellow prisms, mp >300° (91%). This material was too insoluble to permit recrystallisation.

*Anal.* Calcd. for  $C_{10}H_{11}BrN_2OS$ : C, 41.83; H, 3.83; Br, 27.87; N, 9.76; S, 11.15. Found: C, 42.17; H, 3.90; Br, 28.21; N, 10.11; S, 11.28.

When the oxime was treated with trifluoroacetic anhydride it formed a precipitate. This dissolved in a 1:1 mixture of trifluoroacetic anhydride and hexadeuterioacetone;  $^1H$  nmr:  $\delta$  = 2.07, 2.71 ppm (two 3H, s, methyls), 7.73 (1H, t, J = 7.8 Hz, C5-H), 8.21, 8.63 (two 1H, d, J = 7.8 Hz, C4-H, C6-H), 7.93 (1H, s, acidic or hydroxyl).

This spectrum was unchanged over four days. When any of the salts were treated with mild aqueous base the starting oximes were recovered.

7-Acetyl-3-methyl-5-methylthio-1,2-benzisothiazole Oxime.

This was treated with hydrobromic acid as for **3a**. Light yellow needles mp 250° were obtained (86%). These were too insoluble to permit  $^1H$  nmr studies or recrystallisation.

*Anal.* Calcd. for  $C_{11}H_{13}BrN_2OS_2$ : C, 39.65; H, 3.90; Br, 24.00; N, 8.41; S, 19.22. Found: C, 39.54; H, 3.81; Br, 24.26; N, 8.54; S, 18.90.

The oxime was treated with perchloric acid as above. The product was recrystallised from nitromethane as yellow needles mp 222-223° (96%);  $^1H$  nmr (hexadeuterioacetone):  $\delta$  = 2.49, 2.73, 3.15 ppm (three 3H, s, methyls), 8.16, 8.32 (two 1H, s, C4-H, C6-H).

*Anal.* Calcd. for  $C_{11}H_{13}ClN_2O_5S_2$ : C, 37.45; H, 3.68; Cl, 10.07; N, 7.94; S, 18.16. Found: C, 37.12; H, 3.85; Cl, 10.16; N, 7.54; S, 18.18.

The  $^1H$  nmr of the oxime in trifluoroacetic anhydride was  $\delta$  = 2.56, 2.59, 2.78 ppm (three 3H, s, methyls), 7.65, 7.69 (two 1H, d, J = 1.5 Hz).

7-Acetyl-5-dimethylamino-3-methyl-1,2-benzisothiazole Oxime.

This was treated with hydrobromic acid as above. Pale yellow prisms were obtained, mp >300° (96%). These were too insoluble for  $^1H$  nmr or recrystallisation.

*Anal.* Calcd. for  $C_{12}H_{17}Br_2N_3OS$ : C, 35.05; H, 4.14; Br, 38.89; N, 10.23; S, 7.79. Found: C, 34.87; H, 4.00; Br, 39.22; N, 10.36; S, 7.57.

The oxime dissolved in a mixture of trifluoroacetic anhydride and hexadeuterioacetone, giving a deep yellow solution;  $^1H$  nmr:  $\delta$  2.04, 2.61 ppm (two 3H, s, C-methyls), 3.16 (6H, s, N-methyls), 7.95, 7.86 (two 1H, s, C4-H, C6-H).

Acknowledgements.

We wish to thank Mr. T. Wolowiec and M. K. Marat for the preparation of nmr spectra, and Mr. W. Buchannon for the preparation of mass spectra. We also wish to thank the Natural Science and Engineering Council of Canada for financial support.

#### REFERENCES AND NOTES

- [1] N. Losac'h, *Adv. Heterocyclic Chem.*, **13**, 161 (1971).
- [2] N. Losac'h in *Comprehensive Heterocyclic Chemistry*, Vol IV, A. R. Katritzky and C. W. Rees, eds, Pergamon Press, Oxford 1984.
- [3] D. M. McKinnon and A. A. Abouzeid, *J. Heterocyclic Chem.*, submitted.
- [4] E. I. G. Brown, D. Leaver and T. J. Rawlings, *J. Chem. Soc., Chem. Commun.*, 83 (1969).
- [5] E. Haddock, P. Kirby and A. W. Johnson, *J. Chem. Soc. (C)*, 2514 (1970).
- [6] E. Haddock, P. Kirby and A. W. Johnson, *J. Chem. Soc. (C)*, 3642 (1971).
- [7] E. Haddock, P. Kirby and A. W. Johnson, *J. Chem. Soc. (C)*, 3994 (1971).
- [8] K. Clarke, B. Gleadhill and R. M. Scrowston, *J. Chem. Res. (S)*, 197 (1980).
- [9] D. M. McKinnon and K. R. Lee, *Can. J. Chem.*, **66**, 1405 (1988).
- [10] J. R. Beck and J. H. Yahner, *J. Org. Chem.*, **43**, 2048, 2053 (1978).
- [11] T. Schaefer, R. Sebastian, S. A. Salman, J. D. Baleja, G. H. Penner and D. M. McKinnon, *Can. J. Chem.*, in press.
- [12] D. M. McKinnon and A. A. Abouzeid, *J. Heterocyclic Chem.*, in press.
- [13] F. Effenberger, W. Agster, P. Fischer, K. H. Jogum, J. J. Stezkowski, E. Daltrozzo and C. Kollmannsberger-von Nell, *J. Or. Chem.*, **48**, 4649 (1983).