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A NEW INTRAMOLECULAR CYCLISATION REACTION—I

NOVEL SYNTHESIS OF BENZO(k,l)THIOXANTHENE-3,4-DICARBOXYLIC ANHYDRIDE AND DERIVED DYESTUFFS

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Abstract—A new direct synthesis of benzo(k,l)thioxanthene-3,4-dicarboxylic anhydride from 4-nitronaphthalene-1,8-dicarboxylic anhydride and 2-aminobenzenethiol is reported; 4-(2-aminophenylthio) naphthalene-1,8-dicarboxylic anhydride and 4-phenylthionaphthalene-1,8-dicarboxylic anhydride are also formed. Similar reaction in presence of amyl nitrite or sodium nitrite results in formation of larger amounts of 4-phenylthionaphthalene-1,8-dicarboxylic anhydride, together with other products arising from the oxidation of 2-aminobenzenethiol; one such product is the new heterocycle 9,10-dithiaphenanthrene. 4-(2-Aminophenylthio)-naphthalene-1,8-dicarboxylic anhydride is rapidly converted by amyl nitrite or sodium nitrite in dimethylformamide into benzo(k,l)thioxanthene-3,4-dicarboxylic anhydride, constituting a novel one-stage intramolecular cyclisation reaction of greater convenience than the conventional two stage Pschorr cyclisation.

Benzo(k,l)thioxanthene-3,4-dicarboximides have been described in patent specifications[1] as yellow to red dyestuffs for synthetic fibres. We have described recently[2] the synthesis of these dyes by Pschorr cyclisation of 4-(2-aminophenylthio)-1,8-naphthalimides and also by condensation of alkylamines with benzo(k,l)thioxanthene-3,4-dicarboxylic anhydride **1**.

In all these preparations, an integral part of the synthesis involves condensation of a 4-halogeno- or 4-nitronaphthalene-1,8-dicarboxylic anhydride **2**, or derived imides, or of 3- and 4-halogeno- or nitro-7H-benzimidazo(2,1-a)benz(d,e)-isoquinolin-7-ones with 2-aminobenzenethiol, followed by Pschorr cyclisation[3] of the resultant products. The initial condensations with 2-aminobenzenethiol can lead[2] to the formation of undesirable by-products, and the final Pschorr cyclisation stage can result[2] in formation of hydrolysis products of the diazonium compound in addition to **1** and its derivatives. During the synthesis of **3** from **2** and 2-aminobenzenethiol in boiling dimethylformamide (DMF), the additional formation of an orange product was noted.[2] This was not observed in a similar synthesis from 4-halogenonaphthalene-1,8-dicarboxylic anhydride and its formation is thus dependent on the presence of the nitro group in the starting material. We have since confirmed the identity of this orange product as **1**.

This surprising formation of **1** prompted further investigation and we report here the novel formation of **1** from **2** and 2-aminobenzenethiol in DMF (Scheme 1) at temperatures lower than those favourable for formation of **3**. The reaction, preferably at room temperature, is rapid, and, under such conditions, **1** precipitates directly from the reaction liquor over 5–30 min. Small volumes of solvent are preferable for isolation of maximum amounts of **1**, since it is the least soluble product, but contamination with **3** and **4** occurs under such conditions. Typical reaction products (filtered directly from the reaction liquor) from different solvent volumes are shown in Table 1.

