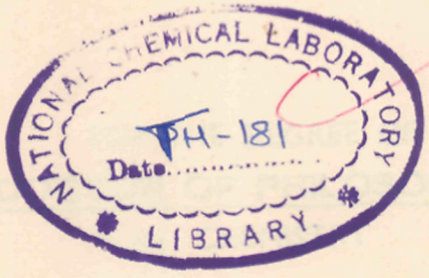

A STUDY OF SOME REACTIONS OF DYES AND DYE INTERMEDIATES USING NMR SPECTROSCOPY : SOME DERIVATIVES OF ANTHRAQUINONE AND s- TRIAZINE

A THESIS
SUBMITTED TO
KARNATAK UNIVERSITY, DHARWAR

FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY
IN CHEMISTRY

BY
R. J. DESHPANDE, M. Sc.

NATIONAL CHEMICAL LABORATORY
POONA
1974

Statement required to be submitted under Rule O-174 I of the Karnatak University, Dharwar.

No part of this thesis has been submitted for a degree or diploma or other academic award. The literature concerning the problems investigated has been surveyed, and all the necessary references are given in the thesis. The present work has been clearly indicated separately. The experimental work has been carried out entirely by me. In accordance with the usual practice, due acknowledgement has been made wherever the work presented is based on the results of other workers.

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R. J. Deshpande
Candidate.

POONA
January 1974.

(K. Venkataraman)
RESEARCH GUIDE.

CONTENTS

P A R T - I

THE ACTION OF ALLYL BROMIDE ON LEUCO ANTHRAQUINONES

***

INTRODUCTION

"The anthraquinonoid vat dyes remain the most important class of all dyes for cotton and other cellulosic fibers because of their outstanding all-round fastness".[1] Because of the sparing solubility of the anthraquinonoid vat dyes in organic solvents, purification by chromatographic methods and crystallization are difficult. The chromatographic separation of vat dyes has been carried out at high temperatures by Unni and Venkataraman,[2] but this did not solve the problem of making them amenable to NMR spectroscopy. Further, their volatility is inadequate for mass spectroscopy.

As long ago as 1928, a German patent[3] described the simultaneous reduction of quinones with zinc and alkali and methylation of the leuco derivatives with methyl-_p_-toluenesulphonate or dimethyl sulphate, but the reaction was not used as a method for isolating anthraquinonoid vat dyes in the pure state and for improving their solubility and volatility until Manjrekar[4] studied the NMR and mass spectra of the methyl ethers of the leuco compounds of violanthrone (dibenzanthrone), isoviolanthrone (isodibenzanthrone) and their derivatives.have The methyl ethers of the leuco derivatives have greatly increased solubility in solvents such as benzene and chlorobenzene, and are amenable to chromatography and crystallisation.

"The general procedure for obtaining the reductive methylation product was to reduce the vat dyes with aqueous sodium dithionite and sodium hydroxide at 60-70°, cool to room temperature and shake the solution vigorously with dimethyl sulphate (about 6 moles) for 30 minutes when the product separated".[4] An important property of the ethers of leuco derivatives is their ready conversion to the parent vat dyes by adding the solution in conc. sulphuric acid at 0° to ice.

The NMR spectra of the methyl ethers or acetates of the leuco compounds in tetramethylurea have been studied.[5,6] Although, the reductive methylation products of anthraquinonoid vat dyes are much more soluble in organic solvents than the parent quinones, many do not have adequate solubility for NMR spectroscopy. Manjrekar[4] prepared the benzyl and trityl ethers of anthrahydroquinone (9,10-dihydroxyanthracene) and found that these derivatives were much more soluble than the corresponding methyl ether, but the attempts to prepare benzyl and trityl ethers of 5,10-dihydroxyviolanthrene were unsuccessful.

PRESENT WORK

The present work was undertaken with a view to prepare a few allyl ethers of leuco anthraquinones and to study their solubility behaviour in various organic solvents for the determination of their NMR spectra. Allyl ethers are known to be more soluble in organic solvents than methyl ethers, and the protective group can be readily removed by mild acid treatment.

A suspension of anthraquinone in 10% aqueous sodium hydroxide was reduced with sodium dithionite, and the clear solution was allowed to react with excess allyl bromide (about 4 moles) at room temperature. The reaction was exothermic and instantaneous. A colourless crystalline product was obtained in above 90% yield. It was freely soluble in benzene, chloroform, carbon tetrachloride, methanol and ethanol. The product was also obtainable by using allyl chloride or p-toluene sulphonate; but it was not the expected diallyl ether (1) of anthrahydroquinone. The mass spectral molecular weight (M^+ 250) and elemental analysis did not agree with $C_{20}H_{18}O_2$, the molar formula of (1). The IR spectrum in carbon tetrachloride shows strong absorption bands at 1665 cm^{-1} (anthraquinone carbonyl) and 3400 cm^{-1} (OH). In conjunction with M^+ at 250 and the IR data, the NMR

spectrum (Fig.1) in CCl_4 indicated structure (2), 9-allyl-9-hydroxy-10-anthrone. In the NMR spectrum, a methylene doublet (J=7 Hz) seen at 7.51,* assigned to the allylic methylene. The terminal methylene on a double bond and the vinyl protons appear as a multiplet in the region between 4.8 to 5.81. A one proton singlet at 6.3 exchangeable with D_2O is assigned to the hydroxyl grouping. The aromatic protons are seen as a complex multiplet in the region between 2.0 to 2.89.

In the mass spectrum (Chart 1) of (2), the molecular ion is insignificant (0.1%). The ion (3) formed by allylic cleavage is the base peak. The base peak subsequently loses CHO and CO groups respectively to give radical ions at m/e 180 (2%) and m/e 152 (17%).

A literature search for (2) showed that it was prepared in 1910 by Kondo[7] in about 22% yield. He reduced anthraquinone in aqueous alkali with zinc dust and treated the boiling solution with excess of allyl bromide.

The reaction of allyl bromide on the di-anion of the anthrahydroquinone seems to be a Claisen type rearrangement. As soon as the monoallyl ether (4) is formed, it undergoes the same changes as the allyl ether of a 2,6-dialkylphenol. Claisen migration to an o-position is immediately followed by a Cope type rearrangement to (6), which picks up a proton to form the stable exanthrone

*Chemical shifts are cited on τ scale.

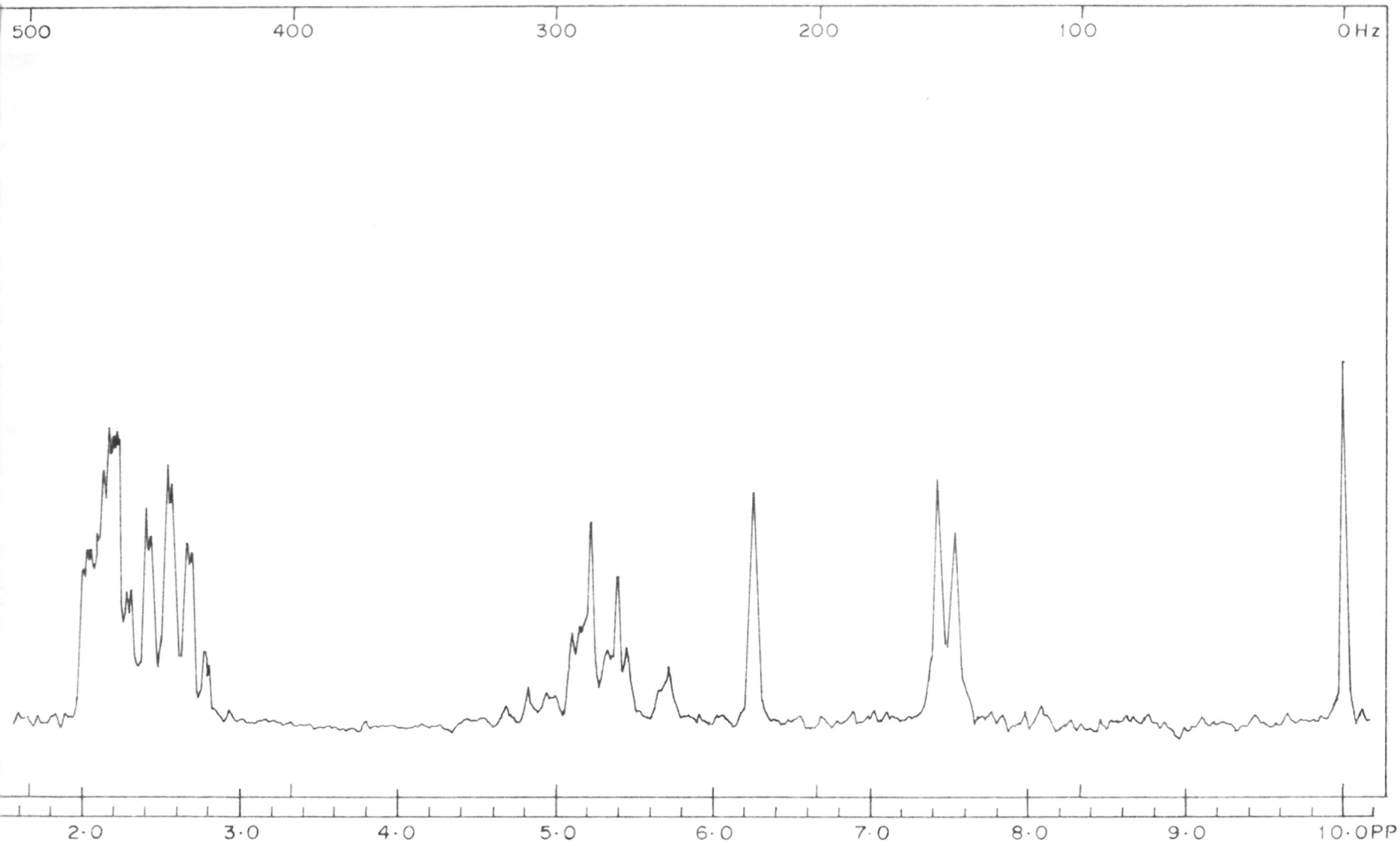
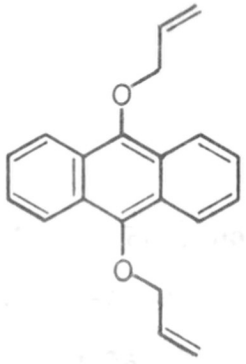
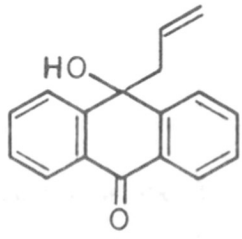


FIG. 1 NMR SPECTRUM OF 9-ALLYL-9-HYDROXY-10-ANTHRONE IN CCl_4

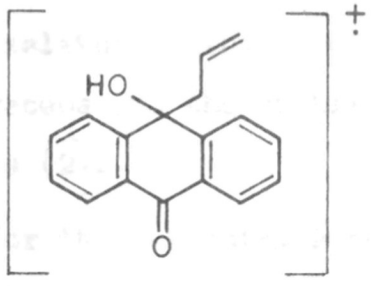


(1)

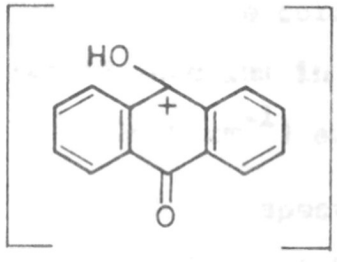


(2)

CHART 1



m/e 250 (0·1%)



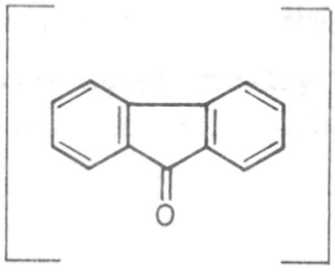
(3)

m/e 209 (100%)

$+ \quad H_2\overset{+}{C} - CH = CH_2$

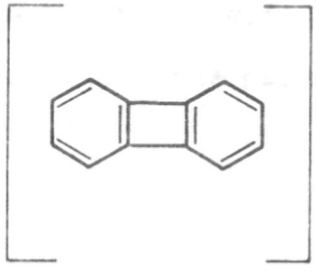
m/e 41 (2%)

$-\dot{C}HO$



m/e 180 (2%)

$-CO$

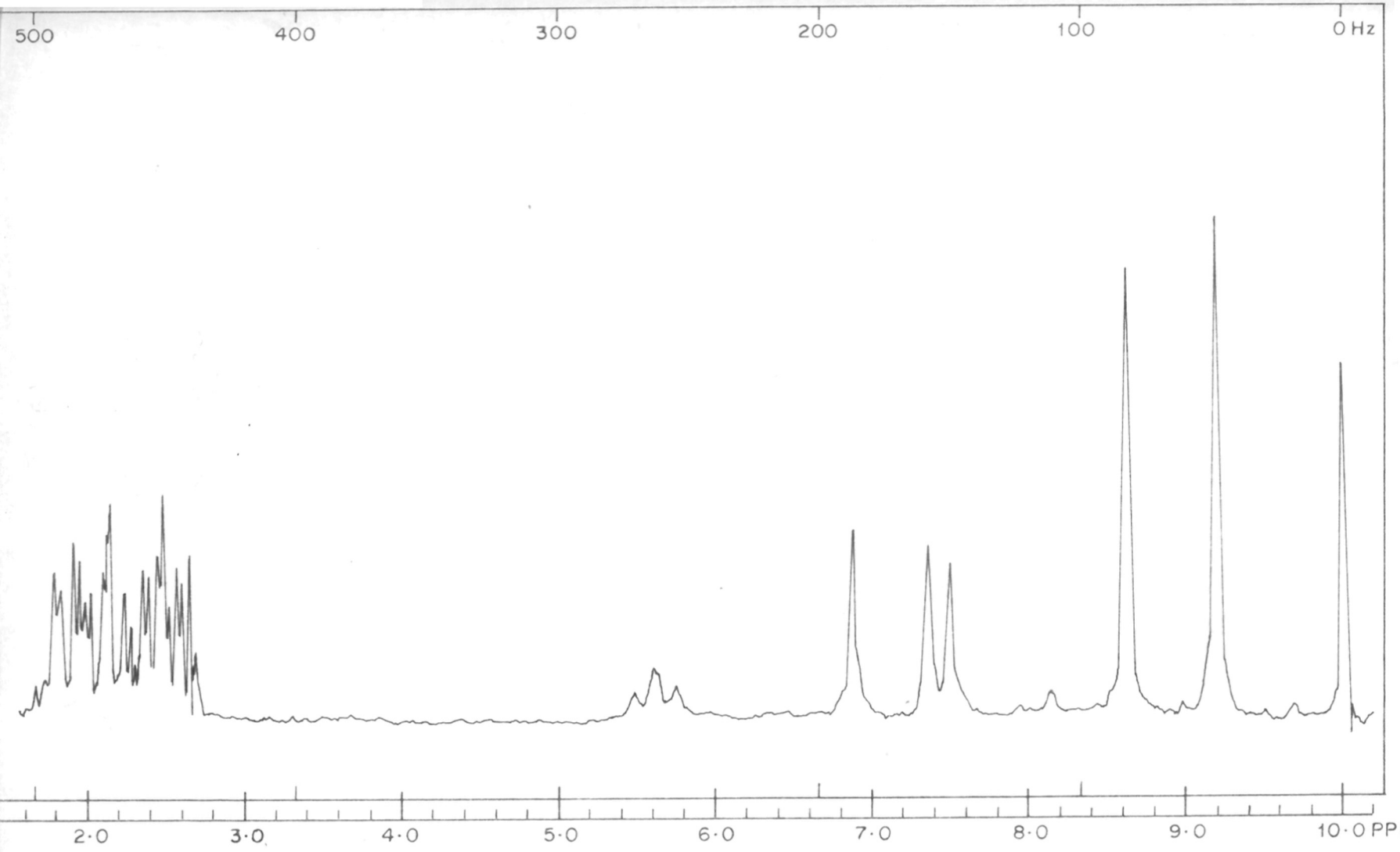


m/e 152 (17%)

derivative (2) (Chart 2). The Claisen change is effected thermally at temperatures of the order of 200°, although rearrangement in trifluoroacetic acid at room temperature has been reported.[8] The remarkably rapid C-allylation of anthrahydroquinone to the oxanthrone (2) at a temperature of 18-20° must be related to the reactivity of the meso-positions in anthracene and the stability of oxanthrone derivatives such as (2).

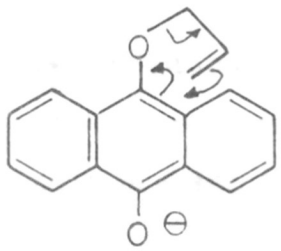
Support for the mechanism suggested in Chart 2 is found in the action of γ,γ-dimethylallyl bromide (isoprenyl bromide) on the dianion of anthrahydroquinone. Because of the double [3,3] sigmatropic shift, there is no end-group interchange and the product proved to be (7) and not (8). The colourless compound, $C_{19}H_{18}O_2$, showed in its IR spectrum in $CHCl_3$ characteristic absorptions for C=O (1665 cm^{-1}) and OH (3400 cm^{-1}) groups.

The NMR spectrum (Fig.2) of (7) shows two 3-proton singlets at 8.66 and 9.21 assigned to $=CMe_2$ of the prenyl side chain. One of the vinylic methyls is shifted to a higher τ value (9.21) when compared to the absorption position of the other (8.66). This can only be explained by assuming that one of the vinylic methyl groups is sterically held above or below the plane of the

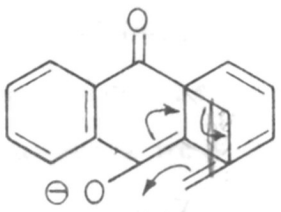


FIG·2 NMR SPECTRUM OF 9-$\mathcal{V},\mathcal{V}$-DIMETHYLALLYL-9-HYDROXY-10-ANTHRONE IN $CDCl_3$

CHART 2

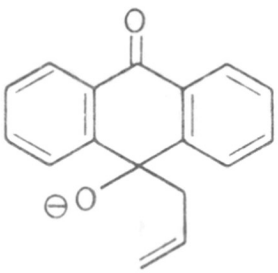


(4) II



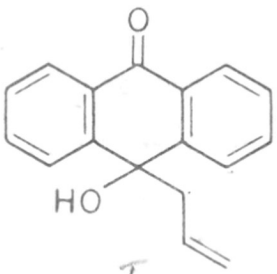
(5)

Benzite



(6) III

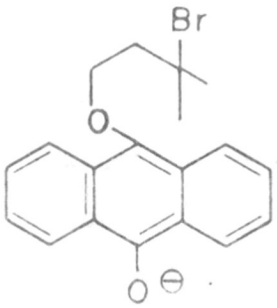
H^+

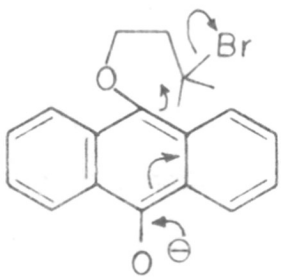


I
(7)

Block 1

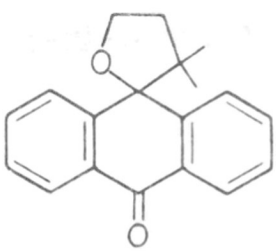
CHART 3





$-Br^{\ominus}$

In one line

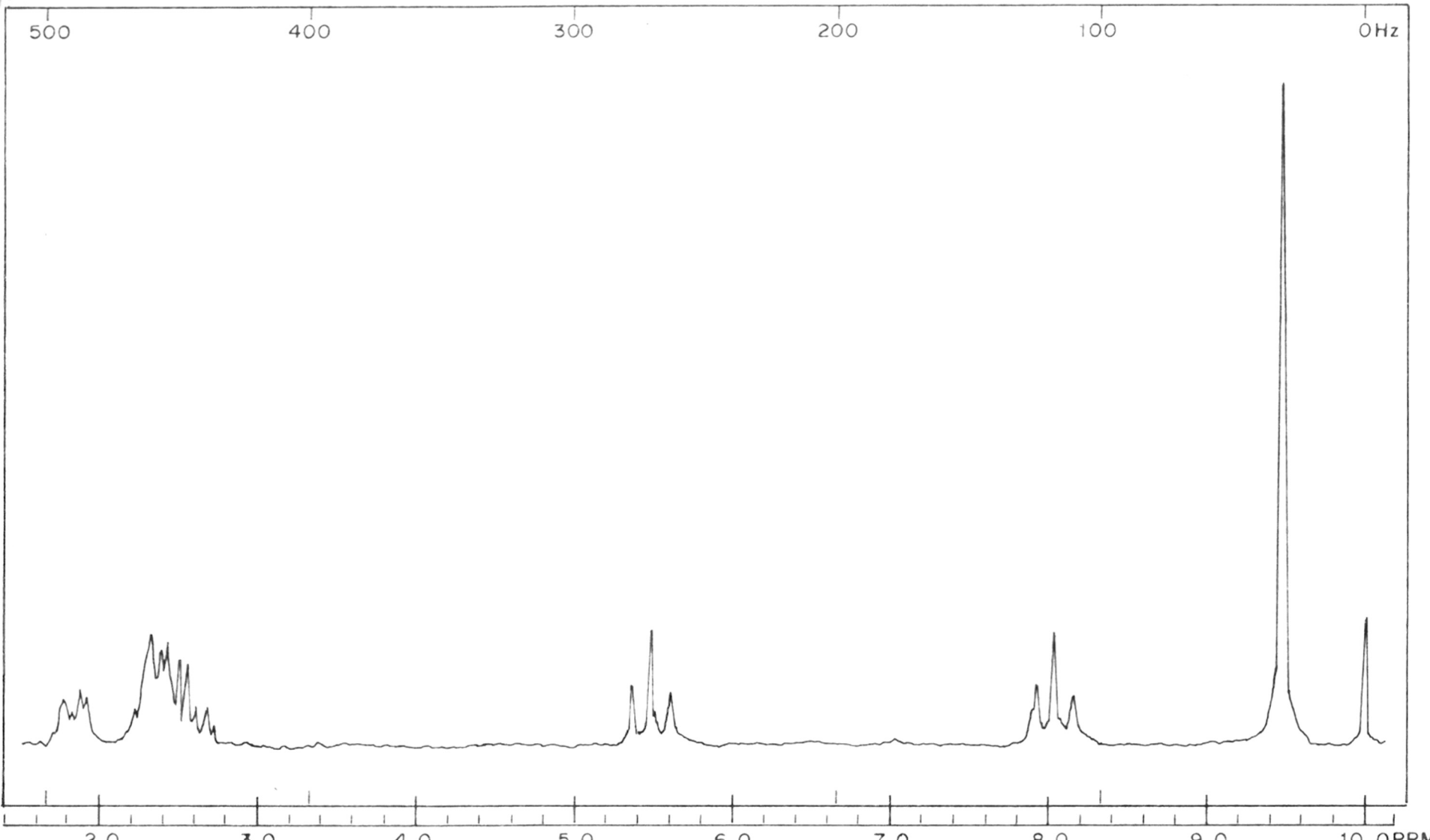


Block 3

(8) VI

benzene ring and thereby abnormally shielded because of the ring current effect. The allylic methylene, is seen as a doublet (J=8 Hz) at 7.47 while it appears at 7.51 in (2). A single-proton triplet (J=8 Hz), at 5.67 was assigned to the vinylic proton. The aromatic protons appear as a complex multiplet in the region between 1.74 to 2.78. The hydroxyl proton is seen at 6.92. Thus the compound undoubtedly is 9-(γ,γ-dimethylallyl)-9-hydroxy-10-anthrone (7) and not the 9-(α,α-dimethylallyl)-9-hydroxy-10-anthrone (8).

During the bromination of isoprene a by-product was 2,4-dibromo-2-methyl-n-butane, formed by the addition of 2 moles of hydrogen bromide. The reaction of this dibromide with leuco anthraquinone was slow, and the colourless product ($C_{19}H_{18}O_2$; M⁺ 278), formed by the mechanism in Chart 3, was shown by spectral evidence to have the structure (9); The IR spectrum in $CHCl_3$ has a carbonyl peak 1667 cm^{-1} and no OH absorption; The NMR spectrum (Fig. 3) in $CDCl_3$ shows a 6-proton singlet at τ 9.45 assigned to a gem-dimethyl group attached to a saturated carbon atom, two methylene triplets, (J=7 Hz) at 8.05 and 5.5 assigned to a methylene adjacent to a saturated carbon atom and the other to O-CH_2), 4-H and 5-H, being adjacent to a peri-carbonyl group are deshielded and



FIG·3 NMR SPECTRUM OF (9) IN $CDCl_3$

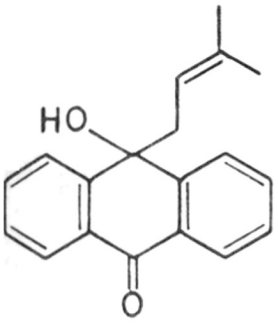
appear as a multiplet in the region between 1.76 to 2.0; the remaining aromatic protons are seen as a complex multiplet between 2.37 to 2.75.

(C) [In the mass spectra of (7) ~~and (9),~~ the molecular ion is not seen ~~in the former;~~ The peak at m/e 210, ~~is~~ obtained by the loss of ~~isoprenyl group in (7) with a~~ migration of a proton, ~~whereas~~ the initial loss of C_5H_9 from the molecular ion gives ~~ion (3) of Chart 1 in the mass spectrum of (9),~~ which then undergoes the ~~indicated~~ fragmentations.]

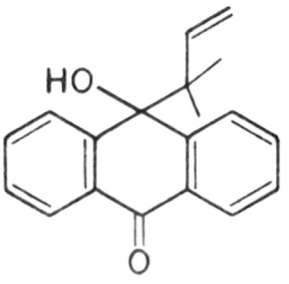
Kondo[7] tried unsuccessfully to synthesise benzanthrone (10), which is a commercially important dye intermediate, by the dehydrohalogenation of the dibromide of allyl oxanthrone (2). (D) [The action of sulphuric acid on (2) at room temperature or 90° gave a mixture of compounds from which no pure product was isolable; TLC gave no evidence of the formation of benzanthrone. The addition of copper led to a minute yield of benzanthrone. Negative results were also obtained by treating (2) with sulphuric and boric acids, an aluminium chloride-sodium chloride melt, and aluminium chloride.]

The action of hydrobromic acid in presence of benzoyl peroxide gave anthraquinone, also produced by treatment with neutral permanganate, lead tetraacetate, and

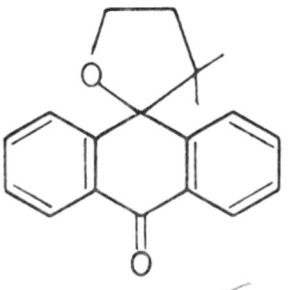
Block 2



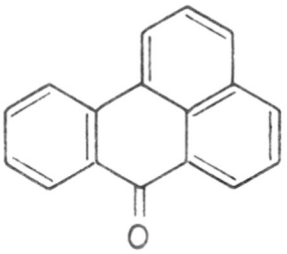
(7) IV



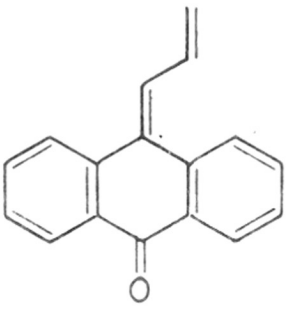
(8) V



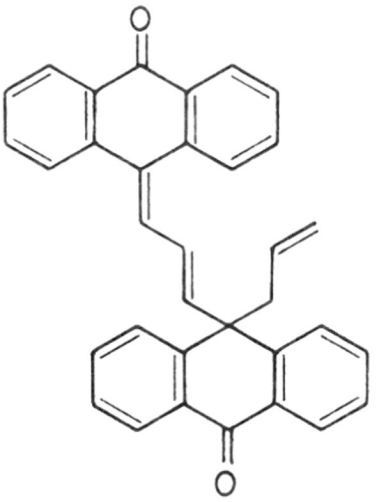
(9) VI



(10)

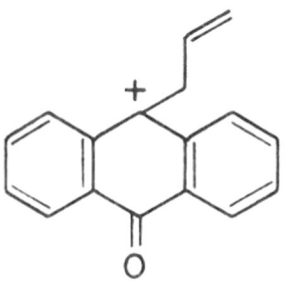


(11) VII

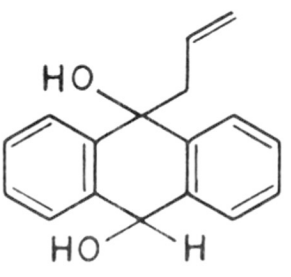


(12) VIII

Block 4



(13) IX



(14) X

potassium hydroxide in dimethylsulphoxide. Acetylation of (2) did not proceed with acetic anhydride in pyridine or in presence of perchloric acid; but with boiling acetic anhydride and fused sodium acetate gave 9-acetoxy-9-allyl-10-anthrone. The structure supported by its NMR spectrum in $CDCl_3$; allylic methylene doublet at 7.21; terminal methylene and vinylic protons multiplet in the region between 4.82 to 5.65; MeCO at 7.9 and aromatic protons as in (2). The IR spectrum in CCl_4 shows the absence of OH and the presence of an ester carbonyl at 1750 cm^{-1} in addition to the anthrone CO at 1670 cm^{-1}.

p-Toluenesulphonic acid had no action on (I) at room temperature, but dehydration was extremely rapid at 70°. After removing the solvent in presence of hydroquinone, two compounds (A) and (B) were isolated. Compound (A), m.p. 109-110°, $C_{17}H_{12}O$, has the structure (VII). The IR spectrum shows strong absorption at 1665 cm^{-1} and no hydroxyl absorption. In the mass spectrum, the base peak is M-1 (m/e 231), which loses CO and CHO to give m/e 203 (28%) and m/e 202 (40%). The NMR spectrum ~~(Fig. 4)~~ shows a 2-proton multiplet between 4.13 to 4.9 (terminal CH_2) and two vinylic CH protons as a complex multiplet between 2.99 to 3.22. The allylidene-anthrone (VII) was postulated as an intermediate in the Bally-Scholl mechanism for the formation of benzanthrone from anthrone via an aldol

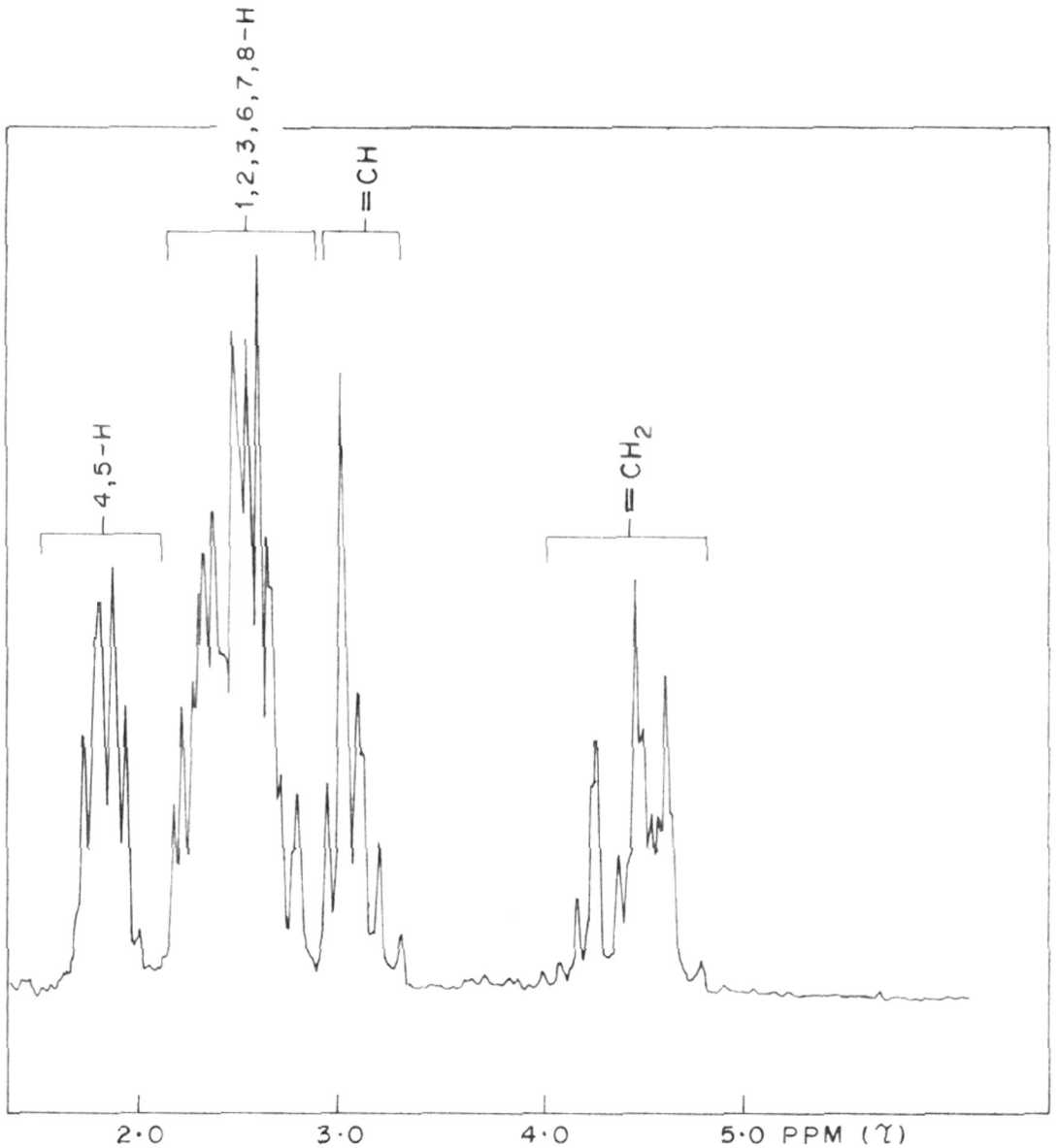


FIG. 4 NMR SPECTRUM OF 9-ALLYLIDENE-10-ANTHRONE IN CCl_4

condensation with acrolein; but it has not been possible so far to convert (11) to benzanthrone.

Compound (B), m.p. 210-12°, $C_{34}H_{24}O_2$ (M.+ 464), has the structure (12), probably formed by the action of (11) on the carbonium ion (13). The NMR spectrum of (12) in $CDCl_3$ shows the presence of a C-allylic group (methylene doublet at 7.0 and 3-proton multiplet between 4.8 and 5.68). A one proton multiplet between 3.3 to 3.72 was assigned to a conjugated CH. The presence of the allyl group was also confirmed by the initial loss of 41 from the molecular ion (M.+ 464) in the mass spectrum of (12).

