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Preparation of 2-Amino-6-nitrobenzothiazole

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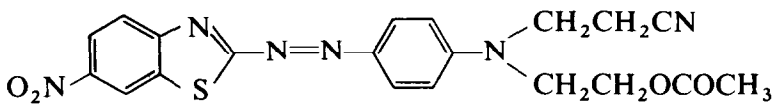
ABSTRACT

2-Amino-6-nitrobenzothiazole, a useful diazo component in the preparation of azo dyes, was prepared by hydrolysis of 2-acetylamino-6-nitrobenzothiazole, which was itself synthesised by oxidative ring-closure of 1-acetyl-3-phenylthiourea with nitric acid in sulphuric acid. 1-Acetyl-3-methyl-3-phenylthiourea was similarly ring-closed with nitric acid to produce 2-acetylimino-3-methyl-6-nitrobenzothiazole. Bis(2-methylamino-5-nitrophenyl)disulphide was obtained on alkaline hydrolysis of 2-acetylamino-3-methyl-6-nitrobenzothiazole.

1 INTRODUCTION

Disperse azo dyes of good properties have been obtained by the use as diazo component of 2-amino-6-nitrobenzothiazole (I).[1] 2-Benzothiazolylazo dyes, compared with their phenylazo counterparts, when applied to polyesters have higher absorptivity, better fastness to light, and show a bathochromic shift of 60–90 nm in the visible absorption maxima.[2] A typical representative of this type of dye is the red dye **II**[3] (Colour Index Disperse Red 177).



II

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2-Amino-6-nitrobenzothiazole diazotised and coupled to *N*-phenylmorpholine[4] also affords good dyes for acetate and polyester fibres and it has also been used for the preparation of reactive dyes for cellulose.[5]

2-Amino-6-nitrobenzothiazole can be also employed for the preparation of fungicides[6] and herbicides[7] and has been used as a starting material for the synthesis of mitomycin analogues[8] (used against leukaemia P338-infected mice).

2 EXPERIMENTAL

2.1 Ring closure of 1-acetyl-3-phenylthiourea

To a solution of 1 g (0·0052 mol) 1-acetyl-3-phenylthiourea (**III**) in 10 ml sulphuric acid (96%) was added dropwise a mixture of 1 ml (0·0157 mol) nitric acid (65%) and 1 ml sulphuric acid (96%) with good stirring and cooling to maintain a temperature below 20°C. After the addition was complete the mixture was kept for 10 min at 25°C and was poured into 100 ml water and cooled to 10°C. The solid was filtered and washed with 100 ml water (yield 0·9 g; 74%). M.p. 294–296°C (dec.). Recrystallisation from acetone gave 2-acetylamino-6-nitrobenzothiazole (**IV**), m.p. 299–301°C (dec.).

$C_9H_7N_3O_3S$ requires: C, 45·6; H, 3·0; N, 17·7; S, 13·5. Found: C, 45·6; H, 3·1; N, 18·1; S, 13·65%.

^{1}H-NMR (hexadeuteriodimethyl sulphoxide, 50°C: δ(NH) = 12·69, δ(H-7) = 9·05, δ(H-5) = 8·32, δ(H-4) = 7·92, $\delta(COCH_3)$ = 2·30.

^{13}C-NMR: δ(C-2) = 163·21, δ(C-3a) = 153·33, δ(C-4) = 120·33, δ(C-5) = 121·44, δ(C-6) = 142·86, δ(C-7) = 118·57, δ(C-7a) = 132·10, δ(CO) = 169·94, $\delta(CH_3)$ = 22·70.

MS electron impact (EI) *m/z* (relative intensity): 195 (100, $M^+ - 42$), 43 (58, CH_3CO), 237 (30, M^+), 165 (30), 122 (21), 149 (20).

2.2 Ring closure of 1-acetyl-3-methyl-3-phenylthiourea

A solution of 1 g (0·0048 mol) 1-acetyl-3-methyl-3-phenylthiourea (**VI**) in 10 ml sulphuric acid (96%) was treated as above with a mixture of 1 ml (0·0157 mol) nitric acid (65%) and 1 ml sulphuric acid (96%). The reaction liquor was poured onto 200 ml water, cooled to 10°C and the solid which separated was filtered and washed with 100 ml water (yield 0·7 g; 58%). M.p. 293–296°C (dec.). Recrystallisation from acetone gave 2-acetylimino-3-methyl-6-nitrobenzothiazole (**VII**), m.p. 304–306°C (dec.).

