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4-Arylamino-6-chloro-1,3,5-triazin-2(1H)-ones: nucleophilic substitution of a model compound in acid medium to produce novel fibre reactive triazinyl derivatives

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Abstract

A model 4-arylamino-6-chloro-1,3,5-triazin-2(1H)-one has been synthesised and reacted with a variety of nitrogen, oxygen and sulphur nucleophiles in an acidic medium. Unlike the parent compound, the products from reaction with pyridine, nicotinic acid and *p*-aminobenzene-β-sulphatoethylsulphone are capable of reaction with cellulose in an alkaline medium.

Keywords: 4-Arylamino-6-chloro-1,3,5-triazin-2(1H)-one; Acid catalysis; Reactive group; Nicotinic acid; Triazine-2-oxide; Betaine

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1. Introduction

4-Substituted-6-chloro-1,3,5-triazin-2(1H)-one (CTO) compounds are formed as unwanted by-products, during both manufacture and application of dichlorotriazinyl (DCT) dyes. In the latter case base catalysed hydrolysis occurs during the cellulose fixation process (Scheme 1).

Although only partially hydrolysed, CTO compounds are resistant to further base catalysed nucleophilic substitution reactions with either cellulose or hydroxide ions. This is due to deprotonation of the weakly acidic hydroxyl group on the triazine ring and the resultant deactivation of the remaining chlorine atom.

It is known, however, that CTO and DCT dyes fix to cellulose in weakly acidic media at elevated temperatures. The combination of high temperatures and acid conditions can result in fibre tendering and renders this approach suitable only for polyester–cellulose dyeing.

Consistent with the above observations, is the known [1] medium dependency of the relative rates of the substitution of the first and second chlorine atoms of DCT compounds (Scheme 2).

In alkaline solution (pH 8–12), $k_1 > k_2$ and in acidic solution (pH 0–2) $k_2 > k_1$. A demonstration of the importance of pH is shown by the preparation of cyanuric acid (**III**; R = OH) from chlorodihydroxytriazine (**II**; R = OH). This can be performed in dilute sodium hydroxide solution [2] at 125 °C, or more simply, in dilute mineral acid [3] at room temperature.

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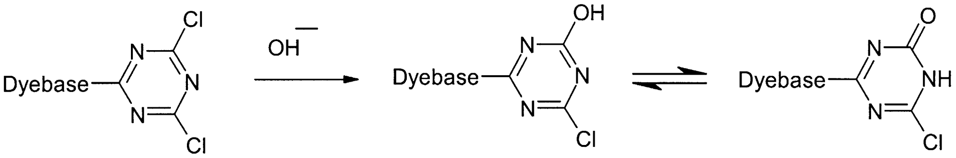
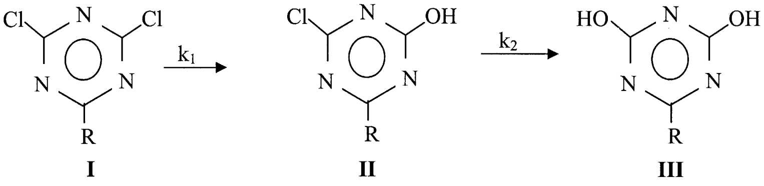


Scheme 1.

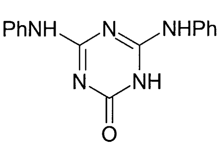


Scheme 2.

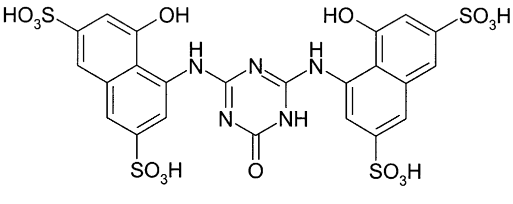
The literature contains few references to nucleophlic substitution reactions of CTO compounds in acidic medium. Matsui et al. [4] refluxed 4,6-dichloro-1,3,5-triazin-2(1H)-one (dichlorohydroxytriazine; **I**, R = OH) with an excess of aniline under neutral and acid conditions to give the dianilino derivative (**IV**) and a patent [5] describes the reaction of dichlorohydroxytriazine (**I**; R = OH) with two moles of 1-amino-8-hydroxynaphthalene 3,6-disulphonic acid (H-Acid), also in acid medium, to furnish the novel coupling component (**V**). Renfrew and Phillips [6] have also shown that the reaction of *p*-aminobenzene-β-sulphatoethylsulphone (PABSES) with dichlorohydroxytriazine —(**I**; R = OH) results in replacement of both chlorine atoms to give compound (**VI**). A mono substituted species was not observed.