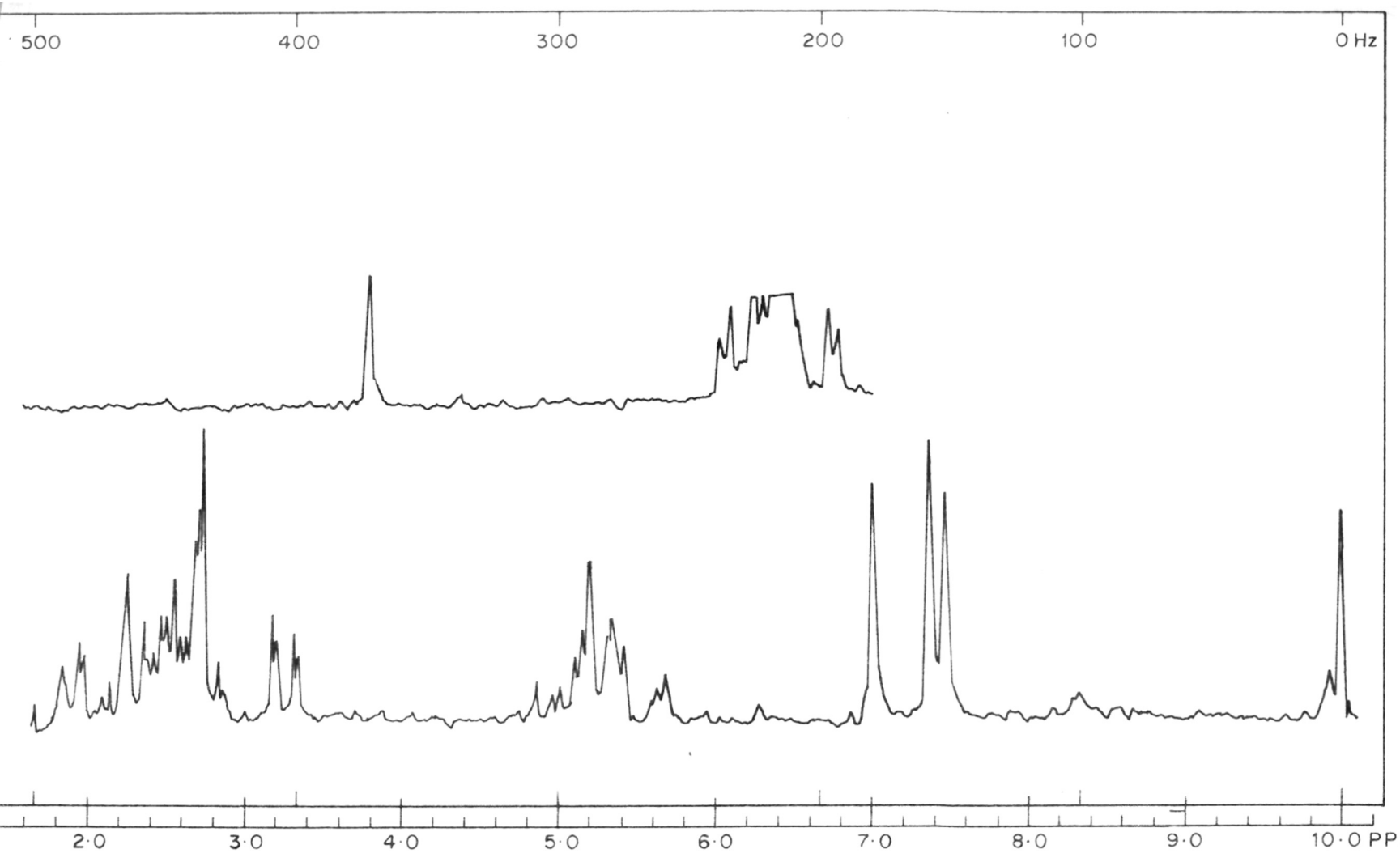
Reduction of (2) in methanol by sodium borohydride gave (14), $C_{17}H_{16}O_2$ (M.+ 252). The NMR spectrum of (14) shows the expected signals for the allyl group together with a 2-proton singlet at 7.4, exchangeable with D_2O, can be assigned to for 9- and 10-OH. The aromatic protons form an A_2B_2 system of two multiplets at 2.4 and 2.73 integrating for four protons each (α- and β-protons of the anthracene ring).

The action of allyl bromide on the leuco derivative of 1-hydroxyanthraquinone gave two products (C) and (D) in the ratio of about 7.5:10, obtained respectively by extracting the alkaline solution with chloroform and by acidifying the aqueous solution. The alkali-insoluble product (C), m.p. 118-20°, $C_{17}H_{14}O_3$ (M.+ 266), shows a

chelated carbonyl absorption at 1640 cm^{-1} in the IR spectrum. In the mass spectrum, the base peak is at m/e 225, corresponding to the loss of the allylic side chain. Structure (15) assigned to (C), was confirmed by its NMR spectrum (Fig. 5) in $CDCl_3$ in which the bonded α-hydroxyl appears at -2.37, and two quartets at 1.85 and 3.3 assigned to 5-H and 3-H respectively; 3-H is shielded because of the adjacent hydroxyl group.

The alkali-soluble product (D), m.p. 92-93°, is isomeric with (C) (M^+ 266). The IR spectrum of (D) shows a broad strong absorption at 3350 cm^{-1} (hydroxyl group) and a free carbonyl at 1662 cm^{-1}. The NMR spectrum of (D) in $CDCl_3$ (Fig. 6) shows the non-bonded phenolic hydroxyl at 0.94, The aliphatic hydroxyl at position 9 which appears at 7.0 in (C), is not seen in (D). The methylene doublet and 3-proton multiplet of the allylic group seen in (C) is also absent. Instead, the NMR spectrum shows two groups of multiplets, one at 4.76 to 5.76 and other at 6.82 to 7.54 integrating for 4 and 2 protons respectively. IR, NMR and mass spectral data are in agreement with the structure (16), The appearance of one of the methylenes attached to the anthrone unit) is abnormally low value and is not clearly understood. However, the data does not suggest any other alternate structure.

547.673.1(043)
DES



FIG·5 NMR SPECTRUM OF 4,9-DIHYDROXY-9-ALLYL-10-ANTHRONE IN $CDCl_3$

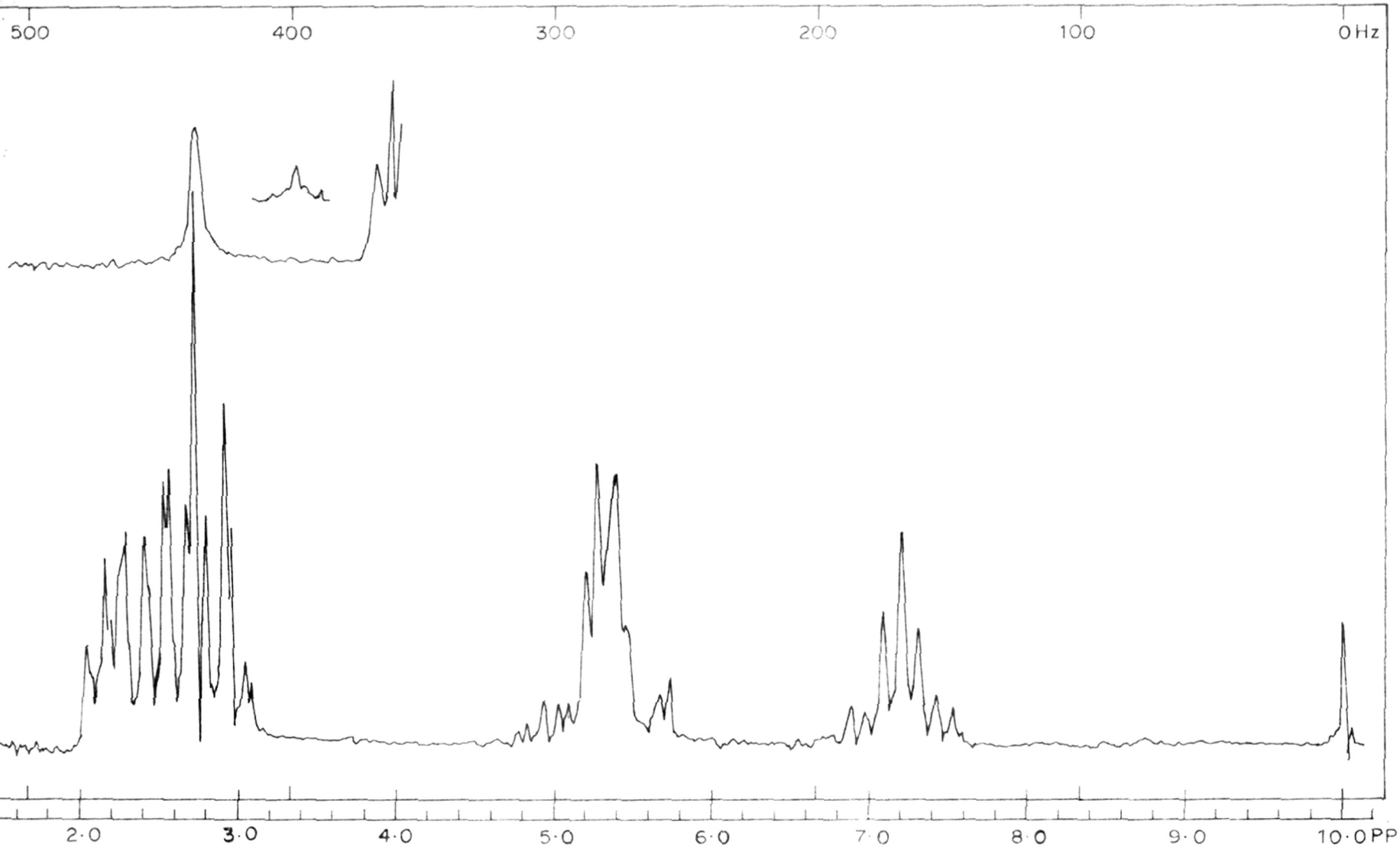
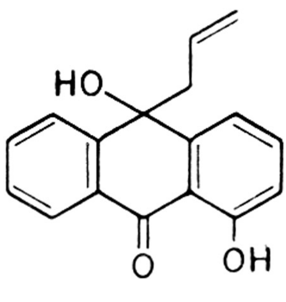


FIG. 6 NMR SPECTRUM OF (16) IN $CDCl_3$

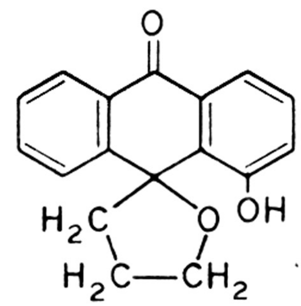
Normally the allyl bromide should react with a phenolic hydroxyl giving the O-allyl ether. However, it is found in the present investigation that under the experimental conditions, the phenolic hydroxyls are unaffected. When the leuco derivative of 2-hydroxy-anthraquinone was treated with allyl bromide, the product gave a fluorescent solution in aqueous sodium hydroxide. Two possible structures (17) and (18) were considered, and the NMR spectrum (pyridine and acetone) favoured (18). NMR spectrum of (18) in acetone shows a low-field 3-proton multiplet in the region between 1.66 to 2.02. These can be assigned to 4-H, 5-H and 8-H; The α-proton adjacent to the 2-hydroxyl is highly shielded and appear as a meta-coupled doublet (J=2 Hz) at 2.47.

Treatment of leuco α-aminoanthraquinone with allyl bromide gave a mixture of compounds, from which (19) was isolated in 65% yield by chromatography. The structure (19) was based on its IR, NMR spectra.

Cf. dimis- Eq. methyl ethers by DMS-K2CO3; acetate; benzoate or tosylate



(15) XI

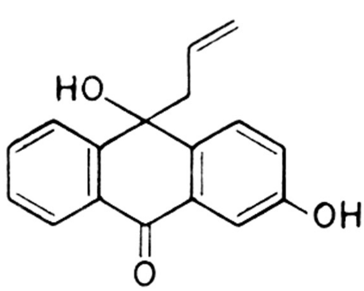


(16) XII

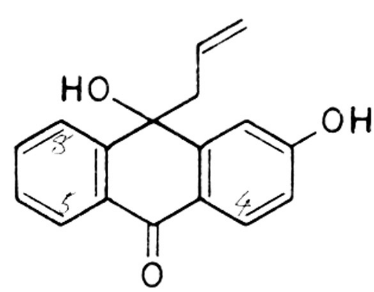
Study (XII) in detail

Prepare (XII) analogue without OH

Block 5

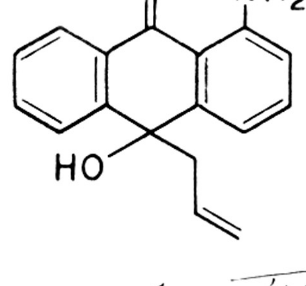


(17) XIII



(18) XIV

In 2 lines



(19) XV

EXPERIMENTAL Procedure

I

9-Allyl-9-hydroxy-10-anthrone (2)

(a) Anthraquinone (10.4 g., 0.05 mole) was suspended in 10% aqueous sodium hydroxide at room temperature. The vat was prepared by adding sodium dithionite (15 g); allyl bromide (12 g., 0.1 mole) was then added and the mixture shaken for 30 minutes when a colourless precipitate separated. Excess alkali and sodium dithionite were tested for as usual. The colourless precipitate was filtered, washed with water and air dried (12 g). Crystallisation from petroleum ether (60-80°) gave colourless rhombic prisms; m.p. 104-105° (lit.[7] 108°) (Found: C, 81.9; H, 5.8. $C_{17}H_{14}O_2$ requires C, 81.6; H, 5.6%). Allyl p-toluenesulphonate? & chloride gave a similar results.

(b) To the alkaline vat of anthraquinone (1 g), allyl chloride (1 ml) was added. The product was worked up as in (a), yield of (2) 0.9 g., m.p. 104-105°.

(c) Hydrogen (0.0025 mole) was absorbed in a suepension of anthraquinone (0.52 g., 0.002 mole) in 5% aqueous sodium hydroxide (30 ml) in presence of platinum oxide catalyst (20 mg). To the red solution at room temperature, allyl bromide (1.2 g., 0.01 mole) was added under vigorous stirring. After 30 min. the colourless product was filtered, washed and dried (0.16 g). Crystallisation from petroleum ether gave (2), m.p. 104-105°.

(d) The alkaline vat of anthraquinone (1 g) was treated with allyl p-toluenesulphonate (3 ml) at room temperature. After 1 hr. the product was extracted with chloroform. The colourless residue (0.6 g) from the extract was repeatedly crystallised from pet.ether, yielding (2), m.p. 104-105°.

9-γ,γ-dimethylallyl-9-hydroxy-10-anthrone (7)

An alkaline vat of anthraquinone (0.5 g., 0.025 mole) was treated with dimethylallyl bromide (1.5 g., 0.1 mole) at room temperature. The product (0.45 g) crystallised from pet.ether in colourless needles, m.p. 142-43°. (Found: C, 82.3; H, 6.8. $C_{19}H_{18}O_2$ requires C, 82.0; H, 6.5%). The yield was improved by carrying out the reaction at 0-5°.

The action of 2-methyl-2,4-dibromo-n-butane on 9,10-dihydroxyanthracene; preparation of (8)

2-Methyl-2,4-dibromo-n-butane (6 g) (prepared by the addition of 2 moles hydrobromic acid to isoprene) was added to an alkaline vat of anthraquinone (2 g). The mixture was shaken at room temperature overnight and extracted with chloroform. The product crystallised from pet.ether in colourless rhombic prisms, m.p. 130-32°. (Found: C, 82.3; H, 6.6. $C_{19}H_{18}O_2$ requires C, 82.0; H, 6.5%).

9-Acetoxy-9-allyl-10-anthrone

Compound (I) (0.5 g), acetic anhydride (8 ml) and fused sodium acetate (1 g) were heated ~~together~~ under reflux for 6 hr. Worked up as usual, the product (0.48 g) crystallised from pet.ether in colourless needles, m.p. 124-25°. (Found: C, 78.4; H, 5.5. $C_{19}H_{16}O_3$ requires C, 78.1; H, 5.5%).

The action of p-toluenesulphonic acid on (I); preparation of (VII) and (VIII)

A solution of (I) (2 g) in dry benzene (40 ml) was heated at 70-75° with p-toluenesulphonic acid (2 g) for 30 min. After cooling to room temperature, the benzene solution was filtered to remove p-toluenesulphonic acid. The filtrate showed two major yellow spots on TLC ~~over~~ silica gel. The two compounds were then separated on a column of silica gel using benzene as solvent. The fast moving compound (0.2 g) was isolated after removal of solvent under reduced pressure in presence of hydroquinone. It crystallised from pet.ether in lustrous pale yellow plates, m.p. 109-110°, and was identified as ~~the~~ dimer (VII). (Found: C, 88.1; H, 5.5. $C_{17}H_{12}O$ requires C, 87.9; H, 5.2%).

The second product (0.2 g) crystallised from benzene-pet.ether in shining yellow prisms, m.p. 210-12° and was identified as the dimer (VIII) (Found: C, 88.0; H, 5.1. $C_{34}H_{24}O_2$ requires C, 87.9; H, 5.2%).

Action of sodium borohydride on (I); preparation of (X)

To a solution of (I) (0.5 g) in methanol (5 ml), sodium borohydride (0.5 g) was added at room temperature with stirring. The reaction was exothermic. After 2 hr. the product was worked up as usual. Crystallisation from benzene-pet.ether gave colourless crystals (0.38 g), m.p. 143-45° (Found: C, 81.2; H, 6.5. $C_{17}H_{16}O_2$ requires C, 81.0; H, 6.3%).

9-Allyl-4,9-dihydroxy-10-anthrone (XI) and compound (XII)

4-Hydroxyanthraquinone (2 g., 0.009 mole) in 5% sodium hydroxide (50 ml) was reduced with sodium dithionite (3 g), and treated with allyl bromide (4.2 g; 0.036 mole) at room temperature for 3 hr. The alkaline solution was extracted with chloroform. The product (0.75 g), recovered from chloroform, crystallised from pet.ether in pale yellow plates, m.p. 119-120° and it was identified as (XI). (Found: C, 77.0; H, 5.6. $C_{17}H_{14}O_3$ requires C, 76.7; H, 5.3%).

The aqueous solution, after extraction with chloroform, was acidified with acetic acid and the precipitate was filtered, washed and dried (1 g). Crystallisation from pet.ether gave pale yellow needles, m.p. 92-94°, and identified as (XII). (Found: C, 77.1; H, 5.6. $C_{17}H_{14}O_3$ requires C, 76.7; H, 5.3%).

9-Allyl-2,9-dihydroxy-10-anthrone (XIV)

When the alkaline vat of β-hydroxyanthraquinone (1 g) was treated with allyl bromide (2.1 g) as in the previous experiment, the entire product remained in the alkali solution and no part was extractable with chloroform. Acidification with acetic acid gave a precipitate (1 g) which crystallised from ethanol-water in pale yellow crystals, m.p. 189-91°. (Found: C, 76.5; H, 5.5. $C_{17}H_{14}O_3$ requires C, 76.7; H, 5.3%).

9-Allyl-9-hydroxy-4-amino-10-anthrone (XV)

A solution of α-aminoanthraquinone (1 g) in alkaline dithionite was treated with allyl bromide (2.2 g) at room temperature for 1 hr. Extraction with ether led to a gummy residue, which was dissolved in benzene and chromatographed on a silica gel column. The major slow-moving greenish yellow band yielded a product (0.6 g) which crystallised from hexane in greenish yellow prisms, m.p. 102-103°. (Found: C, 77.3; H, 5.8; N, 5.1. $C_{17}H_{15}NO_2$ requires C, 77.0; H, 5.7; N, 5.3%).

A for IJC

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P A R T - II

CONSTITUTION OF YELLOW PIGMENTS FROM α-AMINOANTHRAQUINONES AND s-PHTHALOYL CHLORIDE .

***

INTRODUCTION

A dye is a coloured substance that can be applied in dispersion to a substrate. The principle characteristics of a pigment are: (a) it has no affinity for fibres or other substrates, and (b) it is substantially insoluble in the medium in which it is used.

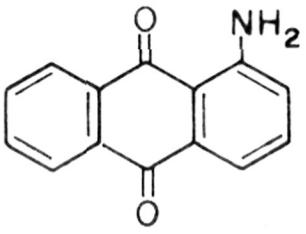
Pigment-using industries are interested in inexpensive bright yellow pigments with good fastness properties. According to the patent literature[1], useful pigments are obtained by the condensation of α-aminoanthraquinone (1) and its nuclear substituted derivatives with the chlorides of diacids. Thus the condensation of α-aminoanthraquinone (1) and s-phthaloyl chloride (2) gives a yellow pigment, "particularly suitable for textile applications" (Textile Yellow Toner Y 5776, HAR).[1]

A 1955 patent[2] describes the preparation of a novel yellow pigment which was obtained by condensation of two moles of (1) and one mole of (2) using nitrobenzene as solvent. The constitution of yellow pigment, commercially known as Patrician Yellow 21-2817, has been mentioned in Colour Index (Additions and Amendments 2, Jan.1972) as (3). The same yellow pigment was obtained[3] as early as 1910 by heating (1) with phthalic anhydride and phosphorus pentachloride.

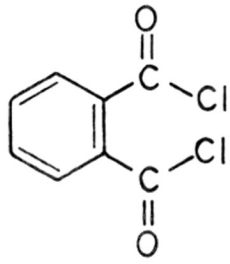
In 1959, Randall and Taras[4] reported the condensation of one mole of (1) and one mole of (2). They obtained a yellow pigment which fluoresced under ultraviolet light. According to them, the product contained a bright greenish yellow component of unknown constitution.

A British patent[5] claims the preparation of yellow anthraquinone pigments "with improved shade and strength" by heating (2) with (1) containing 2-10% of different aminoanthraquinones. Compounds of the general formula (4) (R = C_2H_4, CH=CH, o-phenylene, substituted o-phenylene, or 2,3-pyridinediyl and R^1=H, Cl, NO_2 or $BzNH$) are the subject of another patent;[6] they were prepared by heating aminoanthraquinone in anhydrous solvents such as nitrobenzene or o-dichlorobenzene (ODCB) with 0.5-2 moles of a dicarboxylic acid anhydride in the presence of 0.5-2 moles of phosphorous oxychloride, an acid binding agent and an amide as catalyst.

Condensation of derivatives of 1-aminoanthraquinone, and 1-amino-4-benzamidoanthraquinone such as 1-amino-4-methoxyanthraquinone with (2), which gave orange and red pigments, have been described in the patent literature.[7,8]



(1)



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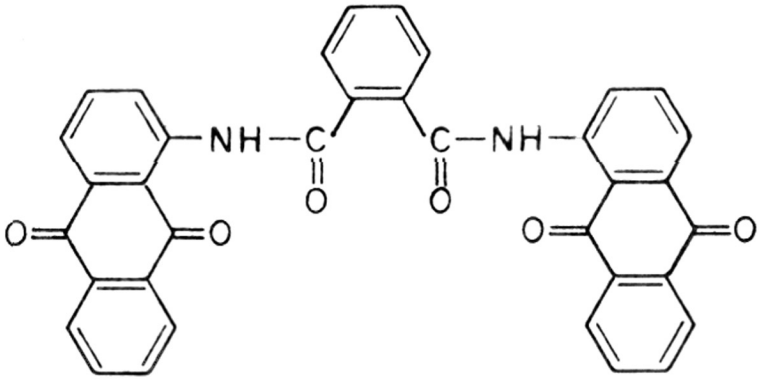

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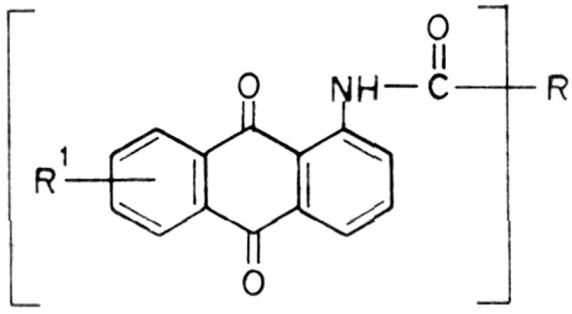

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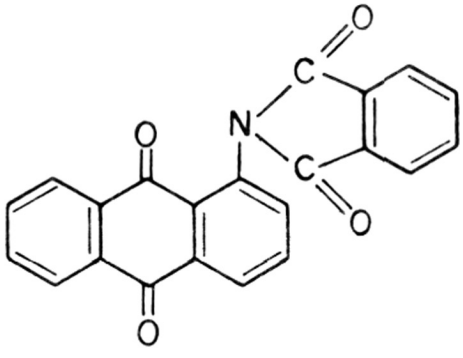


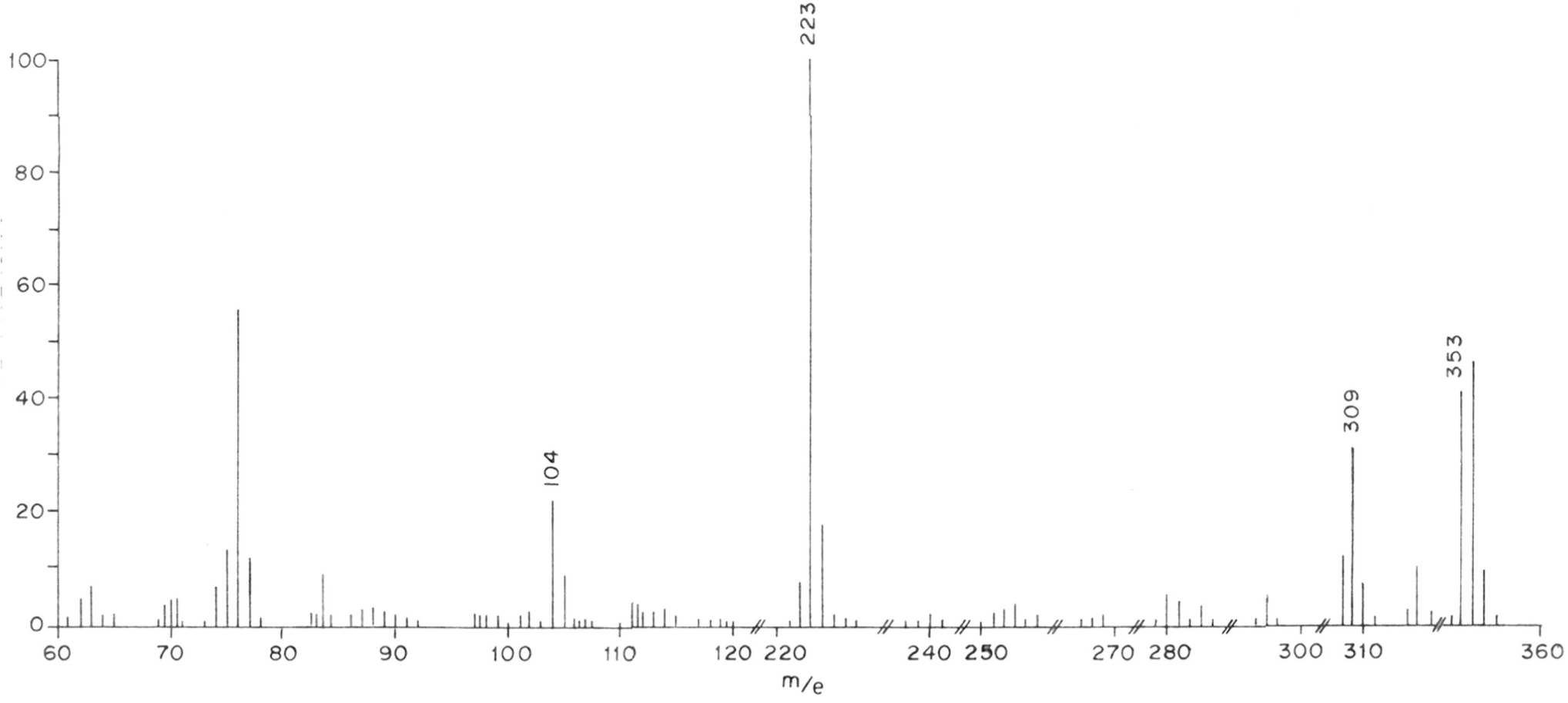
(5)

PRESENT WORK

With a view to study the constitution of the pigment or pigments obtained by the condensation of one or two moles of (1) with one mole of (2), the present work was undertaken. When the condensation was carried out, using one mole each of (1) and (2), as described in USP 2,914,542,[4] the pigment (A) crystallised from ODCB in bright greenish yellow microscopic needles which decomposed at 340-42° with a red sublimate. Elemental analysis does not distinguish between (3) and (5), although the N content favours (3). The mass spectral molecular weight (M^+ 353) is in agreement with (5; $C_{22}H_{11}NO_4$). The IR spectrum in nujol mull shows four strong absorption bands in the carbonyl region at 1710, 1683, 1668 and 1635 cm^{-1}. In the IR spectra of phthalimide and N-methylphthalimide the carbonyl absorption appears[9] as two strong bands in the regions 1790-1720 cm^{-1} abd 1710-1670 cm^{-1}. The non-appearance of a band above 1710 cm^{-1} and the appearance of a bonded NH stretching vibration do not favour structure (5). The amide carbonyl in 1-benzamidoanthraquinone absorbs at 1680 cm^{-1} and the diamilide of phthalic acid at 1626 cm^{-1}. When compared with these values, the carbonyl absorption at 1710 cm^{-1} in the IR spectrum of (A) cannot be explained on the basis of the alternate structure (3).

The prominant peaks in the mass spectrum (Fig.1) of (A) are at m/e 309 and m/e 223. The peak at m/e 223, which is the base peak, corresponds to ∝-aminoanthraquinone. The ion at m/e 309 is formed by the loss of CO_2 from the parent molecular ion. This type of rearrangement, involving oxygen transfer and loss of CO_2 has been observed[10,11] in the mass spectra of N-methyl and N-phenylphthalimide. Because of these conflicting results an attempt was made to record the NMR spectrum of (A), but it had inadequate solubility.

Reductive methylation of pigment (A) was then carried out in order to get a more soluble derivative, because earlier work in this laboratory has shown[10] that when polycyclic quinones, such as violanthrone are reduced with aqueous sodium hydroxide and dithionite and then methylated, the methyl ethers of the leuco compounds have considerable solubility in organic solvents such as benzene and chloroform.[12] The product (C), prepared in this manner by reduction and subsequent methylation of the leuco compound of pigment (A) with dimethylsulphate, was purified by passing a chloroform solution through basic alumina column. Repeated crystallisation from benzene gave greenish yellow lustrous compound, m.p. 253-54°. The elemental analysis is more in agreement with(6) than (7).


100
80
60
40
20
0
223
104
309
353
60
70
80
90
100
110
120 220
240 250
270 280
300 310
360
m/e

FIG·1

However, there was no peak in the mass spectrum (Fig. 2) above m/e 383 and if this is assumed to be $M^{+\cdot}$, it is in agreement with (7). The mass spectral fragmentation pattern will be discussed later. The IR spectrum(nujol) shows carbonyl absorption at 1675 cm^{-1} and NH stretching vibration at 3325 cm^{-1}. The NMR spectrum (Fig.3) in $CDCl_3$ shows an extremely complex pattern in the aromatic region and is difficult to analyse because of the aromatic protons appearing in a very narrow range. The methoxyl protons appear at 5.93 and 6.0. The bonded NH- proton is seen at -1.3. Based on the mass spectral molecular weight, and the NMR and IR spectra, the structure (8), was considered for the reductive methylation product (C) and consequently the structure (9), 3,4-phthaloylmorphanthridine-6,11-diene for pigment (A).

In the mass spectrum (Fig. 2) of (C) the ion at m/e 383 is not significant (11%). It loses two methyl radicals successively from two methoxyl groups (peak at m/e 368 and m/e 353). The ion at m/e 353 then loses CO_2 giving a peak at m/e 309 (8%), also observed in the parent quinone. The peak at m/e 223 which forms the 67% of the base peak (m/e 368), corresponds to the molecular ion of α-aminoanthraquinone. The other prominent ion is at m/e 253 (45%) corresponding to 1-amino-9,10-dimethoxyanthracene (10). The fragmentation

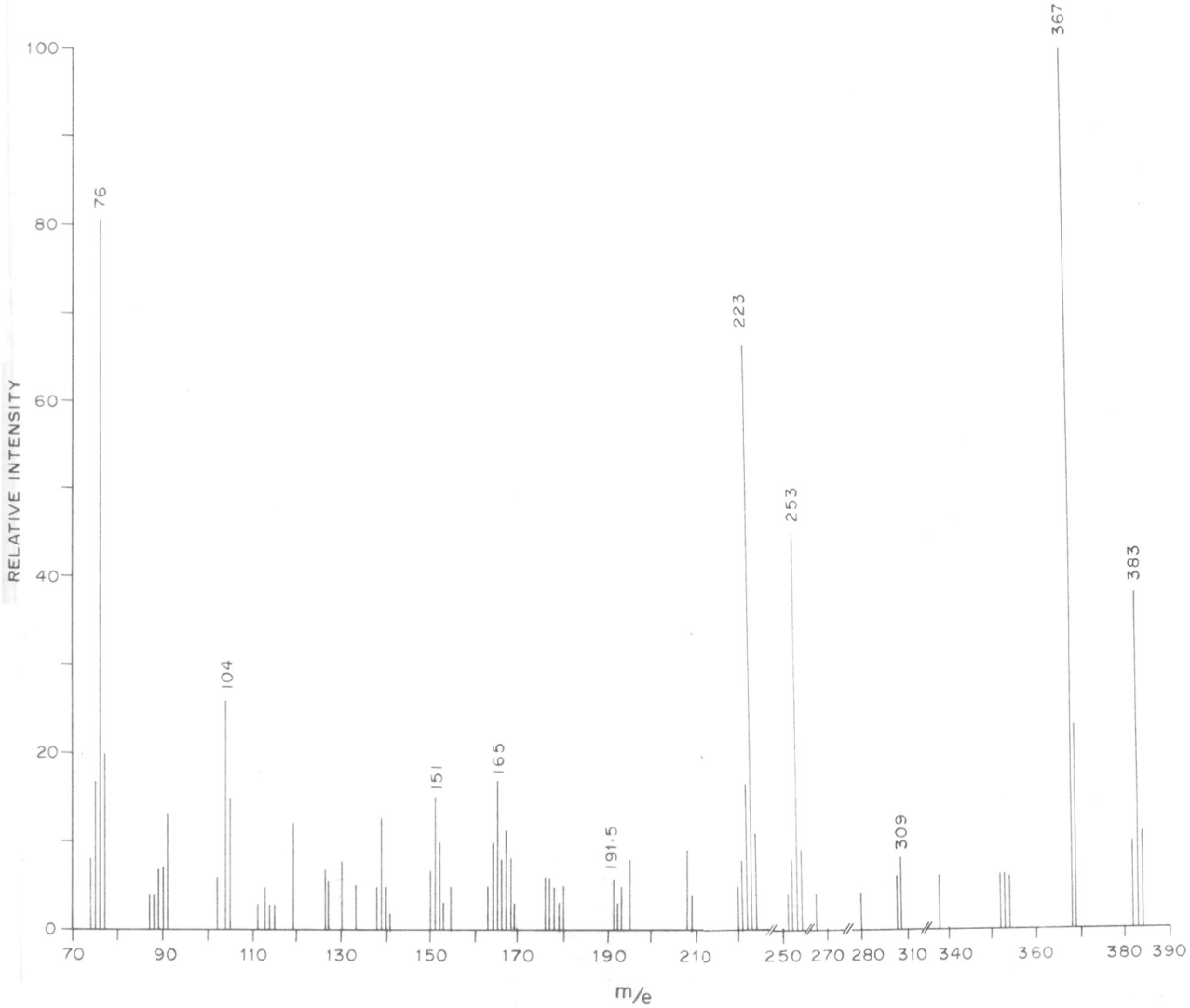
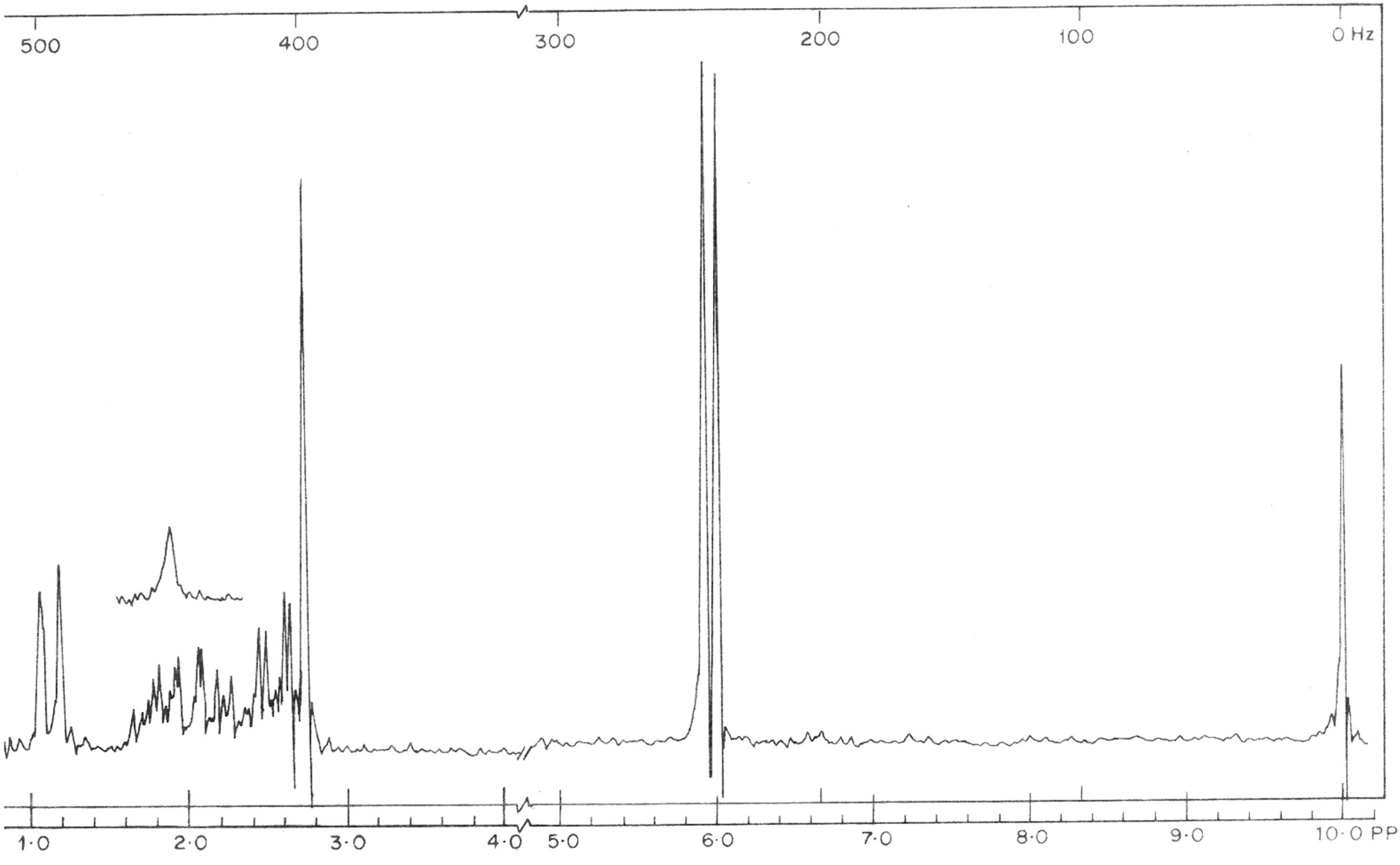

RELATIVE INTENSITY
100
80
60
40
20
0
76
104
151
165
191·5
223
253
309
367
383
70
90
110
130
150
170
190
210
250
270
280
310
340
360
380
390
m/e

FIG. 2



FIG·3 NMR SPECTRUM OF REDUCTIVE METHYLATION PRODUCT OF PIGMENT (A) IN $CDCl_3$

pattern below m/e 223 resembles that of α-aminoanthraquinone which has been reported.[13]

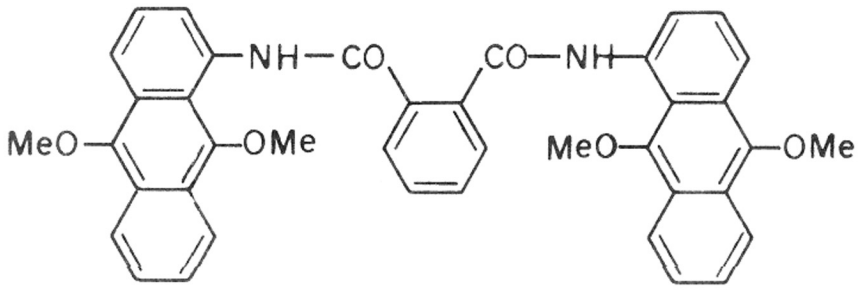
From the mass spectra, the molecular weights of the pigment (A) and its reductive methylation product (C) appear to be 353 and 383 respectively. The IR spectrum of the pigment shows bands at 1710, 1683, 1668 and 1635 cm^{-1}. These data cannot be reconciled with the suggested structure (3). The alternate structure (9) seems to be more likely, but the IR spectrum of (C) shows only one strong carbonyl band at 1675 cm^{-1} and not two bands, normally expected for the morphanthridine-6,11-dione (11) system. It may be recalled at this stage that morphanthridine 6,11-dione (11) is formed[14] from N-phenylphthalimide when it is heated to 290° in a melt of aluminium chloride and sodium chloride. Another way of synthesising (11) is by the Schmidt reaction on anthraquinone by treatment in a mixture of conc. sulphuric acid and methylene chloride with sodium azide at 20-25°.[15] Morphanthridine-6,11-dione (11) was prepared by the latter method in the present investigation in order to study its behaviour in the mass spectrum and the absorption position of the carbonyl groups in the IR spectrum.

