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DERIVATIVES OF 1,3,5-TRIAZINE—I*

CONDENSATION OF *o*-HYDROXYBENZANILIDES WITH CYANURIC CHLORIDE AND FISSION OF THE TRIAZINE RING

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Abstract—The condensation of cyanuric chloride with *o*-hydroxybenzanilides takes place on the amide nitrogen. Treatment of the condensation products with acetic anhydride and pyridine opens the triazine ring and yields benzoxazine derivatives, whose structures are discussed.

Dyes containing the 1,3,5-triazine nucleus, prepared by suitable condensations with cyanuric chloride, have been the subject of numerous patents.[1,2] Fierz-David and Matter[3] were the first to study the preparation of dyes of this type, and there is no reference in the literature to any later investigation of the constitution of cyanurated dyes. The main function of the triazine ring was to act as a chromophoric insulator, enabling the combination of azo or other dye units to form more complex dyes, and for this purpose cyanuric chloride had several advantages over phosgene. Very recently chromogens attached to cyanuric chloride, leaving one or two chlorine atoms free for direct chemical combination with cellulose, have been marketed as "reactive dyes" (Procions, I.C.I., Cibacrons, Ciba), constituting a landmark in the history of synthetic dyes.

Some years ago one of us prepared azoic coupling components by condensing 1, 2 or 3 molecules of the *m*- or *p*-aminoanilide (I; R or R^1 = NH_2; R^1 or R = H) of 2-hydroxy-3-naphthoic acid with one molecule of cyanuric chloride, but the shades produced on cotton by coupling with diazonium salts were of no practical interest, although some of the "naphthols" (e.g. II) had excellent affinity for the fibre.[4]

In connection with this work it was subsequently observed that 2-hydroxy-3-naphthanilide (Naphtol AS) itself condensed with cyanuric chloride in presence of ethanolic sodium hydroxide. The reaction takes place on the NH and not the OH group, and the product, colourless needles, m.p. 182°, has the structure III, as shown by its alkali solubility and ability to couple with diazonium salts. It can be dissolved in 1 per cent sodium hydroxide solution at 0° and recovered unchanged after a few minutes by acidification. Salicylanilide similarly yielded IV. Although the products III and IV are soluble in aqueous sodium hydroxide, they do not give a ferric coloration, unlike 2-hydroxy-3-naphthanilide and salicylanilide. The infra-red spectra of III and IV show a hydroxyl band around 3350 cm^{-1}, a carbonyl band around 1670 cm^{-1}, and strong absorption bands in the 1505, 1260 and 850 cm^{-1} regions which

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[*] Communication No. 410 from the National Chemical Laboratory Poona, India.

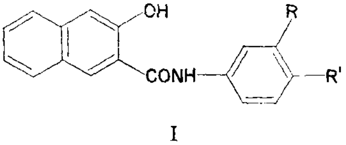
[1] K. Venkataraman, *The Chemistry of Synthetic Dyes* Vol. I, p. 583; Vol. II, pp. 864, 891. Academic Press, New York (1952).

[2] E. M. Smolin, and L. Rapoport, *s-Triazines and Derivatives*. Interscience, New York (1959).

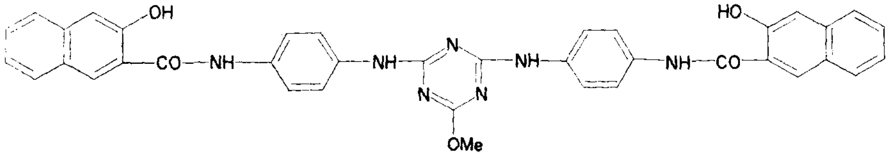
[3] H. Fierz-David and M. Matter, *J. Soc. Dyers Colourists* 53, 424 (1937).

[4] R. V. Talavdekar, Ph.D. Thesis, Univ. of Bombay (1951).