Occasionally, during the manufacture of DCT dyes, hydrolysis takes place rendering the products unsaleable for conventional alkaline fixation. Accordingly, this work was undertaken to study the chemical reactions of 4-substituted-6-chloro-1,3,5-triazin-2(1H)-ones, in acid medium with a view to generating novel fibre reactive compounds for conventional use in alkaline medium.

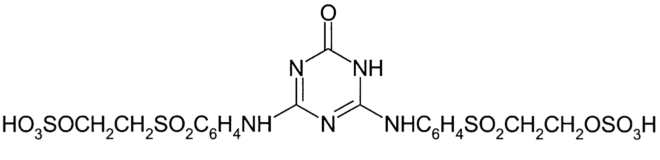
A simple model CTO compound, viz 6-chloro-4-*p*-sulphoanilino-1,3,5-triazin-2(1H)-one (**VIII**; Scheme 3) was synthesised for use in this study.



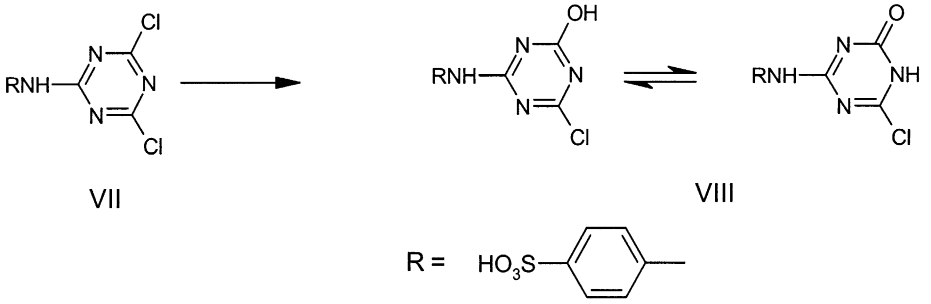
IV



V



(VI)



Scheme 3.

2. Experimental

HPLC was performed with a Hewlett Packard 1100 series fitted with a quaternary pump.

The column was a 10 cm Purospher RP-18 (5 μm) packing and a LiChrocart 125-4 HPLC column cartridge; solvent A; acetonitrile; solvent B, water with 0.25% dicyclohexyl-amonium phosphate; flow rate 2 ml/min; temperature 40 °C; injection volume 5 μl; samples were analysed using a diode array detector. The following gradient programme was used:

	Minutes	% A	%B
	0	30	70
	5	50	50
	6	40	60
	7	30	70
Stop time	7		

Retention times (t_R) are in minutes.

Mass spectra were recorded with a Micromass Instruments LCT orthogonal time-of-flight mass spectrometer fitted with a Z-Spray electrospray ion source operating in negative mode at 3 Kv needle potential. Nitrogen was used as a drying and sheath gas. Data was stored in the continuum mode on a Micromass Instruments MassLynx data station utilizing Version 3.5 software pack. Infusion was at a rate of 20 μl/min with a Harvard Instruments syringe pump utilized for sample introduction.

Infrared spectra were recorded using a Nicolet Magna FT-IR Spectrophotometer 750. Ultraviolet spectra were taken with a Camspec M350 Double Beam UV–Visible Spectrophotometer.

2.1. Phosphate buffer

Mixed phosphate buffer comprised potassium dihydrogen phosphate (two parts) and disodium hydrogen phosphate (one part).

