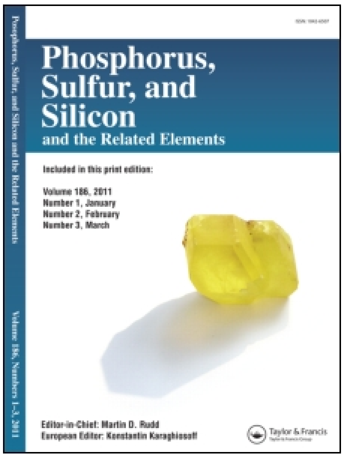

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CONVENIENT ONE-POT CONVERSION OF 2-PHENYL-3,1-BENZOXAZIN-4-ONE TO 2-(O-BENZOYLAMINOPHENYL)-1,3,4-OXADIAZOLIN-5-THIONE

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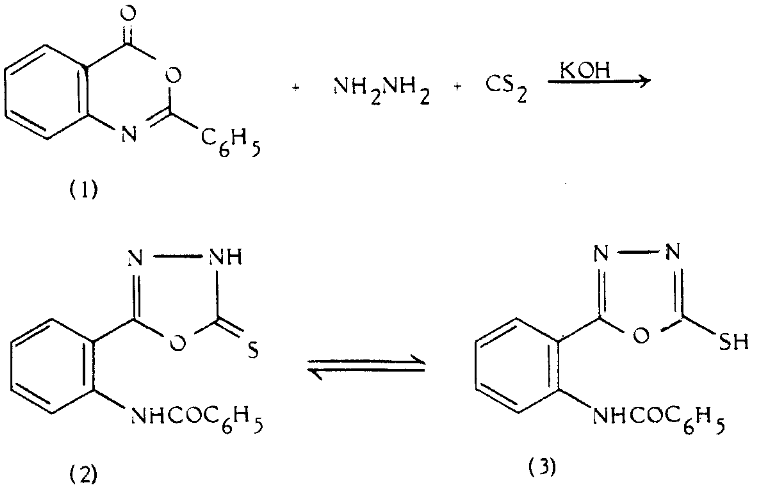
2-Phenyl-3,1-benzoxazin-4-one (**1**) reacted with a mixture of hydrazine hydrate and carbon disulphide in the presence of potassium hydroxide to give 2-(o-benzoylaminophenyl)-1,3,4-oxadiazolin-5-thione (**2**) which was also formed in better yield by the reaction of o-benzoylaminobenzhydrazide (**5**) with carbon disulphide and potassium hydroxide. The reaction of (**2**) with ethyl iodide, formaldehyde in the presence of morpholine, and with amines was also investigated.

Key words: 2-Phenyl-3,1-benzoxazin-4-one; 2-(o-benzoylaminophenyl)-1,3,4-oxadiazolin-5-thione; o-benzoylaminobenzhydrazide.

1,3,4-Oxadiazoles are known to possess marked biological activity.[1-4] In continuation to our previous work on the reactivity of benzoxazinones towards amines and hydrazines,[5-7] we would like to report our preliminary communication on the novel reaction of 3,1-benzoxazin-4-ones with a mixture of hydrazine hydrate and carbon disulphide in the presence of alkali as a one-pot reaction for the synthesis of 1,3,4-oxadiazolin-5-thiones. Thus when 2-phenyl-3,1-benzoxazin-4-one (**1**) was treated with hydrazine hydrate and carbon disulphide in alcoholic potassium hydroxide, 2-(o-benzoylaminophenyl)-1,3,4-oxadiazolin-5-thione (**2**) was formed.