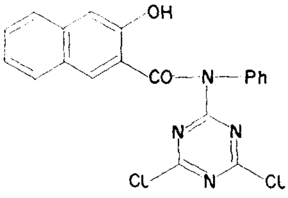
are characteristic of cyanuric chloride.[2] 2-Hydroxy-3-naphthanilide and salicylanilide show no hydroxyl band; in the carbonyl region an absorption band at 1612 cm^{-1} indicates strong chelation. Benzanilide did not react with cyanuric chloride; and in *p*-hydroxybenzanilide (conveniently prepared by refluxing *p*-hydroxybenzoic acid in toluene with phenyl phosphazoanilide)[5] the phenolic hydroxyl reacted to form the alkali-insoluble product V. The azoic alkali-insoluble pigment obtained by coupling 2-hydroxy-3-naphthanilide with diazotized aniline failed to react with cyanuric chloride, showing the need for a hydroxyl group capable of ready interaction with a base, the mechanism of which is discussed in the following paper.



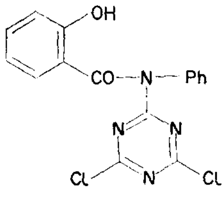
I



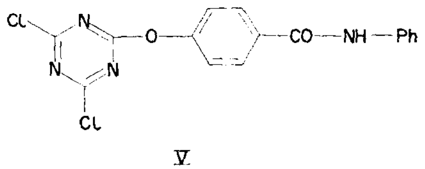
II



III



IV



V

Boiling acetic anhydride left III and IV unaffected, but in presence of a few drops of pyridine they led to crystalline compounds which were free from chlorine and were obviously not the simple O-acetyl derivatives. Two products were obtained in each case: one on cooling the acetic anhydride solution and the other on dilution of the mother-liquor. The products A, m.p. 288°, and B, m.p. 304°, from III analysed respectively for $C_{20}H_{14}N_2O_3$ and $C_{18}H_{11}NO_3$. Similarly IV gave compounds C, m.p. 243°, and D, m.p. 242°, analysing respectively for $C_{16}H_{12}N_2O_3$ and $C_{14}H_9NO_3$. The formulae of A and C corresponded to structures VI and VII, but the infra-red

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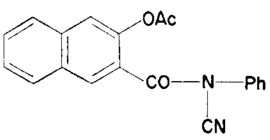
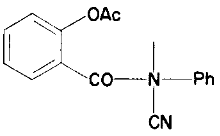
[5] H. W. Grimmel, A. Guenther and J. F. Morgan, *J. Amer. Chem. Soc.* **68**, 539 (1946).

spectra did not show the characteristic —C≡N stretching vibration in the 2220 cm^{-1} region. The condensation of acetylsalicyl chloride with phenylcyanamide in pyridine solution gave a product with the authentic structure VII, m.p. 141°; the infra-red spectrum had a band at 2230 cm^{-1} corresponding to the —C≡N stretching vibration. Compound C therefore did not have the structure VII.

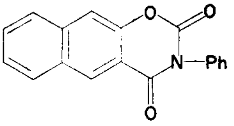


VI

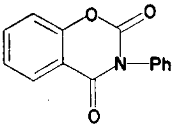


VII

When compound A was heated with 10 per cent sodium hydroxide solution, 2-hydroxy-3-naphthanilide was recovered, and A was converted to B by heating with 10 per cent hydrochloric acid or dissolving in conc sulphuric acid and pouring into water. Compound C behaved similarly, yielding salicylanilide by alkaline hydrolysis and compound D by treatment with sulphuric acid. Both B and D were insoluble in sodium hydroxide solution. The infra-red spectrum of B showed bands at 1764 cm^{-1} (lactone) and 1686 cm^{-1} (carbonyl absorption of tertiary amide). Compound D exhibited similar absorption bands at 1756 cm^{-1} and 1680 cm^{-1}. Neither B nor D showed a band due to a phenolic hydroxyl group in the 3350 cm^{-1} region. Structures VIII and IX were therefore assigned to B and D, and confirmed by an alternative synthesis using a known procedure.[6] 3,4-Dihydro-1,3,2-benzoxazine-2,4-dione (IX; phenyl replaced by hydrogen) was prepared by Einhorn and Mettler[6] by the condensation of salicylamide with ethyl chloroformate; IX was prepared earlier by Bogisch[7] by the same method, which we have now used for the synthesis of VIII. A homologue of IX has been described by Deck and Dains[8], who obtained it by heating phenyl salicylate with S-methyl-N,N-di-*o*-tolylisothiourea, followed by acid hydrolysis.