The mass spectral fragmentation of (11) is different from that of pigment (A) and it resembled to that of benzazepine.[16] The fragmentation occurs by successive loss of

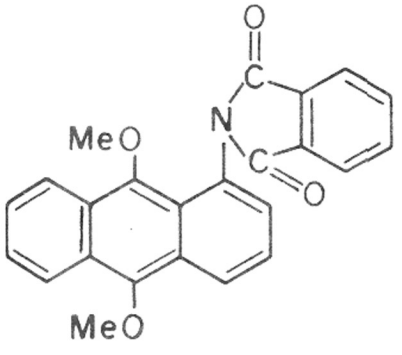
two molecules of CO from the molecular ion (M^+ 223) to give m/e 195 and then the carbazole radical cation (m/e 167). Another prominent peak (m/e 222) is due to the loss of a hydrogen radical from the molecular ion. The loss of CO_2 is not observed. The IR spectrum of (11) in nujol shows strong carbonyl bands at 1667 cm^{-1} and 1640 cm^{-1}.

It has been reported[17] that morphanthridine-6,11-dione and its substituted products undergo ready alkaline hydrolysis to the corresponding amino acids (12) with hot 2N aqueous sodium hydroxide. Under the identical conditions pigment (A) remained intact. However, by refluxing pigment (A) with 10% sodium hydroxide in cellosolve, ∝-amino-anthraquinone was obtained in quantitative yield and not the expected amino acid (13) based on the structure (9) to (A). Hydrolysis of pigment (A) also occured in conc. sulphuric acid at room temperature, ∝-aminoanthraquinone being obtained on pouring the acid solution to ice-cold water. If the morphanthridine-6,11-dione ring system is present in the pigment, it should give (13) and not ∝-amino-anthraquinone. From these results, structure (9) for pigment (A) was ruled out.

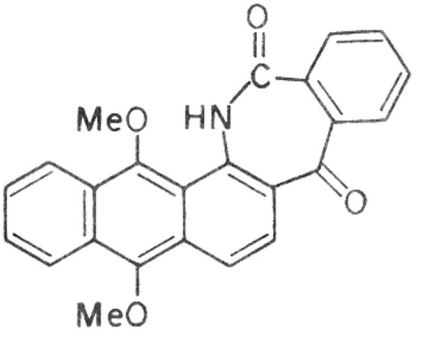
The original structure (3) is more consistant with the chemical reactions. The condensation of two moles of (1) with one mole of (2) as described in the patent literature[2] was carried out and the reddish yellow product(B)



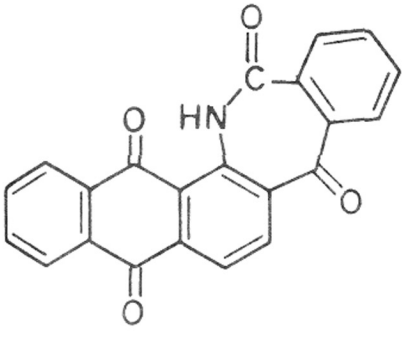
(6)



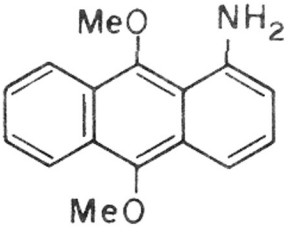
(7)



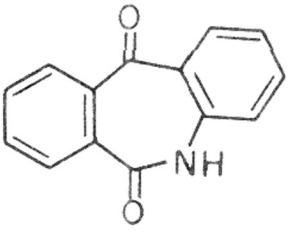
(8)



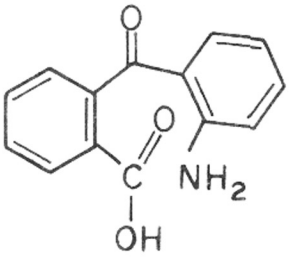
(9)



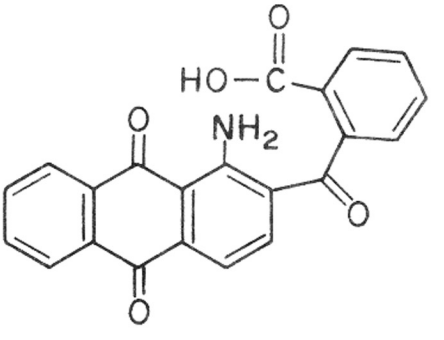
(10)



(11)



(12)



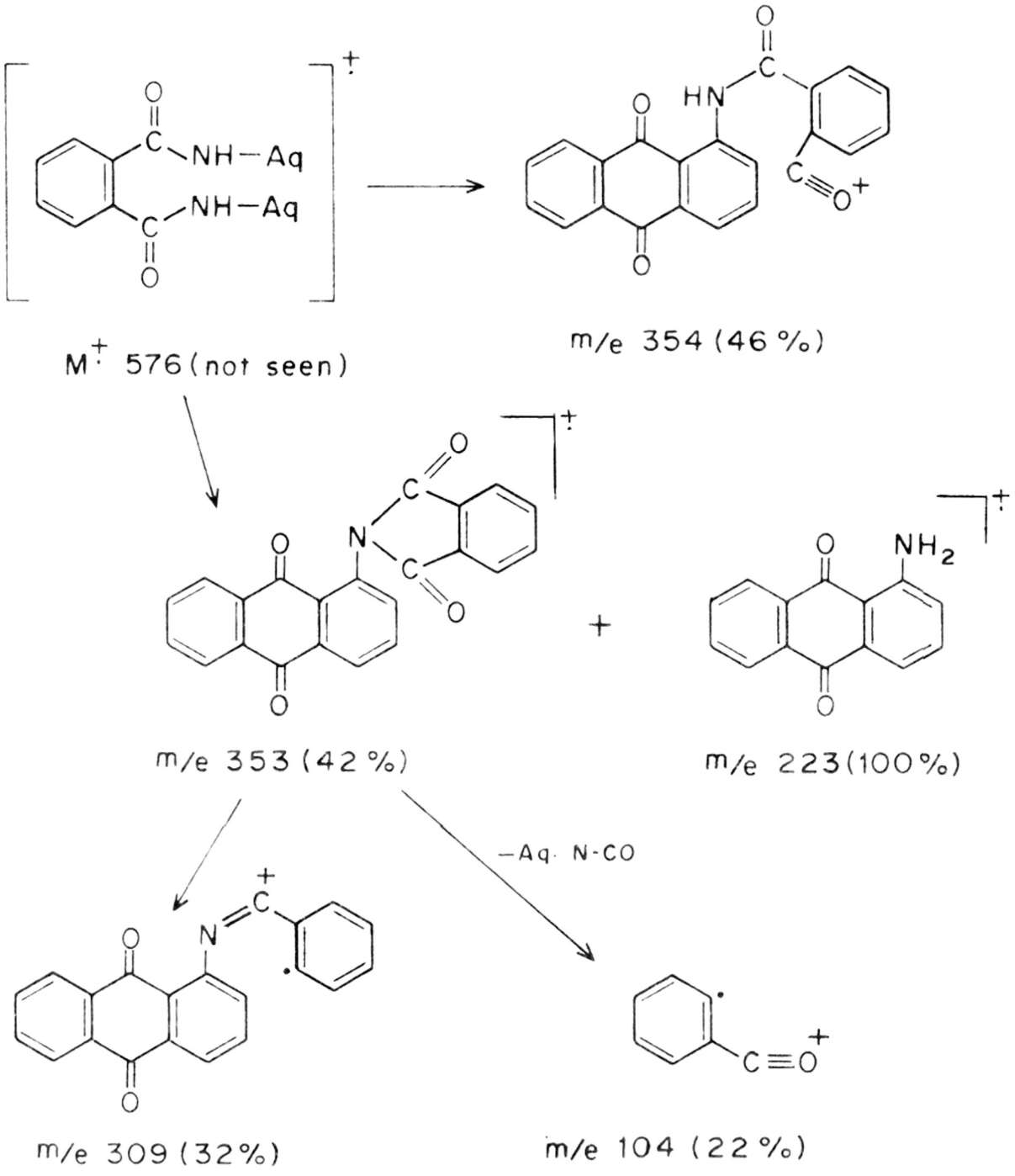
(13)

was crystallised from ODCB. It gave a superposable IR spectrum with pigment (A). The identity of the two pigments (A) and (B) was further established by carrying out the reductive methylation of (B) and the mixed m.p. with (C) was not depressed. Similarly, the condensation of (1) with phthalic anhydride and phosphorous oxychloride in presence of urea and calcium oxide as reported in a patent[6] also resulted in the formation of the same pigment. These reactions also favour structure (3). However, it is difficult to explain the IR and mass spectral data. The only way to account for the peak at m/e 353 in the mass spectrum (Fig. 1) is decomposition of the pigment in the mass spectrometer thermally or by electron impacts, the molecular ion is not seen, but only the next fragment ion. To clarify these points, the thermal stability of (A) was checked.

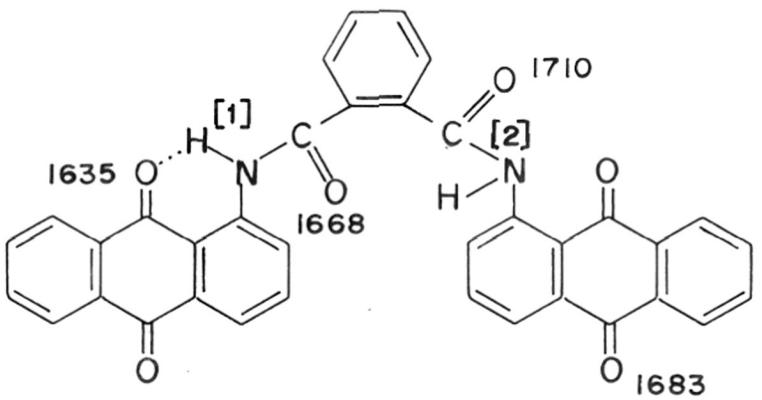
When the pigment (A) was heated under reduced pressure at 360°, the sublimate was found to be a mixture of two compounds: (a) α-aminoanthraquinone (1), and (b) 1-anthraquinonylphthalimide (5) which was separated from (1) by extracting with hot ethanol and crystallising from benzene and characterised by its IR and mass spectra (M^+ 353). Bloom and Freyermuth[18] claimed the synthesis of (5) by adding (1) to a mixture of pyridine and anhydrous aluminium

chloride, followed by the addition of phthalic anhydride. However, no details of the preparation of (5) are available. The IR spectrum (nujol) of (5) shows C=O bands at 1786, 1762 cm^{-1} and no NH absorption is seen. In the mass spectrum the molecular ion m/e 353, is the base peak and no intense peak at m/e 223 observed. In the mass spectrum (Fig.1) of pigment (A) the base peak is at m/e 223, corresponding to the radical ion of ∝-aminoanthraquinone. Thus it is clear that in the mass spectrometer, (A) is first thermally decomposing to N-(1-anthraquinonyl)phthalimide and ∝-aminoanthraquinone; the molecular ion of the former is seen as the peak of highest mass and the base peak corresponds to ∝-aminoanthraquinone (chart 1). Similarly, when the reductive methylation product of the pigment was heated above its m.p. under reduced pressure it decomposed to give two products corresponding to the reductive methylation products of (5) and (1). From these facts it is clear that the structure (3) suggested earlier for the pigment is correct. However, to reconcile the C=O stretching vibrations in the IR spectrum, one has to invoke some steric factors to keep the anthraquinonyl units in (3) in different planes. It can be assumed that only one of the two amide NH groups is strongly bonded with the adjacent C=O group of an anthraquinone unit, while the second amide NH is in a favourable steric situation to bond with the CO

CHART 1 MASS SPECTRAL FRAGMENTATION OF PIGMENT (A)



Aq = (1-ANTHRAQUINONYL)



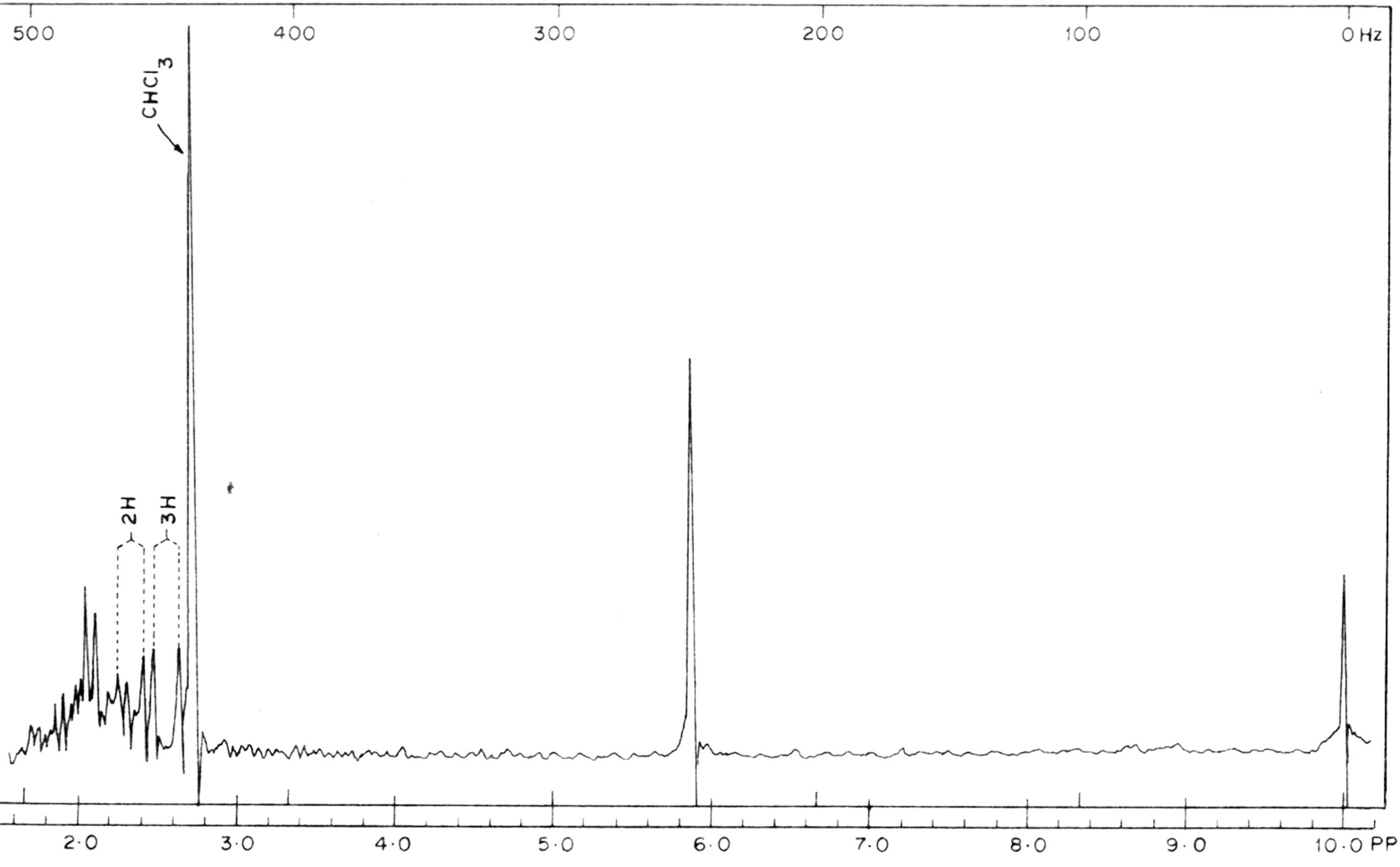
group marked [1] rather than a carbonyl of the second anthraquinone unit. In such a molecule there will be four types of carbonyl absorptions and all are seen in the IR spectrum of pigment (A). Thus the bands at 1710, 1683, 1668 and 1635 cm^{-1} can be assigned in the indicated order to the amide [2], the non-bonded anthraquinonyl carbonyls, the bonded amide C=O[1] and the bonded anthraquinone C=O. In the reductive methylation product the anthraquinone carbonyls are absent and only one amide band is seen at 1675 cm^{-1} as expected.

Condensation of 1-aminoanthraquinone with either one mole or two moles of s-phthaloyl chloride gave only pigment (A) and no trace of N-(1-anthraquinonyl)phthalimide

(5) was detected. An attempt to apply the Gabriel synthesis for the preparation of (5) by condensing 1-chloroanthraquinone with potassium phthalimide in dimethylformamide was unsuccessful.

The reaction of s-phthaloyl chloride with 1-amino-4-methoxyanthraquinone (14) in which the p-methoxyl will increase the basicity of the amino group, was next studied. The reaction of two moles of 1-amino-4-methoxyanthraquinone with one mole of s-phthaoyl chloride has been described in the patent literature[7] and the bis amide structure (15) has been assigned to the product. The reaction was repeated and structure (15) was confirmed. In its mass spectrum it resembled (3) in not showing the molecular ion, but a peak at m/e 383 corresponding to (16) and the base peak at m/e 253, corresponding to 1-amino-4-methoxyanthraquinone. The mass spectral fragmentation data for (15) and other compounds studied in the present investigation are given in Table 1.

However, when one mole of (14) was treated with one mole of s-phthaloyl chloride, the product was not(15), but (16) as shown by the IR, NMR and mass spectra. The IR spectrum in nujol shows the absence of NH absorption, and carbonyls are seen at 1782, 1760, 1714 and 1667 cm^{-1}. The NMR spectrum (Fig. 4) in $CDCl_3$ shows two distinct o-coupled

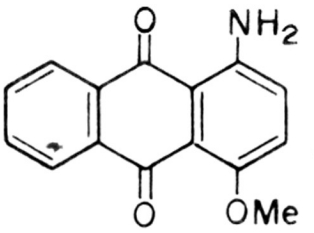


FIG·4 NMR SPECTRUM OF N-(4-METHOXY-1-ANTHRAQUINONYL) PHTHALIMIDE IN $CDCl_3$

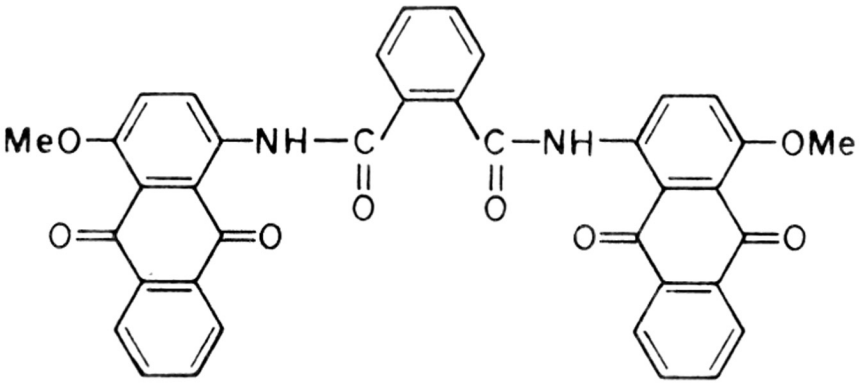
doublets (J=9 Hz) at 2.44 and 2.67 and are assigned to 2-H and 3-H respectively. The remaining aromatic protons appear as a complex multiplet in the region between 1.72 and 2.44. The OMe singlet is seen at 5.87. The absence of bonded NH absorption is noteworthy. The mass spectrum of (16) shows the molecular ion ($M^{\cdot+}$ 383) as the base peak. The peak at m/e 253, corresponding to 1-amino-4-methoxyanthraquinone is insignificant (2.0%) whereas it is the base peak in the mass spectrum of (15) (Table 1).

The condensation of one mole of 1-amino-2-methyl-anthraquinone (17) with one mole of (2) yielded the corresponding phthalimide compound (18). The assigned structure was based on IR, NMR and mass spectra. The NMR spectrum of (18) in $CDCl_3$ shows a low field o-coupled doublet (J=9 Hz) at 1.5 assigned to 4-H. The corresponding doublet for 3-H is shielded because of the adjacent methyl group and is merged in the complex multiplet in the region between 1.63 and 2.33 for the remaining aromatic protons. The 2-Me group absorbs at 7.63.

When this work on the constitution of pigment (A) was in progress, a pigment sample, Helio Fast Yellow E-3R, was kindly supplied by Farben Fabriken Bayer. Colour Index, 3rd edition, 1971, mentions Helio Fast Yellow E-3R (Pigment Yellow 99) as belonging to anthraquinone class, but the



(14)



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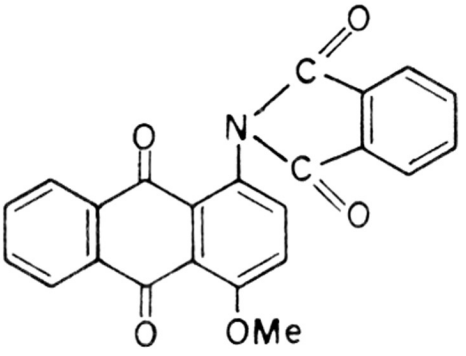

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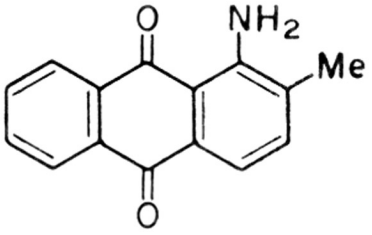
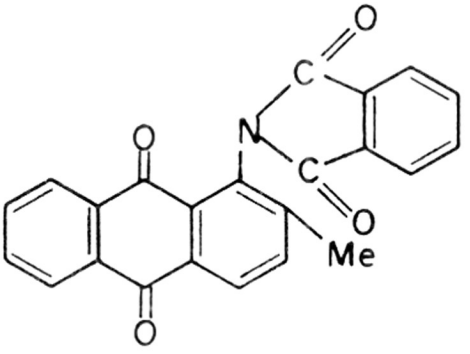
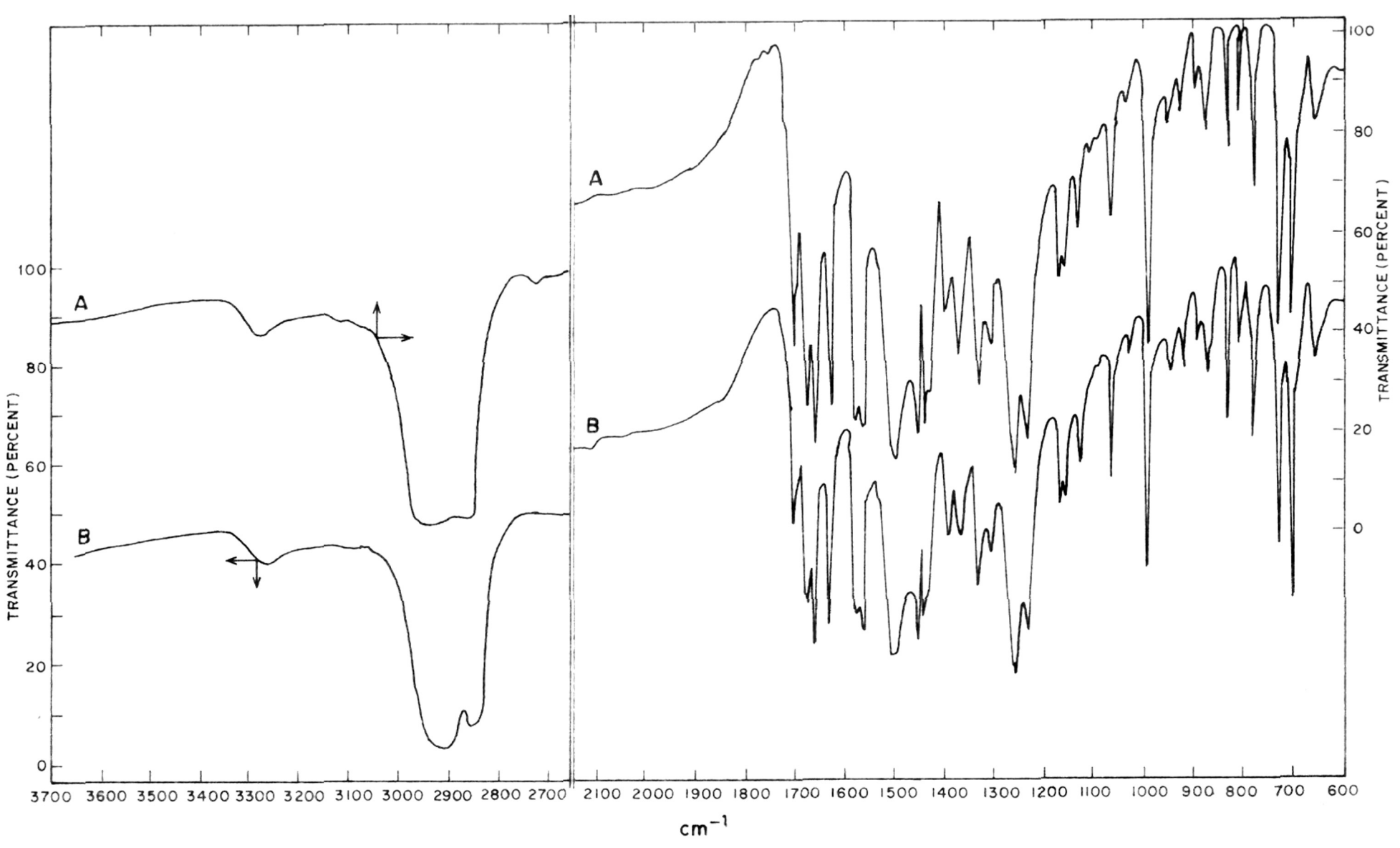


(17)



(18)

constitution has not been disclosed. The commercial sample crystallised from ODCB in yellow microscopic needles, decomposing at 340-42° with a red sublimate. The IR spectra of Pigment Yellow 99 and pigment (A) were identical in all respects. The identity of the two pigments was further established by the ready hydrolysis of the commercial sample to 1-aminoanthraquinone (1) on treatment with conc. sulphuric acid at room temperature. The reductive methylation products of pigment (A) and CI Pigment Yellow 99 gave superposable IR spectra. Helio Fast Yellow E-3R (CI Pigment Yellow 99) must therefore have the structure (3). CI Pigment Yellow 123, more recently marketed by an American firm, Inmont Corporation, under the name Patrician Yellow 21-2817, has also been assigned the same structure in the Colour Index, Additions and Amendments, 2, Jan. 1972. Since it is unlikely that two commercial pigments having the same structure have two different numbers in Colour Index, a sample of Pigment Yellow 123 was obtained from Inmont Corporation, New Jersey. It crystallised from ODCB in reddish yellow microscopic needles which decomposed at 340-42° with a red sublimate. It gave an IR spectrum (Fig. 5) superposable with those of Pigment Yellow 99 and pigment (A). The reductive methylation products of the two commercial samples also gave superposable IR spectra (Fig. 6).



FIG·5 IR SPECTRA OF :- A· PIGMENT YELLOW-123
B· PIGMENT YELLOW-99

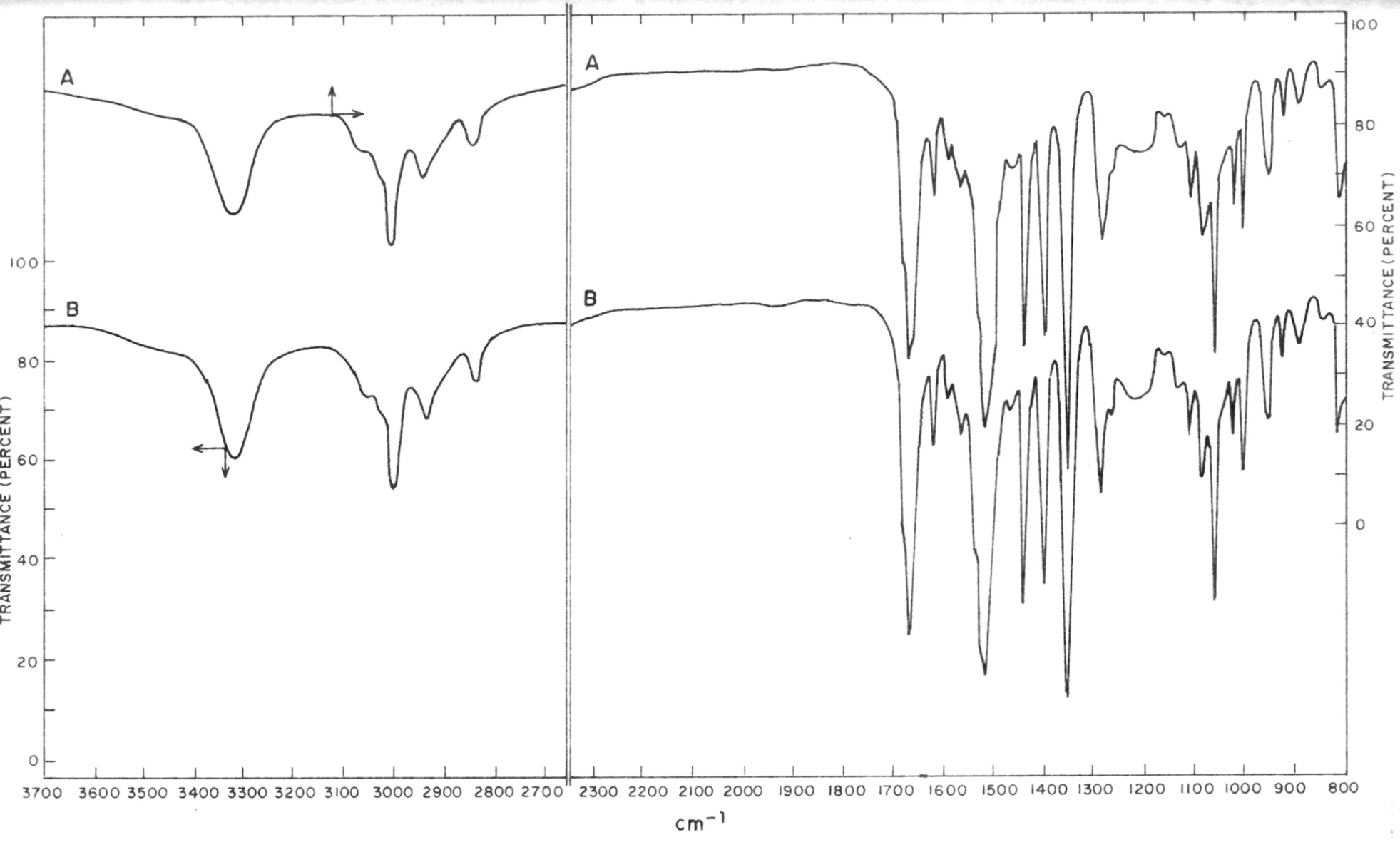


FIG. 6 IR SPECTRA OF REDUCTIVE METHYLATION PRODUCTS OF :- A. PIGMENT YELLOW-123
B. PIGMENT YELLOW-99

The identity of the four pigments (A), (B), Pigment Yellow 99, and Pigment Yellow 123, was further established by the determination of the X-ray powder diffraction patterns by Dr. A.P.B. Sinha and Dr. H.B. Mathur of this laboratory. Pigment Yellow 123 is highly crystalline with 15 diffraction lines. Pigment (B) is the next in crystallinity with 9 diffraction lines, while Pigment Yellow 99 and (A) have 6 and 5 diffraction lines respectively. Pigment (A) with 5 diffraction lines has "d" values very close to those of the very intense lines of Pigment Yellow 123, but the observed differences are the largest for (A) as compared to (B) and Pigment Yellow 99. Since the observed "d" values coincide for all the samples, they are chemically identical.

