

Synthesis of 3-Hydroxy-2,1-benzisothiazole (1)

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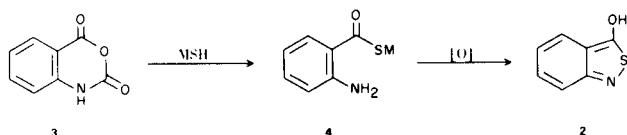
Received April 2, 1973

Sir:

Numerous 3-hydroxy-1,2-benzisothiazoles (**1**) have been reported (**2**), however, the 3-hydroxyl derivative of the corresponding 2,1-benzisothiazole (**2**) is unknown. R. K. Buckley and co-workers (**3**) reported an unsuccessful attempt to prepare **2** from the diazonium salt obtained from 3-amino-2,1-benzisothiazole (**6**).



We wish to report the synthesis of 3-hydroxy-2,1-benzisothiazole (**2**). This was accomplished through a facile two-step process from the readily available isatoic anhydride (**3**). The first step in this facile process is the formation of the metal salt of thioanthranilic acid (**4**), as described by Fanning and Roberts (**4**). The intermediate **4** was not isolated, due to the inherent instability of this type of molecule (**4**), but was oxidatively cyclized to the desired product **2** *in situ*.

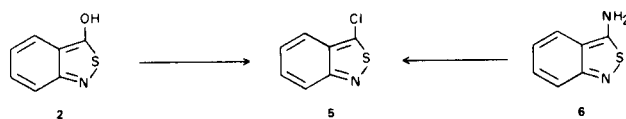


When **3** was slowly added to a stirred solution of an equivalent amount of metal hydrosulfide in water at room temperature, a rapid evolution of carbon dioxide ensued. After this effervescence was complete, the mixture was flushed with nitrogen (to remove the excess hydrogen sulfide) and then slowly treated with a slight excess of 10% hydrogen peroxide, while the temperature was maintained between 25° and 40° by occasional cooling. The resulting mixture was stirred for an additional 30 minutes, filtered, and the pH of the filtrate adjusted to 6. The precipitated product was recrystallized from water to afford a 54% yield of 3-hydroxy-2,1-benzisothiazole (**2**) as yellow needles that had a melting point of 137.5-140° dec. Sublimation produced an analytically pure sample, m.p. 138-139.5° dec., which gave a positive ferric chloride

test (methanol) for enols, [λ max (ethanol) (ϵ): 217 nm (6.14×10^4), 230 nm (shoulder), and 353 nm ($4.68 \cdot 10^3$); m/e 151 (M^+), 123 ($M-28$); pmr (DMSO- d_6) δ 6.95-7.90 (m, 4), 9.80 ppm (broad, 1); ir (potassium bromide) 3090, 1620, 1600, 745 cm^{-1}].

Anal. Calcd. for C_7H_5NOS : C, 55.61; H, 3.33; N, 9.26. Found: C, 55.64; H, 3.35; N, 9.34.

Conclusive structure proof of 3-hydroxy-2,1-benzisothiazole (**2**) was obtained by conversion to the known (3) 3-chloro-2,1-benzisothiazole (**5**). This was accomplished by heating **2** (10 g.) in phosphorus oxychloride (100 ml.) on a steam bath for 1.5 hours, followed by the removal of the excess phosphorus oxychloride *in vacuo*. The residue was poured onto crushed ice, and then extracted with ether. Removal of the solvent afforded 5.6 g. of yellow liquid which was distilled, 72-75°/1 mm. This analytically pure 3-chloro-2,1-benzisothiazole (**5**) compared favorably in its physical and spectral properties with those reported for **5**, which was previously prepared by Buckley and co-workers (**3**) *via* the Sandmeyer reaction on 3-amino-2,1-benzisothiazole (**6**).



REFERENCES

- (1) A preliminary account of this work was presented to the Organic Division at the 164th National Meeting of the American Chemical Society, New York City in 1972.
- (2) M. Davis in "Advances in Heterocyclic Chemistry, 14" (A. R. Katritzky and A. J. Boulton, Eds.), pages 43-98, Academic Press, New York and London, 1972.
- (3) R. K. Buckley, M. Davis, and K. S. L. Srivastava, *Aust. J. Chem.*, **24**, 2405 (1971).
- (4) A. T. Fanning, Jr., and T. D. Roberts, *Tetrahedron Letters*, 805 (1971).