*2.1.1. 6-Chloro-4-p-sulphoanilino-1,3,5-triazin-2(1H)-one (**VIII**)*

Cyanuric chloride (9.32 g; 99%; 0.05 m) was dissolved in acetone (100 ml) and drowned in ice water (250 ml) to give a white suspension. Sulphanilic acid (8.65 g; 0.05 m) was suspended in water (50 ml) and sodium hydroxide solution (2 M) added to give pH 4.8. This solution was added dropwise with stirring, at −5 to 0 °C, to the suspension of cyanuric chloride, while keeping the pH at 3.5–5.5. After 1 h, a negative Ehrlich's test was given and HPLC showed a single band at t_R 1.61. Salt (15% w/v) was added to the reaction mixture and the solid filtered off. The white solid was added to water (250 ml) and sodium bicarbonate (10 g) added to give a pH of 8.4. The reaction mixture was stirred at room temperature for 5 days then at 40 °C for a further 5 days. The pH was adjusted to 6.5 with concentrated hydrochloric acid to give a white precipitate which was isolated by filtration, washed with ice cold water (30 mls) and dried in an electric oven at 88 °C to give the product (12.2 g). A small portion was recrystallised from water. HPLC showed a single band at t_R 0.66 and mass spectral analysis showed ions at m/z 301$(M-H)^-$ (100), 283 $(M-H-H_2O)^-$ (24), 201 (40) and 199 (44). ν_{max} (KBr)/cm^{-1} 3458, 1695, 1653, and 708. Found: C, 29.6; H, 1.9; N, 15.4; Cl, 9.4. $C_9H_5N_4O_4$

SCl.Na_2.H_2O requires C, 29.6; H, 1.9; N, 15.4; Cl, 9.7%.

2.1.2. 6-Anilino-4-p-sulphoanilino-1,3,5-triazin-2(1H)-one (**IX**)

6-Chloro-4-*p*-sulphoanilino-1,3,5-triazin-2(1H)-one (1 g; approx. 50% strength) was added to water (100 ml) and the suspension stirred for 1 h to give a clear solution. The solution was cooled to 10 °C and aniline (0.12 g) added. Hydrochloric acid (2 M) was added to give a pH of 3.8 and the reaction continued for 0.5 h. HPLC showed essentially 100% conversion to a new produce, t_R 0.79. Potassium chloride (10% w/v) was added and the reaction allowed to stand for 4 days. The solid which formed was filtered off (0.64 g). HPLC showed a single band at t_R 0.79 and a mass spectral analysis showed a molecular ion at *m*/*z* 358 $(M-H)^-$ (100).

2.1.3. 6-N-Methylanilino-4-p-sulphoanilino-1,3,5-triazin-2(1H)-one (X)

To 6-chloro-4-*p*-sulphoanilino-1,3,5-triazin-2(1H)-one (2.1 g; approx. 50% strength) was added boiling water (100 mls) to give a clear solution. The solution was cooled to 50 °C, *N*-methylaniline (1 g) added and the pH adjusted to 4.5 with 2 M hydrochloric acid. The reaction mixture was stirred at 40–50 °C for 2 h to give a white precipitate then cooled to 20 °C. The pH was raised to 11.5 with 2 M sodium hydroxide, the resultant solution screened and then the pH lowered to 2.5 to give a white precipitate. The pH was finally raised to 4.5, the white solid isolated by filtration and oven dried to give the produce (1.1 g). HPLC showed a single peak at t_R 0.70 and mass spectral analysis gave ions at *m*/*z* 372 $(M-H)^-$ (100) and 745 $(2M-H)^-$ (36). ν_{max} (KBr)/cm^{-1} 3450, 1766, 842, 768, 712, and 635. Found: C, 48.2; H, 3.9; N, 17.7; S, 8.4. $C_{16}H_{14}N_5O_4SNa$ requires C, 48.6; H, 3.6; N, 17.7; S, 8.1%.