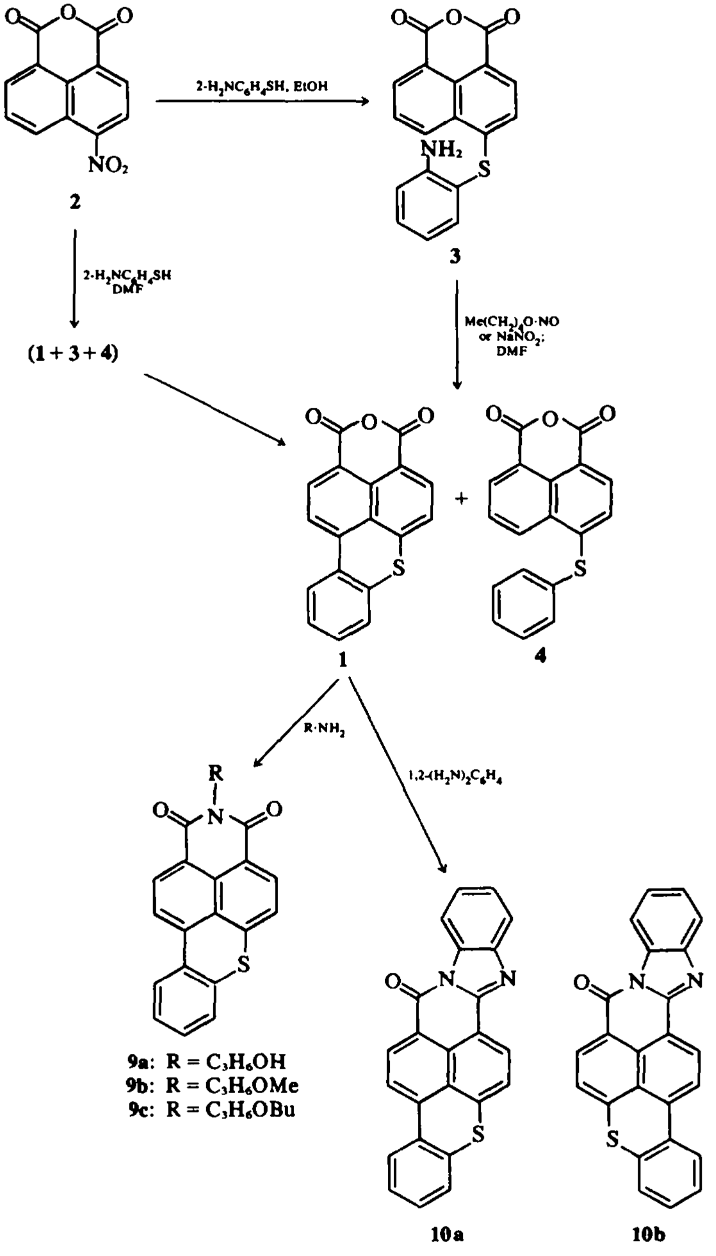
Addition of amyl nitrite or sodium nitrite to the

Table 1. Typical reactions of 2-aminobenzenethiol with 4-nitronaphthalene-1,8-dicarboxylic anhydride **2** for 1 h at room temp.

	2-Aminobenzenethiol	DMF	Yield[a]	%[b]	M.p.°C
2(g)	(g)	(ml)	(g)		
A 2·43	2·50	60	0·40	13·2	311–314
B 2·43	2·50	45	0·87	28·7	306–308
C 2·43	2·50	30	1·26	41·6	297–300
D 2·43	2·50	15	1·66	54·7	284–292
E 2·43	2·50	10	1·98	65·2	269–278

[a] First crop filtered material. Products from reactions A and B are essentially **1**, with increasing contamination with **3** and **4** in reactions C to E.

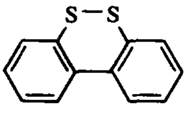
[b] % yield based on conversion of **2** to **1**.



SCHEME 1.

reaction liquor, initially, during, or in the final stages of the reaction had little beneficial effect on the formation of **1**, the tendency being for formation of increased amounts of **4** and for the nitrites to react with oxidation products of 2 - aminobenzenethiol with formation of predominantly high molecular weight reaction products, *cf*[2]. Compounds **1** and **4** were separated from these by extraction with sodium hydroxide; principal low molecular weight alkali-insoluble material was 2,2′ - diaminodiphenyl - disulphide and N - (2 - mercaptophenyl) - 4 - (2 - aminophenylthio) - 1,8 - naphthalimide. Also isolated from the alkali insoluble material, particularly in cyclisations effected in presence of amyl nitrite or sodium nitrite, was 9,10 - dithiaphenanthrene **5**; mass spectrometry indicated the formation also of a compound of *m*/*e* 244 ($C_{12}H_8N_2S_2$, confirmed by high resolution mass measurement), probably azobenzene - 2,2′ - disulphide.