IR data of the compounds investigated in the present work is given in Table 2.

TABLE - 1

Mass spectral fragmentation data of Pigment (A.)

m/e	356	355	354	353	352	316	315
I(%)	2	11	46	42	2	3	11
m/e	314	311	310	309	308	298	291
I(%)	4	2	8	32	13	2	6
m/e	296	284	283	282	281	280	279
I(%)	1	1	4	1	5	6	1
m/e	270	269	268	267	255	254	258
I(%)	1	2	1	1	2	1	4
m/e	252	251	250	241	240	239	238
I( )	3	2	1	1	2	1	1
m/e	227	226	225	224	223	222	221
I(%)	1	1	2	18	100	8	1
m/e	214	213	207	206	196	195	194
I(%)	1	1	1	1	2	10	2
m/e	193	182	180	179	178	177	176.5
I(%)	1	1	1	1	2	3	7
m/e	176	169	168	167	166	165	164
I(%)	1	1	5	11	7	3	7
m/e	163	152	151	150	148	146	140
I(%)	1	3	13	6	6	9	6
m/e	139	138	137	130	120.5	114	113
I(%)	13	5	2	5	4	3	3
m/e	111.5	111	105	104	77	76	75
I(%)	4	4	9	22	12	56	14

Reductive methylation product of Pigment (A.)

m/e	384	383	382	369	368	354	353
I(%)	11	38	10	23	100	6	6
m/e	338	309	308	280	267	254	253
I(%)	6	8	6	4	4	9	45
m/e	252	224	223	222	221	220	209
I(%)	8	11	67	17	8	5	4
m/e	208	195	193	192	191.5	180	179
I(%)	9	8	5	3	6	5	3

Table 1 contd.

m/e	178	177	176.5	176	169	168.5	168
I(%)	5	7	2	6	3	8	3
m/e	167	166	165	164	163	154.5	153
I(%)	11	8	17	10	5	5	3
m/e	152	151	150	141	139	138	133
I(%)	10	15	7	2	13	5	5
m/e	130	127	126.5	126	119	115	114
I(%)	8	5	7	5	12	3	3
m/e	113	111	105	104	102	91	90
I(%)	5	3	15	26	6	13	7
m/e	89	88	87	83.5	77	76	75
I(%)	7	4	4	5	20	80	17

Compound (15)

m/e	384	383	366	355	354	337	326
I(%)	11	45	6.5	6	13.5	2	4
m/e	324	309	308	254	253	252	240
I(%)	3	4.5	4	19	100	10.5	5
m/e	239	238	236	235	227	225	224
I(%)	12	40.5	10	7	5	12	54
m/e	211	210	208	207	206	196	191.5
I(%)	6	34	7	6	5	10	5
m/e	183	182	181	180	178	167	166
I(%)	5.5	31	5	9	3	6.5	5
m/e	164	154	153	152	151	140	139
I(%)	9	8.5	9	11.5	5.5	6	13
m/e	138	137	130	128	127	126	125
I(%)	8.5	6.5	9.5	8	23.5	19	8
m/e	113	105	104	102	101	100	
I(%)	6	11	31	8	10	7	-

Compound (16)

m/e	384	383	367	366	365	355	354
I(%)	22.5	100	3	11	4.5	9	22.5

Table 1 contd.

m/e	337	326	324	310	309	306	295
I(%)	2	5	3	3	5	4	2.5
m/e	282	281	280	253	240	239	238
I(%)	2.5	2.5	2.5	2	2.5	1	1.5
m/e	227	208	206	191.5	180	164	152
I(%)	3.5	2.5	2.5	6	5	4.5	4.5
m/e	151	139	138	137	130	105	104
I(%)	3.5	2	35	2	4.5	5	15

TABLE - 2

IR data (cm-1)

Compound	Imide C=O	Amide C=O	Quinone	NH
Pigment (A)		1710; 1635	1683; 1668	3250(b)
N-(1-anthraquinonyl)phthalimide	1786(w) 1762(w) 1724(s)	-	1667	-
Reductive methylation product of (A)	-	1675(s)	-	3325
(15)	-	1685	1667; 1640	3150(b)
(16)	1782(w); 1760(w); 1714(s)	-	1667	-
(18)	1784(w); 1759(w); 1715(s)	-	1667	-

w - weak; s - strong; b - broad

EXPERIMENTAL

Preparation of pigment (A)

α-Aminoanthraquinone (10.6 g; 0.05 mole), ODCB (90 ml), thionyl chloride (0.5 g) and s-phthaloyl chloride (10 g; 0.05 mole) were heated together with stirring during 3 hr. to 170° and the mixture kept for 2 hr. at 175-80°. After cooling to 50°, the bright greenish yellow precipitate was filtered, washed with ODCB and then with DMSO and dried (12.0 g). Crystallisation from ODCB gave bright greenish yellow microscopic needles, decomposing at 340-42° with the formation of red sublimate. It was identified as (3) (Found: C, 75.0; H, 3.5; N, 4.9. $C_{36}H_{20}N_2O_6$ requires C, 75.0; H, 3.5; N, 4.9%).

Preparation of pigment (B)

α-Aminoanthraquinone (10.6 g; 0.05 mole) in nitrobenzene (180 ml) was heated with s-phthaloyl chloride (5.0 g; 0.025 mole) with stirring. The temperature was slowly raised to 110° during 1 1/2 hr. and kept at 110° for 3 hr. The product was worked up as in the above experiment. Decomposing at 340-42° with red sublimate. Superposable IR spectrum with Pigment (A). Yield?

Action of phosphorous oxychloride and phthalic anhydride on α-aminoanthraquinone

To a homogeneous solution of α-aminoanthraquinone (5.6 g) and phthalic anhydride (3.0 g) in nitrobenzene (80 ml),

~~calcium~~ calcium oxide (0.5 g), urea (0.5 g) and phosphorous oxychloride were added at 30°. The mixture was stirred and heated to 110° during 3 1/2 hr., then maintained at 110° for 2 hr. After cooling to 60°, the reaction mixture was diluted with methanol (50 ml). The reddish yellow precipitate was filtered, washed with successively with methanol, hot 1% hydrochloric acid solution and finally with water and dried at 90° (1.5 g). Crystallisation from ODCB gave yellow microscopic needles (dec. 340-42°), identical with Pigment (A).

Reductive methylation of pigment (A)

The above product (2 g) was suspended in 10% aqueous sodium hydroxide (30 ml) and treated with sodium dithionite (3 g). Dimethyl sulphate (6 ml) was added at room temperature to the clear red vat and the mixture was kept on a shaker for 30 min. Excess alkali and sodium dithionite were tested as usual. The greenish yellow precipitate was crystallised repeatedly from benzene; the greenish yellow lustrous plates (1 g), had m.p. 253-54° (Found: C, 74.4; H, 5.0; N, 4.3. $C_{40}H_{32}N_2O_6$ requires C, 75.5; H, 5.0; H, 4.4%).

Purification of Helio Fast Yellow E-3R

The commercial sample was refluxed with ODCB, filtered hot and cooled gradually. The greenish yellow microscopic crystals were filtered, washed with ODCB and

dried. Like pigment (A) the compound decomposed at 340-42° with the formation of a red sublimate.

Purification of Patrician Yellow 123-2817

The commercial sample crystallised from ODCB in reddish yellow microscopic needles, which decomposed with the formation of a red sublimate at 340-42°.

Reductive methylation of Helio Fast Yellow E-3R and Patrician Yellow 21-2817

Reductive methylation of the pigments (2.0 g) was carried out as mentioned earlier. The products, after crystallisation from benzene, had m.p. 253-54°, undepressed on admixture with the reductive methylated derivative of pigment (A).

Alkaline hydrolysis of pigment (A)

The pigment (1 g) was refluxed with 10% sodium hydroxide in methyl cellosolve (ethylene glycol monomethyl ether) (100 ml) for 30 min. After cooling to room temperature, the red solution was diluted with an equal amount of water, when a red precipitate separated. It was filtered, washed with water and dried (0.75 g). Crystallisation from ethanol gave red needles, m.p. and mixed m.p. with 4-aminoanthraquinone, 252-53°.

Acid hydrolysis of pigment (A)

The pigment (0.2 g) was dissolved in conc.sulphuric acid (1 ml) and left at room temperature for an hour. Afterwards the red solution was poured into ice cold water and the red precipitate was filtered, washed and dried(0.17 g). The red needles from ethanol were identified as α-aminoanthraquinone, m.p. 252-53°.

Similarly, Helio Fast Yellow E-3R and Patrician Yellow 21-2817 gave α-aminoanthraquinone on treatment with conc. sulphuric acid.

Action of heat on pigment (A): Preparation of (5)

The pigment (1 g) was heated at ~~re~~ 2 mm. pressure for 3 hr. in a sublimation apparatus immersed in a metal bath at 360°. The reddish yellow sublimate was collected (0.8 g), extracted with boiling ethanol and filtered. Crystallisation of the residue (0.4 g) from benzene gave reddish yellow shining prisms, m.p. 296-98°; identified as (5). (Found: C, 74.4; H, 3.2; N, 4.5. $C_{22}H_{11}NO_4$ requires C, 74.8; H, 3.1; N, 4.0%).

Concentration of the ethanol solution gave red needles (0.3 g), m.p. 252-53° of α-aminoanthraquinone.

Preparation of morphanthridine-6,11-dione

To a mixture of conc. sulphuric acid (30 ml) and methylene chloride (20 ml) was cooled to 15°, anthraquinone (6 g) was added followed by sodium azide (2.2 g) in small portions over a 1 hr. period at 20°. The reaction mixture was stirred at room temperature for 3 hr., allowed to stand overnight, and then poured over a mixture of ice and water. The crude product was filtered, washed and dried (6.0 g). Crystallisation from acetic acid gave colourless crystals, m.p. 246-47° (lit.[17] 246.5-9°).

1-Nitro-4-methoxyanthraquinone

1-Nitro-4-hydroxyanthraquinone (30 g) in dry acetone (200 ml) was refluxed with dimethyl sulphate(40 ml) in presence of anhydrous potassium carbonate (120 g) for 24 hr. The solvent was distilled off. The residue was treated with water and left overnight. The solid was filtered, washed and dried, extracted with chloroform (1000 ml). The extract was concentrated and cooled when yellow needles separated (6 g), m.p. 266-68°. In the literature,[19] it is prepared by nitrating 1-methoxyanthraquinone with one mole of nitric acid. However, no m.p. is mentioned. (Found: C, 67.4; H, 3.4; N, 5.0. $C_{15}H_9NO_5$ requires C, 67.1; H, 3.2; N, 4.9%).

1-Amino-4-methoxyanthraquinone (14)

1-Nitro-4-methoxyanthraquinone (6 g) was refluxed with methanol (100 ml) containing sodium hydrogen sulphide (4 g) for 2 hr. The solvent was distilled off. The residue was taken in water and acidified. The violet precipitate was filtered, washed and dried (4 g); violet needles from toluene, m.p. 185-86° (lit.[20] m.p. 186°).

N-(4-methoxy-1-anthraquinonyl)phthalimide (16)

1-Amino-4-methoxyanthraquinone (2.5 g), ODCB (40 ml), thionyl chloride (0.1 ml) and s-phthaloyl chloride (2.2 g) were heated together as in the preparation of pigment (A). The product was purified by chromatography, and crystallisation from benzene gave yellow prisms, m.p. 270-71°. (Found: C, 72.4; H, 3.7; N, 3.6. $C_{23}H_{15}NO_5$ requires C, 72.1; H, 3.4; N, 3.7%).

N,N'-Bis(4-methoxy-1-anthraquinonyl)phthalamide (15)

s-Phthaloyl chloride (1.8 g) was added to a solution of 1-amino-4-methoxyanthraquinone (2.7 g) in nitrobenzene (30 ml) at 50° and the mixture was heated to 90-100° during 2 hr. The orange compound was filtered at 50° and the dried mixture was heated to 90-100° (2.0 g). Crystallisation from ODCB gave an orange amorphous powder; m.p. 303-305°. (Found: C, 71.4; H, 3.9; N, 4.9. $C_{38}H_{24}O_8N_2$ requires C, 71.7; H, 3.8; N, 4.4%).

N-(2-methyl-1-anthraquinonyl)phthalimide (18)

1-Amino-2-methylanthraquinone (11.8 g), ODCB(150 ml), thionyl chloride (0.5 g) and s-phthaloyl chloride (10.5 g) were heated together with stirring to 180° during 2 hr. and maintained at 180° for 3 hr. After cooling to 50°, the pale yellow solid was filtered, washed with ODCB and dried (12.0 g). Crystallisation from benzene gave pale yellow prisms; m.p. 253-54° (Found: C, 76.3; H, 4.0; N, 4.0. $C_{23}H_{13}NO_4$ requires C, 76.6; H, 3.6; N, 3.8%).

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P A R T - III

THE ACTION OF THIONYL CHLORIDE ON HYDROXYANTHRAQUINONES

***

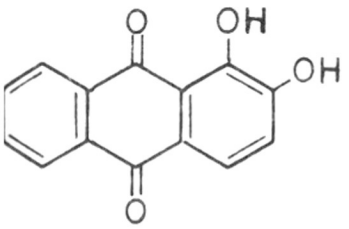
INTRODUCTION

In 1924 Green[1] reported the action of thionyl chloride on alizarin (1) and obtained thionyl alizarin (2), which was stable under anhydrous conditions, but reverted to alizarin in contact with moisture. He further studied[2] the action of boiling thionyl chloride on quinizarin (3). The product (A), deep red needles, m.p. 225-226°, has the molecular formula $C_{14}H_7ClO_3$. On boiling with acetic anhydride, alone or in presence of sulphuric acid, it gave quinizarin diacetate. Quinizarin was obtained by heating (A) with sulphuric acid or aqueous alkali. Oxidation of (A) with alkaline potassium permanganate yielded phthalic acid. The product of methylation with diazomethane was not uniform and contained varying amounts of chlorine. It differed in all these properties with 1-chloro-4-hydroxy-anthraquinone (4), m.p. 193°, which gave quinizarin only if heated with sulphuric acid and boric acid at 140° for several hours. Chlorine in (A) behaved as in an acid chloride. The deep red colour was in favour of an *o*-quinonoid structure. Based on these findings, Green gave structure (5), 10-chloro-1-hydroxy-4,9-anthraquinone to compound (A). Green[2] found that even prolonged reaction time did not give the dichloro-compound (6).

Raudnitz[3] in 1929 studied the reaction of thionyl chloride on quinizarin under pressure. He obtained Green's compound (A) upto 120° even after 10 hours. Increase of temperature up to 130° gave a red dichloro and a yellow trichloro compound. Further increase in the temperature, 160° to 180° resulted in the formation of a compound containing four chlorine atoms. The reaction of thionyl chloride on quinizarin under pressure at 135-40° for four hours gave exclusively a dichloro compound, ruby-red prisms, m.p. 241°, for which two structures (6) and (7) were considered. Structure (7) was favoured on the basis of the following chemical reactions. It was more stable to conc. sulphuric acid than (5), and gave 2-chloroquinizarin (8) on heating at 150° for several hours. It was stable to hot aqueous potassium hydroxide in which it did not dissolve. The reaction with aromatic amines was rather slow when compared with (A) and the same monoarylamino-chloro product was obtained even on longer heating in presence of boric acid.

Raudnitz[3] attributed the red colour of (7) to its o-quinonoid character, the isomeric 1-hydroxy-2,4-dichloroanthraquinone is bright yellow.

In connection with a study of 1,4-dihydroxy-anthrone and 1-hydroxy-4,9-anthraquinone (9) Zahn[4] reported



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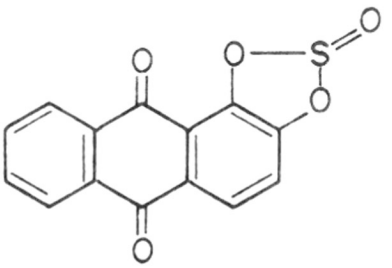

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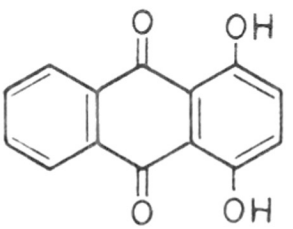

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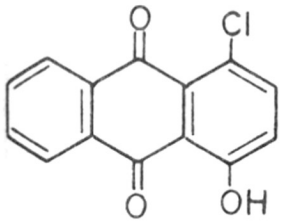

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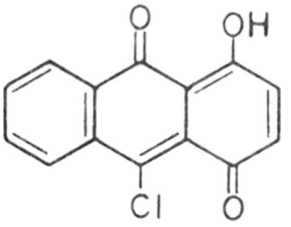

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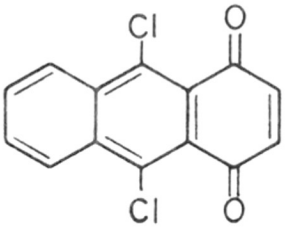

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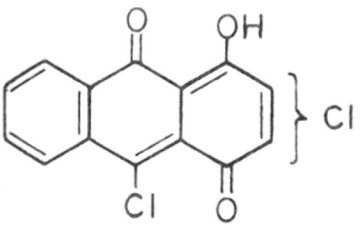

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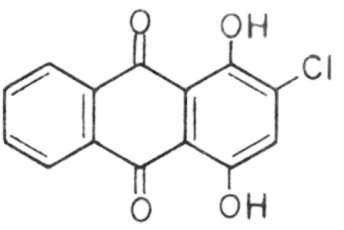

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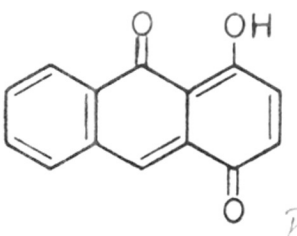

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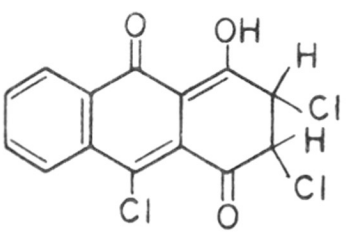

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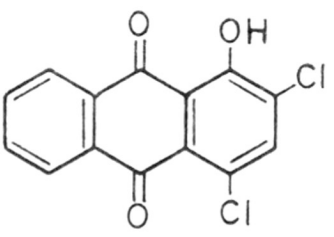

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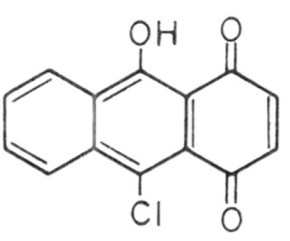

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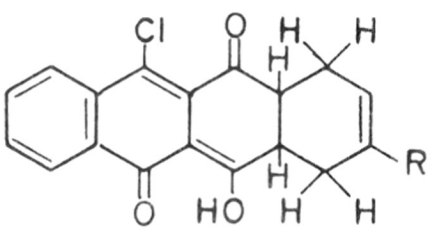
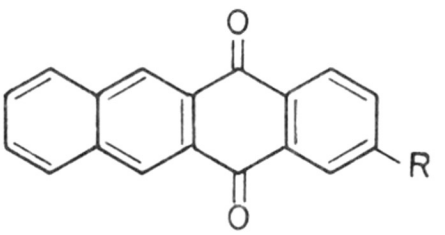


(13)

(R = H, CH_3, Cl)



(14)

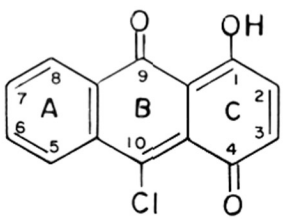
that there was perfect analogy between (A) and (9) in their properties, supporting structure (5) for (A). He prepared the monoacetyl derivative of (A) by cautious acetylation in pyridine. Halogens were added in the 2,3-positions to form dihalides of (A) and (9). Thus (5) yielded (10), which easily gave off hydrogen halide and changed into (7). However, the compound obtained by Zahn differed in its properties with the product described by Raudnitz[3] as having structure (7). He repeated Raudnitz's preparation and found that purification via the acetyl derivative yielded 1-hydroxy-2,4-dichloroanthraquinone(11).

Waldmann and Poppe[5] obtained (A) in 12% yield by heating maleic anhydride and 4-chloro-1-naphthol in aluminium chloride-sodium chloride melt at 180-220°. Although this reaction should normally yield (12), Waldmann assumed that the product had the structure (5) as the result of "a shift of the hydroxyl hydrogen". The formation of quinizarin from maleic anhydride and 1,4-dihydroxy-naphthalene was cited in support.

Recently Winkler[6] synthesised naphthacenequinones (14) by the Diels-Alder addition of (A) and 1,3-dienes. The adducts (13) were dehydrogenated to known and new hydroxynaphthacenequinones.

PRESENT WORK

An attempt is made in the present work to reinvestigate the reaction between quinizarin and thionyl chloride and the constitution of the product (A). If (A) is represented as (5), the NMR spectrum should show an AB pattern for the 2,3-protons of ring C as the two protons are nonequivalent. Two distinct o-coupled doublets should be seen separated by about 1 ppm. On the other hand, if



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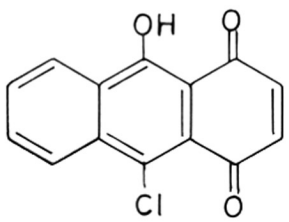


(12)

(A) has the structure (12), one would expect a singlet for the 2,3-protons.

Product (A), prepared according to Green[2] was sparingly soluble in solvents, such as $CDCl_3$ and acetone, but had adequate solubility in arsenic trichloride for determining the NMR spectrum. In the NMR spectrum (Fig. 1) of (A), the 2,3-protons do not appear as two o-coupled doublets, but as a two proton singlet at 3.03. The remaining two α-protons and two β-protons of ring A, which form an A_2B_2 system appear as two multiplets centered

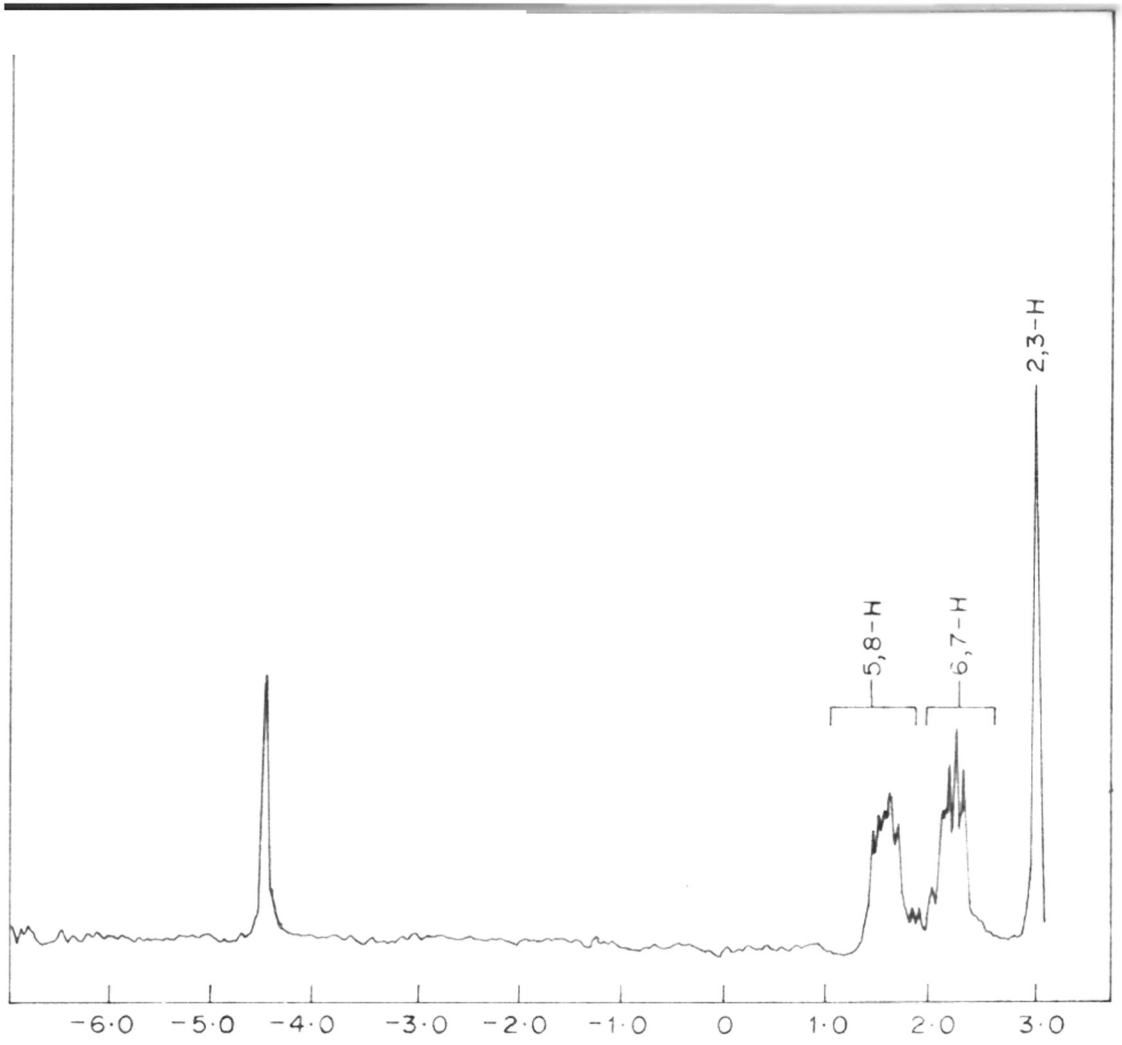


FIG. 1 NMR SPECTRUM OF 10-CHLORO-9-HYDROXY-1,4-ANTHRAQUINONE IN $AsCl_3$

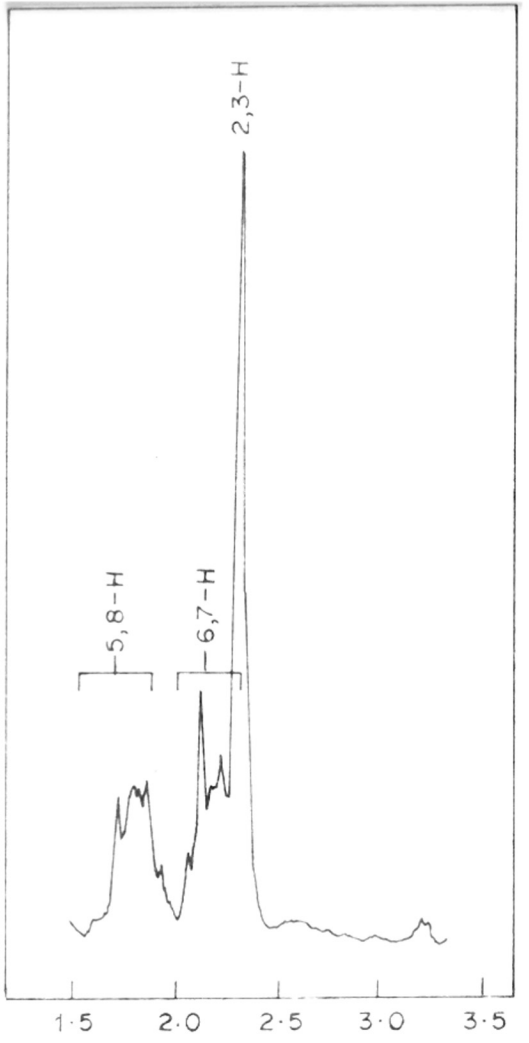


FIG.2 NMR SPECTRUM OF 9,10-DICHLORO-1,4-ANTHRAQUINONE IN $CDCl_3$

around 1.55 and 2.23 respectively. In quinizarin the two α-protons and two β-protons of the unsubstituted ring are seen as two multiplets at 1.81 and 2.15 respectively. The bonded hydroxyl group in (A) appears at -4.53. On the basis of the NMR spectrum of (A), structure (5) was ruled out.

The complex nature of the reaction of thionyl chloride with quinizarin was well understood when the reaction was carried out for several hours. Different products were obtained dependent upon the time of treatment. After 24 hours, only 40% of (A) was obtained. Column chromatography of the methanol extract of the residue gave yellow needles, m.p. 190-91°, $C_{14}H_6O_2Cl_2$, νmax. 1666 cm^{-1} (quinone C=O). Analysis showed the presence of two chlorine atoms. The NMR spectrum (Fig. 2) of the dichloro compound in $CDCl_3$ shows a two proton singlet at 2.37 assigned to the 2,3-protons. The 2,3-protons of ring C in (A) appear at 3.03 because of the interaction of arsenic trichloride with 1,4-carbonyls. The two 2-proton multiplets are seen at 1.82 and 2.18 (α- and β-H in ring A). Thus the compound has structure (6) which Green[2] did not obtain.

Although the NMR evidence supports structure (12), it is difficult to explain its formation unless one understands the behaviour of quinizarin in various chemical reactions, particularly its behaviour on reduction and its

reaction with primary amines,[7] in which quinizarin behaves predominantly as 9,10-dihydroxy-1,4-quinone (15). Quinizarin did not react with sulphuryl chloride which was unexpected on the basis of structure (3). It is reported[8] that the prolonged reaction of quinizarin with excess chlorine in glacial acetic acid gave the dichloro compound (17) in which the chlorine adds on the double bond at the angular carbon atom. These are some of the reactions cited for the unusual behaviour of quinizarin. The probable reaction of (15) with thionyl chloride to give (12) is through the formation of a chloro sulphite (16), a vinylogous ester, which on further heating decomposes through a cyclic intermediate as depicted in Chart 1. The chlorosulphite intermediate(16) breakdown is an "internal return" reaction which is normally observed in the reaction of alcohols with thionyl chloride to yield the corresponding alkyl halides. If excess of hydrogen chloride is formed in the reaction by the initial condensation of the 9,10-dihydroxy-1,4-anthraquinone and thionyl chloride, an ordinary displacement reaction may also take place. If the reaction is stopped at an intermediate stage, the product is predominantly (12) with traces of (6), and if the reaction is carried out for a prolonged time, the main product is (6). However, the second mode of reaction, as shown in chart 2, is unlikely and hydrogen chloride gas when formed in the reaction is

CHART 1

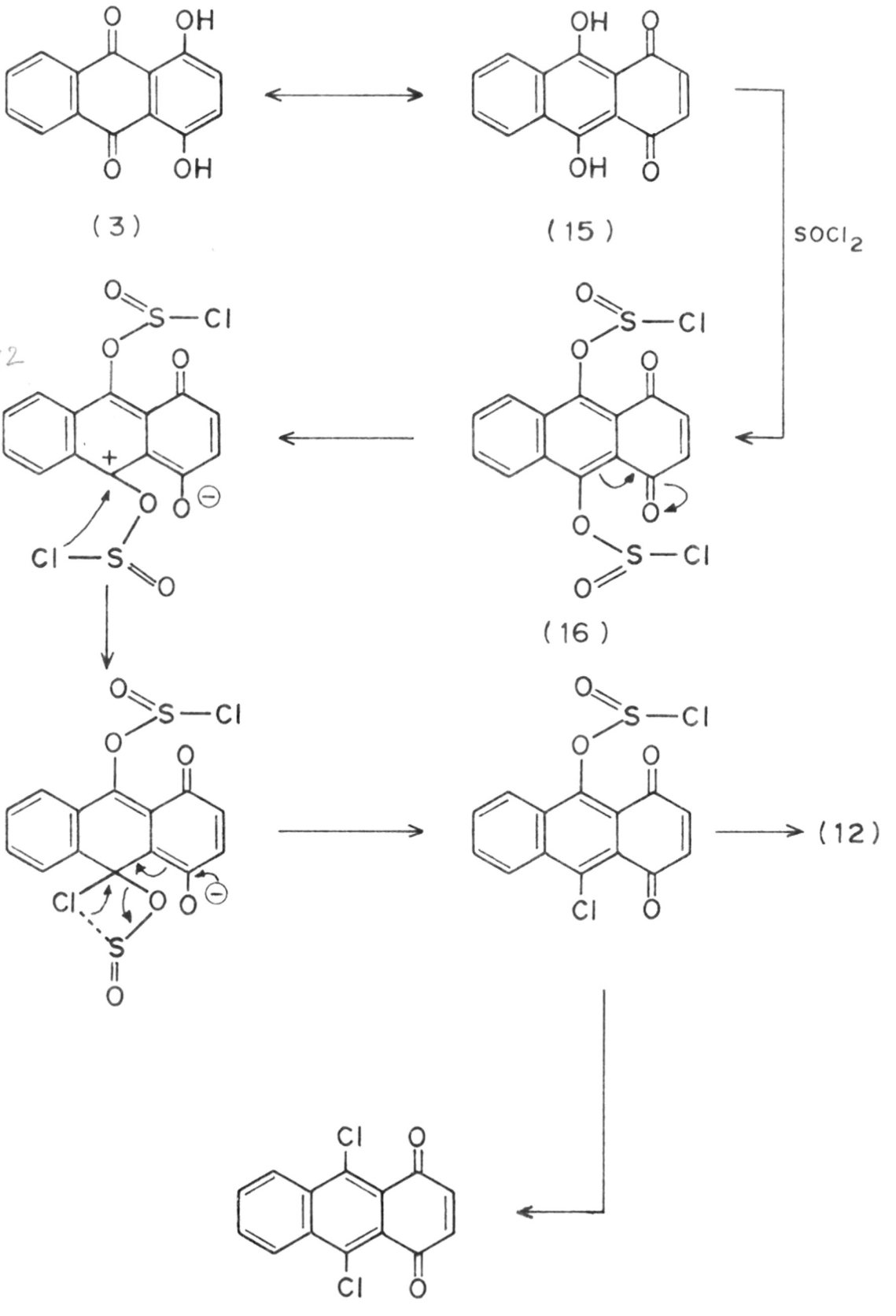
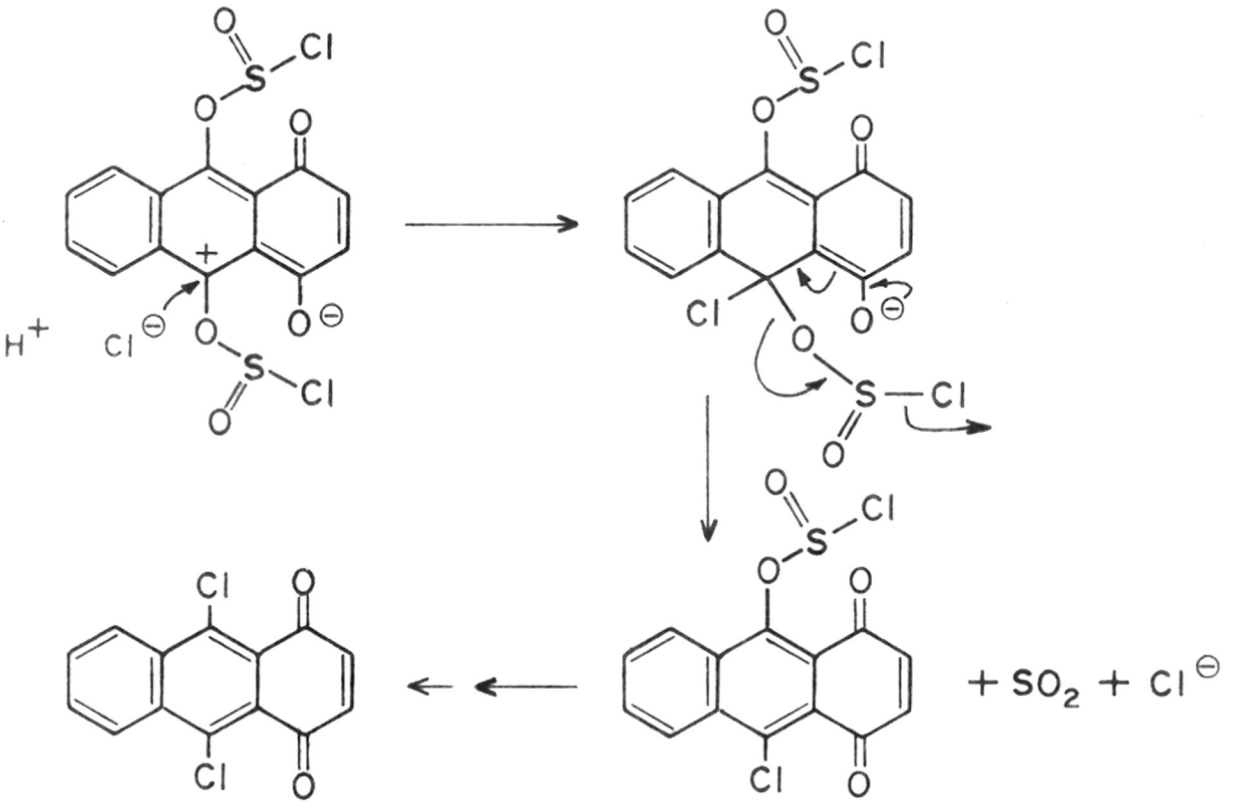
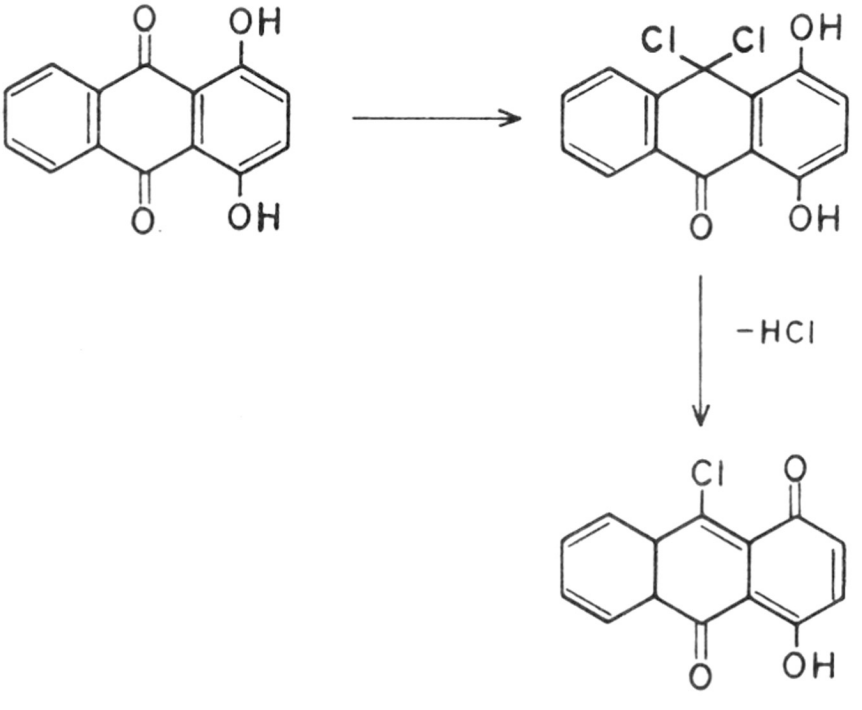


