2,1-Benzisothiazoles. XII. [1]. The Use of *N*-Substituted-2,1-Benzisothiazolium Salts as Synthetic Equivalents of *o*-Aminobenzaldehydes. A Simple Synthesis of Some 2-Quinolones

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N-Substituted-2,1-benzisothiazolium salts **2** react with ethyl cyanoacetate in pyridine solution to give substituted 3-cyano-2-quinolones **5**.

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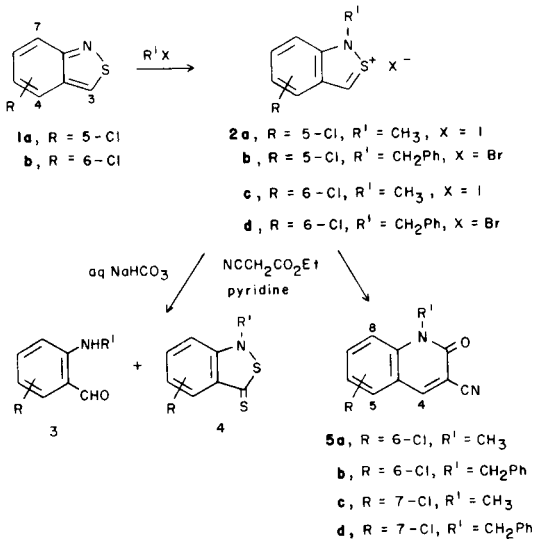
In 1973 we reported [2] that the decomposition of *N*-substituted-2,1-benzisothiazolium salts **2** by aqueous base produced *o*-aminobenzaldehydes **3**. Recently, McKinnon and his coworkers [3] have shown that 2,1-benzisothiazolines-3-thiones **4** are also produced. These authors examined also the reaction of carbanions on the salts **2** obtaining, in low yield, products corresponding to nucleophilic attack by the carbanion on the carbon atom of the heterocyclic ring.

o-Aminobenzaldehydes are useful synthetic intermediates, particularly for heteroannelation reactions [4], but have a reputation, perhaps unjustified, of being unstable and rather inaccessible compounds. We have been interested in using the easily-prepared salts **2** as synthetic equivalents of the aldehydes **3**, and as an example of this idea we now report that a simple, one-step reaction of these salts **2** with ethyl cyanoacetate in hot pyridine affords reasonable yields, *ca.* 50%, of 3-cyano-2-quinolones **5**. The *N*-methyl products **5a, 5c** crystallize from the reaction mixture on dilution with chloroform; the *N*-benzyl derivatives **5b, 5d** are more soluble and are isolated by extraction and evaporation of the extract.



The reaction probably proceeds by attack of the ethyl cyanoacetate anion on the heterocyclic carbon atom, closure of the quinolone ring with expulsion of ethoxide ion, and extrusion of the sulfur atom from a cationic intermediate.

EXPERIMENTAL

The *N*-substituted-2,1-benzisothiazolium salts **2a, 2b** and **2c** were prepared as described previously [2]. 1-Benzyl-6-chloro-2,1-benzisothiazolium bromide (**2d**), prepared in the same way from 6-chloro-2,1-benzisothiazole (**1b**) and benzyl bromide, formed very pale yellow needles (ethanol), mp 196°; pmr (DMSO-d_6): δ 6.09 (s, 2H, CH_2), 7.38-7.51 (m, 5H, aromatic), 8.00-8.31 (m, 3H, aromatic), 10.51 (s, 1H, heterocyclic).

Anal. Calcd. for $C_{14}H_{11}BrClNS$: C, 49.47; H, 3.42; S, 9.70. Found: C, 49.36; H, 3.26; S, 9.41.

General Procedure for Quinolone **5** Synthesis.