The mass spectrum of the new heterocycle **5** showed the molecular ion as base peak, with, as major fragmentations, progressive loss of the two sulphur atoms, (all molecular compositions confirmed by high resolution mass measurement):


5

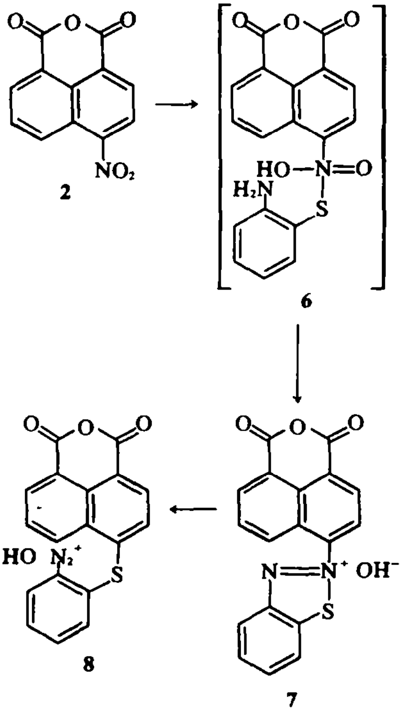
$$\begin{tikzcd}
\begin{array}{c} m/e\ 216 \\ C_{12}H_8S_2 \\ (100\%) \end{array} \arrow[r, "-S", "m^*\ 156{\cdot}7"'] & \begin{array}{c} m/e\ 184 \\ C_{12}H_8S \\ (85{\cdot}4\%) \end{array} \arrow[r, "-S", "m^*\ 125{\cdot}6"'] \arrow[d, dashed] & \begin{array}{c} m/e\ 152 \\ C_{12}H_8 \\ (10{\cdot}4\%) \end{array} \arrow[d, dashed] \\
 & \begin{array}{c} m/e\ 171 \\ C_{11}H_7S \\ (26{\cdot}25\%) \end{array} \arrow[r, dashed, "-S"] & \begin{array}{c} m/e\ 139 \\ C_{11}H_7 \\ (24{\cdot}6\%) \end{array}
\end{tikzcd}$$

In the absence of 2 - aminobenzenethiol however, 3, prepared by conventional methods,[2] was cyclised by sodium nitrite or amyl nitrite in DMF to 1 without formation of the above by-products, but with additional formation of 4. Mixtures of 1, 3 and 4, isolated from the reaction between 2 and 2 - aminobenzenethiol similarly gave 1 and 4, separable by differential solubility in DMF.

Thus, 2 is converted to 1 directly, but with additional formation of 3 and 4; whilst complete elimination of 3 may be effected by addition of amyl nitrite or sodium nitrite to the reaction liquor, this results, in presence of 2 - aminobenzenethiol, in formation of 2,2′ - diamino - diphenyldisulphide, 5, and high molecular weight products. The use of nitrites is thus preferred in absence of 2 - aminobenzenethiol. Optimum conversion of 2 to 1 involves therefore reaction with 2 - aminobenzenethiol under conditions enabling maximum amounts of 1 and 3 to be filtered directly from the reaction mixture, removing 2 - aminobenzenethiol from this mixture, and cyclising with amyl nitrite in DMF.

The conventional Pschorr cyclisation involves diazotisation in strongly acidic conditions, followed by intramolecular cyclisation in aqueous copper sulphate. Other intramolecular cyclisations of diazonium compounds involve thermal decomposition of diazonium fluoroborates,[4-6] diazonium sulphates[7] and diazonium chlorides[8] in aqueous[4] or acidic[5,9] media, optionally in presence of cuprous halides[10] or cupric sulphate.[9] In all these methods, formation of large amounts of hydroxy derivatives by replacement of the diazonium group can occur. While we observed[2] the formation of such hydroxy compounds during the Pschorr synthesis of 1 and derived dyestuffs, no formation of 4 - (2 - hydroxyphenylthio) naphthalene - 1,8 - dicarboxylic anhydride was apparent in this present work, as would be anticipated on the basis of a similar reaction mechanism to the above cyclisation. The high yield and rapid formation of 1 is additionally surprising in view of the known[11] replacement of diazonium groups by hydrogen in DMF; such reaction would be expected to result in larger amounts of 4 than were observed in this present work.