CHART 2



(6)

CHART 3

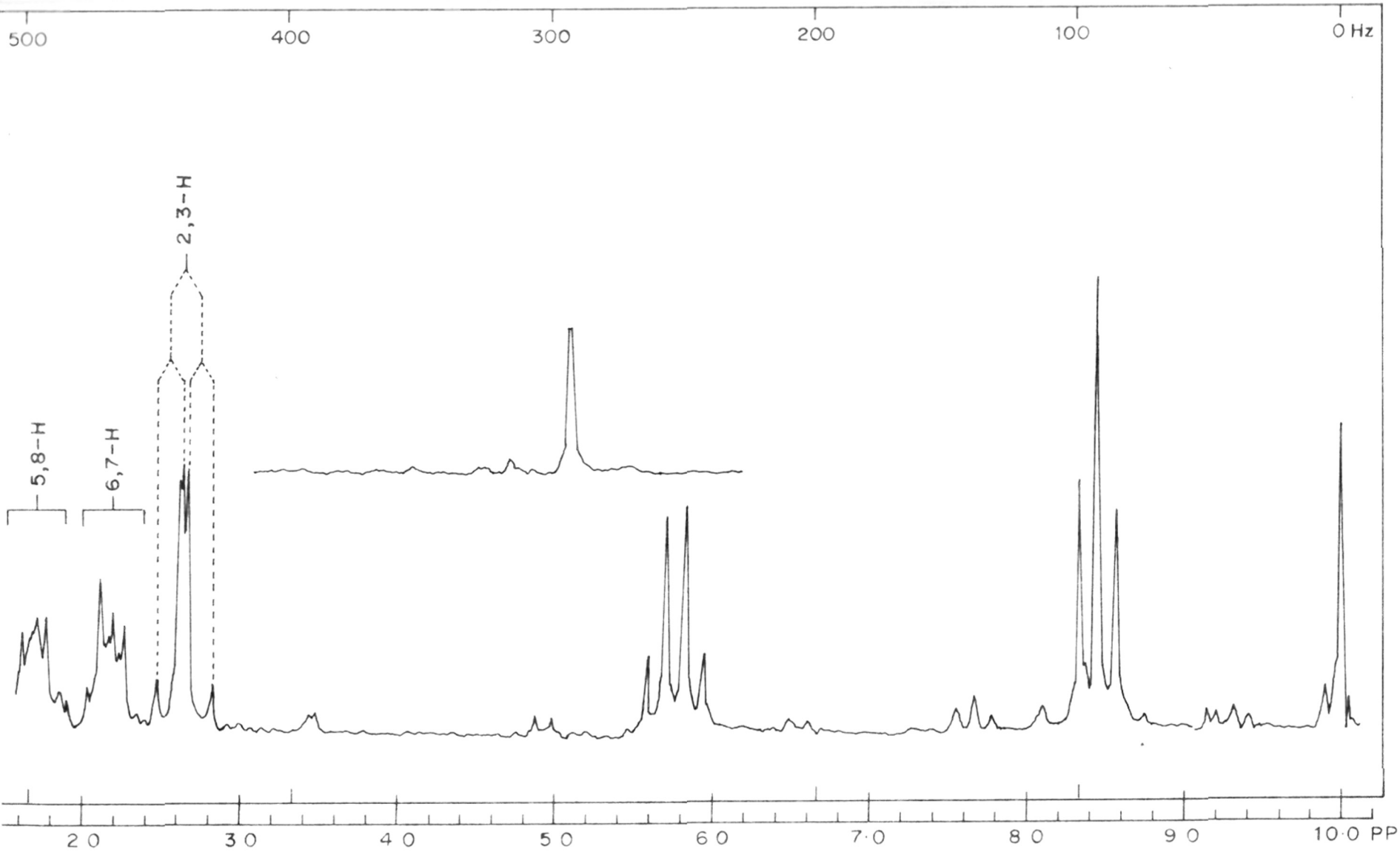


(5)

driven out of the solution and its ionisation in the reaction medium is not favourable.

Green[2] suggested that the carbonyl oxygen atom is replaced by two chlorine atoms (chart 3) in the first step and in the second step, one of these chlorine atoms combines with the hydrogen atom of the neighbouring hydroxyl group giving hydrogen chloride and product (A). However, this was ruled out by him as the 1,4-diacetoxyanthraquinone, anthraquinone and 1-hydroxyanthraquinone did not react[9,10] with thionyl chloride. In this connection, the claim of a recent patent[11] which describes the preparation of 1-hydroxy-2,4-dichloroanthraquinone (11) in 80% yield by refluxing quinizarin and thionyl chloride in dimethyl formamide is noteworthy.

Structure (12) also finds powerful support from two considerations: (a) the obviously higher resonance energy of (12) in comparison with (5), because the former contains an additional aromatic ring; and (b) anthra-4,9-quinone has not been isolated so far. Even an attempt[12] to prepare the extended quinone system, anthra-1,5-quinone (18) by mild dehydrogenation of 1,5-dihydroxy-2,6-dimethoxy-anthracene resulted in the formation of 5-hydroxy-6-methoxy-1,2-anthraquinone.

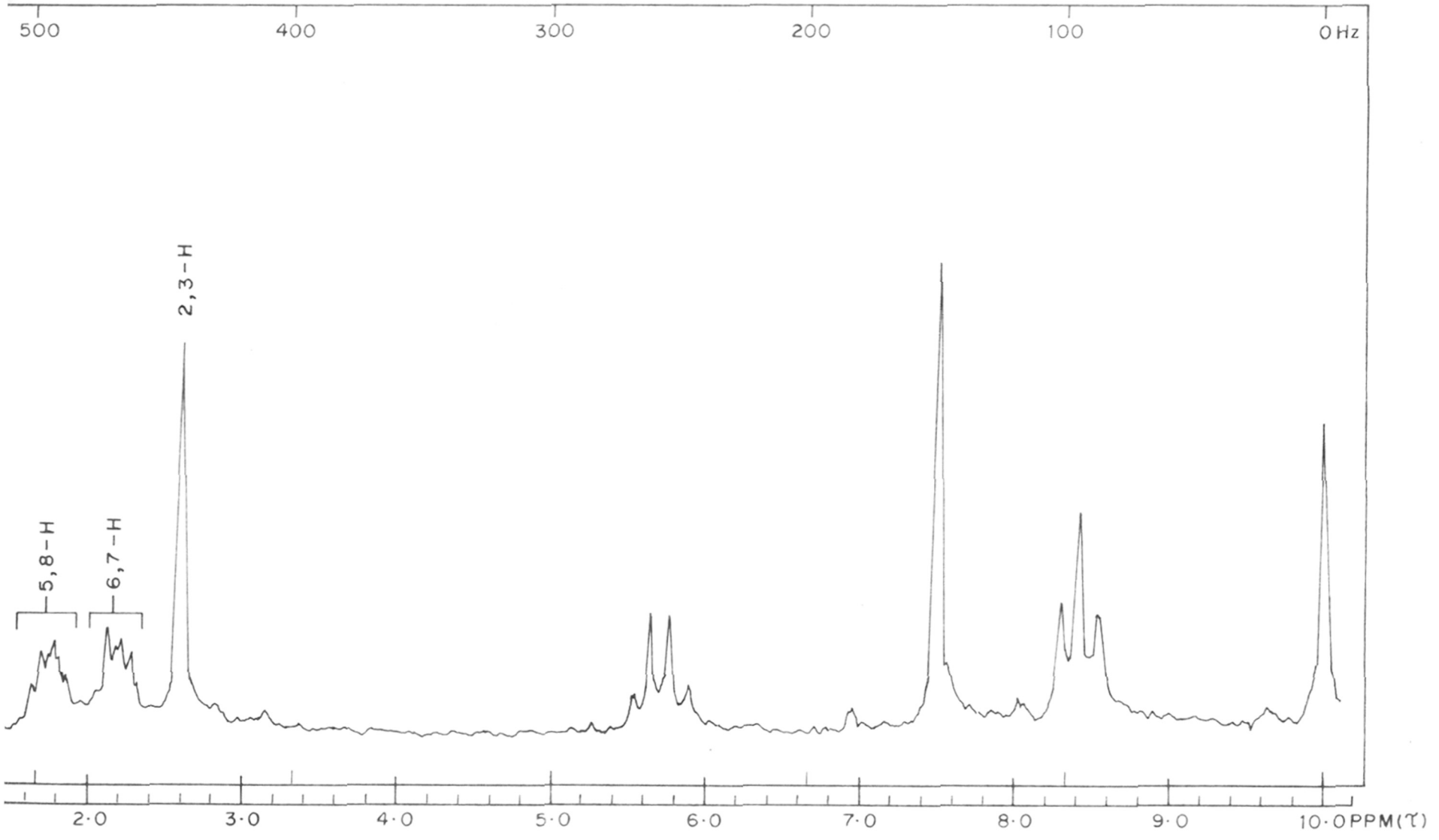


FIG·3 NMR SPECTRUM OF 10-ETHOXY-9-HYDROXY-1, 4-ANTHRAQUINONE IN $CDCl_3$

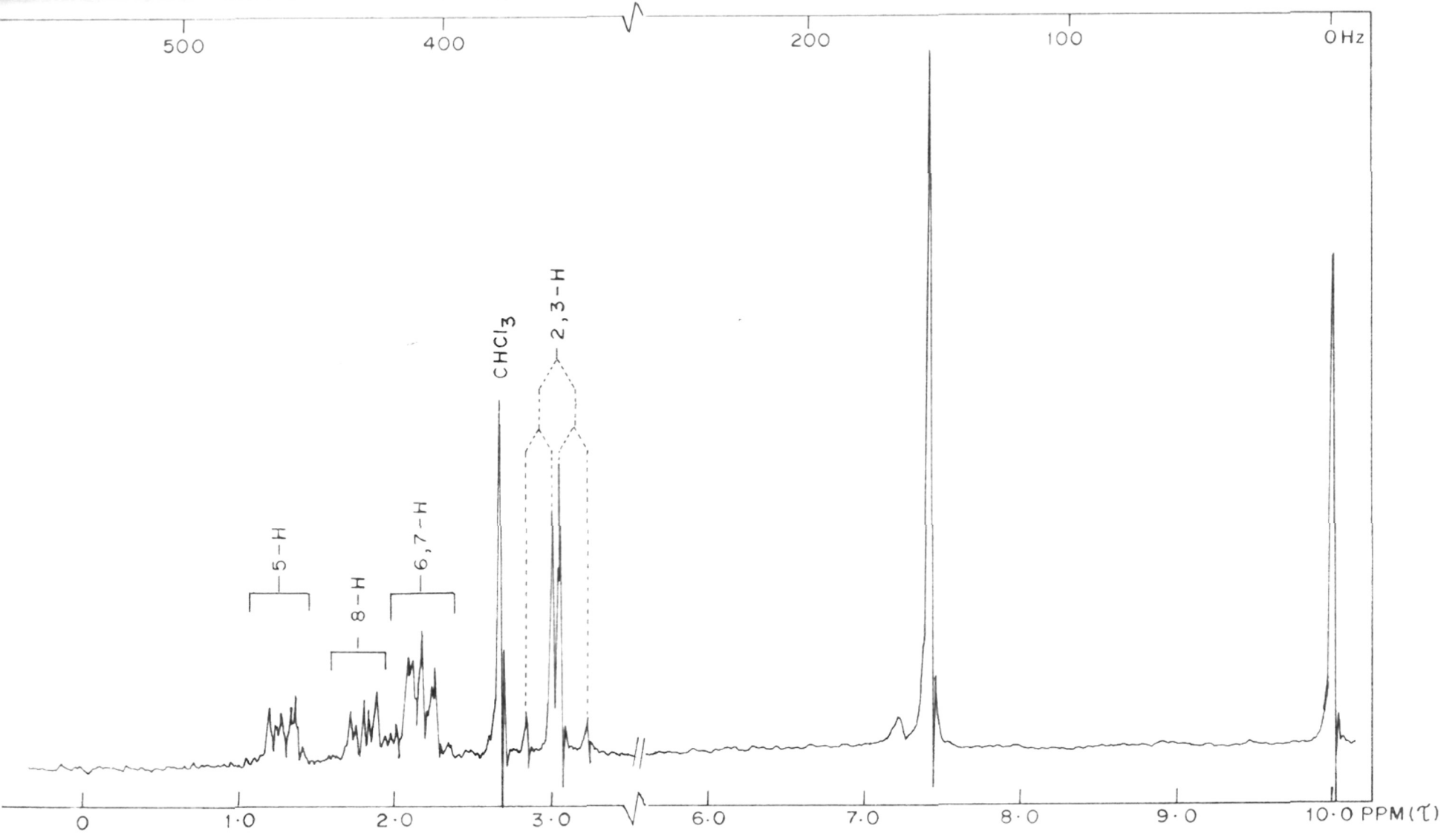
Green[2] was able to replace Cl by OEt in (A) by treatment with ethanol and hydrogen chloride. The preparation of this compound (B) was repeated and it was found that the NMR spectrum (Fig.3) of (B) in $CDCl_3$ shows the following signals: A 3-proton triplet (J=7 Hz) and a 2-proton quartet (J=7 Hz) at 8.5 and 5.78 are assigned to OEt. The four protons of ring A appear as an A_2B_2 pattern at 1.82 and 2.25 and the chelated hydroxyl at -2.87. The 2,3-protons of ring C are seen as two o-coupled doublets (J=9 Hz) at 2.6 and 2.8 unexpected on the basis of structure (19) for (B). This anamoly is probably due to steric effects resulting in slight variation in electron densitites at 2 and 3 positions. This conclusion is substantiated by acetylating compound (B) in which both 9 and 10 positions are substituted; the 2,3-protons, now are seen as a singlet at 2.68 (Fig. 4). The O-acetyl derivative of (19) was obtained by acetylating with acetic anhydride in presence of pyridine.

The O-acetyl derivative (21) of (A) which Green[2] failed to get has been reported by Zahn,[4] and was prepared in the present work. Its NMR spectrum (Fig. 5) in $CDCl_3$ shows the 2,3-protons as o-coupled doublets as in the NMR spectrum of (19).

Incidentally, the NMR spectrum of 1,4-anthraquinone (22) has not been reported so far, its preparation from



FIG·4 NMR SPECTRUM OF 10-ETHOXY-9-ACETOXY-1,4-ANTHRAQUINONE IN $CDCl_3$



FIG·5 NMR SPECTRUM OF 9-ACETOXY-10-CHLORO-1,4-ANTHRAQUINONE IN $CDCl_3$

quinizarin has been recently described.[13] In arsenic trichloride, a singlet appears at 3.0 for the 2,3-protons, in agreement with the value (3.03) for the corresponding protons of (A) supporting structure (12).

Similar 1,4-quinone system as in (12) was obtained by a study of the action of thionyl chloride on 6,7-dichloroquinizarin (23). 6,7-Dichloroquinizarin was prepared[14] by condensing 4,5-dichlorophthalic anhydride with hydroquinone in aluminium chloride-sodium chloride melt at 220°. The product, obtained by refluxing (23) with thionyl chloride, consisted of red needles, m.p. 266-67°, $C_{14}H_5Cl_3O_3$, had the structure (24); the NMR spectrum in arsenic trichloride shows a 2-proton singlet at 3.0 for the 2,3-protons.

C-arylation of 1,4-diaminoanthraquinone through the bis-sulphimide (25) has been described in a recent patent.[15] Addition of anisole to (25) can be effected by anhydrous aluminium chloride at about 10°. Repetition of this reaction on (12) resulted in a Friedel-Crafts acylation with the formation of (26). The NMR spectrum (Fig.6) of (26) in $CDCl_3$ shows two o-coupled doublets (J=9 Hz) for the 2,3-protons at 3 and 3.27. The four protons of the anisole nucleus appear as a singlet at 2.93. The mass spectrum (M^+ 330) and elemental analysis agree with structure (26).

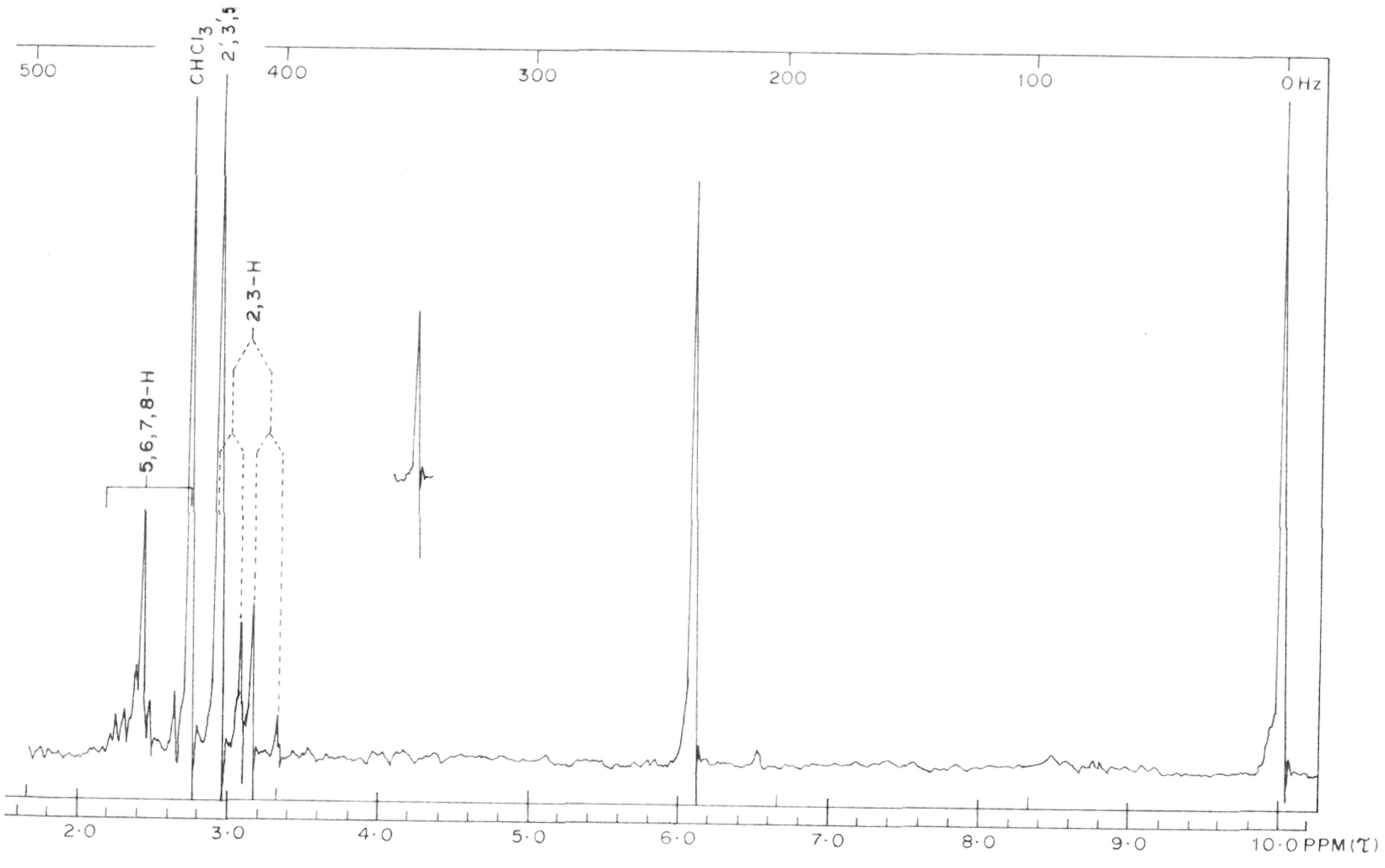
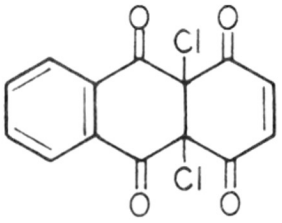


FIG. 6 NMR SPECTRUM OF 10-(4'-METHOXYPHENYL)-9-HYDROXY-1, 4-ANTHRAQUINONE IN $CDCl_3$



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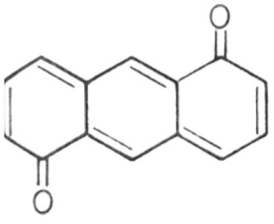

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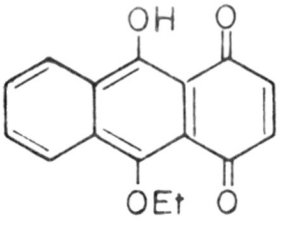

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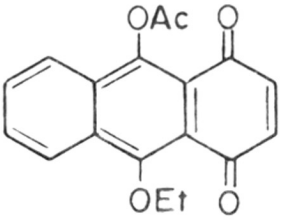

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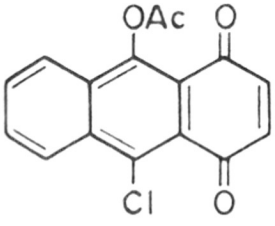

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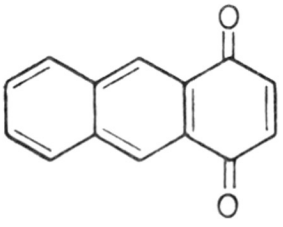

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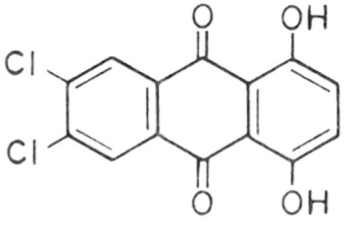

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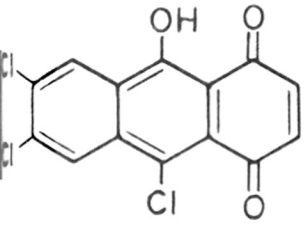

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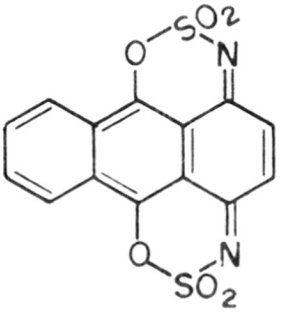

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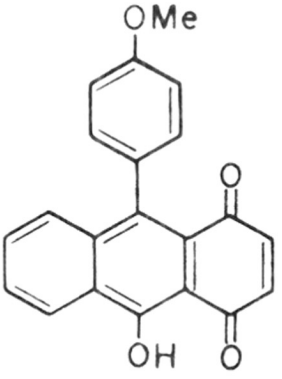

(26)

The chemical shifts of the protons of the compounds studied in the present investigation are tabulated in Table 1.

TABLE 1

Compound	Solvent	Chemical shift (τ)	Multiplicity	No. of protons	Assignments
(6)	$CDCl_3$	2.37	s	2	2,3-H
		2.18	m	2	6,7-H
		1.82	m	2	5,8-H
(12)	$AsCl_3$	3.03	s	2	2,3-H
		2.22	m	2	6,7-H
		1.55	m	2	5,8-H
		-4.53	s	1	9-OH
(19)	$CDCl_3$	8.5	t	3	10-OEt
		5.78	q	2	
		2.8	d(J=9 Hz)	1	2,3-H
		2.6	d(J=9 Hz)	1	
		2.25	m	2	6,7-H
		1.82	m	2	5,8-H
		-2.87	s	1	9-OH
(20)	$CDCl_3$	8.5	t	3	10-OEt
		5.77	q	2	
		7.57	s	3	9-$COCH_3$
		2.68	s	2	2,3-H
		2.27	m	2	6,7-H
		1.83	m	2	5,8-H

Table 1 contd.

(21)	$CDCl_3$	7.4	s	3	9-$COCH_3$
		3.08	d(J=9 Hz)	1	2,3-H
		3.0	d(J=9 Hz)	1	
		2.0-2.33	m	2	6,7-H
		1.83	m	1	8-H
		1.33	m	1	5-H
(24)	$AsCl_3$	3.0	s	2	2,3-H
		2.53	s	1	5-H
		2.42	s	1	8-H
		-4.47	s	1	9-OH
(26)	$CDCl_3$	6.1	s	3	4'-OMe
		3.27	d	1	2,3-H
		3.0	d	1	
		2.93	s	4	2',3',5',6'-H
		2.23-2.75	m	4	5,6,7,8-H
		-4.1	s	1	9-OH

EXPERIMENTAL

10-Chloro-9-hydroxy-1,4-anthraquinone (12)

Quinizarin (1 g) was refluxed with thionyl chloride (15 ml) for 8 hr., solution occurred after a few minutes. The deep red liquid was concentrated to half bulk. On cooling it deposited fine, dark red needles (0.8 g), m.p. 225-226° (lit.[2] m.p. 225-226°).

10-Chloro-9-hydroxy-1,4-anthraquinone (12) and 9,10-dichloro-1,4-anthraquinone (6)

Quinizarin (30 g) was refluxed with thionyl chloride (120 ml) for 24 hr. The deep red liquid was concentrated to half bulk. On cooling, dark red microscopic needles separated, which were filtered, washed with dry benzene and dry ether; yield 13.0 g., m.p. 225-26°, identified as (12).

The mother liquor and washings were mixed and distilled under reduced pressure. The residue was triturated with a small amount of dry ether, and the brown amorphous product (17 g) collected. When 1 g. of the product was extracted with boiling methanol (200 ml) and the extract concentrated (50 ml), a yellowish red compound (0.6 g) separated on cooling. Chromatography on a silica gel column and benzene-hexane (60:40) gave 9,10-dichloro-

1,4-anthraquinone (0.35 g), yellow needles from methanol, m.p. 190-91° (Found: C, 60.8; H, 2.1; Cl, 25.2. $C_{14}H_6Cl_2O_2$ requires C, 60.4; H, 2.2; Cl, 25.6%).

10-Ethoxy-9-hydroxy-1,4-anthraquinone (19)

10-Chloro-1-hydroxy-4,9-anthraquinone (2.5 g) was refluxed with ethanol (200 ml) containing 3% dry hydrogen chloride for 4 hr. The red solution became dark green and flourescent. The hot solution was filtered, concentrated and cooled. The product, purified by column chromatography on silica gel and benzene. Crystallised from ethanol in orange-red needles, m.p. 144-45° (lit.[2] 135°) (Found: C, 72.0; H, 4.6. $C_{16}H_{12}O_4$ requires C, 71.6; H, 4.5%).

10-Ethoxy-9-acetoxy-1,4-anthraquinone (20)

Treatment of (19) with pyridine and acetic anhydride at room temperature and crystallisation from methanol gave yellow needles, m.p. 150-51° (Found: C, 69.5; H, 4.4. $C_{18}H_{14}O_5$ requires C, 69.8; H, 4.5%).

9-Acetoxy-10-chloro-1,4-anthraquinone (21)

A mixture of acetic anhydride (5 ml), pyridine (5 ml) and (12) (0.5 g) was heated at 60-70° until a clear solution was obtained. It was cooled immediately to room temperature and poured into ice water. The yellow precipitate

crystallised from benzene-hexane in yellow microscopic needles, m.p. 196-97° (lit.[4] 196-97°).

10-(4'-methoxyphenyl)-9-hydroxy-1,4-anthraquinone(26)

Anhydrous aluminium chloride (1 g) was dissolved in anisole (3 ml) at 50°. The solution was cooled to 10° and treated with (12) (1.0 g). A violet solution was formed. The reaction mixture was kept on a shaker for an hour at room temperature, treated with hydrochloric acid (40ml), and heated on a water-bath for an hour. The product was taken up in ether (100ml), and crystallisation from benzene gave reddish brown lustrous prisms (0.5 g), m.p. 212-13° (Found: C, 76.7; H, 4.5. $C_{21}H_{14}O_4$ requires C, 76.4; H, 4.2%).

6,7,10-Trichloro-9-hydroxy-1,4-anthraquinone (24)

6,7-Dichloroquinizarin (2 g) was refluxed with thionyl chloride (25 ml) for 24 hr. The product crystallised from benzene in red needles (1 g), m.p. 266-67° (Found: C, 51.6; H, 1.8; Cl, 32.0. $C_{14}H_5O_3Cl_3$ requires C, 51.5; H, 1.5; Cl, 32.2%).

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P A R T - IV

SYNTHESIS OF *s*-TRIAZOLO-*s*-TRIAZINES

DERIVATIVES OF 2-HYDRAZINO-*s*-TRIAZINE$

***

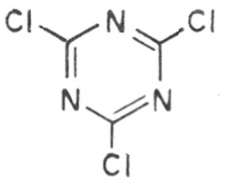
INTRODUCTION

The s-triazine ring provides a useful chromophore insulating group in the synthesis of dyes.[1] Cyanuric chloride (1) which has been known for over eighty years, is a remarkable substance with tremendous potentialities as an intermediate for the synthesis, because the three nitrogen atoms in the aromatic ring system render the three chlorine atoms highly labile and readily susceptible to nucleophilic substitution. Thus it can be condensed successively with three amines, alcohols or phenols in presence of a base. The reactivity of the three chlorine atoms in cyanuric chloride, which has been used in recent years with spectacular success for the production of dyes ("reactive dyes") which enter into covalent combination with cellulose, enables a wide variety of dyes of the general type (2) to be built up.[2]

As early as 1901, Pellizari and Roncaglilo[3] reported the condensation of dicyandiamide (3) with guanazole (4). The assigned structure (5) to the condensation product was subsequently revised by Kaiser *et al.*[4] and structure (6) was assigned to it. This was the first representative of 1,2,4-triazolo[4,3-a]-s-triazine (7) ring system. The synthesis of eight compounds of this

bicyclic ring system (7) have been described in the chemistry of "s-triazine and derivatives".[5] In general, these compounds were synthesised by mixing and heating dicyandiamide (3) and 1,2,4-triazole derivative (8) where R is an aliphatic or aromatic radical. The structures assigned to these compounds were only tentative as the products are either 1,2,4-triazolo-s-triazines or 1,3,4-triazolo-s-triazines. Recently, the synthesis of derivatives of (7) by treating dicyandiamide with hydrazine hydrate has been reported.[7]

The synthesis of s-triazolo[4,3-a]-s-triazine, starting from s-triazines on which the s-triazole ring was built, dates from 1966. In that year, Tisler and co-workers[8] reported the preparation of 3-phenyl-5,7-bismorpholino-s-triazolo[4,3-a]-s-triazine (10) by subjecting the corresponding benzylidene derivative (11) of 2-hydrazino-s-triazine to oxidative cyclisation with lead tetraacetate or bromine. However, the oxidative cyclisation of the corresponding ethylidene derivatives resulted in the formation of a mixture of compounds from which an analytically pure compound could not be obtained. Employing the above method, the oxidative cyclisation of benzylidene derivatives of unsymmetrically substituted 2-hydrazino-s-triazines were also studied[9] by the same



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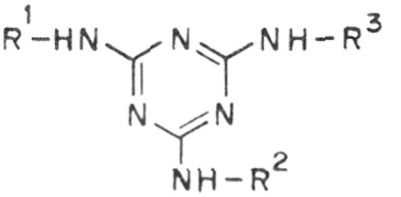

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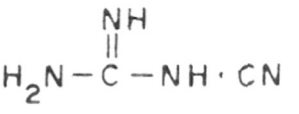

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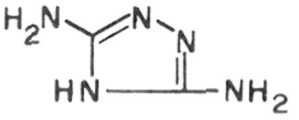

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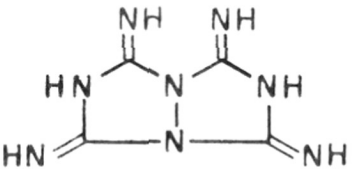

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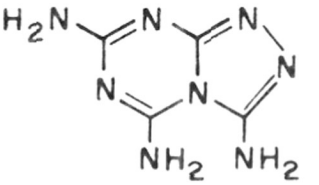

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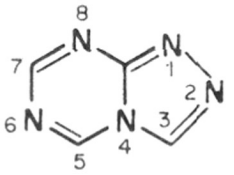

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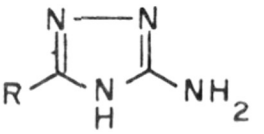

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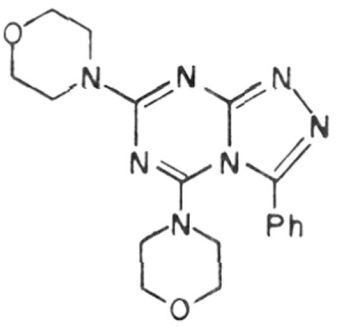

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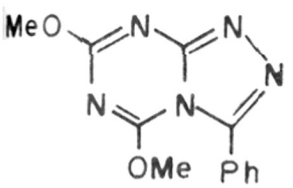

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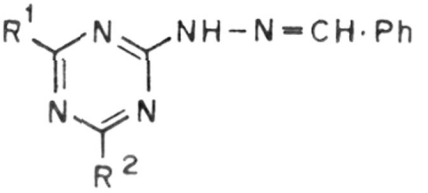

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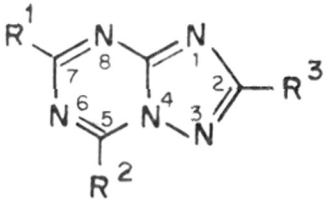

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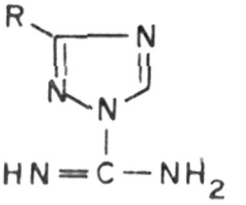

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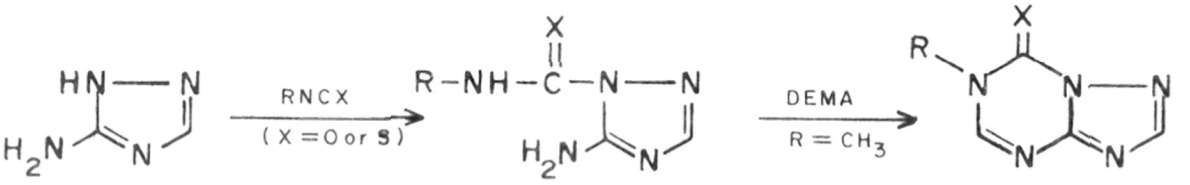
SCHEME 1



(14) (15) (16)

workers. They also observed that the oxidative cyclisation of 2-benzylidenehydrazino-*s*-triazines afforded mainly the 3-phenyl-*s*-triazolo[4,3-a]-*s*-triazines and under the experimental conditions there was no eventual isomerisation to the *s*-triazolo[2,3-a]-*s*-triazine (12) (nomenclature according to Ring Index).

