The Reaction Between 2-Aminobenzenethiol and Diethyl Oxalate. A Structural Reassegnement.

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It is proposed that the reported [2] condensation between 2-aminobenzenethiol and diethyloxalate give rise to 2-ethoxycarbonylbenzothiazole **3** rather than 3-ethoxy-2*H*-1,4-benzothiazin-2-one **2**.

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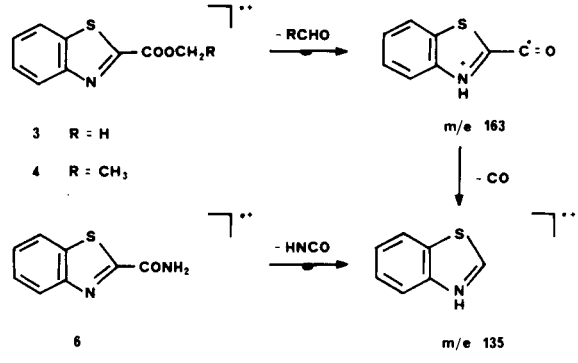
Hofmann [1] synthesized bis-2,2'-benzothiazolyl **1** by reaction between 2-aminobenzenethiol and diethyloxalate (method a in Scheme 1), whereas D'Amico *et al* recently claim [2] that a modified Hofmann's procedure, *i.e.* method b, allows the synthesis of 3-ethoxy-2*H*-1,4-benzothiazin-2-one **2** (mp 72.0-72.5°; ir: ν CO 1715 cm^{-1}; ms: base peak at 135 m/e $[C_7H_3SO]^+$).

We now report that the product assigned as **2** is actually 2-ethoxycarbonylbenzothiazole **3** (lit [3] mp 70-71°).

Although some unequivocal methods for the preparation of **3** are known [4], a new synthesis of this last compound has been successfully achieved following a known method [5] which involves the thermal decomposition of 2,2-disubstituted-2,3-dihydrobenzothiazoles to 2-substituted-benzothiazoles. Thus we obtained an authentic sample of such a compound by heating under nitrogen at 225° the appropriate 2,3-dihydrobenzothiazole **7**. Similarly, compound **4** was obtained starting from **8**.

The ir, ^{1}H-nmr and mass spectra of the compound prepared by thermolysis of **7** correspond with those of the solid obtained following the reported procedure [2]. With one exception (ir ν CO found 1755, quoted [2] 1715 cm^{-1}) our spectral data are in fair agreement with those reported [2].

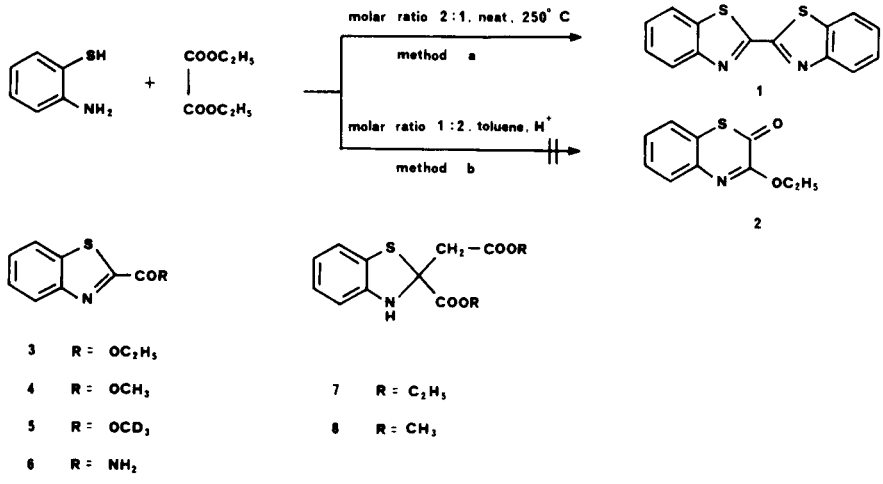
Scheme 2



Furthermore, by transesterification and ammonolysis of the ester **3** we prepared the esters **4** and **5** and the amide **6** respectively, and their melting points also correspond with those literature values available [3]. By transesterification reactions the esters **4** and **5** were obtained together with benzothiazole and 2-deuteriobenzothiazole, respectively.

Compounds **3-6** have similar ^{1}H-nmr as well as electron impact mass spectra. In particular, in these last spectra the base peak occurs at m/e 136 in the case of the compound **5** and at m/e 135 in the case of the compounds **3**, **4**

Scheme 1



and **6**. Hence, it appears reasonable to suggest that the electron impact induced decomposition of the compounds **3-6** involves a protonated benzothiazolyl radical as the most abundant fragmentation species.

The formation of such fragments can be explained by invoking a McLafferty rearrangement of the corresponding molecular ions as reported in Scheme 2.

EXPERIMENTAL

Melting points were determined on a Tottoli apparatus and are uncorrected. The ir spectra were taken on a Perkin-Elmer 257 instrument as Nujol mulls or potassium bromide discs. The ^{1}H-nmr spectra were recorded in deuteriochloroform on a Varian XL 200 instrument operating at 200 MHz. Chemical shifts are given in δ from tetramethylsilane as the internal standard. Gas-mass analysis has been carried out on a Hewlett-Packard 5995C-GC/MS instrument. Values lower than m/e 100 have been omitted in the reported mass spectral data. Preparative layer chromatography (plc) was carried out on Carlo Erba SI F_{254} silica gel-plates (2 mm thickness) using light petroleum ether-ethyl acetate (9:1) as eluent.

2-Ethoxycarbonylmethyl-2-ethoxycarbonyl-2,3-dihydro-1,3-benzothiazole (**7**).