The formation of intermediate addition products in nucleophilic replacements involving aryl mercaptans has been recently demonstrated[12] e.g. in the reaction of thiophenol with 2 - chloro - 1,3 - dimethyl benzimidazolium ions. Compound 7 (Scheme 2) may be envisaged as arising from loss



SCHEME 2.

of water from the addition product **6** of 2 - aminobenzenethiol and **2**. Ring opening of **7** and rearrangement may be envisaged as a possible source of **8**, which may then cyclise to **1** or eliminate the diazo group, giving **4**. The mechanism of the reaction requires further study, since the other principal reaction product **3** is most likely to arise by typical nucleophilic replacement.

The cyclisation of **3** with amyl nitrite in DMF occurs presumably through the diazo reaction, and the formation of **5**, particularly when amyl nitrite or sodium nitrite is added to mixtures of **2** and 2 - aminobenzenethiol, must arise by diazotisation of the amino groups in 2,2′ - diaminodiphenyl - disulphide, elimination of the diazo group by DMF,[11] followed by intramolecular cyclisation. In absence of amyl nitrite or sodium nitrite, **5** is also formed, although in much smaller amount; its formation in absence of nitrites is thus indicative of the presence of nitrosating (diazotising) species arising from the eliminated nitro group. Reaction of 2 - aminobenzenethiol and 4 - chloronaphthalene - 1,8 - dicarboxylic anhydride did not result in the formation of **5**.

In addition to providing a rapid direct synthesis of **1** from **2**, this new method also offers an easier way than Pschorr cyclisation of **3**, replacing the two-stage process of diazotisation and subsequent reaction of the diazonium compound with aqueous copper sulphate, by a one-stage synthesis using amyl nitrite or sodium nitrite in DMF.

The formation of **5** as by-product in reactions in presence of 2 - aminobenzenethiol further indicates the wider potential applicability of this intramolecular cyclisation reaction, a factor which we are investigating further. Reaction of 2,2′ - diaminodiphenyldisulphide with amyl nitrite in DMF resulted in the formation of **5**.

Condensation of **1**, as synthesised in this present work, additionally offers a more rapid method for formation of **9** and **10** (Scheme 1) which have[2] excellent properties as dyestuffs for synthetic fibres. In view of the interest in sulphur heterocycles in dyestuffs chemistry, we are further investigating the applicability of this new synthesis. Preliminary work suggests[13] its use in the synthesis of variously substituted **1**, and also in the introduction of 6-membered sulphur containing heterocyclic rings into other chromophores.

EXPERIMENTAL

All m.ps are uncorrected. Microanalyses were performed by Research Laboratorium Dr. C. Janssen, Beerse, Belgium. The mass spectra were measured on an AEI MS-902 instrument at 70 eV.

Benzo - (k,l) - thioxanthene - 3,4 - dicarboxylic anhydride 1; *direct synthesis from 4 - nitronapththalene - 1,8 - dicarboxylic anhydride* 2

Compound **2** (2·43 g), 2 - aminobenzenethiol (2·5 g) and DMF (10–60 ml) (see Table 1) were stirred at room temperature; an orange–red solid precipitated rapidly and, after 40 min, the mixture was filtered. For low solvent volume reactions, filtration of the viscous paste was facilitated by addition of a small volume of acetone. The residue was washed either with a little DMF, followed by acetone, or by water, the latter giving a less pure reaction product. Compounds **1**, **3** and **4** were very soluble in DMF, but the lower solubility of **1** enabled **3** and **4** to be washed out (together with some **1**). Second crop material was boiled with 5% aq NaOH; the alkaline liquor, on acidification, gave a mixture of **1**, **3** and **4**, which recrystallised (DMF) to **1**, m.p. 330° (lit.,[3] 332–333°). Since hot DMF methylates the anhydride group of **1**, giving additional impurities, a preferred separation of **1**, **3** and **4** involved stirring the mixture in a sufficient cold DMF to dissolve **3** and **4** (and some **1**), and filtering residual insoluble **1** in pure form. Compound **1** thus isolated was identical to that previously[2] described.