The known representatives of *s*-triazolo[1,5-a]-*s*-triazine system (12) (nomenclature according to Chemical Abstracts) were synthesised in 1970 by Bokaldere and Grinshteins.[10] They synthesised 2-substituted 7-amino-1,2,4-triazolo[1,5-a]-*s*-triazines (12; R^2=H, R^1=NH_2; R^3=Me, Et, Pr, Ph, *p*-$MeOC_6H_4$) by the reaction of 3-substituted-5-amino-1-guanyl-1,2,4-triazoles (13) with orthoformic ester or 100% formic acid. Few *s*-triazolo[1,5-a]-*s*-triazines were prepared[11] starting from 3-amino-*s*-triazole (14) by the route mentioned in Scheme 1, using diethoxymethyl acetate (DEMA) as condensing agent. However, the addition of either isocyanate or isothiocyanate to (14) is a complicated reaction as theoritically four mono substituted products are possible depending upon whether the addition taken place at the amino group or at one of the three different ring nitrogens.

PRESENT WORK

Preliminary work in this laboratory has shown[12] that intermediates such as (17) can be used for the preparation of (a) azo dyes such as (21); and (b) intermediates with an additional ring system (e.g. pyrazolone) for constructing more complex dyes or more effective colour insulators than the parent triazine.

When this work was iniated, the few known s-triazolo[4,3-a]-s-triazines were prepared from substituted triazoles and dicyandiamide as reviewed in the introduction. Failure to obtain the 3-alkyl-s-triazolo[4,3-a]-s-triazines by Tisler et al.[8] by the oxidative cyclisation of ethylidene derivatives of 2-hydrazino-s-triazine led us to investigate this problem. In the present work, 3-alkyl and 3-phenyl-s-triazolo[4,3-a]-s-triazines were synthesised and their isomerisation to s-triazolo[1,5-a]-s-triazines (Chemical Abstract nomenclature is being followed in the present work) was studied. The present work dealt with symmetrically substituted 2-hydrazino-s-triazines (17). The 2-hydrazino-s-triazines (17) were readily prepared by the reaction of 4,6-disubstituted-2-chloro-s-triazine with alcoholic hydrazine hydrate in excess. The first 2-hydrazino-s-

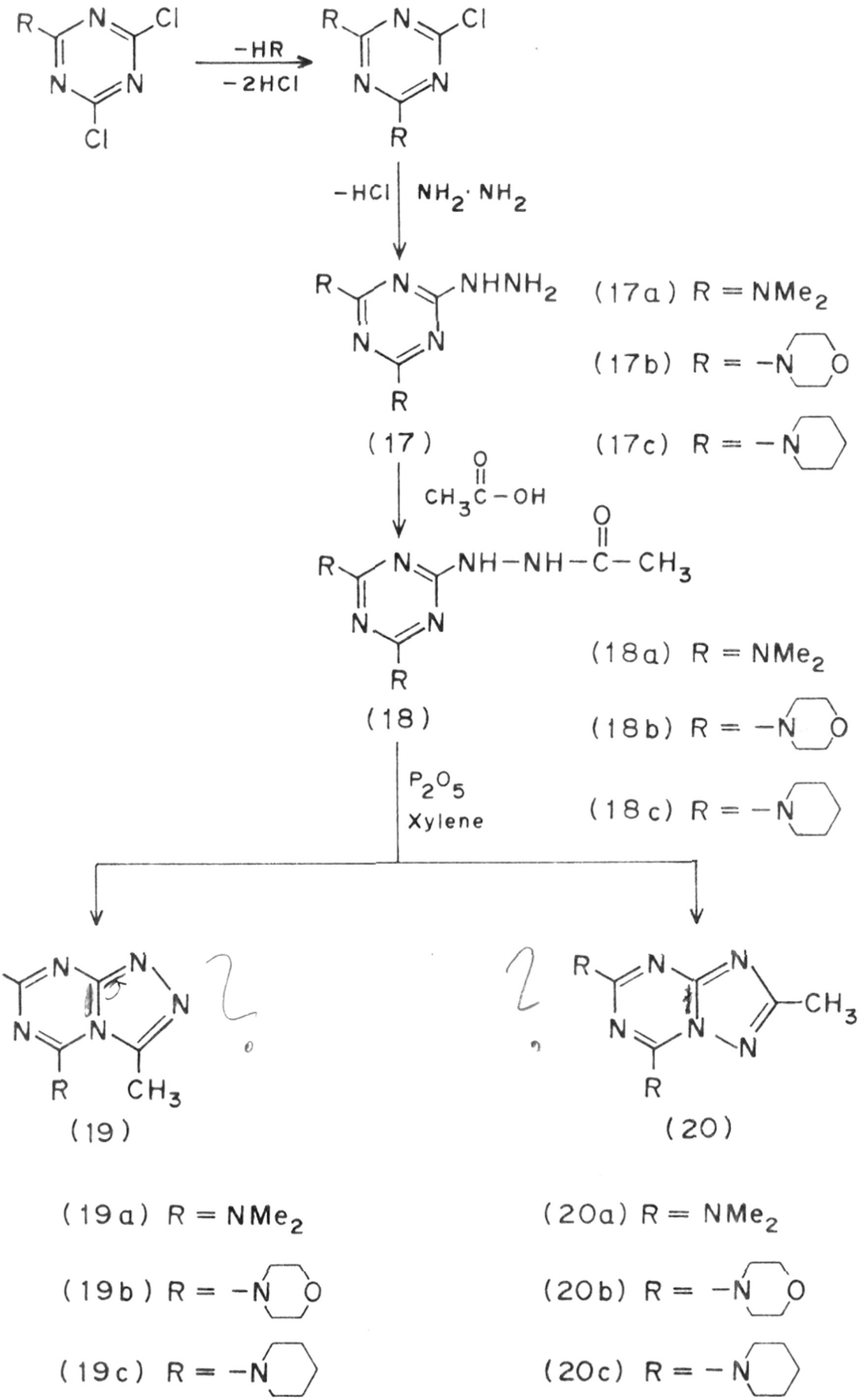
triazine prepared in the present investigation was 2-hydrazino-4,6-bis(dimethylamino)-s-triazine (17a), which was obtained by refluxing the 2-chloro-4,6-bis (dimethylamino)-s-triazine with hydrazine hydrate in ethanol. 2-Chloro-4,6-bis(dimethylamino)-s-triazine was prepared from cyanuric chloride by the replacement of two chlorine atoms by dimethylamino groups.

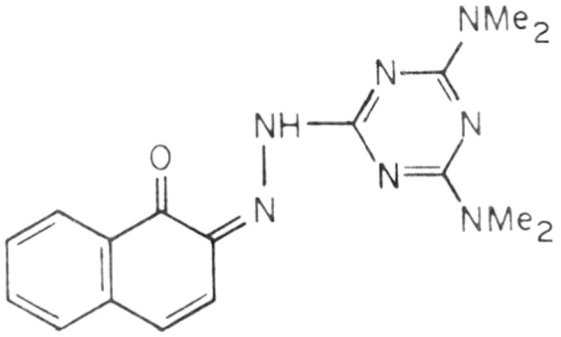
An attempt to prepare the 5,7-bis(dimethylamino) s-triazolo[4,3-a]-s-triazine using ethyl ortho-formate as a condensing agent was unsuccessful. The analogous s-triazolo[4,3-a] pyrimidines (22) have been prepared[13,14] by cyclisation of 2-hydrazino pyrimidines (23) with ortho-esters. It has been observed in the literature that 2-hydrazinopyridines[15] and 2-hydrazinopyrimidines undergo ring closure with extreme ease in presence of carboxylic acids, acid anhydrides or esters.

Treatment of (17a) with acetic anhydride in presence of pyridine gave the tris-acetamido derivative (24) and not the expected 3-methyl-5,7-bis(dimethylamino) s-triazolo[4,3-a]-s-triazine (19a). The assigned structure (24) was based on the NMR spectrum in $CDCl_3$ which shows three singlets at 6.86, 7.16 and 7.65 integrating for 12, 3 and 6-protons respectively. The singlets at 7.16 and 7.65 can be assigned to three acetyl groups

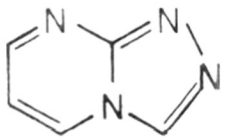
attached to the nitrogen atoms of the hydrazine moiety. Elemental analysis and molecular weight (M^+ 323) confirmed the structure (24). The hydrazine (17a) when boiled with acetic acid gave a compound, m.p. 175-76° and analysed for $C_9H_{17}N_7O$. IR spectrum in nujol mull shows a characteristic peak at 1685 cm^{-1} assigned to C=O band. Thus the compound was identified as the hydrazide (18a) and not the bicyclic product (19a). The isolation of the uncyclised hydrazide (18a) indicates that a dimethylamino group at 4- and 6-position of the s-triazine nucleus is bulky enough to provide some steric hindrance to the ring closure reaction. The formation of uncyclised intermediate like (18a) was also observed in the pyrimidine[19,20] series.

An attempt to cyclise (18a) by refluxing in anhydrous benzene with p-toluene sulphonic acid resulted in the quantitative recovery of the starting material. Upon refluxing (18a) in dimethyl sulfoxide (DMSO), a compound, decomposing at 315-16°, was obtained. IR spectrum of the DMSO reaction product in $CHCl_3$ shows a peak at 1682 cm^{-1}, which revealed the presence of a carbonyl group, unexpected on the basis of the bicyclic product (19a).


-HR
-2HCl
-HCl
NH2·NH2
CH3C(=O)-OH
P2O5
Xylene
(17a) R = NMe2
(17b) R = -N O
(17c) R = -N
(17)
(18a) R = NMe2
(18b) R = -N O
(18c) R = -N
(18)
(19)
(20)
(19a) R = NMe2
(19b) R = -N O
(19c) R = -N
(20a) R = NMe2
(20b) R = -N O
(20c) R = -N



(21)



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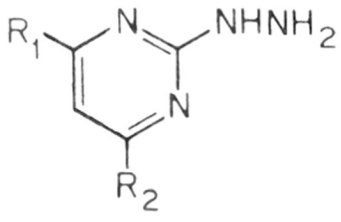
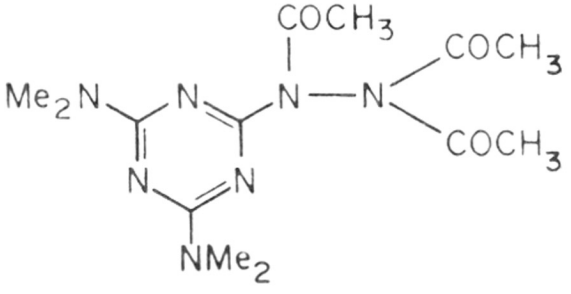
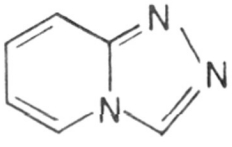


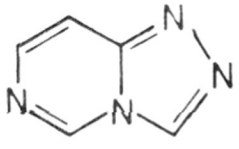
(23)



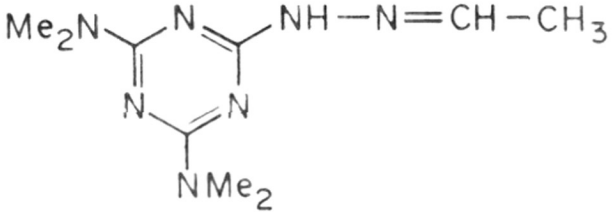
(24)



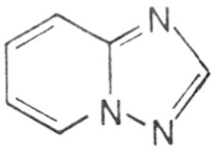
(25)



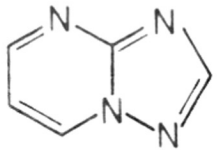
(26)



(27)



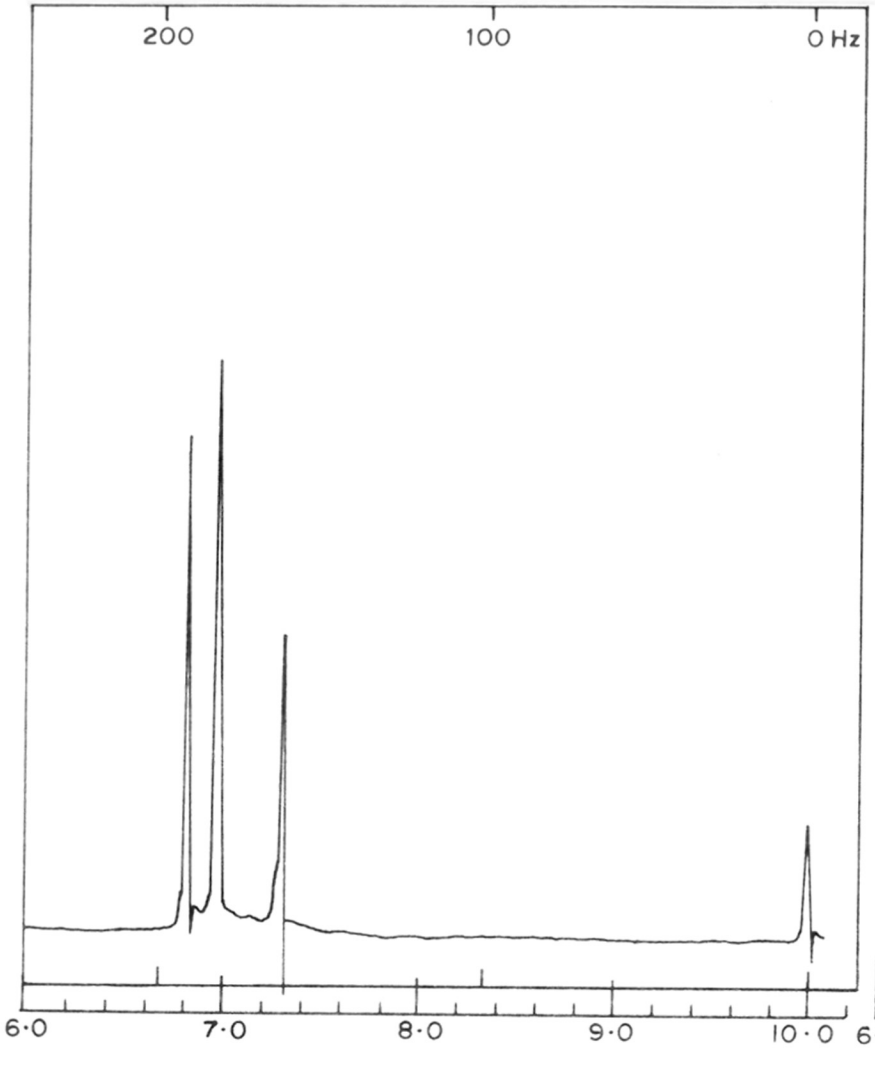
(28)



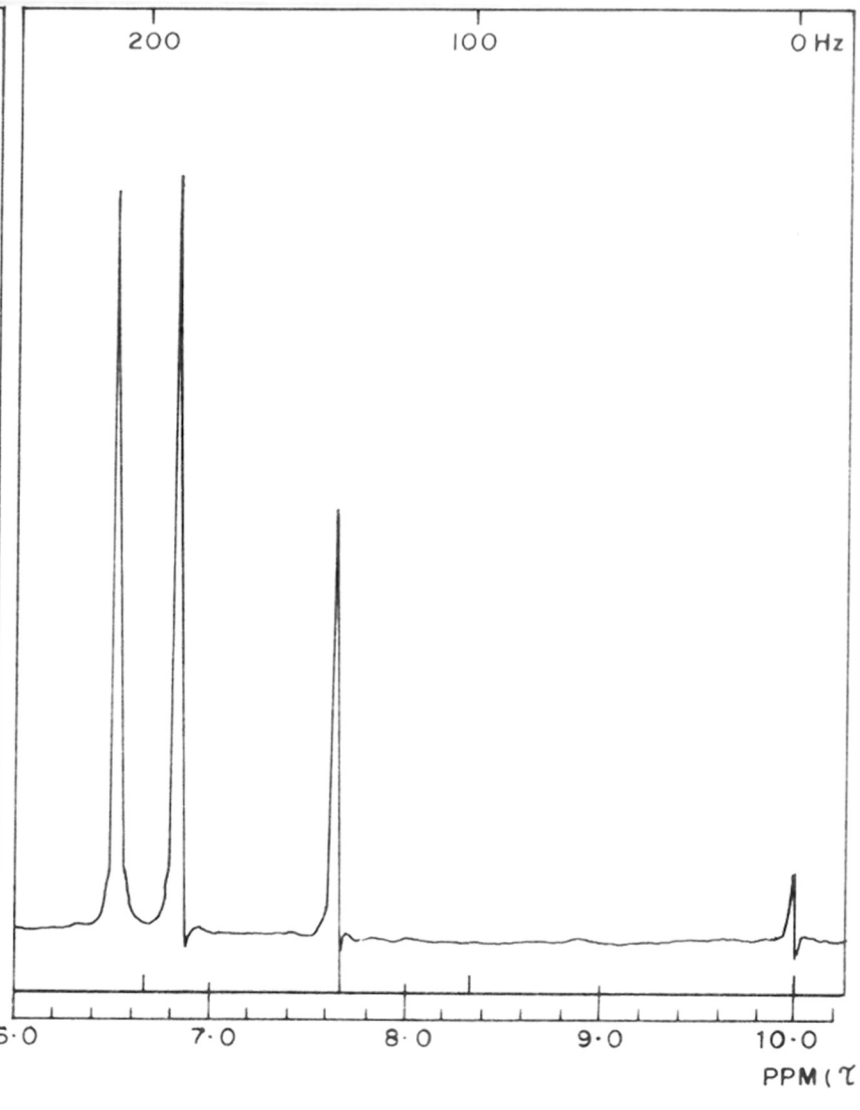
(29)

Cyclodehydration of (18a) was effected by refluxing with phosphorous pentoxide in anhydrous xylene for 20 hrs. After removal of the solvent, the residue was dissolved in water and the acidic solution was made alkaline with 40% aqueous potassium hydroxide. The compound (A), obtained, was crystallised from petroleum ether (60-80°) in colourless needles, m.p.165°. Molecular weight (M^{+} 221) and elemental analysis agreed to the molecular formula $C_9H_{15}N_7$. IR spectrum of (A) in $CHCl_3$ shows the absence of carbonyl group. NMR spectrum (Fig.1) of (A) in $CDCl_3$ shows three singlets at 6.52 (6H), 6.81(6H) and 7.6(3H) assigned to bis-(dimethylamino-) and C-Me groups respectively. Thus compound (A) is a bicyclic product, but two structures (19a) and (20a) were considered for it, because under the experimental conditions there was every possibility of isomerisation of (19a) to (20a). Similar isomerisation in dilute acid, base or merely by the application of heat have been reported in the s-triazolo [4,3-a] pyridine[21] (25) and s-triazolo[4,3-c][22]-pyrimidines (26) and [4,3-a] pyrimidines[18,19,23,24] (22) series.

An attempt was made to synthesise (19a) under the conditions where the eventual isomerisation to (20a) does not take place. The oxidative cyclisation of the ethylidene derivative (27) of 2-hydrazino-s-triazine (19a)



FIG·2 NMR SPECTRUM OF 3-METHYL-5,7-BIS (DIMETHYLAMINO)-s-TRIAZOLO-(4,3-a)-s-TRIAZINE IN $CDCl_3$



FIG·1 NMR SPECTRUM OF 2-METHYL-5,7-BIS (DIMETHYLAMINO)-s-TRIAZOLO(1,5-a)-s-TRIAZINE IN $CDCl_3$

using lead tetraacetate in benzene at 20-30° gave a mixture of products, a reaction which has been reported earlier.[8]

The authentic representatives of (20) were prepared[10,11] by utilising the s-triazole nucleus and building up the s-triazine portion of the fused ring system. However, these methods involved the formation of a mixture of compounds. So it was thought that any variation of the reaction conditions in the cyclodehydration of (18a) with phosphorous pentoxide might lead to the isolation of two compounds. Thus instead of making the reaction mixture strongly alkaline with potassium hydroxide, the acidic solution was brought to nearly neutral (pH 6-7) by adding a saturated solution of aqueous sodium carbonate. The product was thus resulted showed to be a mixture of two compounds on thin layer chromatography (TLC) (silica gel - $CHCl_3$, MeOH; 95:5). They were separated on a silica gel column using the same solvent system. The fast moving compound was found to be identical with product (A) and the slow moving product (B), m.p. 186-87° (M^+ 221) is an isomer of (A). The NMR spectrum (Fig.2) of (B) shows also three singlets for the methyl groups as in (A), but their chemical shifts have shown slight variations. The singlets in the NMR

spectrum of (A) are seen at 6.52 (6H), 6.81(6H) and 7.6(3H), corresponding to both bis(dimethylamino) and C-Me groups respectively. The corresponding signals in (B) (Fig.2) are at 6.81, 6.96 and 7.28. While the chemical shift of one of the bis-(dimethylamino) groups remained same, the other has shifted significantly towards higher field in (B) compared to (A), but the C-Me group suffered a down-field shift in (B) (0.3 ppm) compared with (A). However, on the basis of NMR spectra, it was difficult to assign the correct structure either to (A) or to (B). The only available literature[25] on the proton magnetic resonance data for s-triazolo[4,3-a] pyridine (25) and s-triazolo[1,5-a] pyridine (28) did not help much in assigning the correct structure to (A) or (B).

It has been observed[18,19,22-24,26] in the related s-triazolo azines, the isomerisation of [4,3-a] derivatives to [1,5-a] derivatives can be effected by dilute acid, base or by heat. This fact was utilised in assigning the correct structures to (A) and (B). The compound (B) readily underwent a thermal rearrangement above its m.p. and the product obtained was identical in all respects with (A). Compound (B) also isomerised to (A) in 2% aqueous sodium hydroxide at room temperature. This type of isomerisation in s-triazolo[4,3-a]-s-triazine derivatives was predicted by Guerret et al.[27] and observed by Tisler.[9] The isomeri-

sation of (20a) to (19a) is not favoured indicating that compounds of type (20a) are most stable to acids, alkali and heat. Thus the compounds (B) and (A) were assigned the structures (19a) and (20a) respectively. The bis (dimethylamino) group at position 5 can only show different chemical shifts in both the isomers and not at position 7. However, it is difficult to draw any conclusions regarding their structures from the NMR data, but one can suggest that the C-Me in structure such as (19a) should appear at downfield compared with structure (20a), and is the case in these products.

With the object of examining the utility of NMR spectroscopy in assigning the correct structures to isomeric compounds in the s-triazolo-s-triazine series, two more 2-hydrazino-s-triazines (17b) and (17c) were prepared in the present investigation. N-acetyl-2-hydrazino-4,6-bismorpholino-s-triazine(18b) was prepared by refluxing (17b) with acetic acid. Cyclodehydration of (18b) gave a mixture of two compounds (19b) and (20b). The assigned structures (19b) and (20b) were further confirmed by thermal rearrangement of (19b) to (20b) at 300° in 60% yield.

In the NMR spectra of (19b) and (20b) in $CDCl_3$ the 3-Me group absorbs at 7.31 whereas the 2-Me in the

isomeric compound (20b) is seen at 7.6, a shift of about 0.3 ppm high-field. Similar phenomenon was also observed in (19a) and (20a). Out of the eight methylenes present in the bis-morpholine groups, six methylene groups appear as a multiplet around 6.18 in (19b) and 6.18 in (20b). The remaining two methylenes are seen at 6.5 in (19b) and 5.72 in the corresponding isomer (20b) and can be assigned to two methylene groups attached to the nitrogen of the morpholine group at 5 position.

The $-NMe_2$ substituents in (19b) appear at a higher field compared with its isomer (20a) and this shift can be attributed to the steric interaction between the two substituents at 3- and 5- positions resulting the substituent at 5- going out of plane, while in (20a) there is no methyl group at 3-position, and no significant steric interaction is anticipated. Such steric interaction between the substituents at 3- and 5-positions have been observed in other heterocyclic systems.[25,27,28]

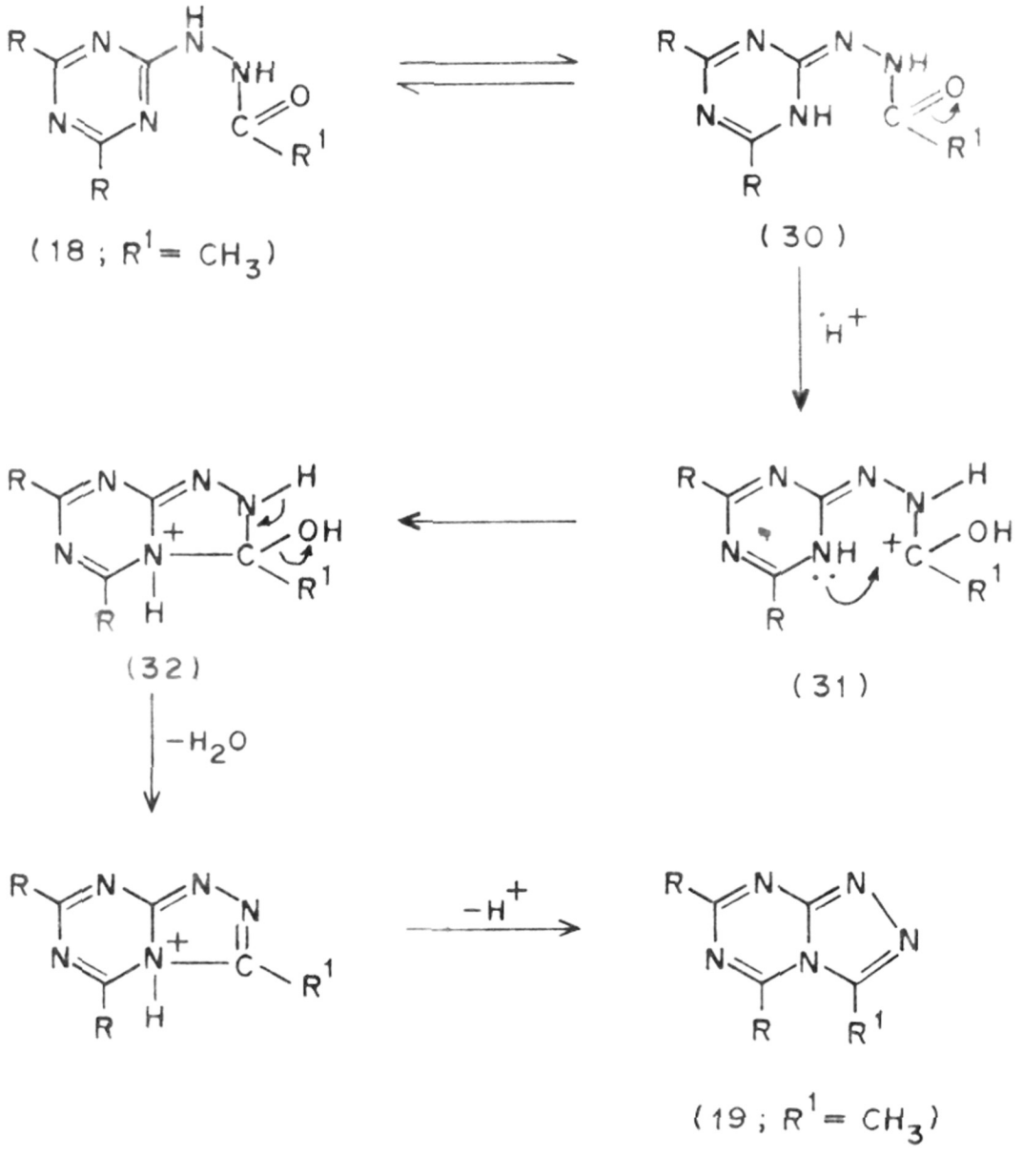
Similarly the cyclodehydration of N-acetyl-2-hydrazino-4,6-bis-piperidino-s-triazine (18c) afforded (19c) and (20c). NMR spectra of the both the isomers were determined in $CDCl_3$ and the chemical shift of the protons are in agreement with the earlier observation (Table 3).

The mechanism of cyclisation of N-acyl derivatives (18) of 2-hydrazino-s-triazines (17) involves the initial formation of the tautomeric compound (30) which undergoes cyclodehydration as shown in Scheme 2. The ease of ring closure may be related to the basic strength of the s-triazine nitrogen atom since the ring closure should involve the attack of an intermediate carbonium ion (31). Because of the presence of three electronegative nitrogen atoms in the aromatic ring system, the triazine ring is readily susceptible to nucleophilic substitution. Since the formation of the bicyclic nucleus involves an electrophilic attack upon the triazine ring, stronger dehydrating agent like phosphorous pentoxide is required for cyclisation.

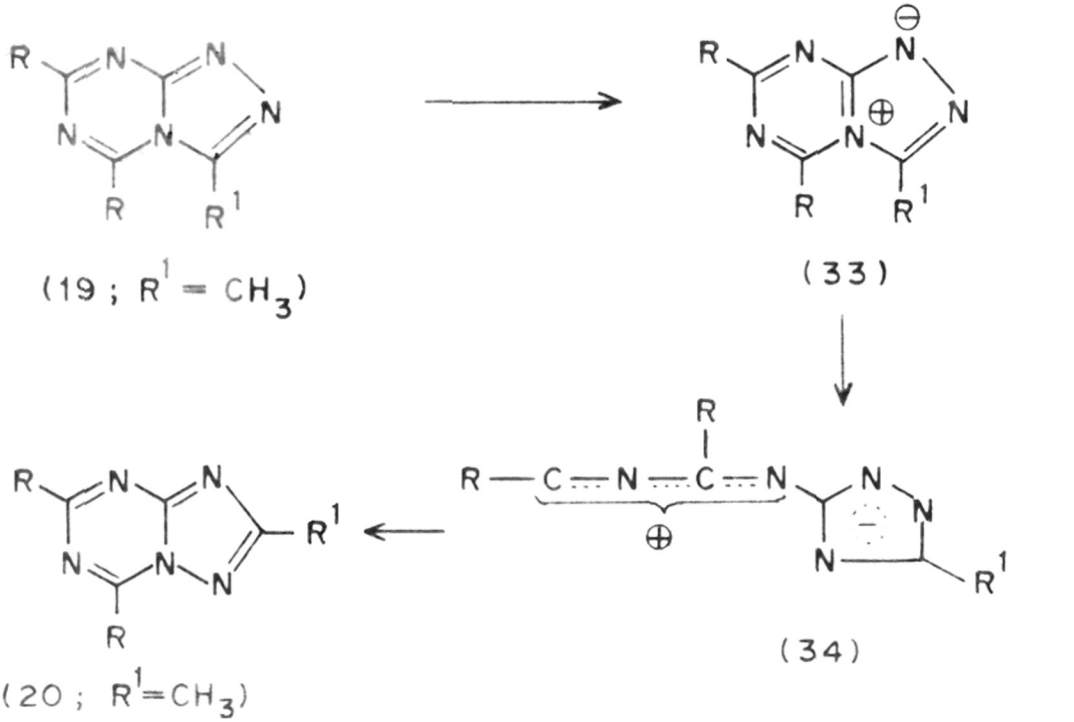
Generally, the rearrangement of s-triazolo[4,3-a]-s-triazines into s-triazolo-[1,5-a]-s-triazines by acid, alkali or heat is termed into Dimroth type rearrangement. "The term Dimroth rearrangement was coined in 1963 as a convenient way of referring to an isomerisation proceeding by ring fission and subsequent recyclisation, whereby a ring nitrogen and its attached substituent exchanged places with an imino group in the α-position to it."[29]

In a recent review on Dimroth-type rearrangements in polyazaindolizine systems, Gurnet et al.[27] have predicted

SCHEME 2

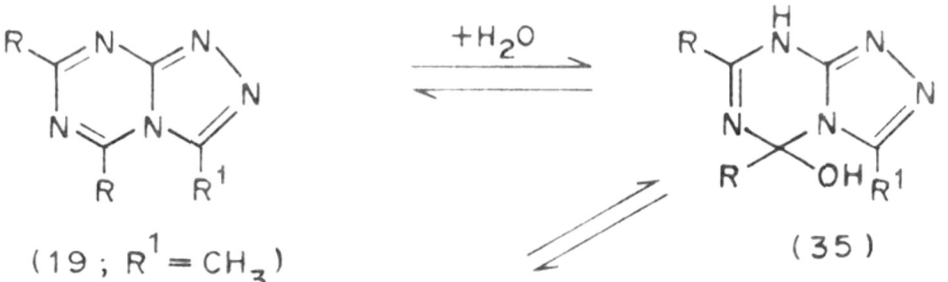


SCHEME 3



that s-triazolo[4,3-a]-s-triazine should rearrange to s-triazolo[1,5-a]-s-triazine. In the present work, Dimroth-type rearrangement in s-triazolo-s-triazines has been proved experimentally. The thermal rearrangement of [4,3-a] derivatives into [1,5-a] derivatives can be explained by assuming the formation of a zwitterionic intermediate (34) (Scheme 3) by the rupture of the 4,5-bond in the limiting stage (33), followed by ring closure to give isomer (20) analogous to the triazolopyrimidines.[24]

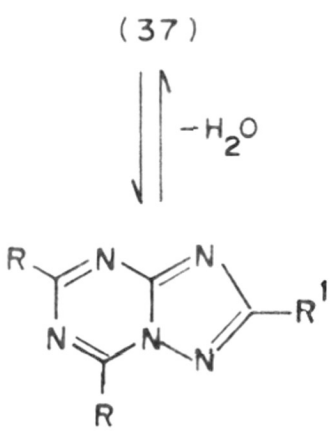
The facile Dimroth-type rearrangement in 2% alkali even at room temperature is not unexpected on the basis of the structure of bicyclic nucleus (19). It is generally accepted that the [1,5-a] derivatives were obtained by the fission of the azine nucleus at the junction with position 4 of the triazole ring and subsequent ring closure at position 2. In the base catalysed rearraggement, the initial step involves nucleophilic attack at position 5 by hydroxide ion (scheme 4). Thus the initial step is dependent on the π electron density at position 5. Electron densitites of a number of polyazaindolizine systems at position 5 have been calculated[27] using HMO method and it was found that an extra nitrogen atom at position 6 or 8 renders 5-position more electrophilic;

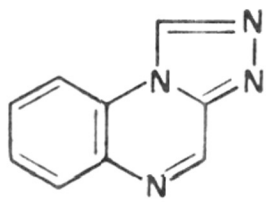


SEVERAL TAUTOMERIC FORMS

SEVERAL TAUTOMERIC FORMS

SEVERAL TAUTOMERIC FORMS





moreover an extra nitrogen atom at position 2 decreases the π electron density at position 5. In the s-triazolo [4,3-a]-s-triazine (19), the nitrogen atoms at position 2,6 and 8 decrease the π-electron density considerably when compared to other similar heterocyclic systems (Table 1). The decreased π-electron density at position 5 in the triazolo triazine series enhcnaces the nucleophilic attack by hydroxide ion. Following hydration, the six membered ring undergoes tautomeric ring opening; the intermediate (36) then recyclises to give(20). There is another factor, steric in nature, which plays an equal role in the isomerisation of [4,3-a] derivatives into [1,5-a] derivatives. We have already seen from the NMR study, that there exists a steric interaction between the two peri groups at 3- and 5-position of the bicyclic nucleus (19). The formation of the hydrated compound (35) with a subsequent change in hybridization of carbon 5 diminishes the steric interaction between the 3 and 5 substituents, thus stabilising (35) and (37), when compared to (19) and (20) respectively. Then, the ring-chain tautomeric fission of the 4,5-bond is more likely to occur in (35) than in (37) because of the residual interaction between the 3- and 5-substituents (scheme 4). The initial hydroxide ion attack at position 5 finds some

TABLE - 1

Electron Density Calculations [27]

Polyazaindolizines	π-Electron density at position 5 by HMO calculation.
Imidazo[1,2-a]pyrazine	0.826
Imidazo[1,2-a]pyridine	0.819
Imidazo[1,2-a]pyrimidine	0.711
s-Triazolo[1,5-a]pyrimidine	0.685
s-Triazolo[4,3-a]pyrimidine	0.667
Imidazo[1,2-c]pyrimidine	0.626
s-Triazolo[1,5-c]pyrimidine	0.631
s-Triazolo[4,3-c]pyrimidine	0.597
Imidazo[1,2-a]-s-triazine	0.528
s-Triazolo[1,5-a]-s-triazine	0.520
s-Triazolo[4,3-a]-s-triazine	0.484

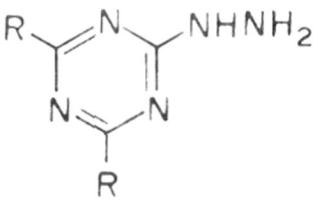
support from the fact that the Dimroth-type rearrangement was not observed in s-triazolo[4,3-a] quinoxaline series[26] (38) which was expected since the 5-position of the pyrazine nucleus is part of the fused benzene ring. It is observed[29] that the addition of electron-donating substituents diminishes the rate of Dimroth rearrangement. However, in the s-triazolo[4,3-a]-s-triazines (19), although the substituents at 3- and 5-position are powerful electron donating groups, the rate of rearrangement is not diminished.

