Reaction Products of 2-Aminobenzenethiol with some β-Diketones

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2-Aminobenzenethiol undergoes condensation reactions with several β-diketones (CH_3, CF_3 and C_6H_5 substituents) to form benzothiazolines. Conversion to benzothiazines and benzothiazoles occurs in some instances, as documented by the isolation and spectroscopic characterization of the products.

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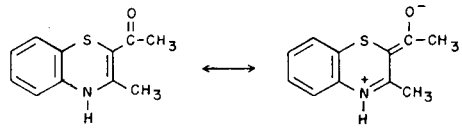
The heterocyclic 2-acetonyl-2-methylbenzothiazoline Ia was reported earlier [1,2] as the condensation product of the reaction of acetylacetone with 2-aminobenzenethiol in ethanol (Scheme 1). We noted that the colourless crystalline compound Ia slowly changed to a bright orange-red product in contact with air, the transformation taking place more readily in dimethylsulfoxide or acidified ethanol solution at elevated temperatures [3]. Other workers had isolated the orange compound as a decomposition product in an attempt to make a triorganoantimony(V) complex of Ia and identified it spectroscopically as 2-acetyl-3-methyl-4*H*-1,4-benzothiazine, IIa. A recent X-ray crystal structure determination has confirmed that ring expansion occurs in the formation of IIa from Ia [5]. Our interest in this transformation was heightened by its contrast with our earlier observation of the reaction of 2-aminobenzenethiol with salicylaldehyde. The benzothiazoline initially formed retains the 5-membered heterocyclic ring upon oxidation and is converted to the corresponding benzothiazole [6].

In this paper we report the isolation of several products derived from the reaction of 2-aminobenzenethiol with certain β-diketones. The condensation products are dependent upon the β-diketone employed; the relationship of the three principal types and the species isolated are summarized in Scheme 1. Analytical and spectral data for the new compounds are reported in the experimental section.

With unsymmetrical β-diketones the initial benzothiazoline formation takes place preferentially with the carbonyl group adjacent to the less electron withdrawing substituent. Under our reaction conditions, Ic and Id were too unstable to be isolated giving IIIc and IIId respectively. The benzothiazine IIf was only isolable using dimethylsulfoxide [7,8] as the solvent rather than ethanol. Formulation of Ia, Ib and Ie as five-membered ring benzothiazolines is indicated by their spectroscopic data. The observations of Liso *et al.* [7] were that benzothiazolines in boiling DMSO solutions undergo both oxidative ring expansion to form 1,4-benzothiazines and decomposition to give 2-substituted benzothiazoles. Our results confirm these reaction pathways and show that for strongly electron withdrawing substituents (CF_3) formation of III *via* decomposition of I is favoured over ring expansion to II. In contrast to other workers [8], we conclude that benzothiazoles IIId and IIIe and not the 1,4-benzothiazines IId and IIe are formed.

The recent X-ray analysis [5] of IIa confirmed its formulation based on spectral data [4] as a resonance hybrid of IIa and IIa':



Our spectral characterization of IIa and IIb includes their ^{13}C nmr spectra, and a comparison (Table 1) with the corresponding data for Ia and Ib gives a clear indication of oxidative ring expansion. The two peaks attributable to the asymmetric ring carbon and the methylene carbon in the spectra of the benzothiazolines are replaced by two new peaks in the aromatic region. Specific tentative assignments are given in the Table. Presumably IIf and other 1,4-benzothiazines [7] have similar six-membered ring structures as substantiated for IIa and IIb.

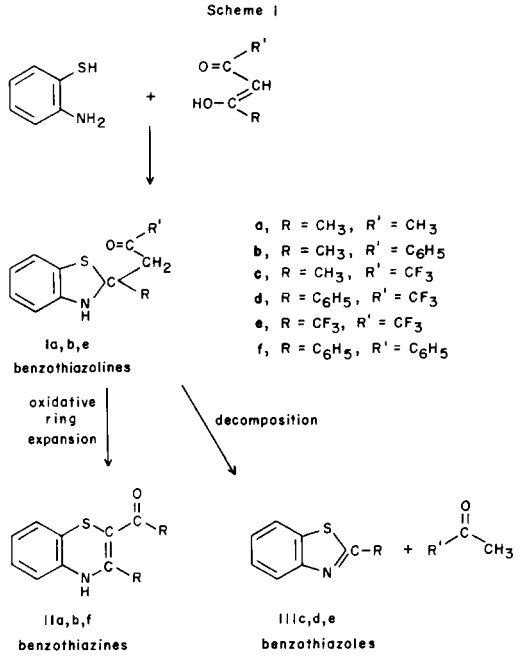
We have not isolated the fluorinated benzothiazolines IId and IIe following the procedure of Soni and Jain [8]. Although a wine-red colour does indeed develop when a 1:1 molar mixture of 2-aminobenzenethiol and the fluorinated β-diketone is heated in DMSO, no solid product could be isolated by concentrating the solution or by the addition of other organic solvents. A wine-red solid was isolated however by the addition of water [7] and subsequent repeated washings. Drying of this solid under vacuum over phosphorus pentoxide resulted in a gradual loss of colour and the formation of a brown oil and (on top)