VIII



IX

From the molecular formulae and the ease of hydrolysis to VIII and IX it was then deduced that A and C were constituted as X and XI. The infra-red spectrum of A showed bands at 1721 and 1241 cm^{-1} (acetate), 1691 cm^{-1} (carbonyl of tertiary amide), 1656 cm^{-1} (broad band indicating C=N—); C showed similar infra-red bands at 1722 and 1220, 1708, 1657 cm^{-1}. The ultra-violet absorption spectra (in ethanol) of C showed maxima at 238 mμ (log ε 4·15) and 293 mμ (log ε 3·6); and D at 238 mμ (log ε 4·21) and 288 mμ (log ε 3·54).

The formation of compounds X and XI during the acetylation of III and IV

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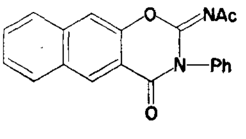
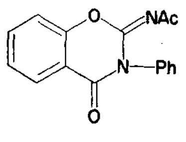
[6] A. Einhorn and C. Mettler, *Ber. Dtsch. Chem. Ges.* **35**, 3647 (1902).

[7] Bogisch, Dissertation, Rostock (1889). Cited in *Beilstein* **27**, 263.

[8] J. F. Deck and F. B. Dains, *J. Amer. Chem. Soc.* **55**, 4986 (1933).



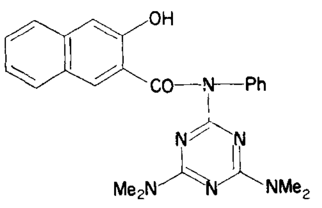
X



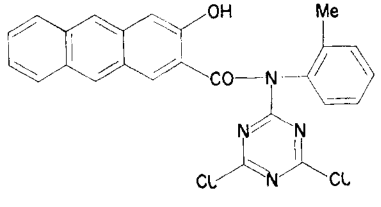
XI

provides an unusual example of the fission of the 1,3,5-triazine ring system,* apart from the parent compound which is very sensitive to hydrolysis.

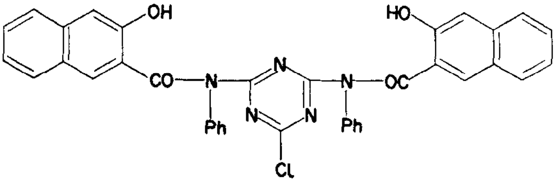
The two chlorine atoms in III were readily replaceable by dimethylamino groups, yielding XII which may be of some interest as an intermediate for basic dyes. Treatment of III with 1 per cent alcoholic sodium hydroxide at 50–55° for 3 hours resulted in smooth hydrolysis to 2-hydroxy-3-naphthoic acid in 87 per cent yield, accompanied by a small amount of III in which chlorine was replaced by hydroxyl. Alkaline hydrolysis of the N-acetyl[9] and N-benzoyl derivatives led to the parent Naphtol AS (I; R and $R^1 = H$), together with acetic or benzoic acid. The difference in the hydrolytic behaviour of the N-cyanuryl derivative on the one hand and the N-acetyl and N-benzoyl derivatives on the other is to be anticipated in view of the difference between cyanuric acid and carboxylic acids; in III therefore the carbonyl group is more readily attacked by hydroxyl ion than the triazine carbon attached to the amide nitrogen.



XII



XIII



XIV

The *o*-toluidide (Naphtol AS-GR; C.I. 37585) of 2-hydroxyanthracene-3-carboxylic acid condensed with cyanuric chloride, yielding XIII. Mild alkaline

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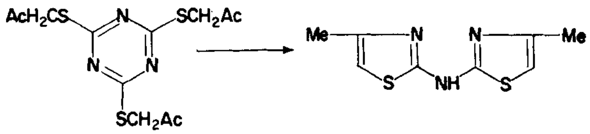
* One example in the literature is the degradation and rearrangement of 2,4,6-tri(acetonylthio)-s-triazine by the action of conc hydrochloric acid [A. Hantzsch, *Ber. Dtsch. Chem. Ges.* **61B**, 1776 (1928)].



