

Reaction of N-acylisatins with *o*-aminophenol and *o*-aminothiophenol¹

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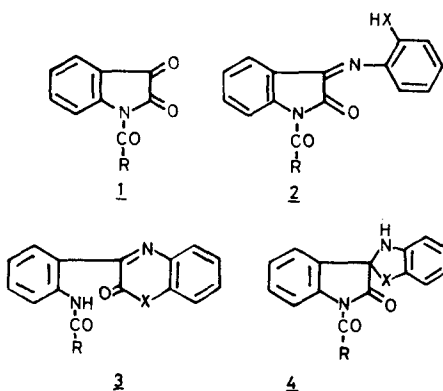
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Abstract. The reaction of N-acylisatins 1a–1d with *o*-aminophenol gives the benzoxazinones 3a–3d. With *o*-aminothiophenol, 1a and 1b give a mixture of products from which were isolated 2f, 3d, 3e, 5a, 6 and 7.

Keywords. Benzoxazinones; benzothiazinones; benzthiazole.

1. Introduction

The reaction of N-acylisatins with aromatic 1,2-diamines has been shown to yield 3-*o*-acylamino-phenyl-2H-quinoxalin-3-ones (Joshi *et al* 1983). We report here the reaction of N-acylisatins with *o*-aminophenol and *o*-aminothiophenol.



	X	R
a :	O	CH ₃
b :	O	CH ₂ CH ₃
c :	O	CH ₂ CH ₂ CH ₃
d :	O	C ₆ H ₅
e :	S	CH ₃
f :	S	CH ₂ CH ₃

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2. Results and discussion

For the reaction product m.p. 169–170°, obtained by the condensation of N-acetylisatin (**1a**) with *o*-aminophenol, structure (**2a**) had been assigned previously (Parisi 1953). We find that in ethanol as well as in acetic acid, the same product, m.p. 179°, is formed, the structure of which should be revised to **3a**. The compound is insoluble in cold 10% aqueous alkali and dissolves only on warming. The IR spectrum, ν_{\max} 1740, 1675 cm^{-1} , does not agree (Joshi *et al* 1983) with **2a** but is in good agreement with the reported spectrum of 3-phenyl-2H-1,4-benzoxazin-2-one (rep. ν_{\max} 1740 cm^{-1}) (Chioccora *et al* 1976). Its $^1\text{H NMR}$ spectrum shows the methyl of $\text{NH}\cdot\text{CO}\cdot\text{CH}_3$ at δ 2.1 ppm in contrast to N-acetylisatin (**1a**) where it appears at δ 2.75 ppm, supporting the structure **3a**, involving the opening of the N–C₂ bond of isatin.

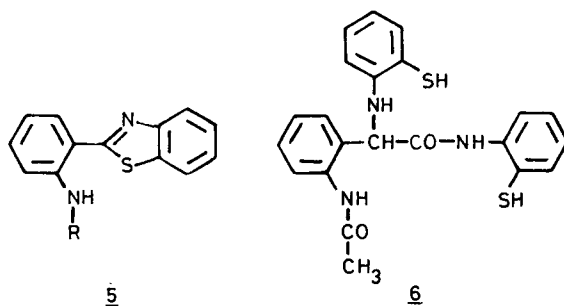
The homologues **1b** and **1c** gave **3b** and **3c** respectively. In **3b**, the $\text{N}\cdot\text{CO}\cdot\text{CH}_2$ appears in the $^1\text{H NMR}$ spectrum as a quartet at δ 2.4 ppm and in **3c** as a triplet at δ 2.2 ppm. In **1b** and **1c**, this methylene appears near δ 3 ppm. N-Benzoylisatin (**1d**) similarly gives **3d**.

Compounds **3a**–**3d** show the molecular ion peaks in their mass spectra and a strong M-28 peak due to loss of CO as has been observed in the case of 2H-1,4-benzoxazin-2-ones (Reichen 1977).

The reaction of N-acylisatins with *o*-aminothiophenol, which is not reported in literature, was more complicated. Several products were formed as seen by TLC and chromatographic separation yielded only some of them in pure state.

The reaction of **1a** with *o*-aminothiophenol in acetic acid gave **3e**, insoluble in cold 10% aqueous alkali, ν_{\max} 1695 cm^{-1} (Ar–CO–S–Ar, reported ν_{\max} 1685 cm^{-1}) (Nyquist and Potts 1959). Its $^1\text{H NMR}$, δ 2.25 ppm (3H, s, $\text{NH}\cdot\text{CO}\cdot\text{CH}_3$), supports the N–C₂ cleavage. The homologue **1b** similarly gives **3f**, its $^1\text{H NMR}$ spectrum showing the $\text{NH}\cdot\text{CO}\cdot\text{CH}_2$ methylene as a quartet at δ 2.4 ppm.