Alternatively, addition of the reaction mixture to excess water, followed by filtration gave above-quantitative yields (based on the conversion of **2**→**1**) of an orange–yellow solid. Alkali insoluble material was separated from this by boiling 5% aq NaOH. Preparative layer chromatography on Kieselgel PF$_{254+366}$(Merck) of alkali-soluble material (applying to the plates from DMF solution and eluting with toluene:acetone 95:5, using a multiple-run technique), gave a product analysis falling generally in the regions 60–65% **1**, 20–30% **3** and 10–15% **4**. Alkali insoluble material was not fully analysed; TLC showed the presence of numerous components, partially separable by preparative layer chromatography. Specifically isolated were 2,2′ - diaminodiphenyldisulphide and 9,10 - dithiaphenanthrene **5**, brownish-yellow prisms, m.p. 138–140° (ethyleneglycol monomethylether) (Found: C, 66·4; H, 3·4; S, 29·2; $C_{12}H_8S$ requires: C, 66·7; H, 3·7; S, 29·6%), and trace amounts of N - methyl - benzo - (k,l) - thioxanthene - 3,4 - dicarboximide, m.p. 305–306° (DMF) (Found: C, 71·7; H, 3·4; N, 4·1; S, 9·8; $C_{19}H_{11}NO_2S$ requires: C, 71·9; H, 3·5; N, 4·4; S, 10·1%).

Mass spectra of remaining incompletely resolved bands indicated the presence of high MW components similar to those previously observed,[2] a component at *m/e* 244 (high resolution mass measurement $C_{12}H_8N_2S_2$ corresponding to azobenzene - 2,2′ - disulphide) and of N - (2 - mercaptophenyl) - 4 - (2 - aminophenylthio) - 1,8 - naphthalimide, *m/e* 428 (cf.[2]).

Increasing the amount of 2 - aminobenzenethiol used in the above reaction did not significantly affect the yields of **1**, **3** and **4**, but resulted in the formation of considerably increased amounts of alkali insoluble material, particularly 2,2′ - diaminodiphenyldisulphide and **5**. Decreased amounts of 2 - aminobenzenethiol tended to inhibit reaction with **2**, resulting in increased formation of 2,2′ - diaminodiphenyldisulphide and also more **3** relative to **1**.

Cyclisation of 4 - (2 - *aminophenylthio*)*naphthalene* - 1,8 - *dicarboxylic anhydride* 3.

A solution of **3** (0·80 g), prepared as previously[2] described, in DMF (15 ml) was treated with amyl nitrite (1 ml) at room temp. After 30 min the liquor was filtered to give orange–red needles (0·32 g), of **1**, m.p. 310–315°. The mother liquors, added to water, afforded an orange red solid, 0·38 g, m.p. 270–280°, mainly **1** and **4** (TLC); compound **4** (and some **1**) was removed by cold DMF. The total yield of **1** was 69·74%.

Alternatively, a solution of **3** (0·4 g) in DMF (4 ml) at

150° was treated with amyl nitrite (0·5 ml), the mixture refluxed for 5 min, cooled and filtered, to give orange–red needles of **1** (0·3 g; 78·9%), m.p. 314–316°.

Similarly, mixtures of **1** and **3**, or of **1**, **3** and **4**, obtained by the reactions given in Table 1, were cyclised as above. Thus, a mixture of **1** and **3** (0·5 g)(first crop, Expt C, Table 1) in DMF (7 ml) was treated with amyl nitrite (1 ml); after stirring for 60 min at room temp, red–brown needles of **1** (0·36 g), m.p. 303–310°, were filtered off. Replacing amyl nitrite in the above by sodium nitrite (0·5 g) gave, after 2 h, 0·33 g of **1**, m.p. 314–318° as first crop material. Mother liquors in both these reactions contained mainly **1** and **4**.