$C_{10}H_9N_3OS$ requires: C, 47·8; H, 3·6; N, 16·7; S, 12·8. Found: C, 47·5; H, 3·7; N, 17·1; S, 12·9%.
^{1}H-NMR (hexadeuteriodimethyl sulphoxide, 50°C): δ(H-7) = 8·98, δ(H-5) = 8·40, δ(H-4) = 7·82, $\delta(NCH_3)$ = 3·90, $\delta(COCH_3)$ = 2·33.
^{13}C-NMR (110°C): $\delta(NCH_3)$ = 32·27, $\delta(CO\underline{C}H_3)$ = 26·36, δ(CO) = 165·66, δ(C-2) = 180·18; other carbons without assignment, δ = 143·15, 141·63, 126·30, 122·26, 118·40.
MS (EI) *m/z*: 236 (100, $M^+ - 15$), 251 (43, M^+), 190 (37), 43 (31), 163 (8), 135 (8), 209 (7).

2.3 Hydrolysis of 2-acetylamino-6-nitrobenzothiazole

2-Acetylamino-6-nitrobenzothiazole (**IV**) (1 g, 0·0042 mol) was refluxed for 30 min in 100 ml 0·5M-sodium hydroxide. After cooling to 10°C the crystals of 6-nitro-2-aminobenzothiazole (**I**) were filtered, washed with 60 ml water and dried (yield 0·6 g; 73%). M.p. 252–253°C (lit.[9] 249°C).

2.4 Hydrolysis of 2-acetylimino-3-methyl-6-nitrobenzothiazole

Aqueous 0·5M-sodium hydroxide (100 ml) and ethanol (40 ml) were poured onto 0·8 g 2-acetylimino-3-methyl-6-nitrobenzothiazole (**VII**) (0·003 18 mol) and the mixture was refluxed for 90 min, during which time the solid dissolved. Ethanol was distilled off and the mixture was refluxed for a further 90 min. The liquor was then cooled to 10°C and neutralised with the acetic acid (to pH *ca.* 5·5). The crystals which deposited were filtered and washed with 20 ml water (yield 0·45 g; 67%). M.p. 246–248°C (after recrystallisation from acetone). The product was identified as bis(2-methylamino-5-nitrophenyl)disulphide (**VIII**).

^{1}H-NMR (hexadeuteriodimethyl sulphoxide, 25°C): δ ($N\underline{H}CH_3$) = 7·38, $\delta(NHC\underline{H}_3)$ = 2·99, δ(H-3) = 6·82, δ(H-4) = 8·17, δ(H-6) = 7·50.
^{13}C-NMR: δ(C-1) = 115·49, δ(C-2) = 154·52, δ(C-3) = 109·43, δ(C-4) = 128·29, δ(C-5) = 134·79, δ(C-6) = 132·69, $\delta(CH_3)$ = 30·03.
MS (EI): *m/z* 183 (100, $M^+ - 183$), 184 (99), 137 (51), 136 (50), 138 (30), 366 (30, M^+), 167 (28), 150 (26).

2.5 Characterisation

^{1}H-, ^{13}C- and ^{15}N-NMR spectra were recorded on a JNM-FX 100 spectrometer (JEOL, Japan) at 99·601 MHz, 25·047 MHz and 10·095 MHz respectively. The compounds were measured in saturated solutions in hexadeuteriodimethyl sulphoxide. As internal standard a signal of solvent

$\delta^1H = 2{\cdot}55$, $\delta^{13}C = 39{\cdot}6$ was used. For ^{15}N-NMR spectra nitromethane (95% ^{15}N, $\delta = 0{\cdot}00$) in a coaxial capillary was used as external standard. Negative ^{15}N chemical shifts denote upfield shifts.

Mass spectra were obtained on a JOEL JMS-01SG-2 (Japan) mass spectrometer equipped with an electron-impact (EI) source. The mass spectrometer conditions were: ionization potential 75 eV; source temperature 75–300°C; resolution 1000 (10% valley definition); for accurate mass measurement resolving power 5000; accelerating voltage 8 kV; beam current 200 μA.