2.1.4. 6-(p-β-Sulphatoethylsulphonyl)-anilino-4-p-sulphoanilino-1,3,5-triazin-2(1H)-one (**XI**)

6-Chloro-4-*p*-sulphoanilino-1,3,5-triazin-2(1H)-one (1.6 g; approx. 50% strength) was added to water (100 ml) and *p*-aminobenzene-β-sulphatoethylsulphone (0.82 g; 95.5%). The reaction mixture was stirred at room temperature and the pH adjusted to 3.5 with sodium bicarbonate solution (M). The pH fell rapidly and was maintained at 3–3.5 with sodium bicarbonate solution. After 2 h the reaction was essentially complete and the pH was raised to 4.9 (sodium bicarbonate). Salting with potassium chloride (13% w/v) gave a white solid which was isolated by filtration and oven dried at 50 °C to give the produce (1.3 g). HPLC showed the product to be 97% pure, with t_R 0.97, and mass spectral analysis gave ions at *m*/*z* 546 $(M-H)^-$ (88), 466 $(M-H-SO_3)^-$ (100) and 448 $(M-H-H_2SO_4)^-$ (78).

2.1.5. 6-Hydroxy-4-p-sulphoanilino-1,3,5-triazin-2(1H)-one (**XII**)

6-Chloro-4-*p*-sulphoanilino-1,3,5-triazin-2(1H)-one (1.6 g; approx. 50% strength) was stirred in water (100 ml) at 20 °C and hydrochloric acid (2 M) added to give pH 2. The reaction was continued for 40 h, the pH fell to 1.06 and a white precipitate was formed. The solid was collected by filtration, washed with a little water and oven dried at 70 °C to give the produce (0.87 g). Recrystallisation from water gave a white solid. HPLC showed one band at t_R 0.64 and mass spectral analysis showed ions at *m*/*z* 283 $(M-H)^-$ (100) and 240 (15). A dimer ion was observed at 567 $(2M-H)^-$ (30). ν_{max} (KBr)/cm^{-1} 3468, 3380, 3311, 2805, 1735, 837, 779, 716, and 601. Found: C, 33.1; H, 2.1; N, 17.4; S, 9.8. $C_9H_7N_4O_5SNa$.H_2O requires C, 33.3; H, 2.8; N, 17.3; S, 9.9%.

2.1.6. 6-Pyridinium-4-p-sulphoanilino-1,3,5-triazine-2-oxide (**XIII**)

6-Chloro-4-*p*-sulphoanilino-1,3,5-triazin-2(1H)-one (2 g; approx. 95% strength) was dissolved in water (80 ml) and pyridine (20 ml) added. The pH was adjusted to 5.0 with 2 M hydrochloric acid and the resultant solution heated to 40–44 °C, with stirring, for 5 h, while keeping the pH at 4.5–5.0 with 2 M sodium carbonate solution. A yellow colour developed after a few minutes. When the reaction was complete (HPLC) the pH was raised to 5.4, sodium chloride (20% w/v) added, and the solution allowed to stand for 24 h. The pale yellow solid which separated was filtered off, washed with 20% brine and oven dried at 90 °C to give a solid

(0.24 g). HPLC showed this material to be impure. The volume of the filtrates was reduced to 50 mls on a rotary evaporator and the resultant solution allowed to stand for 24 h. A second crop (0.1 g) was also impure. The filtrates were allowed to stand for a further 3 days to give a yellow precipitate which was filtered off, washed with acetone and oven dried to give the product as a pale yellow solid (1.51 g). HPLC showed a single band at t_R 0.54, and mass spectral analysis gave a molecular ion at *m*/*z* 344 $(M-H)^-$ (100). λ_{max} 269 nm ($3.8*10^4$) and 311 nm, inflection (ε $3.5*10^3$) ν_{max} (KBr)/cm^{-1} 3440, 1720 (w), and 1652 Found: C, 46.6; H, 3.0; N, 19.1; S, 8.5. $C_{14}H_{10}N_5O_4SNa$, requires C, 45.8; H, 2.7; N, 19.1; S, 8.7%.