From the reaction of **1a** with *o*-aminothiophenol in ethanol, two products were isolated. The less polar one, m.p. 120°, C₁₅H₁₂N₂OS (M⁺ at m/e 268), $^1\text{H NMR}$: δ 2.25 ppm (3H, s, $\text{NH}\cdot\text{CO}\cdot\text{CH}_3$), was identified as the benzthiazole (**5a**). An authentic sample of **5a** was prepared by acetylation of the known **5b** obtained by reaction of anthranilic acid with *o*-aminothiophenol (Hein *et al* 1957).



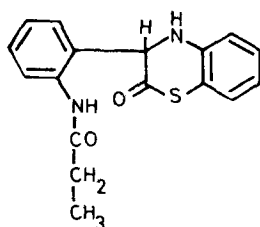
a: R = CO·CH₃

b: R = H

Compound **5a** could have arisen from **4e**. Decarbonylation of **3e** is less likely under the conditions of the experiment since 3-phenyl-2H-1,4-benzothiazin-2-one yields 2-phenyl-benzthiazole only by pyrolysis at 300°C (Rabilloud *et al* 1970).

The more polar product of the reaction mixture from 1a, m.p. 215°, $C_{22}H_{21}N_3O_2S_2$, is soluble in 10% aqueous alkali and insoluble in 2N HCl, ν_{\max} 1710, 1680, 1650 cm^{-1} . Its 1H NMR shows a singlet at δ 2.05 (3H, $NH \cdot CO \cdot \underline{CH_3}$), a singlet (1H) at δ 5.15 (benzylic CH) and 12 aromatic hydrogens as a complex multiplet. The compound is assigned structure 6, its formation involving reaction of one mole of isatin with two moles of thiophenol and also reduction of the azomethine double bond by thiophenol.

From the reaction of the homologue (1b), in addition to 3f, two compounds were isolated in poor yields: 2f, m.p. 145°, $C_{17}H_{14}N_2O_2S$ (M^+ at m/e 310), soluble in 10% aqueous alkali, ν_{\max} 3360, 1770, 1700 cm^{-1} . 1H NMR: δ 3 (3H, q, $N \cdot CO \cdot \underline{CH_2}$.) and 7, m.p. 215°, $C_{17}H_{16}N_2O_2S$ (M^+ at m/e 312), insoluble in alkali, ν_{\max} 1680, 1660, 1650 cm^{-1} , 1H NMR: δ 2.4 (3H, q, $NH \cdot CO \cdot \underline{CH_2}$), 5.1 (1H, s, benzylic CH) ppm. Compound 7 is evidently formed by reduction of the azomethine bond by thiophenol.

7

3. Experimental

Melting points are uncorrected. 1H NMR spectra were recorded in $CDCl_3$, except for 6a which was run in a mixture of $CDCl_3 + DMSO-d_6$, on a Varian EM 360 L spectrometer. Mass spectra were determined on a Varian Mat CH 7 instrument at 70 eV utilizing direct insertion. IR spectra were taken in nujol on a Perkin-Elmer Infracord instrument.

Table 1. Physical constants of compounds prepared.

Sl. No.	Compound	Mol. formula	Mol. wt.	m.p.°C	Solvent of crystallisation
1	<u>3a</u>	$C_{16}H_{12}N_2O_3$	280.3	179	MeOH
2	<u>3b</u>	$C_{17}H_{14}N_2O_3$	294.3	180	"
3	<u>3c</u>	$C_{18}H_{16}N_2O_3$	308.3	147	"
4	<u>3d</u>	$C_{21}H_{14}N_2O_3$	341.3	208	"
5	<u>3e</u>	$C_{16}H_{12}N_2O_2S$	296.3	128	C_6H_6 -hexane
6	<u>3f</u>	$C_{17}H_{14}N_2O_2S$	310.3	125	$CHCl_3$ -hexane
7	<u>5a</u>	$C_{15}H_{12}N_2OS$	268.3	120	C_6H_6
8	<u>6</u>	$C_{22}H_{21}N_3O_2S_2$	423.4	215	CH_2Cl_2
9	<u>2f</u>	$C_{17}H_{14}N_2O_2S$	310.3	145	C_6H_6
10	<u>7</u>	$C_{17}H_{16}N_2O_2S$	312.3	215	CH_2Cl_2 -MeOH

[Microanalytical values obtained for C, H and N were within $\pm 0.5\%$ of the calculated values].

3.1 General procedure

A mixture of N-acylisatin (10 mmol) and *o*-aminophenol or *o*-aminothiophenol (10 mmol) was refluxed for 8 hr either in acetic acid (25 ml) or ethanol (25 ml). In the former case, the solution was poured on ice and the crude solid extracted with chloroform. In the latter case, the alcohol was evaporated in vacuo. The crude product obtained by either method was chromatographed over silica gel in the order C₆H₆, C₆H₆-CHCl₃, CHCl₃ and CHCl₃-MeOH.

The physical constants of the compounds prepared are recorded in table 1.

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