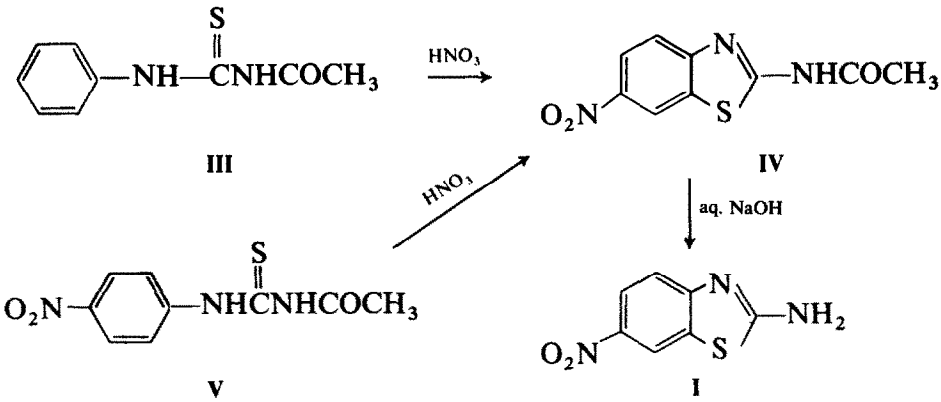
The starting materials used in the cyclisation reactions, viz. 1-acetyl-3-(4-X)phenylthioureas and 1-acetyl-3-methyl-3-phenylthiourea, were prepared from acetyl isothiocyanate and the appropriate aniline, following the procedure described by Nair[10] for benzoyl isothiocyanate. Thus prepared were 1-acetyl-3-phenylthiourea (**III**) (m.p. 172–173°C), 1-acetyl-3-(4-nitrophenyl)thiourea (**V**) (m.p. 195–197°C), 1-acetyl-3-(4-methylphenyl)thiourea (**IX**) (m.p. 175–176°C), 1-acetyl-3-(4-carbomethoxyphenyl)thiourea (**XI**) (m.p. 208–210°C) and 1-acetyl-3-methyl-3-phenylthiourea (**VI**) (m.p. 112–113°C).

3 RESULTS AND DISCUSSION

It is well known that 1-phenylthiourea cyclises to 2-aminobenzothiazole in the presence of halogen compounds.[11] During this reaction, by-products due to bromination in the 6-position of the benzothiazole ring or to addition of the so-called labile bromine can be formed. In the recent patent literature some other reagents for the cyclisation of phenylthiourea have been described, e.g. sulphuryl chloride[12] and sulphur monochloride.[13] A synthesis of 2-amino-6-nitrobenzothiazole has been described[14] involving nitration of 2-acetylaminobenzothiazole with nitric acid in a sulphuric acid solution followed by hydrolysis of the acetyl group with water without isolation of the intermediate product.

In this communication a simple method[15] for the preparation of 2-amino-6-nitrobenzothiazole is described. The mechanism of this reaction is not entirely clear and will be studied by us in more detail. The process involves treating a solution of 1-acetyl-3-phenylthiourea (**III**) in conc. sulphuric acid with an excess of nitric and proceeds in two steps *in situ*, viz. nitration and ring-closure. Reactions using an excess of more than 1·5 mol of nitric acid give relatively pure product and the reaction temperature could be varied from 5 to 65°C without significant influence on the yield.

The same product, viz. 2-acetylamino-6-nitrobenzothiazole (**IV**) was also obtained by treating 1-acetyl-3-(4-nitrophenyl)thiourea (**V**) with nitric acid.