Attempted recrystallisation from water gave an off-white solid which was shown by HPLC and mass spectral analysis to be 6-hydroxy-4-*p*-sulphoanilino-1,3,5-triazin-2(1H)-one (**XII**), *m*/*z* 283 $(M-H)^-$ (100).

2.1.7. 6-(3-Carboxy)-pyridinium-4-p-sulphoanilino-1,3,5-triazine-2-oxide (XIV)

6-Chloro-4-*p*-sulphoanilino-1,3,5-triazin-2(1H)-one (1.6 g; approx 50% strength) was slurried in water (100 ml) to give a translucent solution which was filtered through a bed of filter aid to give a clear solution, pH 5.4, temperature 21 °C. Nicotinic acid (0.5 g) was added with stirring, to give a pH of 4.5, then hydrochloric acid (2 M) to pH 3.5. A pale yellow colour developed and after a few minutes the pH fell to 3.11. The pH was maintained at 3–3.5 and the reaction continued for 2.5 h. HPLC indicated approximately 90% of the starting material had reacted. Sodium bicarbonate solution was added dropwise to give pH 5.9 which resulted in a gelatinous yellow precipitate being produced. Salt (20% w/v) was added, the reaction mixture stirred for 0.5 h, then allowed to stand for 2 days. A pale yellow precipitate resulted which was filtered off, washed with 20% brine, dried in an electric oven at 70 °C to give the product as a pale yellow solid (1.49 g). A small portion was lixiviated in deionised water, filtered, washed and oven dried at 90 °C. HPLC showed a single peak at t_R 0.58, and mass spectral analysis gave ions at *m*/*z*, 388 $(M-H)^-$ (22), 344 $(M-H-CO_2)$ (58), 283 (100) and 265 $(M-H-C_6H_5NO_2)^-$ (43); λ_{max} 270 nm ($3.0*10^4$) and 315 nm, inflection ($3.9*10^3$). ν_{max} (KBr)/cm^{-1} 3440, 2604, 1699, 1641, and 840. Found: C, 40.8; H, 3.1; N, 16.0; S, 7.1. $C_{15}H_9N_5O_6SNa_2.H_2O$, requires C, 39.9; H, 2.5; N, 15.5; S, 7.1%.

2.1.8. Reaction of 6-chloro-4-p-sulphoanilino-1,3,5-triazin-2(1H)-one with benzenesulphinic acid

6-Chloro-4-*p*-sulphoanilino-1,3,5-triazin-2(1H)-one (1.74 g; approx. 50% strength) was added to boiling water (100 ml) and the resultant solution cooled to 37 °C. Sodium benzenesulphinate (1 g) was added at pH 4.9. The pH rose to 5.2 then fell to 4.2 after 10 min. Sodium carbonate (2 M) was added dropwise to maintain a pH of 4.2–4.7 and after 30 min a white precipitate separated. After a reaction time of 1 h, the white solid was filtered off, washed with water and dried over calcium chloride in a vacuum desiccator to give the product (0.83 g). The solid was analysed by HPLC and mass spectrometry and found to be identical to an authentic sample of 6-hydroxy-4-*p*-sulphoanilino-1,3,5-triazin-2(1H)-one (**XII**).

2.1.9. Reaction of 6-chloro-4-p-sulphoanilino-1,3,5-triazin-2(1H)-one with mercaptoacetic acid

6-Chloro-4-*p*-sulphoanilino-1,3,5-triazin-2(1H)-one (2.0 g: approx. 50% strength) was added to hot water (100 ml) and stirred to dissolve. Mercaptoacetic acid (0.68 g) was added at 25 °C, the pH adjusted to 4.5 with 2 M sodium carbonate solution and the reaction mixture stirred for 2 h. HPLC showed no reaction had occurred. A further addition of mercaptoacetic acid (1.4 g) was made, the pH adjusted to 4.5 as before and the reaction mixture heated at 45 °C for a further 3 h. HPLC showed no reaction had occurred.

3. Discussion

Hydrolysis of the DCT precursor of model compound (**VIII**; Scheme 3) was conducted in water as solvent at pH 8.4 (see Experimental). Although taking several days to complete, a relatively pure product was furnished by this method. Reactions at higher pH values resulted in impurities being generated.