[9] E. B. Higgins, *J. Soc. Dyers Colourists* **43**, 213 (1927).

hydrolysis of XIII gave in about 70 per cent yield 2-hydroxyanthracene-3-carboxylic acid, which is difficult to isolate when the arylamide is submitted to the usual drastic methods of hydrolysis with strong sodium hydroxide solution or conc sulphuric acid.[1]

The condensation of 2 moles of 2-hydroxy-3-naphthanilide with one of cyanuric chloride yielded XIV. Towards acetic anhydride and pyridine XIV behaved like the primary condensation product III and gave X.

EXPERIMENTAL

Condensation product (III) *of 2-hydroxy-3-naphthanilide with cyanuric chloride*

To a solution of cyanuric chloride (0·76 g) in acetone (10 ml) at 0–5° a solution of 2-hydroxy-3-naphthanilide (1·1 g) in acetone (20 ml) and 10% NaOH (1·7 ml) was added with stirring. After 1 hr ice-cold water (30 ml) was added and the mixture stirred for 15 min. The precipitate was filtered, washed, and dried *in vacuo* at room temp. It crystallized from benzene (Norit) in colourless needles, m.p. 182° (1·3 g). (Found: C, 58·6; H, 2·7; N, 14·0; Cl, 17·7. $C_{20}H_{12}Cl_2N_4O_2$ requires: C, 58·5; H, 2·9; N, 13·7; Cl, 17·3%).

Under similar conditions benzamide and benzanilide were recovered unchanged.

Hydrolysis of III

A solution of (III; 1 g) in 1% NaOH (100 ml containing 15 ml ethanol) was heated at 50–55° for 3 hr. The solution was filtered and saturated with carbon dioxide. The precipitate (0·2 g) crystallized from alcohol in colourless plates, m.p. 208–210°. (Found: N, 15·7. $C_{20}H_{14}N_4O_4$ requires: N, 15·0%). The filtrate was acidified and the precipitate (0·4 g) crystallized from dilute ethanol in yellow plates, m.p. 219–221°, alone or mixed with 2-hydroxy-3-naphthoic acid.

Condensation product (IV) *of salicylanilide with cyanuric chloride*

To a solution of cyanuric chloride (1 g) in acetone (5 ml) a solution of salicylanilide (1·1 g) in acetone (5 ml) and 10% NaOH (2·2 ml) was added and stirred at 0–5° for 1 hr. On the addition of ice-water a semi-solid mass separated and stuck to the sides of the flask. The aqueous solution was decanted off, and the residue dissolved in benzene (100 ml). The solution was dried over anhydrous calcium chloride, filtered and concentrated, and hexane added till a slight turbidity developed. On cooling, the crystalline product (0·8 g) was recrystallized from benzene–hexane. The colourless needles had m.p. 152°. (Found: C, 53·5; H, 2·9; Cl, 19·0; N, 15·0. $C_{16}H_{10}Cl_2N_4O_2$ requires: C, 53·2; H, 2·8; Cl, 19·7; N, 15·5%).

Condensation product (V) *from* p*-hydroxybenzanilide and cyanuric chloride*

The anilide (0·62 g) and cyanuric chloride (0·55 g) were dissolved in acetone (20 ml) and treated with 10% NaOH (1·2 ml) at 0–5° for 2 hr. Worked up as above the product (0·96 g) crystallized from acetone in broken plates, m.p. 228°. (Found: C, 53·5; H, 2·8; N, 15·7. $C_{16}H_{10}Cl_2N_4O_2$ requires: C, 53·2; H, 2·8; N, 15·5%).