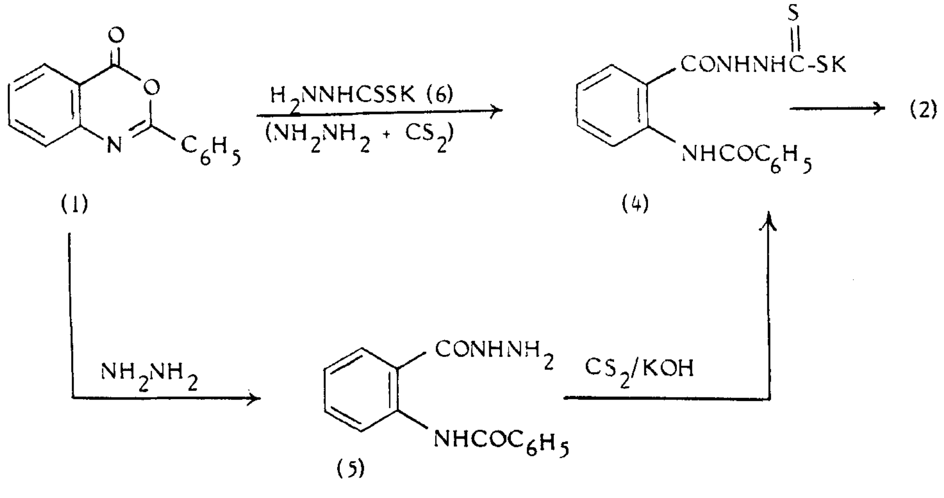
The structure of (**2**) was confirmed by: (i) Microanalytical data. (ii) It dissolves in aqueous sodium hydroxide solution and reprecipitates by the addition of conc. hydrochloric acid. (iii) It's infrared spectrum shows the bands characteristic of ν NH of amides and cyclic thioamides at 3320 cm^{-1}, 3230–3000 cm^{-1}, respectively. The spectrum shows, in addition, the bands characteristic of amide carbonyl, C=S and C=N groups at 1650 cm^{-1}, 1155 cm^{-1} and 1592 cm^{-1}, respectively. (iv) Its ^1H NMR spectrum shows signals at δ 7.1 (s, 1H) assigned for the thioamide proton, δ 7.2–8.3 (m, 9H) of the aromatic protons and δ 10.55 (s, 1H) characteristic of the amide proton. (v) It undergoes many reactions expected for 1,3,4-oxadiazolin-5-thiones (interalia).

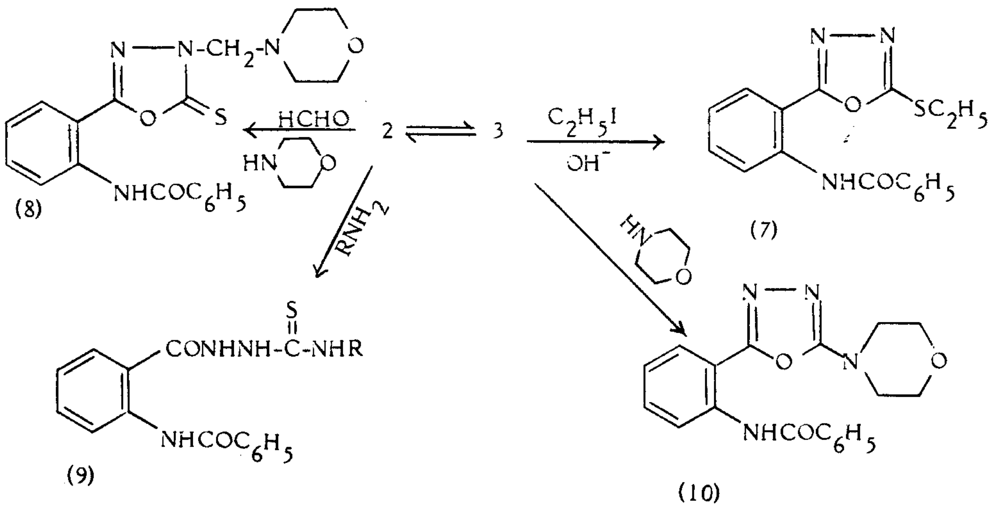
The formation of (**2**) is expected to be by cyclisation of (**4**) which would be formed by either: (i) ring opening of the benzoxazinone ring by the reaction with hydrazine giving o-benzoylaminobenzhydrazide (**5**) followed by reaction with carbon disulphide[8] or (ii) reaction of the benzoxazinone with potassium dithiocarbazinate (**6**) formed by the reaction of hydrazine hydrate with carbon disulphide.[9] However, the former pathway is more probable owing to: (i) the fact that the reaction of the benzoxazinone with hydrazine proceeds almost immediately giving the hydrazide. (ii) It was possible to synthesis (**2**) in better yield by the reaction of the hydrazide (**5**) with carbon disulphide in alcoholic potassium hydroxide which