A mixture of ethyl cyanoacetate (0.28 ml, 2.6 mmoles), dry pyridine (1.1 ml, 13 mmoles) and the salt **2** (2.6 mmoles) was stirred at 110° under reflux for 4 hours. The red mixture was cooled and diluted with chloroform (20 ml). The product either crystallized immediately (**5a, 5c**) or could be isolated by filtering the mixture, washing with water, drying, and evaporation (**5b, 5d**). The products were recrystallized from ethanol (**5a, 5b, 5d**) or ethanol/acetone (50:50) (**5c**).

6-Chloro-3-cyano-1-methyl-2-quinolone (**5a**).

Prepared from **2a** by the above procedure in 57% yield, this formed pale yellow needles, mp 255°; pmr (DMSO-d_6): δ 3.55 (s, 3H, CH_3), 7.44-7.82 (m, 3H, aromatic), 8.55 (s, 1H, heterocyclic); ir (potassium bromide): 3090, 2250, 1670, 1442, 1230, 1122, 955, 845, 780 cm^{-1}.

Anal. Calcd. for $C_{11}H_7ClN_2O$: C, 60.43; H, 3.23; N, 12.81. Found: C, 60.27; H, 3.45; N, 12.54.

1-Benzyl-6-chloro-3-cyano-2-quinolone (**5b**).

Prepared from **2b** by the same method (52% yield) as long yellow needles, mp 192°; pmr (deuteriochloroform): δ 5.51 (s, 2H, CH_2), 7.15-7.62 (m, 8H, aromatic), 8.18 (s, 1H, heterocyclic); ir (potassium bromide): 3070, 2250, 1670, 1580, 1505, 1440, 1240, 815, 740 cm^{-1}.

Anal. Calcd. for $C_{17}H_{11}ClN_2O$: C, 69.28; H, 3.76; N, 9.51. Found: C, 69.36; H, 3.86; N, 9.43.

7-Chloro-3-cyano-1-methyl-2-quinolone (**5c**).

Prepared from **2c** by the same procedure (49% yield), this formed almost colorless needles, mp 250°; pmr (DMSO-d_6): δ 3.60 (s, 3H, CH_3), 7.33-7.84 (m, 3H, aromatic), 8.73 (s, 1H, heterocyclic); ir (potassium bromide): 3080, 2325, 1660, 1605, 1425, 1222, 1005, 830, 780 cm^{-1}.

Anal. Calcd. for $C_{11}H_7ClN_2O$: C, 60.43; H, 3.23; N, 12.81. Found: C, 60.31; H, 3.23; N, 12.77.

1-Benzyl-7-chloro-3-cyano-2-quinolone (**5d**).

Prepared from **2d** in the same way (51%), this formed almost colorless needles, mp 217°; pmr (DMSO-d_6): δ 5.51 (s, 2H, CH_2), 7.22-7.87 (m, 8H, aromatic), 8.80 (s, 1H, heterocyclic); ir (potassium bromide): 3080, 2325, 1660, 1610, 1570, 1444, 1240, 1110, 705 cm^{-1}.

Anal. Calcd. for $C_{17}H_{11}ClN_2O$: C, 69.28; H, 3.76; N, 9.51. Found: C, 69.10; H, 3.84; N, 9.21.

Separation of the *o*-Aminoaldehydes **3** from Thiones **4**.

The products **3** and **4** of the decomposition of the salts **2** by aqueous sodium bicarbonate solution are readily separated by applying a dried chloroform extract of the reaction mixture to a short silica gel column, and eluting with chloroform/methanol (80/20). The *o*-aminobenzaldehyde **3** is thus obtained in pure form. The thione **4** is eluted with chloroform/-methanol (20/80).

REFERENCES AND NOTES

[1] Part XI. M. Davis and K. C. Tonkin, *Aust. J. Chem.*, **34**, 755 (1981).

[2] M. Davis, E. Homfeld and K. S. L. Srivastava, *J. Chem. Soc., Perkin Trans. I*, 1863 (1973).

[3] D. McKinnon, K.A. Duncan and L. M. Millar, *Can. J. Chem.*, **60**, 440 (1982).

[4] An extensive review of such reactions is given by P. Caluwe, *Tetrahedron*, **36**, 2359 (1980).