2-*Acetimino-3-phenyl-4-keto-3,4-dihydro-1,3,2-β-naphthoxazine* (X)

A mixture of (III; 6 g) acetic anhydride (60 ml) and a few drops of pyridine was refluxed for 3 hr and cooled. The brown crystalline product (A) was filtered, washed and dried (2·3 g). Dilution of the filtrate with water and cooling in a refrigerator gave B (0·2 g). Crystallization of A from toluene gave colourless needles, m.p. 288°. (Found: C, 72·8; H, 4·3; N, 8·6. $C_{20}H_{14}N_2O_3$ requires: C, 72·7; H, 4·2; N, 8·5%). Crystallization of B from toluene gave colourless needles, m.p. 304° after shrinking at 268°. (Found: C, 74·4; H, 3·6; N, 4·6. $C_{18}H_{11}NO_3$ requires: C, 74·7; H, 3·8; N, 4·8%).

2-*Acetimino-3-phenyl-4-keto-3,4-dihydro-1,3,2-benzoxazine* (XI)

On refluxing (IV; 2 g) for 2 hr with acetic anhydride (20 ml) and pyridine (0·1 ml) and cooling, the product (C) was collected (0·75 g). Dilution of the filtrate with water yielded D (0·09 g). Crystallization of C from toluene gave colourless needles, m.p. 243°. (Found: C, 69·1; H, 4·3; N, 10·3.

$C_{16}H_{12}N_2O_3$ requires: C, 68·6; H, 4·3; N, 10·0%). Crystallization of D from ethanol gave colourless needles, m.p. 242°. (Found: C, 70·4; H, 4·1; N, 6·2. $C_{14}H_9NO_3$ requires: C, 70·3; H, 3·8; N, 5·9%).

O-*Acetyl*-N-*cyanosalicylanilide* (VII)

A solution of acetylsalicyl chloride (0·5 g) and phenylcyanamide (0·5 g) in pyridine (5 ml) was shaken for 1 hr at 25°. Dilution with water (100 ml) and acidification with HCl gave a product (0·25 g), which crystallized from benzene–hexane in colourless cubes, m.p. 141°. (Found: C, 69·1; H, 4·0; N, 10·0. $C_{16}H_{12}N_2O_3$ requires: C, 68·6; H, 4·3; N, 10·0%).

Alkaline hydrolysis of X

A mixture of X (0·2 g), ethanol (5 ml) and 10% NaOH (20 ml) was heated on a water-bath for 2 hr and filtered. A small amount of undissolved material (0·02 g) was identified as unchanged X. Acidification of the filtrate and crystallization of the precipitate from ethanol gave 2-hydroxy-3-naphthanilide, m.p. 245°.

Acid hydrolysis of X

(a) A solution of X (0·2 g) in conc sulphuric acid (4 ml) was kept at 25° for 30 min and then poured on ice. The precipitate crystallized from toluene in colourless needles (0·17 g), m.p. 304° (after shrinking at 265°). This was identical in its m.p. and infra-red spectrum with the by-product (VIII) obtained in the acetylation of III.

(b) On heating X (0·1 g) at 98° for 1 hr with 10% HCl (20 ml) and ethanol (5 ml), the product (0·07 g) crystallized from benzene in colourless needles, m.p. 304° (after shrinking at 265°).

Acid hydrolysis of XI

Treatment of XI (0·4 g) with conc sulphuric acid (10 ml) and dilution as above gave IX, crystallizing from ethanol in colourless needles (0·2 g), m.p. 242°, identical with IX.

3-*Phenyl*-3,4-*dihydro*-1,3,2-*benzoxazine*-2,4-*dione* (IX)

A solution of salicylanilide (2·4 g) in pyridine (15 ml) and ethyl chloroformate (1 ml) was stirred at 85° for 2 hr. The pale brown precipitate (1·01 g) obtained by pouring into ice-water crystallized from ethanol in colourless needles, m.p. 242° (Bogisch,[7] m.p. 246° corr).

3-*Phenyl*-3,4-*dihydro*-1,3,2-β-*naphthoxazine*-2,4-*dione* (VIII)

2-Hydroxy-3-naphthanilide (1·4 g) was suspended in pyridine (25 ml) and heated with ethyl chloroformate (1 ml) for 3 hr at 80–85° with agitation. The precipitate obtained by pouring on ice was collected, shaken with ethanol (20 ml), 10% NaOH (5 ml) and diluted with water (50 ml). This gave a precipitate (0·56 g), which crystallized from toluene in colourless needles, m.p. 304° after shrinking at 265°. From the alcoholic alkaline filtrate unchanged 2-hydroxy-3-naphthanilide (0·8 g) was recovered.