is a known method for the synthesis of 1,3,4-oxadiazolin-5-thiones.[8] (iii) Indeed when the benzoxazinone (**1**) was allowed to react with potassium dithiocarbazinate a mixture of products was obtained. However, reaction of (**1**) with potassium dithiocarbazinate seems to need further investigation.

The oxadiazolinthione (**2**) reacts normally with ethyl iodide to give 2-(o-benzoylaminophenyl)-5-ethylthio-1,3,4-oxadiazoline (**7**) whose infrared spectrum lacks the broad spectrum in the 3230–3000 cm^{-1} region and that of the C=S group observed in the spectrum of (**2**) while it shows absorptions characteristic of the NH and CO groups of amides. These spectral features indicate that reaction occurred on sulphur. However, the reaction of (**2**) with formaldehyde in the presence of morpholine occurred on nitrogen to give the Mannich base (**8**). When (**2**) was allowed to react with primary amines, namely, *n*-butylamine or benzylamine, it underwent ring opening to give 9a or 9b, respectively. However, its reaction with secondary amines, for example, morpholine involved the displacement of the thiol group to give the 1,3,4-oxadiazoline derivative (**10**).





a; R = C_4H_9 (n-)
b; R = $C_6H_5CH_2$-

The structures of 8–10 were inferred, other than from analytical data, from a study of their infrared spectra which are in good agreement with these proposed structures (cf. experimental).

The synthesis of (**2**) from (**1**) by the previously mentioned method seems to be a convenient straightforward way for the conversion of benzoxazinones to 1,3,4-oxadiazolinthiones. The application of this reaction on some other benzoxazinones is under investigation and will be published later.

EXPERIMENTAL

All melting points are uncorrected. Elemental analyses were carried out at the Microanalytical Unit, Cairo University. I.R. Spectra in KBr were recorded on a Pye-Unicam SP 1200 spectrophotometer. ^1H N.M.R. spectrum of (**2**) was carried out on EM-390-90 MHz NMR spectrometer using dimethyl sulphoxide as a solvent.

Synthesis of 2-(o-benzoylaminophenyl)-1,3,4-oxadiazolin-5-thione (**2**).

Method 1: [from 2-phenyl-3,1-benzoxazin-4-one (1)]: A solution of 2-phenyl-3,1-benzoxazin-4-one (1; 0.01 mole) in ethanol (100 ml) was treated with hydrazine hydrate (1 ml) and set aside for 5 min. with occasional shaking. The reaction mixture was treated with carbon disulphide (3 ml) and potassium hydroxide (0.5 gm) and then heated under reflux on a boiling water-bath for 20 hrs. The reaction mixture was poured into cold water and conc. hydrochloric acid was added drop-wise untill just acidic. The solid formed was filtered off and crystallised from benzene-ethanol mixture to give (**2**), as colourless crystals, m.p. 220–2°C, yield 45%. Found: C, 60.5; H, 4.3; N, 14.3; S, 10.0% $C_{15}H_{11}N_3O_2S$ requires: C, 60.6; H, 3.7; N, 14.14; S, 10.77%.