6-Chloro-1,3,5-triazin-2(1H)-ones are both tautomeric and amphoteric, i.e. they can exist in both a hydroxy and an oxo form, and have weakly acidic and weakly basic properties.

The chloro-1,3,5-triazin-2(1H)-one (**VIII**) was isolated at pH 6.5. Infrared spectroscopy (see Experimental) did not show a strong absorption band at 1700–1800 cm^{-1} region unlike that of the hydroxyl derivative (**XII**; ν_{max} 1735 cm^{-1}), and the *N*-methylanilino derivative (**X**; ν_{max} 1766 cm^{-1}) both of which were isolated at lower pH. Elemental analysis of the chloro derivative (**VIII**) confirmed that the compound was isolated predominantly as the disodium salt of the hydroxytriazine tautomer.

In alkaline medium the chlorine atom on the triazine ring is deactivated by the oxido group and in acidic medium the chlorine is activated by ring protonation (Scheme 4).

To study the chemical reactions of the CTO system, a series of nucleophilic compounds (Table 1) were reacted, in turn, with the model CTO compound (**VIII**) under acidic conditions.

Reaction products were analysed by HPLC and characterised by negative ion mass spectrometry (see Experimental) and the structures are shown in Scheme 5.

Table 1
Dissociation constants of acids, and conjugate acids of amines (water at 25 °C unless stated otherwise)

Nucleophilic compound	pK_{BH+}	pK_a
Aniline [7]	4.6	
N-Methylaniline [7]	4.7	
p-Aminobenzene-β-sulphato-ethylsulphone[a]	1.46[b]	
Pyridine [7]	5.2	
3-Carboxypyridine [7]	4.76	
Benzenesulphinic acid [8]		1.29[c]
Mercaptoacetic acid [8]		3.68, 10.55

[a] Analogous to *p*-methylsulphonylaniline [7].

[b] Measured at 30 °C.

[c] Measured at 20 °C.

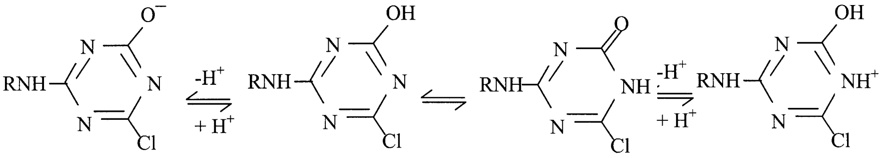
All of the benzenoid amines in Table 1, i.e. aniline, *N*-methylaniline and *p*-aminobenzene-β-sulphatoethylsulphone reacted cleanly and easily with the model triazine-2(1H)-one (**VIII**) to give the expected products (**IX**, **X** and **XI**). Product (**XI**), unlike the parent compound is now fibre reactive in alkaline medium by virtue of the presence of a β-sulphatoethylsulphonyl group. Moreover, a reactive dye utilising this chemistry would enjoy the benefits of a substantivity conferring triazinyl group while offering an AOX free system.

Reaction of the parent CTO compound (**VIII**), in turn, with pyridine and 3-carboxypyridine (nicotinic acid) gave the novel zwitterionic triazinyl compounds (**XIII**) and (**XIV**), as pale yellow solids. Compound (**XIII**) contains one sulphonic acid group and elemental analysis indicates the presence of one sodium cation. Accordingly, compound (**XIII**) is assigned the betaine structure shown. However, the charges are too far apart to provide counterions for each other within a single molecule and charge pairing must involve at least two molecules.