Table 1

Assignments in the ^{13}C NMR (ppm δ) Spectra of Selected Benzothiazolines and the Corresponding Benzothiazines

Compound	-CH_3	-C(O)-CH_3	-C(O)-	-CH_2-	=C=
Ia	29.36	30.39	205.91	55.72	74.17
IIa	20.93	29.75	190.06	—	—
Ib	29.58	—	197.28	51.41	74.91
IIb	21.07	—	188.67	—	—

Scheme I



a white cotton-like solid. These products are shown to be IIIe and Ie, respectively. The wine-red colour is not developed if a 1:1 mixture of the reactants is heated either without a solvent or in ethanol; however, addition of DMSO develops the colour in both cases. Neither reactant gives a colour separately in boiling DMSO solution. A solution of Ie in DMSO develops the wine-red colour when heated. The colour that develops in these reactions can probably be attributed to the formation of an intermediate containing DMSO [7] which is converted to either Id and Ie or IIId and IIIe as DMSO is removed under reduced pressure. It is worth noting that IIa and IIf were both isolated following the DMSO procedure.

EXPERIMENTAL

Elemental analyses were performed by The Guelph Chemical Laboratories, Guelph, Ontario and by M-H-W Laboratories, Phoenix, Arizona. Infrared spectra were obtained on Beckman Acculab-6 and Perkin-Elmer 180 spectrophotometers as Nujol mulls between potassium bromide plates. Proton nmr spectra were recorded on Varian A-60A and Varian T-60 spectrometers with TMS as the internal standard. The ^{13}C nmr spectra in DMSO solution were obtained with a Bruker WH-400 nmr spectrometer in the pulsed Fourier Transform mode. Mass spectra were recorded with a Varian Mat-7 mass spectrometer at an ionizing energy of 70 eV. Melting points are uncorrected.

Preparation of Benzothiazolines, Ia, IIb and Ie (An attempted synthesis of the compound with R = R' = ϕ following this procedure was unsuccessful).

These were prepared by following methods described previously for Ia [2]. Generally, an equimolar ratio of 2-aminobenzenethiol and β-diketone was mixed in ethanol and allowed to stand at room temperature for several hours. The reaction was carried out under an atmosphere of dinitrogen to avoid air oxidation. On reduction of the volume of the solvent, Ia and Ib, separated as prismatic crystals which were filtered and recrystallized from ether. Compound Ie was isolated from the light brown oil obtained on removal of the solvent under low pressure. On careful distillation of the oil under vacuum and below 40° Ie deposited on the upper part of the flask as a cotton-like sublimate which was scraped off and separated from the oil (identified as IIIe).

Ia. 2-Acetonyl-2-methylbenzothiazoline.

Analytical and some spectral data were reported earlier [2].

Ib. 2-Benzophenonyl-2-methylbenzothiazoline.

This compound had mp 70-73°; ir: 3358 cm^{-1} (> NH str), 1672 cm^{-1} (>C=O); ^1H nmr (deuteriochloroform): ppm δ 1.83 (s, 3H, $-CH_3$), 3.67 (b, 2H, $-CH_2-$), 5.23 (b, 1H, >NH), 6.5-8.8 (m, 9H, ring); ms: 269 (M^+), 254 ($M-CH_3$)$^+$, 162 [M-{H_2 + (ϕ-C=O)}]$^+$, 150 [M-{CH_2-CO-ϕ}]$^+$.

Anal. Calcd. for $C_{16}H_{15}NOS$: C, 71.34; H, 5.61; N, 5.22. Found: C, 71.33; H, 5.56; N, 5.08.

Ie. 2-Trifluoromethyl-2-trifluoroacetonylbenzothiazoline.

This compound had mp 55-56°; ir: 3370 cm^{-1} (>NH str), 1770 cm^{-1} (>C=O); ^1H nmr (deuteriochloroform): ppm δ 3.55 (s, 2H, $-CH_2-$), 5.20 (b, 1H, >NH), 6.60-7.35 (m, 4H, ring); ms: 315 (M^+), 246 [M-{CF_3}]$^+$, 204 [M-{CF_3-CO-CH_2)}]$^+$, and 203 (IIIe).

