HETEROCYCLIC BIOANTIOXIDANTS

4*. CHLOROLYSIS OF 3-NITRO-4-s-BENZYLCOUMARIN

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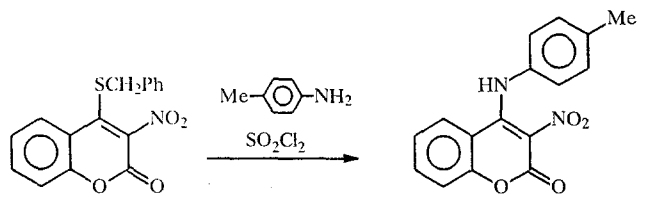
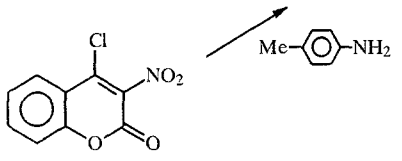
3-Nitro-4-S-benzylcoumarin reacts with sulfuryl chloride to give an unstable compound, which in turn reacts with p-toluidine to give 3-nitro-4-p-tolylaminocoumarin.

Nitrothiophenols are known to form stable sulfenyl chlorides, which are conveniently obtained by chlorolysis of the appropriate S-benzyl compounds [2, 3].

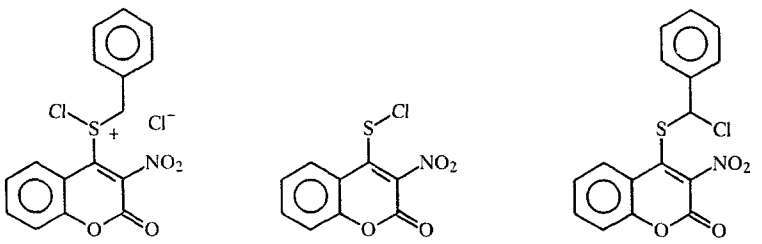
We have now shown that 3-nitro-4-S-benzylcoumarin (I) reacts with sulfuryl chloride to give a product which could not be isolated from the reaction mixture without decomposition, which excludes the stable 3-nitro-4-chlorocoumarin (II) from the possible chlorolysis products. The reaction product could be either the adduct (III), the sulfenyl chloride (IV), or the benzyl chloride (V), by analogy with the usual chlorolysis products of aliphatic benzyl sulfides [4], but it was not possible to isolate any chlorine-containing product.



I VI



II



III IV V

*For Communication 3, see [1].

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Treatment of the chlorolysis reaction mixture with p-toluidine gave 3-nitro-4-p-tolylaminocoumarin (VI) in 70% isolated yield. This compound (VI) was also obtained directly from 3-nitro-4-chlorocoumarin (II).

Hence, the chlorolysis product of 3-nitro-4−S-benzylcoumarin (I) behaves as a sulfenylating agent, as might be expected by analogy with the corresponding nitroaromatic systems [2, 3], and as an alkenylating agent. Its behavior on chlorolysis emphasizes the differences between 4-substituted 3-nitrocoumarins and the analogous aromatic systems.

EXPERIMENTAL

Thin-layer chromatography was carried out on Silufol UV-254 plates in the systems benzene-ethyl acetate, 4:1, and hexane−ether, 1:1, and column chromatography on silica gel L 100/250 (Chemapol), eluent hexane, or mixtures of hexane and ether, 9:1, and hexane-ethyl acetate, 9:1. IR spectra were obtained on a Perkin-Elmer 580 instrument.

The elemental analyses of the products were in agreement with the calculated values. 3-Nitro-4-S-benzylcoumarin (I) was obtained as in [5].

3-Nitro-4-p-tolylaminocoumarin (VI, $C_{16}H_{12}N_2O_4$). **A.** To a suspension of 0.5 g (1.6 mmole) of 3-nitro-4-S-benzylcoumarin (I) in 5 ml of alcohol- and water-free chloroform was added at 18-20°C three drops of DMF and 0.15 ml (1.72 mmole) of sulfuryl chloride, giving a homogeneous solution. After 2 h, when the reaction mixture no longer contained the sulfide (I) (by TLC), 0.44 ml (3.2 mmole) of triethylamine and 0.17 g (1.6 mmole) of p-toluidine were added, kept for 1 h at 18-20°C, then poured into cold water and extracted with chloroform. Chromatographic purification on a column of silica gel gave the coumarin (VI), mp 188-189°C (from acetone), lit. mp [6] 193.5°C (from alcohol). IR spectrum, ν (in KBr): 3274 (NH), 1696 (C=O), 1612 (C=C), 1601 (Ar), 1550 (antisymm. NO_2), 1367 (symm. NO_2). Yield 0.33 g (70%).

In control experiments, the reaction mixture when all the (I) had reacted did not contain 3-nitro-4-chlorocoumarin (II) (analytical TLC), nor was it possible to isolate any chlorine-containing product after treatment of the mixture with water, or after evaporating the solution to dryness and recrystallizing the residue from anhydrous solvents, or chromatography on a column of silica gel.

B. To a solution of 0.5 g (2.22 mmole) of 3-nitro-4-chlorocoumarin (II) and 0.24 g (2.22 mmole) of p-toluidine in 5.0 ml of DMF was added 0.25 g (2.78 mmole) of sodium bicarbonate, and the mixture stirred for 2 h at 18-20°C. After dilution with 20 ml of water, the greenish-yellow solid was filtered off and air-dried. mp 188-189°C (from acetone), mp of monohydrate 145-146°C (acetone−water, 3:1). Yield 0.63 g (96%).

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