The same procedure of cyclodehydration was extended further to other N-acyl derivatives of (17). The formyl derivatives (39) of appropriately substituted 2-hydrazino-s-triazines were prepared by boiling the hydrazine with 85% formic acid. The action of formic acid with the analogous 2-hydrazinopyrimidines has been studied[13,30-32] and the bicyclic products of type (29) are obtained. However, in the present work, the uncyclised hydrazides are obtained in quantitative yield even after boiling for 2 hr. with formic acid. Similar observation was made earlier by Tisler.[9] The hydrazine (17a) gave the corresponding N-formyl derivative (39a) at room temperature with evolution of heat on treatment with 85% formic acid.

However, the cyclodehydration of (39a), (39b) and (39c) afforded mainly to the corresponding s-triazolo [4,3-a] derivatives (40a), (40b) and (40c) in 65, 37 and 58% yield respectively, and the corresponding isomeric products (41a), 41b) and (41c) formed in very minute amount as detected by TLC of the mother liquors. Thermal isomerisation of (40a) and (40b) involved the decomposition of the product. However, they can be isomerised by treatment with 2% methanolic sodium hydroxide solution at room temperature. Isomerisation of (40a) to (41a) was effected in 2% methanolic sodium hydroxide. Refluxing in 2% methanolic sodium hydroxide resulted in the fission of (41a).

In the NMR spectra of (40a) and (41a) in $CDCl_3$, the 3-proton appears as a broad singlet at 1.47 and the corresponding proton in the 2-position of (41a) is seen at 2.1. The methyl groups corresponding to the bis-(dimethylamino) group at 7-position are seen almost at the same place in both the isomers. The methyls of the NMe_2 group at 5-position in the two isomers appear at 6.62 and 6.47 respectively for (40a) and (41a) indicating that the shift is not very much compared with the corresponding methyl compounds substantiating the earlier observation.

The reaction of 2-hydrazino-s-triazines (17) with an equimolar amount of benzoyl chloride in dry benzene at



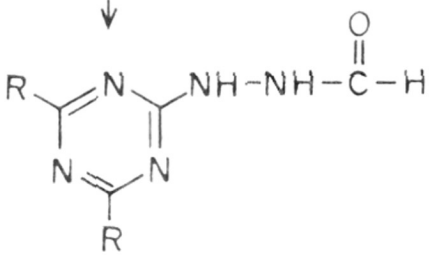
(17)

(17a) R = NMe_2

(17b) R = 

(17c) R = 

HCOOH



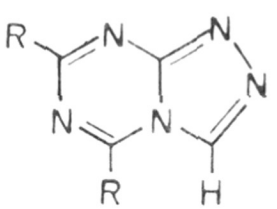
(39)

(39a) R = NMe_2

(39b) R = 

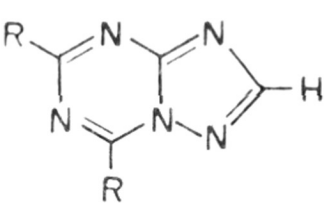
(39c) R = 

P_2O_5



(40)

2% NaOH



(41)

(40a) R = NMe_2

(40b) R = 

(40c) R = 

(41a) R = NMe_2

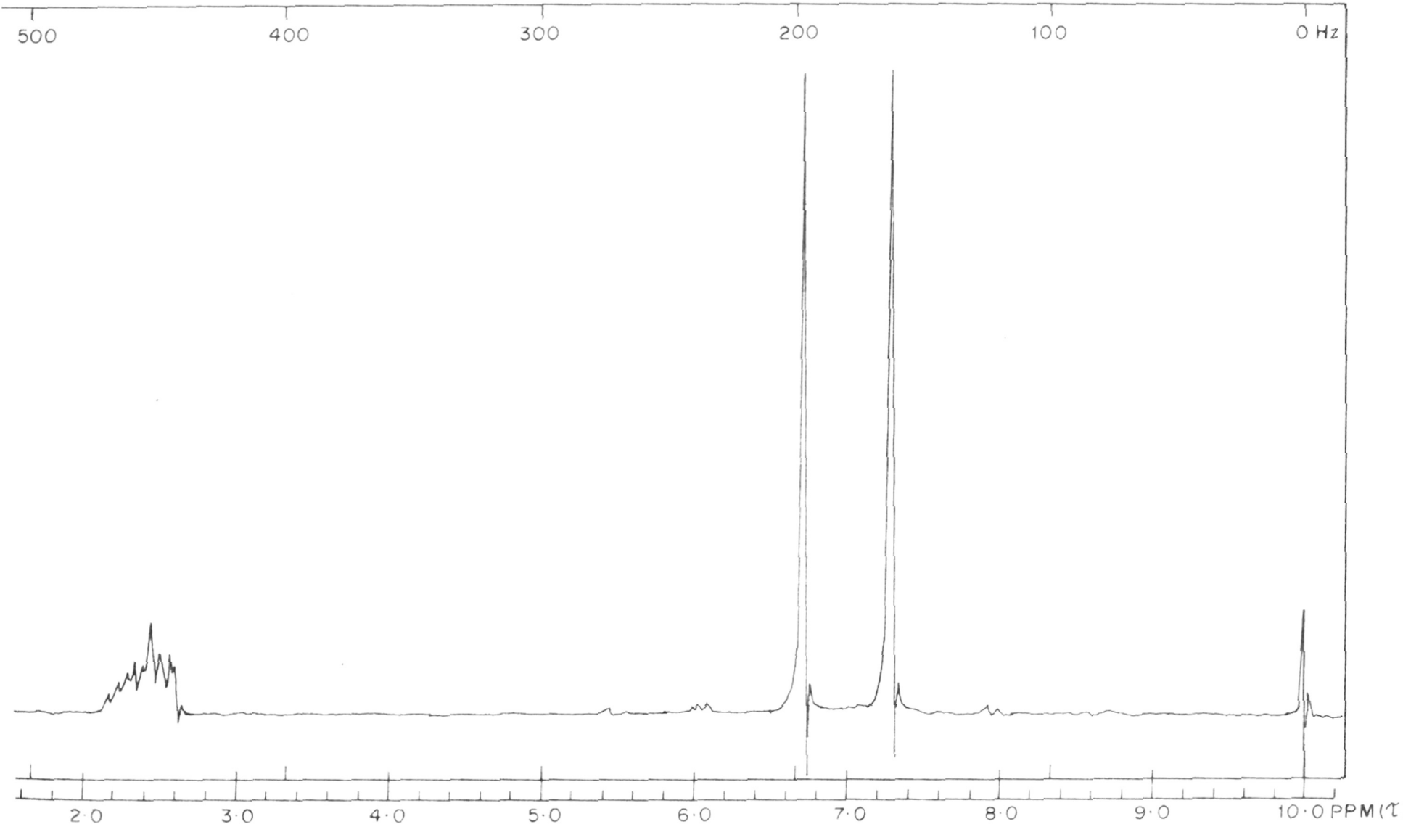
(41b) R = 

(41c) R = 

room temperature gave the normal benzoylation product along with dibenzoyl derivative. The monobenzoyl derivatives were purified by column chromatography. However, yields were better when Schotten-Baumann procedure for benzoylation was used.

Cyclodehydration of benzoyl derivatives with phosphorous oxychloride has been carried out in the pyridine,[15] pyrazine and quinoxaline[26] series. We have cyclised the benzoyl derivatives with phosphorous pentoxide. Cyclodehydration of (42a) afforded the mixture of two compounds (43a) and (44a) in a ratio of about 7:1. Similarly the cyclisation of (42c) gave (43c) and (44c) in about 12:1 ratio. However, the cyclisation of (42b) resulted mainly in the formation of (43b) and the isomeric product (44b), obtained in an insignificant amount, but enough to determine its m.p. and analysis. The structures of the 3-phenyl-s-triazolo[4,3-a]-s-triazines, (43a) and (43b) were further confirmed by the unambiguous synthesis of these compounds by subjecting the corresponding 2-benzylidene-hydrazine-s-triazines, (45a) and (45b), to oxidative cyclisation with lead tetraacetate, a method already reported[8,9] in the literature.

The NMR spectrum (Fig.3) of (43a) in $CDCl_3$ shows the following signals. The 7-N methyls appear at



G·3 NMR SPECTRUM OF 3-PHENYL-5,7-BIS(DIMETHYLAMINO)-s-TRIAZOLO-(4,3-a) -s- TRIAZINE IN $CDCl_3$

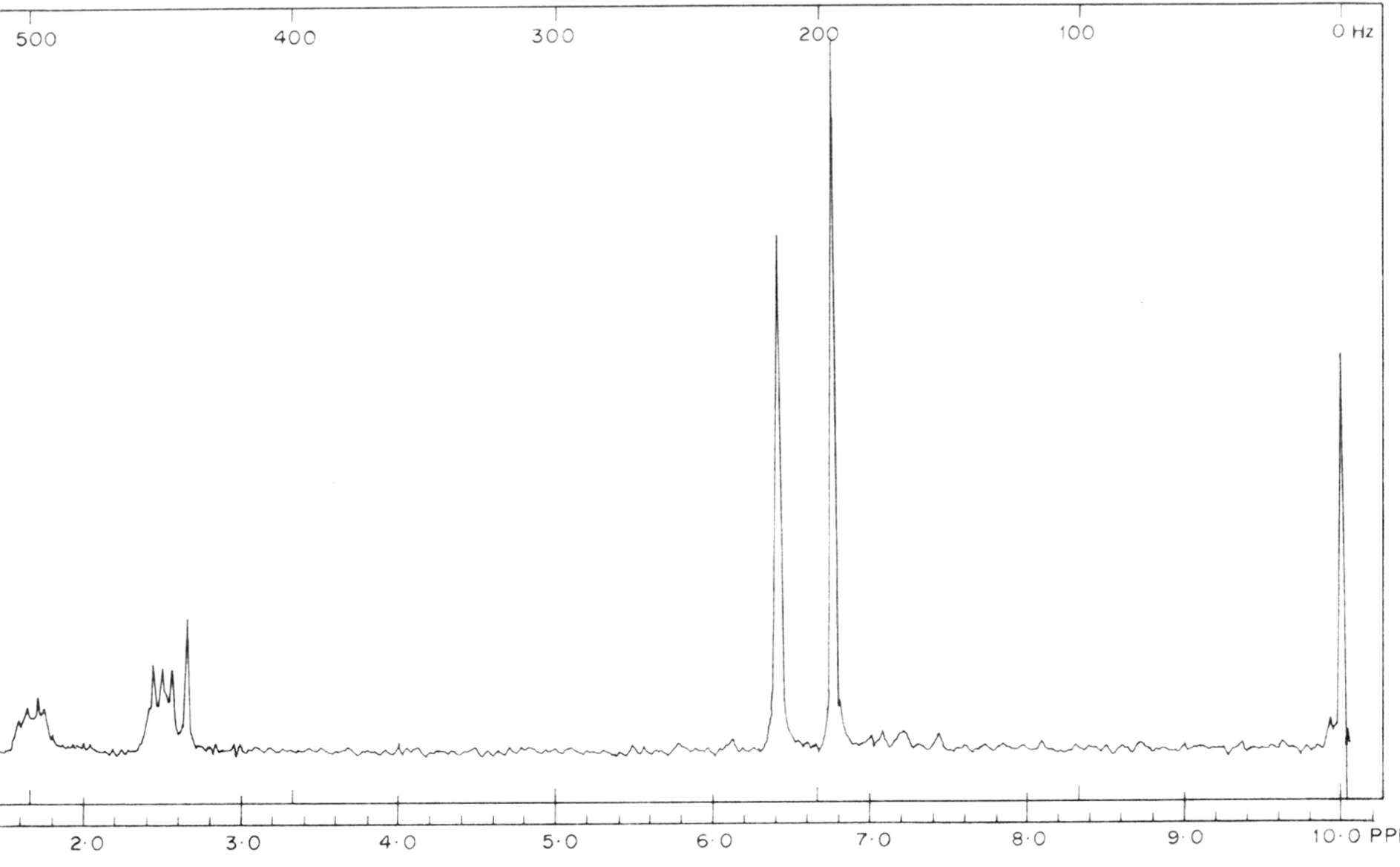
6.78. The 5-N-methyls absorb at 7.3. In the absence of 3-phenyl group the chemical shift of the 5-NMe_2 are 6.62 in (40a) and 6.96 in (19a) (see Table 2).

TABLE 2

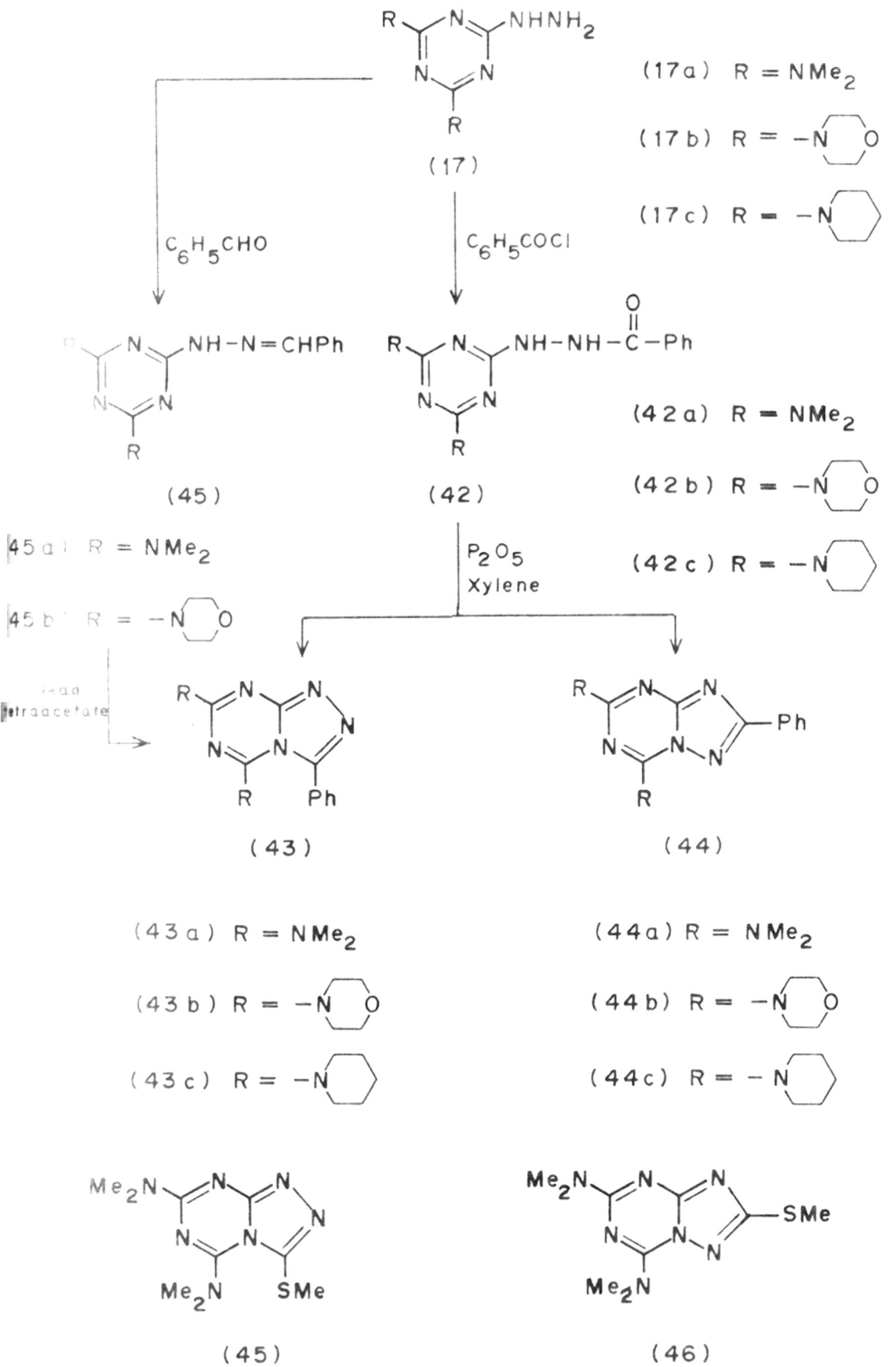
Chemical shift of the NMe_2 groups in 5,7-bis(dimethylamino)-s-triazolo[4,3-a]- and [1,5-a]-s-triazines

Compound	40a H	19a Me	43a Ph	41a H	20a Me	44a Ph
5-NMe_2	6.62	6.96	7.3	6.47	6.52	6.48
7-NMe_2	6.83	6.81	6.78	6.8	6.81	6.8

The effect of the phenyl group on N-methyl protons at 7-position is insignificant. The anomalously high-field shift of the 5-NMe_2 may be explained in terms of non-planar conformation forced on the 3-phenyl group with the result the 5-NMe_2 group would be shielded by the 3-phenyl group. The protons of the 3-phenyl group are seen as multiplet in the region between 2.2 to 2.7. In the NMR spectrum (Fig.4) of its isomer (44a), the protons of the 2-phenyl group resolved into two multiplets, the ortho-protons are centered at 1.75 and other three protons at 2.65.



FIG·4 NMR SPECTRUM OF 2-PHENYL-5,7-BIS(DIMETHYLAMINO)-s- TRIAZOLO(1,5-a) -s- TRIAZINE IN $CDCl_3$


(17a) R = NMe2
(17b) R = -N O
(17c) R = -N
(17)
C6H5CHO
C6H5COCl
(45)
(42)
(42a) R = NMe2
(42b) R = -N O
(42c) R = -N
45a) R = NMe2
45b) R = -N O
P2O5
Xylene
(43)
(44)
(43a) R = NMe2
(43b) R = -N O
(43c) R = -N
(44a) R = NMe2
(44b) R = -N O
(44c) R = -N
(45)
(46)

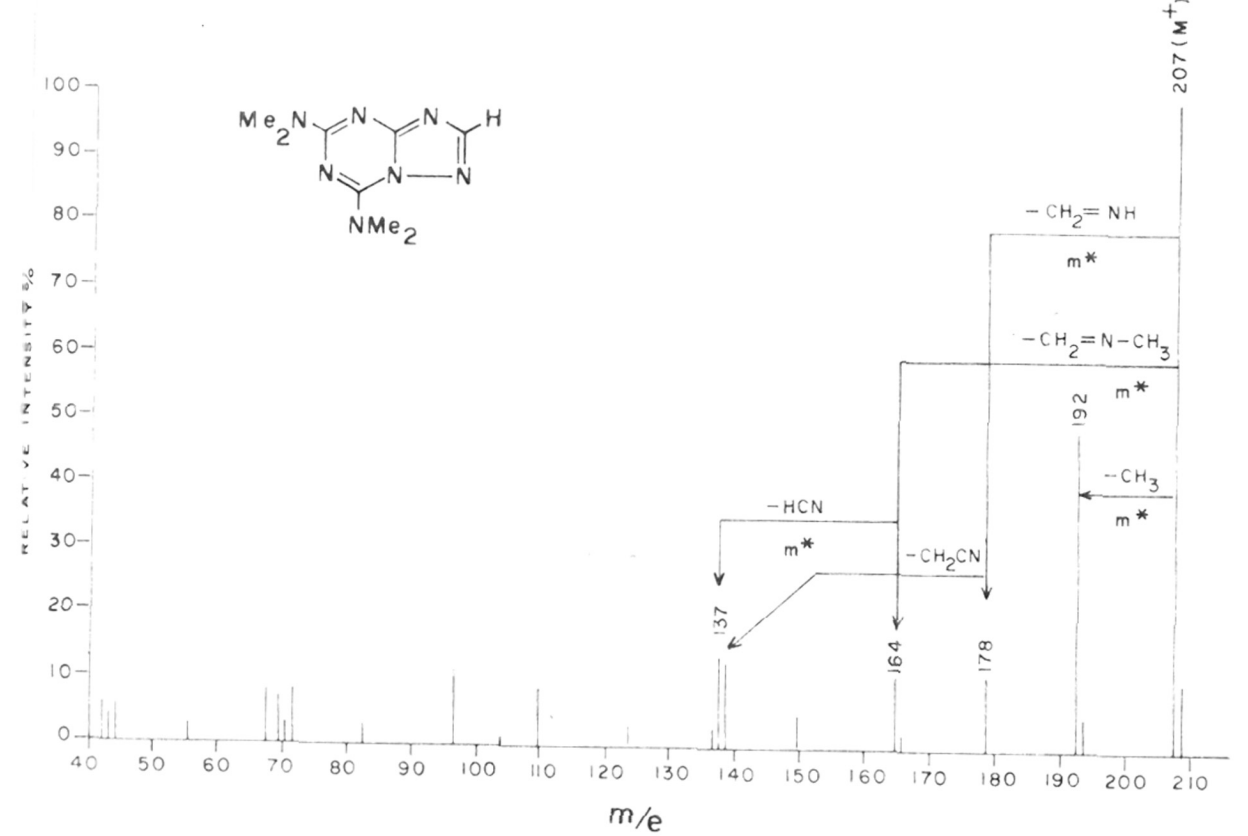
This o-shift phenomenon must therefore be attributed to the magnetic anisotropy of the neighbouring triazole ring. When multiplet resonances occur, the o-phenyl protons reside preferentially near the plane of the triazole ring and are shifted downfield by the magnetic field of the triazole ring. The absorption pattern of the 2-phenyl protons in (44a) further confirms that the 3-phenyl group in (43a) exists in nonplanar conformation. A planar conformation of the 2-phenyl would place 5-NMe_2 in the plane of the bicyclic nucleus and consequently are deshielded and appear at 6.48. The chemical shift of the 7-NMe_2 group remains the same for both the compounds. Similar effects have been observed[25,33] in other heterocyclic ring systems with substituent phenyl groups.

Similar observation (Table 3) was made in the NMR spectra of (43b) and (44c).

Mass spectral fragmentations of triazolo-s-triazines have not been studied to this date, although a number of similar nitrogen heterocyclic systems have been reported.[34,35] The members of this bicyclic system gave a strong molecular ion substantiated by the appearance of a doubly charged ion. In all the compounds studied (see Table 4), the molecular ion itself is the base peak.

All the s-triazolo[1,5-a]-s-triazine underwent fragmentation by a common pathway. Fragmentation pattern of (41a) is similar to (40a) (Fig.5) with a difference in the intensities of the fragment ions.

All the s-triazolo[4,3-a]-s-triazine showed three fragmentation pathways (Scheme 5). The molecular ion (a) of (40a) lost Me to give ion (b), m/e 192 (25.5%). The second pathway involved the elimination of a neutral fragment from the dimethylamino substituent as formimine (CH_2=NH) with a simultaneous migration of a methyl group to a ring nitrogen atom (ion c). The observed M-27 peak was accompanied by a corresponding meta-stable peak. Similar rearrangement reactions have been reported to occur in other heterocyclic systems containing a dimethylamino substituent.[36-40] The ion (d), m/e 164, was formed by the loss of a neutral radical -CH_2=N-CH_3 from the molecular ion which is confirmed by the presence of a corresponding meta-stable peak. Rahamim et al.[40] have predicted the loss of CH_3-N=CH_2 in the fragmentation of 2-dimethylamino-5-benzenesulphonamidopyrimidine. The further breakdown of ion (d) by loss of HCN from 5-membered ring to ion (g), m/e 137, is also confirmed by the presence of a corresponding meta-stable peak. The probable further fragmentation of ion (g) is shown in Scheme 5, but needs confirmation by high resolution data and deuteration studies.


207 (M+)
Me_2N
NMe2
H
$-CH_2=NH$
m*
$-CH_2=N-CH_3$
m*
192
$-CH_3$
m*
-HCN
m*
$-CH_2CN$
137
164
178
RELATIVE INTENSITY %
m/e

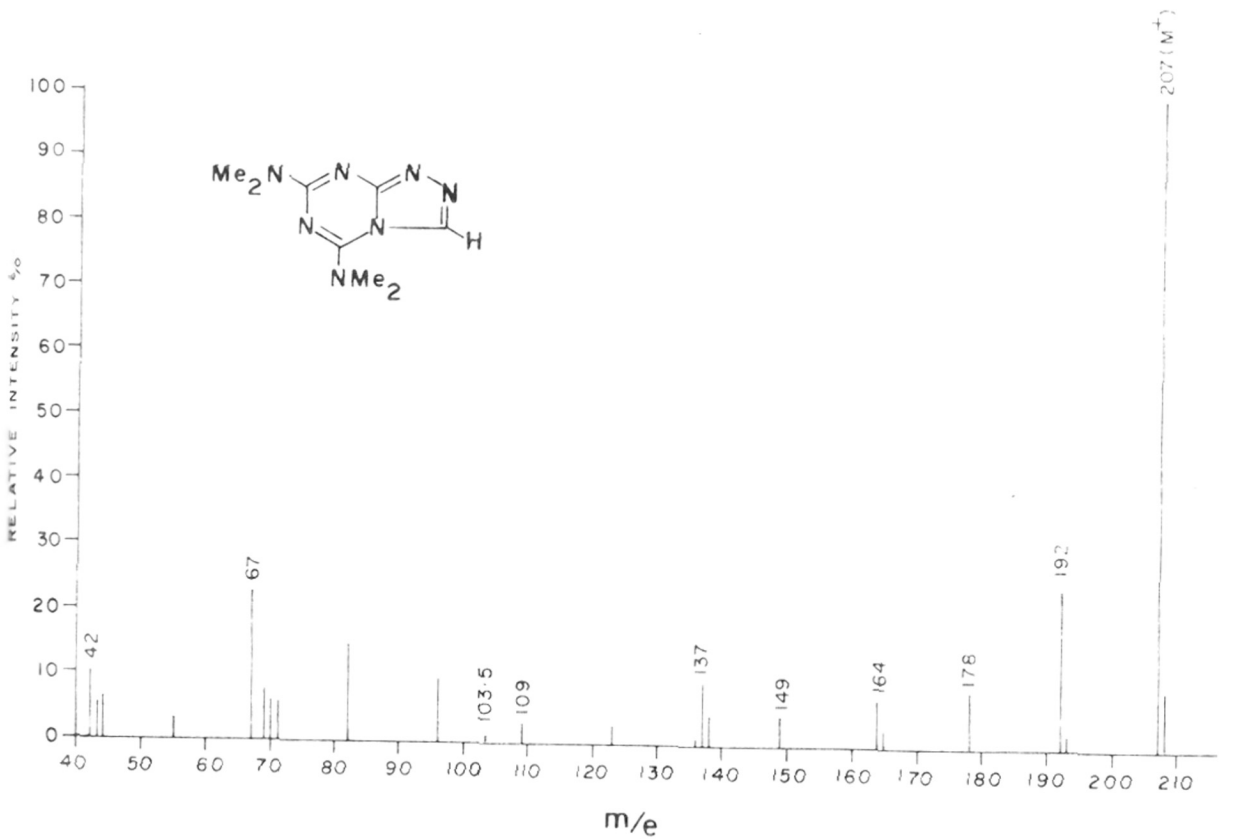
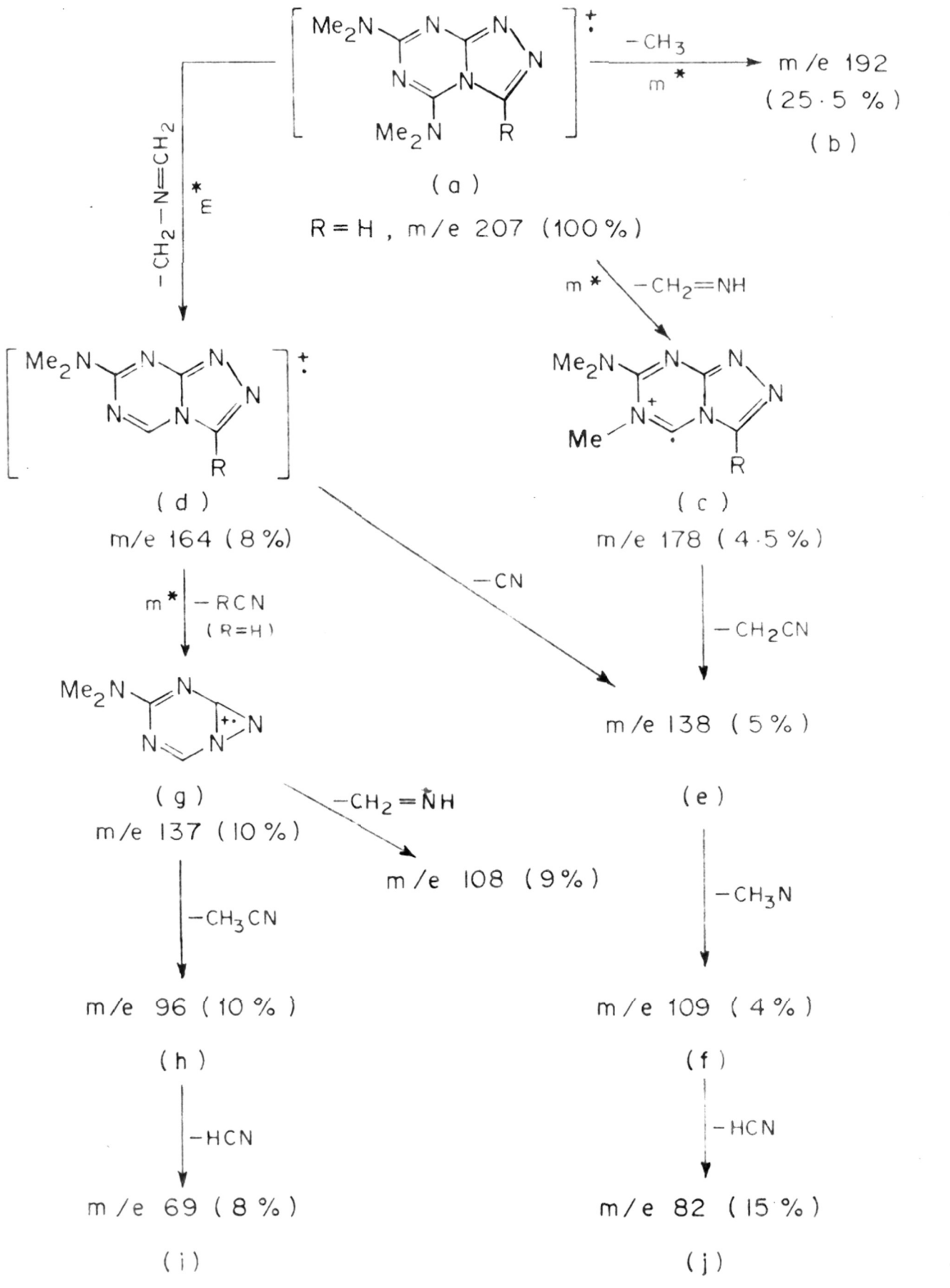

207 (M+)
Me_2N
NMe2
H
67
42
103.5
109
137
149
164
178
192
RELATIVE INTENSITY %
m/e

FIG. 5

SCHEME – 5.


Me2N
N
N
N
N
N
Me2N
R
+·
(a)
R = H , m/e 207 (100 %)
– CH3
m*
m/e 192
(25·5 %)
(b)
– CH2 – N = CH2
m*
E
m*
– CH2 = NH
Me
(c)
m/e 178 (4·5 %)
(d)
m/e 164 (8 %)
– CN
m*
– RCN
(R = H)
– CH2CN
m/e 138 (5 %)
(e)
(g)
m/e 137 (10 %)
– CH2 = NH
m/e 108 (9 %)
– CH3CN
– CH3N
m/e 96 (10 %)
(h)
m/e 109 (4 %)
(f)
– HCN
– HCN
m/e 69 (8 %)
(i)
m/e 82 (15 %)
(j)

In the other pathway, after elimination of formimine, the resultant radical cation (c) loses CH_2CN to form ion (e), m/e 138 (5%). However, no meta-stable transition was detected to support this fragmentation. The ion (e) probably formed by the loss of CN radical from ion (d).

Introduction of methyl substituent into the 3-position (compound 19a) had little effect on the above fragmentation pattern except that the fragment eliminated from ion (d) was CH_3CN. Loss of Me at either from 2- or 3-position, although expected is not observed in these compounds. The loss of Me from the molecular ions come exclusively from the NMe_2 groups. The fragmentation pattern for 3-phenyl-s-triazolo[4,3-a]-s-triazine (43a) was similar and a PhCN fragment eliminated from ion (d). The loss of RCN (R=H, Me or Ph) from the 5-membered ring of the bicyclic system is observed not directly from the molecular ion, but through the intermediacy of an $[M-43]^+$ ion. The ion (g), m/e 137, obtained by the loss of RCN was common to the decomposition of both isomeric ring systems. However, with the triazolopyridines,[34] the major fragmentation pathway involves the loss of RCN from the molecular ion and the $[M-1]^+$ peak is also quite intense.

The method of synthesis of *s*-triazolo-*s*-triazines by cyclodehydration of the *N*-acyl derivatives of 2-hydrazino-*s*-triazines is better compared to other methods. The easily accessible starting materials and reagents makes the method of choice and yields are comparatively better. Besides, the availability of several symmetrical and unsymmetrical substituted *s*-triazines makes the method of wide applicability and variation of the reaction conditions result in the formation of one product exclusively. The preparation of 2-methyl-5,7-*bis*-(dimethylamino)-*s*-triazolo-[4,3-a]-*s*-triazine may be cited in support.