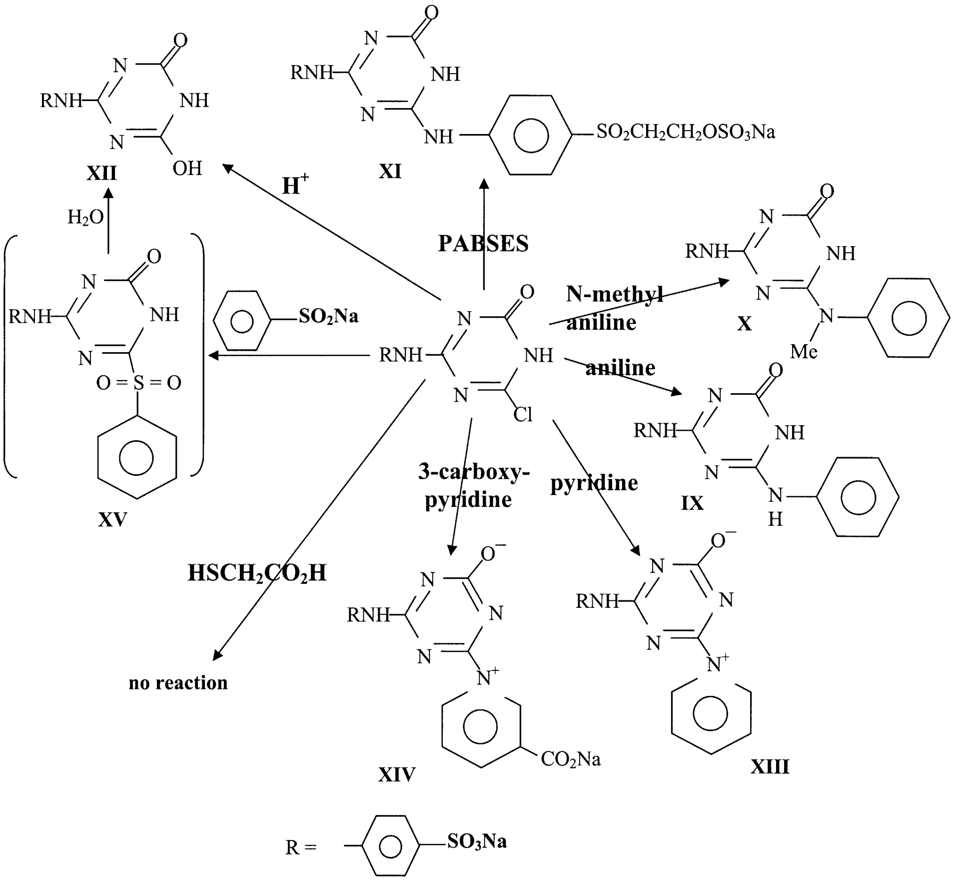
Compound (**XIV**) shows a similar electronic spectrum to that of compound (**XIII**), and is also assigned a betaine structure.

The reactions with pyridine and nicotinic acid were straightforward, but the latter reaction was the faster due to the greater concentration of free base (nicotinic acid pK_a 4.76) under the acidic reaction conditions employed. Preliminary studies have shown that the new triazinyl compounds (**XIII**) and (**XIV**) react with cellulose fibres under alkaline conditions, and dyes based on the nicotinic acid species will be the subject of a future publication.

Two sulphur nucleophiles, mercaptoacetic acid and sodium benzenesulphinate, were also reacted, in turn, with compound (**VIII**) in acidic medium. The absence of significant thiolate ions in the former



Scheme 4.



Scheme 5.

reaction (pK_a 10.55) resulted in starting materials being recovered unchanged. In the latter reaction rapid replacement of the chlorine atom took place. However, the benzenesulphonyl derivative (**XV**) proved unstable under the reaction conditions and the reaction yielded the 6-hydroxy-1,3,5-triazin-2(1H)-one derivative (**XII**). This compound was independently synthesised by treatment of compound (**VIII**) with dilute hydrochloric acid.

4. Conclusion

A model 6-chloro-4-arylamino-1,3,5-triazin-2(1H)-one was reacted with a variety of nitrogen, oxygen and sulphur nucleophiles in acidic medium. Reaction with nicotinic acid and with *p*-aminobenzene-β-sulphatoethylsulphone furnished fibre reactive species, which unlike the starting compound were able to be fixed to cellulosic substrates under alkaline conditions.

Acknowledgements

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