Anal. Calcd. for $C_{11}H_7NOSF_6$: C, 41.91; H, 2.24; N, 4.44. Found: C, 41.57; H, 2.28; N, 4.43.

Preparation of Benzothiazines IIa, IIb and IIf.

These are formed as orange side products in the synthesis of the corresponding benzothiazoline if the reaction is carried out with prolonged exposure to air. The products are obtained in quantitative yield as orange-red needles when an ethanolic solution of the benzothiazoline is allowed to stand at room temperature for several days. Compound IIa is obtained in high yield by refluxing overnight a mixture of 2-aminobenzenethiol and acetylacetone in 1:1 molar ratio in ethanol in the presence of a few drops of acetic acid. On cooling orange needles separated out. Compound IIa can also be prepared in high yield in DMSO following the method of Soni *et al.* [8]. Compound IIf was obtained as dark red needles by the DMSO method [8].

IIa. 2-Acetyl-3-methyl-4*H*-1,4-benzothiazine [4,5].

This compound had mp 185-186° (lit 194-195°); ir, nmr and ms reported earlier [4].

Anal. Calcd. for $C_{11}H_{11}NOS$: C, 64.36; H, 5.40; N, 6.82. Found: C, 64.87; H, 5.29; N, 6.90.

IIb. 2-Benzoyl-3-methyl-4*H*-1,4-benzothiazine.

This compound had mp 182-185° dec; ir: 3260 cm^{-1} (>NH str), 1610 cm^{-1} (>C=O); ^1H nmr (deuteriochloroform): ppm δ 2.17 (s, 3H, $-CH_3$), 7.2-8.0 (m, 5H, >NH + ring); ms: 267 (M^+), 162 [M-(ϕ-C=O)]$^+$, 105 (ϕ-C=O)$^+$.

Anal. Calcd. for $C_{16}H_{13}NOS$: C, 71.88; H, 4.90; N, 5.24. Found: C, 72.00; H, 4.94; N, 5.38.

IIf. 2-Benzoyl-3-phenyl-4*H*-1,4-benzothiazine.

This compound has mp 171-172°; ir: 3258 cm^{-1} (>NH str), 1582 cm^{-1} (>C=O); ms: 329 (M^+), 224 [M-(ϕ-C=O)]$^+$, 105 (ϕ-C=O)$^+$.

Preparation of Benzothiazoles IIIc, IIId and IIIe.

These were obtained during the attempted synthesis of the corresponding benzothiazolines. On removal of ethanol under low pressure IIId was isolated as a colourless solid (with a bluish tinge). Distillation of the residue under vacuum at 80°/1 mm gave IIIc as a colourless oil in that preparation, while IIIe was obtained as a light brown oil at 40°/5 mm. In the latter case, Ie was also isolated as a sublimate.

IIIc. 2-Methylbenzothiazole.

This was obtained as the major product along with some 2-methyl-2-trifluoromethylbenzothiazole IV. No attempt was made to separate these

components. Compound IV would be expected if the initial condensation took place near the $-CF_3$ end of the β-diketone. Subsequent elimination of a ketene would give IV. This was inferred from the fact that the mass spectra of this product showed a weak peak at m/e 219 corresponding to IV and the base peak at m/e 149 due to IIIc. The ^1H nmr spectra can best be explained if it is assumed that the product is a mixture of about 90% IIIc and 10% IV. The methyl signal due to IIIc appears at δ 2.72 ppm. A weak and broad peak at δ 1.82 ppm may be assigned to the $-CH_3$ group in IV. This signal is broadened due to the proximity of the protons to the asymmetric carbon atom. The ir spectra (thin film between potassium bromide plates) shows >NH str at 3205 cm^{-1} and the aromatic CH str in the region 3100-2800 cm^{-1}. The CHN analysis based on 90% IIIc and 10% IV is shown below: Calcd.: C, 62.27; H, 4.63; N, 9.09. Found: C, 60.68; H, 4.59; N, 8.54.

IIId. 2-Phenylbenzothiazole.

This compound had mp 110-112°; ir: no peak due to >NH or >C=O str; ^1H nmr (DMSO): ppm δ 7.35-7.80 (m, 5H, ring), 7.95-8.40 (m, 4H, ring); ^{13}C nmr (DMSO): ppm δ 121.98-129.32 (m, ring); ms: 211 (M^+).

IIIe. 2-Trifluoromethylbenzothiazole.

This compound had ^1H nmr (deuteriochloroform): ppm δ 7.3-8.4 (m, ring); ir: no >NH or >C=O str signals; ms: 203 (100%) (M^+); minor peaks at 315 (3%), 265 (4%), 246 (7%) due to the presence of some Ie as an impurity.

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