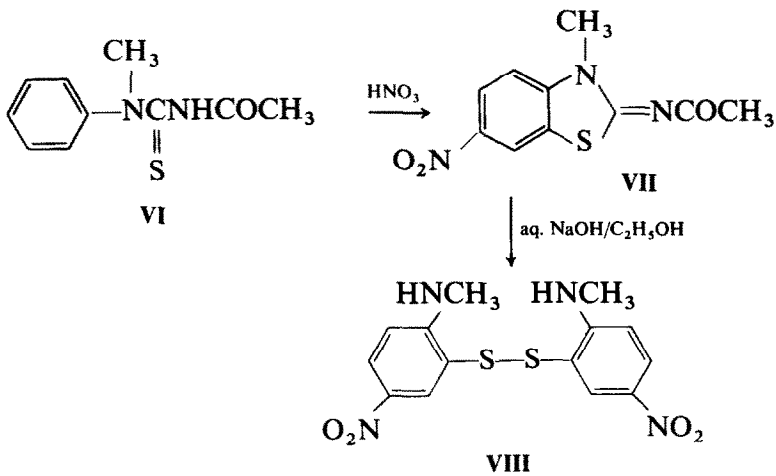


Scheme 1

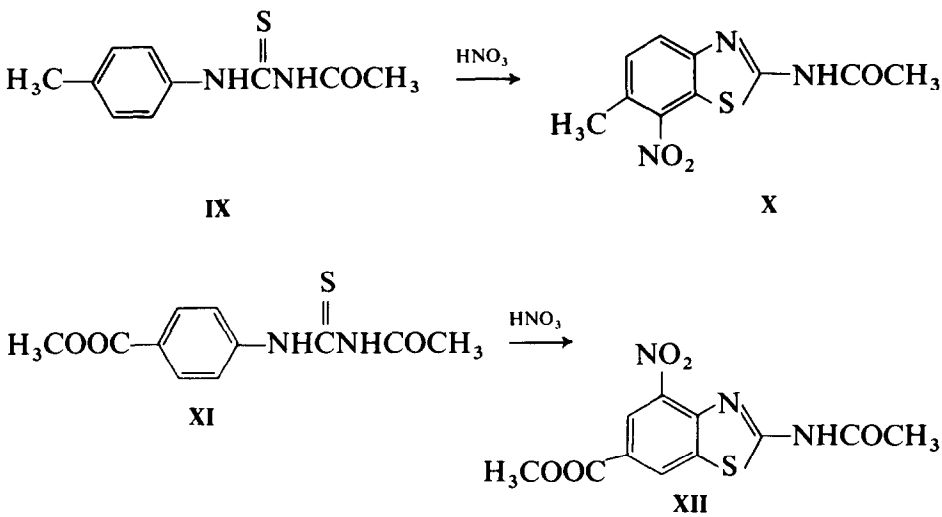
1-Acetyl-3-methyl-3-phenylthiourea (**VI**) ring-closed under the same conditions giving 2-acetylimino-3-methyl-6-nitrobenzothiazole (**VII**). If the phenyl ring of 1-acetyl-3-phenylthiourea was substituted in the 4-position by an electron-donor substituent such as CH_3 (**IX**), then the principal reaction product was a compound melting at 295–297°C and having the following characteristics:

^{1}H-NMR: $\delta(COCH_3) = 2{\cdot}29$, $\delta(CH_3) = 2{\cdot}80$, δ(H-4) = 8·09, δ(H-5) = 7·64, δ(NH) = 12·70; $^3J(H,H) = 8{\cdot}30$ Hz.
MS (EI) *m/z*: 209 (100, $M^+ - 42$), 192 (81, $M^+ - 42 - 17$), 43 (60, CH_3CO), 251 (51, M^+), 164 (33), 136 (24).

Ring-closure and nitration in the 7-position of the benzothiazole ring has thus occurred, giving 2-acetylamino-6-methyl-7-nitrobenzothiazole (**X**).



Scheme 2



Scheme 3

If the phenyl ring of 1-acetyl-3-phenylthiourea is substituted in the 4-position by an electron-acceptor substituent, e.g. $COOCH_3$ (**XI**) then, in addition to cyclisation, nitration in the 4-position of the benzothiazole also occurs, giving 2-acetylamino-4-nitro-6-carbomethoxybenzothiazole (**XII**), m.p. 317–320°C.

^{1}H-NMR: $\delta(COCH_3) = 2{\cdot}32$, $\delta(COOCH_3) = 3{\cdot}98$, δ(H-5) = 8·64, δ(H-7) = 9·02, δ(NH) = 13·09; ^4J(H, H) = 1·40 Hz.
MS (EI): *m/z* 253 (100, $M^+ - 42$), 43 (64, $COCH_3$), 295 (22, M^+), 210 (22), 280 (15), 254 (15), 222 (13).

The direct synthesis of 2-amino-6-nitrobenzothiazole from 1-phenylthiourea by treatment with nitric acid was not successful.

For the preparation of 2-acetylamino-6-nitrobenzothiazole from 1-acetyl-3-(4-nitrophenyl)thiourea some other oxidising agents were tested, but with little success. The use of perchloric acid gave no reaction, whilst with hydrogen peroxide, potassium dichromate, or potassium permanganate in excess 1-acetyl-3-(4-nitrophenyl)thiourea was converted to only a small amount of the product (2-acetylamino-6-nitrobenzothiazole), the main reaction being exchange of the sulphur atom for oxygen with the formation of the urea.

Alkaline hydrolysis was preferred for the degradation of 2-acetylamino-6-nitrobenzothiazole because of its relative stability in acidic media. The hydrolysis of this compound was successfully effected by boiling in 0·5 mol sodium hydroxide, and from the reaction liquor pure (according to TLC, ^{1}H-NMR and melting point) 2-amino-6-nitrobenzothiazole (**I**) was

obtained. The degradation of 2-acetylimino-3-methyl-6-nitrobenzothiazole (**VII**) in alkaline medium led to ring-opening with formation of bis(2-methylamino-5-nitrophenyl) disulphide (**VIII**).

2-Amino-6-nitrobenzothiazole exists in solution of hexadeuteriodimethyl sulphoxide as a classical amino compound, viz. $\delta(NH_2) = -291{\cdot}78$; $^1J(N, H) = 87{\cdot}40$ Hz (triplet); $\delta(N\text{-}3) = -144{\cdot}50$, $\delta(NO_2) = -9{\cdot}55$.

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