Reaction of 2 - *aminobenzenethiol and* 4 - *nitronaphthalene* - 1,8 - *dicarboxylic anhydride in presence of amyl nitrite*

Compound **2** (2·43 g), 2 - aminobenzenethiol (1·9 g) and DMF (16 ml) were stirred 5 min at room temp, amyl nitrite (2 ml) added, and stirring continued for 4 h during which time an orange–brown solid (A, 1·8 g), m.p. 290–300°, deposited; the mother liquors, added to water, afforded an orange yellow solid (B, 3·2g), m.p. 116–130°. Both fractions were boiled for 15 min in 5% aq NaOH, insoluble material filtered, and the filtrates neutralised to give mixtures of **1** and **4** (from A, 0·4 g, m.p. 298–300°; from B, 1·9 g, m.p. 289–295°). These, recrystallised (DMF), or, preferably, stirred in sufficient cold DMF to dissolve **4** (and some **1**), gave **1**, m.p. 320–324° (1·7 g). Alkali insoluble material (containing 2,2′ - diaminodiphenyldisulphide, **5**, and high molecular weight material) was not investigated further.

Alternatively, **2** (1 g), 2 - aminobenzenethiol (0·6 g), DMF (5 ml) and amyl nitrite (4 ml) were stirred at room temp for 30 min and the liquor filtered to give orange prisms (0·7 g; m.p. 270–280°), a mixture of **1**, **3** and **4**. This mixture, after being washed free of residual 2 - aminobenzenethiol with a little benzene, on treatment with amyl nitrite in DMF, as above, gave **1** and **4**, separated by cold DMF. The use of larger amounts of nitrite resulted in the preferential formation of **4**.

Reaction of 2 - *aminobenzenethiol and* 4 - *nitronaphthalene* - 1,8 - *dicarboxylic anhydride in presence of sodium nitrite*

Compound **2** (5 g) and 2 - aminobenzenethiol (3·6 g) were stirred for 5 min at room temp in DMF (30 ml) and sodium nitrite (1·5 g); hydrated copper sulphate (2 g) was added, and stirring continued during 2 h. On filtering, a bright orange solid (5·2 g) was collected. Alkali extraction, as above (alkali-insoluble material, 2·6 g, m.p. >360°), gave, on acidification of the alkaline liquor, an orange–red solid (2·8 g; m.p. 260–270°) (mixture of **1** and **4**), which, after extraction of **4** (and some **1**) with cold DMF, gave **1** (1·9 g; m.p. 312–318°).

Condensation of 2 - *aminobenzenethiol and* 4 - *nitronaphthalene* - 1,8 - *dicarboxylic anhydride in other solvents*

Replacing DMF in the above syntheses by other solvents was not satisfactory. In diethyleneglycoldimethylether, the principal reaction product was **3** (with 2,2′ - diaminodiphenyldisulphide). In benzene, toluene, or acetic acid, little reaction occurred other than oxidation of the thiol. Reaction in ethanol has been previously shown[2] to give mainly **3**.

Benzo(k,l)thioxanthene - 3,4 - *dicarboximides*, **9**

Compound **1** (1 g), prepared as above, was refluxed in ethanol (40 ml) for 2 h with 3 - aminopropan - 1 - ol (0·4 ml), 3 - methoxypropylamine (0·45 ml) or 3 - n - butoxypropylamine (0·67 ml). On addition of the liquors to cold water, and filtering, the respective imides **9a**, **9b** and **9c** (Scheme 1) were obtained in 84%, 87% and 86% yield. These were identical with the products prepared by other methods, and dyed synthetic fibres in identical shades to those previously[2] described.

Benzimidazo(1,2-*b*)*thioxantheno*(2,1,9-*d,e,f*)*isoquinolin*-7-*one* **10a** *and benzimidazo* (1,2-*a*)*thioxantheno* (2,1,9 - *d,e,f*)*isoquinolin* - 8 - *one* **10b**.

Compound **1** (0·35 g), prepared as above, was refluxed with o - phenylenediamine (0·4 g) in glacial acetic acid (10 ml) for 3 h, the liquor cooled and filtered, to give reddish–pink needles (0·37 g; m.p. 289–295°) of the isomer mixture of **10a** and **10b**. This mixture dyed polyester fibres in intense fluorescent orange scarlet shades, similar to those obtained from a similar isomer mixture obtained[13] by Pschorr cyclisation of 3- and 4 - (2 - aminophenylthio) - 7H - benzimidazo (2,1 - a)benz(d,e)isoquinolin - 7 - one. This new synthesis gave a more facile route to, and improved yields of, **10a** and **10b**, without the formation of undesirable by-products.

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