Method 2: [from o-benzoylaminobenzhydrazide (5)]: A solution of o-benzoylaminobenzhydrazide (5; 0.01 mole) in alcoholic potassium hydroxide (0.012 mole in 100 ml ethanol) was treated with carbon disulphide (0.01 mole). The reaction mixture was heated on a boiling water-bath for 20 hrs. and left to cool. The mixture was poured into cold water and acidified with conc. hydrochloric acid. The solid formed was filtered off and crystallised from benzene-ethanol mixture to give (**2**), as colourless crystals, m.p. 220–2°C, yield 75%. No depression of m.p. was observed when the product was mixed with the corresponding product obtained in the previous experiment.

Reaction of (**2**) *with ethyl iodide; Formation of* (**7**): Ethyl iodide (0.01 mole) was added to a solution of (2; 0.01 mole) in 10% aqueous sodium hydroxide solution (10 ml). The reaction mixture was heated on a boiling water-bath for 10 min. and left to cool. The solid formed was filtered off and crystallised from light petroleum (b.p. 60–80°) to give (**7**), as colourless crystals, m.p. 106–8°C; yield 60%. Found: C, 63.5; H, 4.6; S, 9.5% $C_{17}H_{15}N_3O_2S$ requires: C, 62.76; H, 4.61; S, 9.84%, ν NH 3260 cm^{-1}; ν CO 1670 cm^{-1}, ν C=N 1591 cm^{-1}.

Reaction of (**2**) *with formaldehyde in the presence of morpholine; Formation of the Mannich base* (**8**): A mixture of (2; 0.005 mole), formaldehyde solution (2 ml) and morpholine (0.01 mole) in ethanol (20 ml) was heated under reflux for 6 hrs. After cooling the solid formed was filtered off and crystallised from ethanol to give (**8**), as colourless crystals, m.p. 153–5°C; yield 70%. Found: C, 61.2; H, 4.7; S, 8.4% $C_{20}H_{20}N_4O_3S$ requires: C, 60.60; H, 5.05; S, 8.08% ν NH 3340 cm^{-1}, ν CO 1665 cm^{-1}, ν C=N 1600 cm^{-1}, ν C=S 1168 cm^{-1}.

Reaction of (**2**) *with amines*: The mixture resulting from the addition of 0.01 mole of the appropriate primary or secondary amine to a solution of (2; 0.01 mole) in ethanol (20 ml), was heated under reflux for 15 hrs. and left to cool. The solid formed was filtered off and crystallised from a suitable solvent to give (9a, b and 10).

a) *Reaction of* (**2**) *with n-butylamine*: The solid separated was crystallised from benzene-ethanol mixture to give (9a), as colourless crystals, m.p. 179–81°C; yield 72%. Found: C, 61.9; H, 5.5; N, 15.5; S, 8.4% $C_{19}H_{22}N_4O_2S$ requires: C, 61.62; H, 5.95; N, 15.14; S, 8.65% ν NH 3200 cm^{-1}, ν CO 1665 cm^{-1}, ν C=S 1160 cm^{-1}.

b) *Reaction of* (**2**) *with benzylamine*: The solid formed was crystallised from ethanol to give (9b), as colourless crystals, m.p. 196–8°C; yield 78%. Found: C, 65.3; H, 4.8; N, 14.5; S, 7.6% $C_{22}H_{20}N_4O_2S$ requires: C, 65.34; H, 4.95; N, 13.86; S, 7.92% ν NH 3260, 3140 cm^{-1}, ν CO 1660, ν C=S 1160 cm^{-1}.

c) *Reaction of* (**2**) *with morpholine*: The solid obtained was crystallised from benzene-light petroleum (b.p. 90–100°) mixture, to give (**10**), as colourless crystals, m.p. 197–9°C; yield 52%. Found: C, 64.6; H, 5.5; N, 16.5% $C_{19}H_{18}N_4O_3$ requires: C, 65.14; H, 5.14; N, 16% ν NH 3260 cm^{-1}, ν CO 1665 cm^{-1}, ν C=N 1615 cm^{-1}.

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