N-*Benzoyl*-2-*hydroxy*-3-*naphthanilide*

Benzoylation of 2-hydroxy-3-naphthanilide was effected in alcoholic NaOH by benzoyl chloride at 0–5°, molar proportions being used and the mixture stirred until it was neutral to Brilliant Yellow. The product crystallized from benzene (in which 2-hydroxy-3-naphthanilide is insoluble) in colourless needles, m.p. 189–190°. (Found: N, 4·2. $C_{24}H_{17}O_3N$ requires: N, 3·8%).

Hydrolysis of N-*benzoyl*-2-*hydroxy*-3-*naphthanilide*

The compound (0·5 g) was heated with 10% NaOH (5 ml), water (40 ml) and alcohol (5 ml) for 3 hr at 50°. The solution was saturated with CO_2 and the precipitate (0·35 g) was identified as 2-hydroxy-3-naphthanilide.

Primary condensation product (XIII) *from the* o-*toluidide of* 2-*hydroxyanthracene*-3-*carboxylic acid and cyanuric chloride*

Prepared as in the case of III, the product crystallized from benzene in pale yellow needles, m.p. 210°. (Found: Cl, 14·7; N, 11·6. $C_{25}H_{16}O_2Cl_2N_4$ requires: Cl, 15·0; N, 11·8%).

Treatment of XIII (1·5 g) in alcohol (50 ml) and water (100 ml) with 10% NaOH (15 ml) at 50–55° for 3 hr, cooling, and saturating with CO_2 gave a minute amount of a precipitate which was rejected. Acidification of the filtrate gave a yellow precipitate, which crystallized from glacial acetic acid in orange-yellow plates (0·55 g), m.p. 293–294° (dec). (Found: C, 75·1; H, 3·9. Calc. for $C_{15}H_{10}O_3$: C, 75·6; H, 4·2%).

2,4-*Bis-dimethylamino*-6-N-2′-*hydroxy*-3′-*naphthoylanilino*-1,3,5-*triazine* (XII)

To a stirred solution of III (0·5 g) in dimethylformamide (50 ml) 30% aqueous dimethylamine (0·4 ml) and sodium carbonate (0·08 g) in water (10 ml) were added. After heating on a water-bath for 3 hr, the solution was poured into water (150 ml) and extracted with ether. Ether was removed and the residue crystallized from ethanol in colourless needles (0·21 g), m.p. 183°. (Found: C, 67·5; H, 5·8; N, 19·5. $C_{24}H_{24}O_2N_6$ requires: C, 67·3; H, 5·6; N, 19·6%).

Secondary condensation product (XIV) *from* 2-*hydroxy*-3-*naphthanilide and cyanuric chloride*

To a stirred solution of cyanuric chloride (0·38 g) in acetone (10 ml) at 0–5°, a solution of 2-hydroxy-3-naphthanilide (1·1 g) in ethanol (20 ml) and 10% NaOH (1·7 ml) was added. The solution was stirred at 0–5° for 1 hr and then at 45–50° for 1 hr. Water (40 ml) was added and the precipitate (1·22 g) crystallized from chlorobenzene. The colourless plates had m.p. 206°. (Found: C, 69·8; H, 4·1; Cl, 5·8; N, 10·6. $C_{37}H_{24}O_4ClN_5$ requires: C, 69·6; H, 3·8; Cl, 5·6; N, 11·0%). This compound on treatment with acetic anhydride and pyridine under the conditions described in the case of III yielded X.

Acknowledgements—We are indebted to the Council of Scientific and Industrial Research for a Junior Fellowship (to R. Srinivasan), to Imperial Chemical Industries, Limited (Dyestuffs Division) for a grant (to R. V. Talavdekar), to Dr. T. S. Gore and Mr. V. S. Pansare for the microanalyses, and to Mr. C. I. Jose for the infra-red spectra.