This compound was prepared employing diethyl acetylenedicarboxylate instead of the dimethyl ester in the procedure previously reported [6] for the synthesis of compound **8**, yield 85%, oil; ir: 3350, 1745, 1725 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.25 (t, 6H, CH_3), 3.30 (dd, 2H, CH_2CO), 4.15 (q, 2H, OCH_2), 4.24 (q, 2H, OCH_2), 5.31 (s, 1H, NH), 6.7-7.0 (m, 4H, ArH).

Anal. Calcd. for $C_{14}H_{17}NO_4S$: C, 56.94; H, 5.80; N, 4.74. Found: C, 57.10; H, 5.76; N, 4.80.

Thermolysis of Compound **7**.

Compound **7** (0.5 g) was bulb-to-bulb distilled once at 225° (bath temperature) under nitrogen to give a partially crystallized oil in 65% yield. This fraction was at first washed with *n*-hexane, then crystallized from the same solvent to give pure 2-ethoxycarbonylbenzothiazole **3** as colourless plates, mp 70-71° (lit [3] 70-71°); ir: 1755 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.44 (t, 3H, CH_3), 4.50 (q, 2H, CH_2), 7.4-7.5 (m, 2H, ArH), 7.8-7.9 (m, 1H, ArH), 8.1-8.2 (m, 1H, ArH); ms: m/e 107 (4), 108 (17), 109 (4), 134 (15), 135 (100), 136 (12), 137 (4), 148 (4), 162 (23), 163 (11), 164 (2), 207 (46) M$^+$, 208 (5), 209 (2).

Such spectral data are superimposable with those of the solid prepared by us following the reported procedure [2].

Anal. Calcd. for $C_{10}H_9NO_2S$: C, 57.94; H, 4.38; N, 6.76. Found: C, 58.05; H, 4.44; N, 6.80.

Thermolysis of Compound **8**.

The thermolysis of the compound **8** was carried out following the above reported procedure for compound **7**. By working-up as above, 2-methoxycarbonylbenzothiazole **4** was obtained in 38% yield. Compound **4** had mp 88-89° (from chloroform) (lit [3] 90° (from aqueous ethanol)); ir: 1740, 1715 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 3.99 (s, 3H, OCH_3); 7.4-7.5 (m, 2H, ArH); 7.8-7.9 (m, 1H, ArH); 8.1-8.2 (m, 1H, ArH); ms: m/e 103 (3), 104 (2), 106 (1), 107 (6), 108 (16), 109 (3), 110 (1), 116 (2), 117 (1), 121 (4), 122 (1), 133 (4), 134 (24), 135 (100), 136 (9), 137 (5), 148 (4), 149 (1), 162 (13), 163 (5), 164 (1), 193 (41) M$^+$, 194 (4), 195 (2).

Anal. Calcd. for $C_9H_7NO_2S$: C, 55.96; H, 3.65; N, 7.25. Found: C, 56.15; H, 3.70; N, 7.28.

Transesterification of Compound **3** with Methanol.

Hydrogen chloride gas was bubbled for 3 minutes into a methanolic solution (5 ml) of compound **3** (0.25 g, 1.2 mmoles). The solution was heated at 50° overnight. Tlc analysis on silica gel of the reaction mixture showed the formation of a more polar compound and the absence of the starting material. The reaction mixture was evaporated under reduced pressure. The resulting residue was dissolved in ether, then washed with aqueous sodium bicarbonate and dried (sodium sulfate). Gas-mass analysis revealed that the crude residue was essentially constituted of benzothiazole and 2-methoxycarbonylbenzothiazole **4**. Purification by plc afforded benzothiazole (18% yield) and compound **4** as a white solid (75% yield), in the order given. The former was identified by comparison with authentic sample, the compound with lower R_f value was found identical by ir, ^{1}H-nmr spectra with the compound obtained by **8** thermolysis.

Transesterification of Compound **3** with Tetradeuteriomethanol.

By using tetradeuteriomethanol instead of methanol in the above reported transesterification procedure, there was obtained 2-deuteriobenzothiazole and compound **5** in 6% and 88% yield, respectively; compound **5** had mp 87-88° (from chloroform); ir: 1740, 1715 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.4-7.5 (m, 2H, ArH), 7.8-7.9 (m, 1H, ArH), 8.1-8.2 (m, 1H, ArH); ms: m/e 104 (3), 106 (2), 107 (7), 108 (17), 109 (3), 110 (3), 118 (3), 120 (1), 122 (3), 123 (1), 133 (3), 134 (19), 136 (100), 137 (8), 138 (4), 150 (3), 151 (l), 162 (12), 163 (1), 164 (3), 196 (45) M$^+$, 197 (5), 198 (2).

2-Carboxamidobenzothiazole **6** by Ammonolysis of the Ester **3**.

A solution of the compound **3** (50 mg, 0.24 mmole) in ethanol (6 ml) and concentrated aqueous ammonium hydroxide (2 ml) was refluxed overnight and then evaporated. The resulting white solid was crystallized from ethanol affording the pure compound **6** (60% yield), mp 229° (from ethanol) (lit [4a] mp 228-230° (from aqueous acetic acid); ir: 3320, 3220, 1695, 1665 (strong), 1620 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 5.7 (br s, 2H, NH), 7.5-7.6 (m, 2H, ArH), 7.9-8.0 (m, 1H, ArH), 8.0-8.1 (m, 1H, ArH); ms: m/e 108 (43), 109 (5), 135 (100), 136 (8), 137 (4), 150 (3), 178 (66) M$^+$, 179 (7), 180 (3).

Anal. Calcd. for $C_8H_6N_2OS$: C, 53.93; H, 3.40; N, 15.73. Found: C, 54.10; H, 3.38; N, 15.80.

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