Finally, an unsuccessful attempt was made to synthesise the parent ring system, *s*-triazolo-[4,3-a]-*s*-triazine by employing the above method of preparation.

After this work was completed, DeMilo *et al.*[41] have reported the isomerisation of 5,7-*bis*(dimethylamino)-3-(methyl thio)-*s*-triazolo[4,3-a]-*s*-triazine (45) to 2-(methylthio)-*s*-triazolo[1,5-a]-*s*-triazine (46) with excess anhydrous dimethylamine in absolute ethanol at 85°. Based on the NMR study of similar compounds, the assignments for the dimethylamino groups of (45) and (46) were made unambiguously (see Table 3). Synthesis of (41b) starting from 2-amino-*s*-triazine has been reported[42] very recently. Another recent paper[43] describes the preparation of *s*-triazolo-[1,5-a]-*s*-triazine derivatives starting from substituted triazole.

TABLE - 3

NMR data for s-triazolo-s-triazines
(Solvent: $CDCl_3$)

Compound	Chemical shift	Multiplicity	No. of protons	Assignment
19a	7.28	s	3	3-Me
	6.96	s	6	5-NMe_2
	6.81	s	6	7-NMe_2
20a	7.6	s	3	2-Me
	6.81	s	6	7-NMe_2
	6.52	s	6	5-NMe_2
19b	7.31	s	3	3-Me
	6.5	m	4	N-methylenes of 5-morpholino group.
	6.19	m	12	N and O-methylenes of 7-morpholino group + O-methylenes of 5-morpholino group
20b	7.6	s	3	2-Me
	6.18	m	12	N and O-methylenes of 7-morpholino group + O-methylenes of 5-morpholino group.
	5.72	m	4	N-methylenes of 5-morpholino group.
19c	7.29	s	3	3-Me
	6.67	m	4	N-methylenes of 5-piperidyl group.
	6.2	m	4	N-methylenes of 7-piperidyl group.
	8.33	m	12	Remaining methylenes of 5,7-piperidyl groups

Table 3 contd.

20c	7.62	s	3	2-Me
	6.2	m	4	N-methylenes of 7-piperidyl group
	5.86	m	4	N-methylenes of 5-piperidyl group.
	8.33	m	12	Remaining methylenes of 5,7-piperidyl groups
40a	6.83	s	6	7-NMe_2
	6.62	s	6	5-NMe_2
	1.47	s	1	3-H
41a	6.80	s	6	7-NMe_2
	6.47	s	6	5-NMe_2
	2.1	s	1	2-H
40b	6.2	m	8	N-methylenes of 5,7-piperidyl groups
	8.27	m	12	Remaining methylenes of 5,7-piperidyl groups
	1.63	s	1	3-H
43a	7.3	s	6	5-NMe_2
	6.78	s	6	7-NMe_2
	2.2-2.7	m	5	3-Phenyl
44a	6.8	s	6	7-NMe_2
	6.48	s	6	5-NMe_2
	2.65	m	3	2-Phenyl
	1.75	m	2	
43c	6.18	m	4	N-methylenes of 7-piperidyl group.
	6.92	m	4	N-methylenes of 5-piperidyl group
	8.58	m	12	Remaining methylenes of 5,7-piperidyl groups
	2.27-2.97	m	5	3-Phenyl

Table 3 contd.

44c	6.2	m	4	N-methylenesof 7-piperidyl group.
	5.8	m	4	N-methylenes of 5-piperidyl group
	8.32	m	12	Remaining methylenes of 5,7-piperidyl groups.
	2.47-2.93	m	3	2-Phenyl group
	1.8	m	2	
45*	7.28	s	3	3-SMe
	6.96	s	6	5-NMe_2
	6.78	s	6	7-NMe_2
46*	7.39	s	3	2-SMe
	6.83	s	6	7-NMe_2
	6.53	s	6	5-NMe_2

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* NMr values of these compounds have already been reported.[41]

TABLE - 4

Mass spectral data for 5,7-bis(dimethylamino)-s-triazolo-s-triazines.

Compound (19a)

m/e	222	221	207	206	192	178
I%	12	100	2.5	25	3	4
m/e	163	152	147	138	137	110.5
I%	2	5	2	5	15	4
m/e	109	108	107	97	96	82
I%	4	2	3	2	8	24.5
m/e	78	71	70	69	67	44
I%	5	2.5	3	6.5	25	5.5
m/e	43	42				
I%	4	9				

Compound (20a)

m/e	222	221	220	207	206	192
I%	18	100	3	6	57	9
m/e	180	179	178	163	152	138
I%	2	2.5	8	3.5	12	6.5
m/e	137	110.5	109	108	107	97
I%	16	1	9	2	5	3.5
m/e	96	82	71	70	69	67
I%	16	8.5	10	5	11.5	23
m/e	44	43	42			
I%	18	6.5	21			

Compound (40a)

m/e	208	207	193	192	178	165
I%	10	100	3	25.5	4.5	3
m/e	164	149	138	137	136	123
I%	8	5	5	10	1	3
m/e	109	103.5	96	82	71	70
I%	3	1	10	15	6	6.5

Table 4 contd.

m/e	69	67	55	44	43	42
I%	8	23	83	6.5	5.5	10

Compound (41a)

m/e	208	207	198	192	178	165
I%	11	100	5	54	115	2
m/e	164	149	138	137	136	123
I%	115	5	13.5	14	3	3
m/e	109	103.5	96	82	71	70
I%	7	1.5	11.5	3	8	3
m/e	69	67	55	44	43	42
I%	7.5	8	3	6	45	6

Compound (43a)

m/e	284	283	269	268	254	240
I%	185	100	48.5	42	10	12
m/e	214	200	199	180	144	141.5
I%	14	8	5	6	7.5	4
m/e	138	137	109	104	103	97
I%	7	26	12	16.5	2	5
m/e	96	82	77	76	71	70
I%	27	14	26	11.5	22	11.5
m/e	69	68	67	56	55	51
I%	24	8	70	5.5	8.5	10
m/e	50	44	43	42	41	
I%	5	32	15	33	5.5	

Compound (44a)

m/e	284	283	269	268	254	240
I%	18	100	4	22.5	4.5	5
m/e	214	213	200	184	170	141.5
I%	5	6.5	3	2	7	1
m/e	137	109	103	96	82	77
I%	10.5	2.5	10	11.5	36	4.5
m/e	76	71	70	69	68	67
I%	4	4	4	10	4	51
m/e	55	44	43	42		
I%	4	7	5	8		

EXPERIMENTAL

Melting points are uncorrected. NMR spectra were determined on Varian A-60 and T-60 spectrometers in $CDCl_3$. Chemical shifts are quoted in τ values using TMS as internal reference. For TLC and column chromatography, silica gel was used as adsorbent, and chloroform-methanol (95:5) was used as the solvent system. The spots on TLC plate were observed either by exposing the plates to iodine vapours or by spraying with Draggendorff's reagent.

2-Hydrazino-s-triazines (17a) and (17b) were prepared[12,44] from the corresponding 2-chloro-s-triazines which in turn were obtained from cyanuric chloride by the method already known in the literature.[45]

2-Chloro-4,6-bispiperidino-s-triazine

To a fine suspension of cyanuric chloride (18.4 g; 0.1 mole), obtained by dropping a hot solution of cyanuric chloride in acetone (50 ml) on crushed ice (100 g), piperidine (39.4 ml) was added with stirring at 0-5° and the mixture stirred for half an hour. The temperature was then slowly raised to room temperature. The precipitate

was filtered, washed with water and dried. Crystallisation from hexane gave colourless crystals (20 g), m.p. 117-18° (lit.[45] 117-19°).

2-Hydrazino-4,6-bispiperidino-s-triazine (17c)

A mixture of 2-chloro-4,6-bispiperidino-s-triazine (19 g) and hydrazine hydrate (10 ml; 98%) in ethanol was refluxed for 6 hr., concentrated to 50 ml and cooled. The resulting colourless plates were filtered, washed with water and dried (17 g), m.p. 137-39° (lit.[46] 137-39°).

N-acetyl-2-hydrazino-4,6-bis(dimethylamino)-s-triazine(18a)

A solution of (17a) (2 g) was refluxed with glacial acetic acid (20 ml) for an hour. The solvent was distilled under reduced pressure on steam bath (2.3 g). Crystallisation from benzene gave colourless prisms, m.p. 175-76° (Found: C, 45.1; H, 7.2; N, 41.5. $C_9H_{17}N_7O$ requires C, 45.2; H, 7.1; N, 41.0%); $\nu_{max.}^{nujol}$ 1685 cm^{-1} (CO); 3226 cm^{-1} (NH).

The following compounds were prepared employing the above procedure.

N-acetyl-2-hydrazino-4,6-bismorpholino-s-triazine, (18b) m.p. 233-34° (ethanol) (Found:C, 48.5; H, 6.8; N, 30.0. $C_{13}H_{21}N_7O_3$ requires C, 48.3; H, 6.5; N, 30.3%). $\nu_{max.}^{nujol}$ 1681 cm^{-1} (CO,),3226 (NH).

N-acetyl-2-hydrazino-4,6-bispiperidino-s-triazine (18c)

Crystallisation from benzene gave colourless shining plates, m.p. 195-96° (Found: C, 56.8; H, 8.1; N, 31.0. $C_{15}H_{25}N_7O$ requires C, 56.4; H, 7.9; N, 30.7%); $\nu_{max.}^{nujol}$ 1685 cm^{-1} (CO); 3200 cm^{-1} (NH).

N-formyl-2-hydrazino-4,6-bis(dimethylamino)-s-triazine (39a).

A solution of (17a) (2.7 g) in 85% formic acid (15 ml) was left at room temperature overnight. Excess acid was distilled under reduced pressure. The residue was tritulated with ether and the colourless precipitate was filtered, washed with ether and dried (3 g). Colourless plates from benzene, m.p. 189-90° (Found: C, 43.0; H, 6.8; N, 43.5. $C_8H_{15}N_7O$ requires C, 42.7; H, 6.7; N, 43.5%).

N-formyl-2-hydrazino-4,6-bismorpholino-s-triazine (39b)

A solution of (17b) (2 g) in 85% formic acid (10 ml) was refluxed for an hour. It was worked up as in the above experiment. Colourless needles from ethanol, m.p. 238-39° (lit.[9] m.p. 239-40°).

N-formyl-2-hydrazino-4,6-bispiperidino-s-triazine (39c)

It was prepared employing the above procedure. Colourless plates (benzene), m.p. 167-68° (Found: C, 55.4; H, 7.2. $C_{14}H_{23}N_7O$ requires C, 55.1; H, 7.5%). ν_{max}^{nujol} 1700 (CO), 3175 (NH).

N-benzoyl-2-hydrazino-4,6-bis(dimethylamino)-s-triazine (42a)

A solution of (17a) (29) in dry benzene (100 ml) was treated with benzoyl chloride (1.2 ml; 0.01 mole) cautiously with constant stirring at room temperature, and left at room temperature for 3 hr. The crystalline product was filtered, washed with benzene and dried(2 g), and purified by chromatography. Crystallised from ethanol in colourless shining plates, m.p. 222-23°(Found: C, 55.8; H, 5.9; N, 32.0. $C_{14}H_{19}N_7O$ requires C, 55.8; H, 6.3; N,32.5%).

The same procedure was adopted for preparing the following compounds:

N-benzoyl-2-hydrazino-4,6-bismorpholino-s-triazine (ℓ 42b)

Colourless shining plates (EtOH), m.p. 214-15°; yield 77% (Found: C, 56.4; H, 6.3; N, 25.5. $C_8H_{23}N_7O_3$ requires C, 56.1; H, 6.0; N, 25.5%). $\nu^{nujol}_{max.}$ 1684 cm^{-1} (CO); 3224 cm^{-1} (NH).

N-benzoyl-2-hydrazino-4,6-bispiperidino-s-triazine (42c)

Colourless plates from benzene, m.p. 187-88°; yield 85% (Found: C, 63.3; H, 7.1; N, 25.4. $C_{20}H_{27}N_7O$ requires C, 63.0; H, 7.1; N, 25.7%). $\nu^{nujol}_{max.}$ 1660 (CO) 3200 (NH).

Ethylidene derivative of 2-hydrazino-4,6-bis (dimethylamino)-s-triazine (27)

To a solution of (17a) (2Ø g) in ethanol (20 ml), acetaldehyde was added at room temperature. The reaction mixture was heated to boiling and cooled. The resulting crystalline compound was filtered, washed with ethanol and dried (1.6 g). Colourless needles from ethanol, m.p. 185-86° (Found: C, 49.0; H, 7.8; N, 43.6. $C_9H_{17}N_7$ requires C, 48.5; H, 7.6; N, 43.9%).

Benzylidene derivative of 2-hydrazino-4,6-bis (dimethylamino)-s-triazine (45a)

A solution of (17a) (2.5 g) in ethanol (50 ml) was treated with benzaldehyde (0.95 g) and refluxed for 5 min. On cooling colourless needles were separated, m.p. 153-54° (ethanol) (Found: C, 59.4; H, 7.0; N, 34.3. $C_{14}H_{19}N_7$ requires C, 59.0; H, 6.7; N, 34.4%).

Similarly benzylidene derivative of 2-hydrazino-4,6-bismorpholino-s-triazine (45b) was prepared; m.p. 221-22° (lit.[8] 222-23°).

2-Methyl-5,7-bis(dimethylamino)-s-triazolo[1,5-a]-s-triazine (20a)

To a refluxing solution of (18a) (1.2 g) in dry xylene (100 ml) was added phosphorus pentoxide (5 g) in

two portions over an 8 hr. interval with stirring. Further, the mixture was refluxed for 12 hr. The solvent was distilled under reduced pressure on steam bath and the solid residue was dissolved in ice-cold water (100 ml). The aqueous solution was made basic with 40% potassium hydroxide solution, extracted with chloroform. The extract was washed with water, dried over anhydrous sodium sulphate and solvent removed. The solid was crystallised from pet.ether (60-80°)in colourless needles (0.9 g), yield 81%; m.p. 165° (Found: C, 48.6; H, 6.6. $C_9H_{15}N_7$ requires C, 48.9; H, 6.8%).

3-Methyl-5,7-bis(dimethylamino)-s-triazolo[4,3-a]-s-triazine (19a) and 2-methyl-5,7-bis(dimethylamino)-s-triazolo[1,5-a]-s-triazine (20a)

General procedure: To a refluxing solution of (18a) (2 g) in dry xylene (250 ml) was added phosphorous pentoxide (30 g) in three portions (each 10 g) with stirring over a 45 min. interval. Then, the mixture was refluxed for 10 hr. with stirring.The solvent was distilled under reduced pressure and the aqueous solution (50 ml) of the solid mixture was neutralised by the addition of saturated solution of sodium carbonate (pH 6-7). The neutral solution was extracted thrice with chloroform (each 50 ml portion). The combined extracts (150 ml) were washed with

TABLE - 5

Starting material Comp. No.	s-Triazolo-s-triazine Comp. No.	m.p. °C	Yield %	Formula	Analyses Calc. % C	H	N	Found % C	H	N
(17b)	(19b)	206-7[a]	16.0	$C_{13}H_{19}N_7O_2$	51.2	6.4	32.1	51.0	6.4	-
	(20b)	231-33[b]	10.5					51.4	6.0	32.4
(17c)	(19c)	152-53[b]	26.0	$C_{15}H_{23}N_7$	59.8	7.6	32.6	59.8	7.2	-
	(20c)	165-66[c]	29.0					60.0	7.3	32.6
(39a)	(40a)	196-7[d]	65.5	$C_8H_{13}N_7$	46.4	6.3	-	46.8	6.6	-
(39b)	(40b)	241-43[e]	37.0	$C_{12}H_{16}N_7O$	49.5	5.8	33.6	49.5	6.1	33.9
(39c)	(40c)	161-62[b]	58.0	$C_{14}H_{21}N_7$	59.8	7.5	-	59.6	7.6	-
(42a)	(43a)	172-73[b]	51.0	$C_{14}H_{17}N_7$	59.4	6.0	-	59.2	6.3	-
	(44a)	230-31[b]	8.0					59.6	5.8	-
(42b)	(43b)	237-39[a]	42.0	$C_{18}H_{21}N_7O_2$	58.8	5.8	26.7	58.6	5.9	26.4
	(44b)	264-76[b]						59.3	5.6	-
(42c)	(43c)	192-93[d]	63.0	$C_{20}H_{25}N_7$	66.1	6.8	27.0	66.4	6.5	27.0
	(44c)	175-76[c]	5.0					66.1	6.8	-

Crystallised from (a) ethylacetate; (b) benzene-pet.ether mixture: (c) pet.ether; (d) benzene; (e) ethanol.

a slight amount of water, dried over anhydrous sodium sulphate. Removal of the solvent and chromatographic separation of the solid gave the compounds:

(a) 3-Methyl-5,7-bis(dimethylamino)-s-triazolo[4,3-a]-s-triazine (19a) (0.56 g). Crystallised from benzene-pet.ether in colourless plates, m.p. 186-87° (Found: C, 49.0; H, 6.9. $C_9H_{15}N_7$ requires C, 48.9; H, 6.8%).

(b) 2-Methyl-5,7-bis(dimethylamino)-s-triazolo[1,5-a]-s-triazine (1.2 g) (20a), colourless needles from pet. ether, m.p. and mixed m.p. with the product obtained in earlier experiment did not depress. Total yield 95%.

Rearrangement of 3-methyl-5,7-bis(dimethylamino)-s-triazolo[4,3-a]-s-triazine (19a) to 2-methyl-5,7-bis (dimethylamino)-s-triazolo[1,5-a]-s-triazine (20a)

Compound (19a) (0.05 g) was heated to 200° in a metal bath and kept at 200° for 5 min. and cooled; colourless needles from pet.ether (0.04 g), m.p. 165°, mixed m.p. with the authentic compound did not depress.

Similarly compound (19b) was isomerised to (20b) in 60% yield at 300°.

Rearrangement of (19a) to (20a) in 2% aqueous sodium hydroxide

When compound (19a) was treated with 2% aqueous sodium hydroxide (5 ml) for 2 hr., it isomerised to (20a).

Rearrangement of 5,7-bis(dimethylamino)-s-triazolo[4,3-a]-s-triazine (40a) to 5,7-bis(dimethylamino-s-triazolo[1,5-a]-s-triazine (41a)

When compound (40a) (0.1 g) was treated with 2% methanolic solution of sodium hydroxide (5 ml) at room temperature for 2 hr. it rearranged to (41a). The methanolic solution was passed through a column of silica gel using $CHCl_3$-MeOH (95:5) as eluant. The fast moving fraction collected and solvent removed (0.05 g). Colourless needles from benzene-pet.ether, m.p. 157-58° (Found: C, 46.6; H,6.5. $C_8H_{13}N_7$ requires C, 46.4; H, 6.3%).

Attempted oxidative cyclisation of ethyledino-2-hydrazino-4,6-bis(dimethylamino)-s-triazine (27)

Compound (27) (0.5 g), lead tetraacetate (1 g) and benzene (30 ml) were stirred at room temperature for 15 min. The mixture was then heated to boil and filtered hot. The residue obtained after removal of solvent was found to be a mixture from which analytically pure sample could not be obtained.

Similar result was obtained with bromine.

Oxidative cyclisation of 2-benzylidenehydrazino-4,6-bismorpholino-s-triazine (45b); preparation of (43b)

A solution of (45b) (1.1 g) in glacial acetic acid was treated with lead tetraacetate (1.4 g) at room temperature with stirring. The reaction mixture was left at room temperature, for 30 min. It was diluted with water (40 ml) and neutralised with sodium carbonate. The precipitated product was filtered, washed and dried (0.3 g). Colourless plates from ethylacetate; m.p.238-39° (lit.[8] 238-40°); mixed m.p. with (43b) prepared earlier did not depress (superposable IR spectrum).

Oxidative cyclisation of 2-benzylidene-hydrazino 4,6-bis(dimethylamino)-s-triazine (45a) (0.5 g)

The reaction was carried out according to the above procedure (0.25 g). Crystallised from benzene-pet.ether mixture in colourless needles, m.p. 172-73°, identical with (43a).

N,N-trisacetamido-2-hydrazino-4,6-bis(dimethylamino)-s-triazine (24)

A solution of (17a) (2 g) in acetic anhydride (10 ml) and pyridine (1 ml) was refluxed for 30 min. It was poured into ice-cold water. The colourless precipitate was filtered, washed and dried (2.8 g). Crystallisation from benzene gave colourless prisms; m.p. 154-55° (Found:

C, 48.5; H, 6.9; N, 30.6. $C_{13}H_{21}N_7O_3$ requires C, 48.3; H, 6.5; N, 30.3%).

Action of DMSO on N-acetyl-2-hydrazino-4,6-bis (dimethylamino)-s-triazine (18e)

A solution of (18e) (0.5 g) in DMSO (10 ml) was refluxed for 20 hr., cooled, diluted with water and extracted with chloroform. The extract was dried over anhydrous sodium sulphate. The residue (0.175 g), after removal of solvent, crystallised from benzene in colourless plates, decomposing at 330-31° (Found: N, 36.4%).

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S U M M A R Y

PART - I: The action of allyl bromide on leuco anthraquinones

Because of the sparing solubility of the anthraquinonoid vat dyes in common organic solvents, purification by chromatographic methods and crystallisation are difficult. These dyes are also not amenable to NMR spectroscopy and mass spectrometry. Methyl ethers of leuco anthraquinonoid vat dyes have greatly increased solubility and some have adequate solubility for NMR spectroscopy. A few have also been submitted to mass spectrometry.

Extending the work on the preparation of more soluble derivatives of anthraquinonoid vat dyes, the action of allyl bromide on leuco anthraquinones was studied, because allyl ethers of phenols are known to be much more soluble than methyl ethers. Treatment of leuco anthraquinone with excess allyl bromide gave 9-allyl-9-hydroxy-10-anthrone (1) in quantitative yield and not the expected diallyl ether (2). Its NMR spectrum in CCl_4 shows the allylic methylene at 7.51 and a three-proton multiplet in the region between 4.8 to 5.81 (terminal methylene and

vinyl protons of the allyl group). The tertiary hydroxyl is seen at 6.3.

The reaction of allyl bromide on the dianion of anthrahydroquinone seems to be a para-Claisen type rearrangement. As soon as the mono-allyl ether is formed, it undergoes the Claisen migration to an o-position which is immediately followed by a Cope-type rearrangement. The remarkably rapid C-allylation of anthrahydroquinone to the oxanthrone (2) at 15-20° must be related to the reactivity of the meso-position in anthracene and the stability of the oxanthrone derivative.

Support for the para-Claisen rearrangement is found in the action of ٢,٢-dimethylallyl bromide on the dianion of anthrahydroquinone. Because of the double 3,3 sigmatropic shift, there is no end group interchange and the product proved to be (3) and not (4) on the basis of its NMR spectrum. One of the gem-dimethyl groups of the prenyl side chain appears at 9.21, a shift of about 0.6 ppm highfield when compared to the second methyl group. This can be explained by assuming that one of the gem-dimethyl groups is sterically held above

or below the plane of the benzene ring and thereby abnormally shielded because of the ring current effect.

H. Kondo in 1910 tried unsuccessfully to synthesise benzanthrone from allyl oxanthrone (2). Our attempts to convert allyl oxanthrone (2) to benzanthrone by using various cyclising reagents, such as sulphuric acid, aluminium chloride-sodium chloride melt and aluminium chloride in pyridine were also unsuccessful. The reaction of p-toluenesulphonic acid in dry benzene on allyl oxanthrone (2) was interesting. There was no reaction at room temperature, whereas dehydration was extremely rapid at 70°. Two products were obtained and were assigned the structures (5) and (6) based on the spectroscopic data. The allylidene-anthrone (5) was postulated as an intermediate in the Bally-Scholl mechanism for the formation of benzanthrone via an aldol condensation with acrolein. However, it has not been possible so far to convert (5) to benzanthrone.

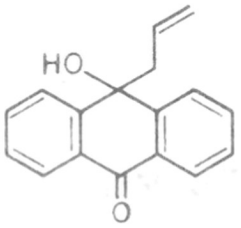
Treatment of the leuco derivative of 4-hydroxyanthraquinone with allyl bromide gave two products, one alkali-soluble and the other alkali-insoluble. The latter was the expected allyl oxanthrone (7). The alkali-soluble isomeric product

has been assigned structure (8). Leuco derivative of β-hydroxyanthraquinone and α-aminoanthraquinone gave the corresponding 9-allyl-9-hydroxy-10-anthrones.

PART II: Constitution of yellow pigments from α-aminoanthraquinones and s-phthaloyl chloride.

Pigment-using industries are interested in inexpensive bright yellow pigments with good fastness properties. The condensation of α-aminoanthraquinone and its nuclear substituted derivatives with the chlorides of diacids which give useful pigments are the subject of many patents.

According to the patent literature, the condensation of one mole of α-aminoanthraquinone with one mole of s-phthaloyl chloride gives a bright greenish yellow pigment of unknown constitution. When the condensation was carried out using one mole each of α-aminoanthraquinone and s-phthaloyl chloride as described in USP 2,914,542, the pigment (A) crystallised from ortho-dichlorobenzene in bright greenish yellow microscopic needles which decomposed at 340-42°. The IR spectrum of (A) shows four strong absorption bands in the carbonyl region at 1710, 1683, 1668 and



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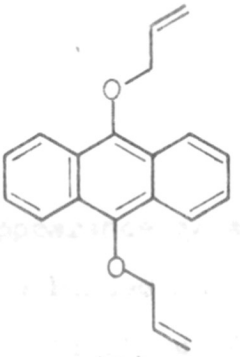

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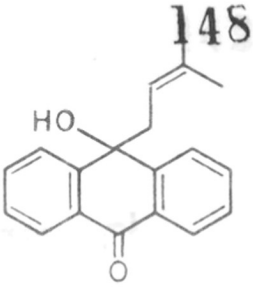

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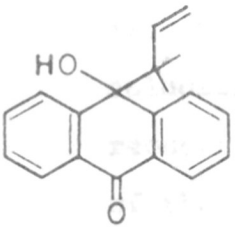

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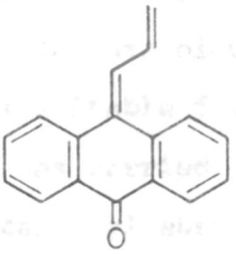

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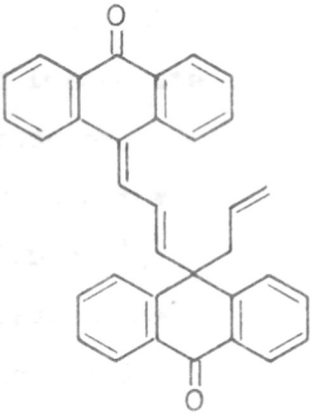

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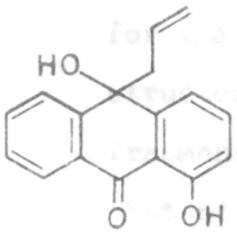

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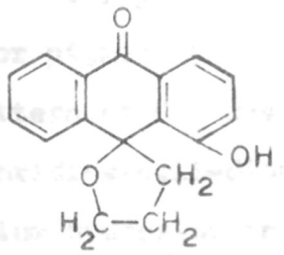

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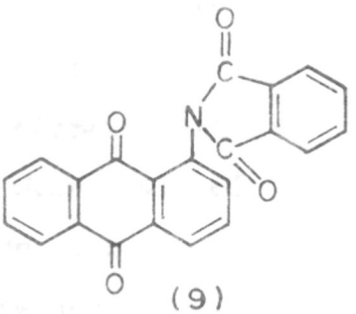

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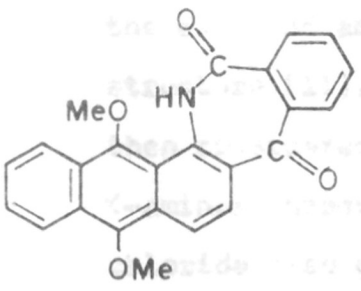

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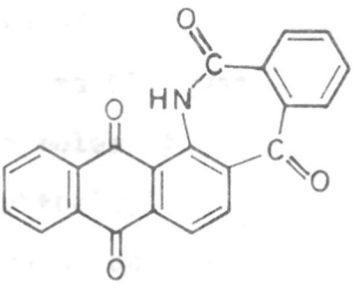

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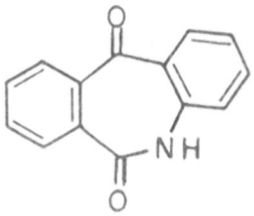

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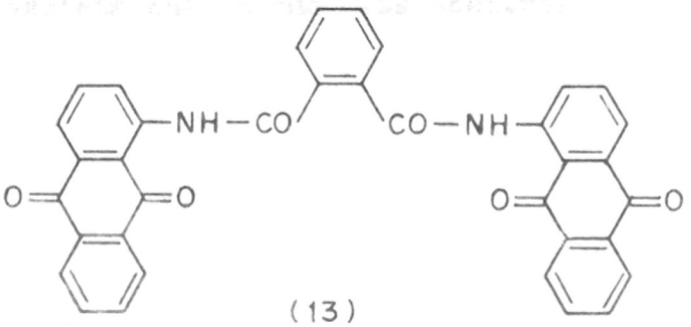


(13)

1635 cm^{-1}. The non-appearance of a band above 1710 cm^{-1} and the appearance of a bonded NH at 3250 cm^{-1} do not favour the phthalimido structure (9). However, the mass spectral molecular weight (M^{+} 353) is in agreement with (9) ($C_{22}H_{11}NO_4$). Because pigment (A) had inadequate solubility in solvents suitable for NMR spectroscopy, reductive methylation was carried out. The IR spectrum of the product shows carbonyl absorption at 1675 cm^{-1}, and NH absorption at 3325 cm^{-1}. The NMR spectrum shows a complex pattern in the aromatic region. Based on IR, NMR and mass spectra, the structure (10) was considered for the reductive methylation product and consequently structure (11) for pigment (A). The mass spectral fragmentation pattern of (A) was not in conformity with that of morphanthridine-6,11-dione (12). Hydrolysis of (A) with 10% sodium hydroxide in cellosolve or conc. sulphuric acid yielded α-aminoanthraquinone and not the expected amino acid. These results ruled out the structure (11). The other possible structure (13) was then considered. The condensation of two moles of α-aminoanthraquinone with one mole of s-phthaloyl chloride also gave the same pigment. Thus structure (13) was confirmed for pigment (A). However, it is difficult to explain the IR and mass spectral data.

The only way to account for the peak at m/e 353 is decomposition of the pigment thermally or by electron impact; the molecular ion is not seen, but only the next fragment ion.

Pigment (A) underwent thermal decomposition and two products were obtained: (a) ‹-aminoanthraquinone and (b) N-(1-anthraquinonyl) phthalimide(9). In the mass spectrum of (A) the base peak is at m/e 223 which corresponds to the radical ion of ‹-aminoanthraquinone, whereas the peak at m/e 223 in the mass spectrum of (9) is insignificant. These results also favour structure (13) for pigment (A). To reconcile the C=O stretching vibrations in the IR spectrum, one has to invoke a steric factor, keeping the anthraquinonyl units in (13) in different planes.

The condensation of two moles of 1-amino-4-methoxyanthraquinone with one mole of s-phthaloyl chloride gave the expected bis-amide which resembled (13) in not showing the molecular ion in its mass spectrum. However, condensation of one mole of 1-amino-4-methoxyanthraquinone with one mole of s-phthaloyl chloride gave N-(4-methoxy-1-anthraquinonyl) phthalimide.

When this work on the constitution of pigment (A) was in progress, a pigment sample, Helio Fast Yellow E-3R was kindly supplied by Farbenfabriken Bayer. Colour Index, 3rd ed., 1971, mentions Helio Fast Yellow E-3R (Pigment Yellow 99) as belonging to the anthraquinone class, but the constitution has not been disclosed. Helio Fast Yellow E-3R was identical in all respects with pigment (A) and must therefore have the structure (13). C.I. Pigment Yellow 123 (Patrician Yellow 21-2817) has also been assigned the same structure in a recent issue of the Colour Index (Additions and Amendments,2,Jan. 1972). Since it is unlikely that two commercial pigments having the same structure have two different numbers in Colour Index, a sample of Pigment Yellow 123 was obtained, but it was found that the two commercial pigments were identical. The identity of the three pigments (Pigment A, CI Pigment Yellow 99 and CI Pigment Yellow 123) was further established by the determination of the X-ray powder diffraction pattern.

PART III: The action of thionyl chloride on hydroxyanthraquinones

Green in 1926 showed that the action of thionyl chloride on quinizarin gave a red compound to which he assigned structure (14), based on its chemical properties. However, the alternate structure (15) cannot be ruled out merely on the basis of chemical properties. The preparation of (A) has been repeated and the structure (15) confirmed by its NMR spectrum in arsenic trichloride. The 2,3-hydrogens appear as a singlet at 3.03 and not two o-coupled doublets expected from structure (14) in which they are nonequivalent.

The prolonged reaction of thionyl chloride on quinizarin gave a mixture of compounds, from which the dichloro compound (16) has been isolated. Replacement of Cl by OEt gave 9-hydroxy-10-ethoxy-1,4-anthraquinone which shows two o-coupled doublets for the 2,3-protons in its NMR spectrum. This anomaly is probably due to steric effects resulting in slight variation in electron densities at the 2- and 3-positions. In the NMR spectrum of the acetyl derivative, the 2,3-hydrogens are seen as a singlet. Structure (15)also finds powerful support from two considerations: (a)

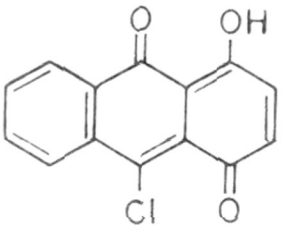
the obviously higher resonance energy of (15) in comparison with (14), because the former contains an additional aromatic ring; and (b) anthra-4,9-quinone has not been isolated so far.

A product with a similar 1,4-quinone system as in (15) was obtained by the action of thionyl chloride on 6,7-dichloroquinizarin.

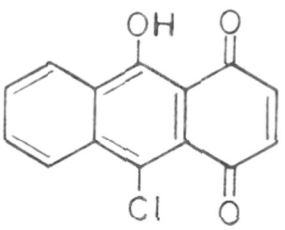
PART IV: Synthesis of s-triazolo-s-triazines: derivatives of 2-hydrazino-s-triazines

The s-triazine ring provides a useful chromophore-insulating group in the synthesis of dyes. Cyanuric chloride is an important intermediate for the synthesis of reactive dyes, because the three nitrogen atoms render the three chlorine atoms highly labile and readily susceptible to nucleophilic substitution. Preliminary work in this laboratory has been shown that 2-hydrazino-s-triazines (17) can be used for the preparation of (a) azo dyes, and (b) intermediates with an additional ring system (e.g. pyrazolone) for constructing more complex dyes or more effective colour insulators than the parent triazine.

When this work was initiated, the known s-triazolo[4,3-a]-s-triazines were prepared from



(14)



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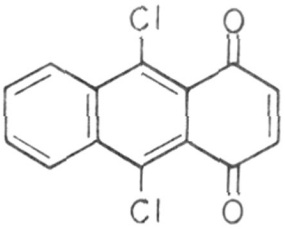

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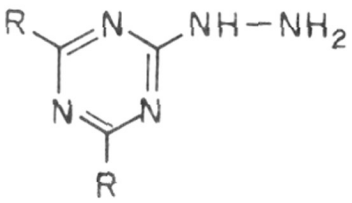

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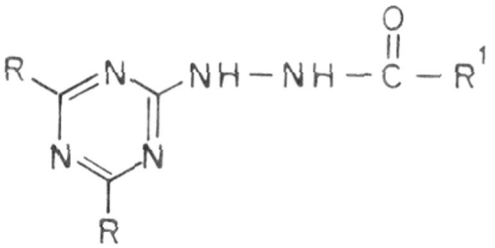
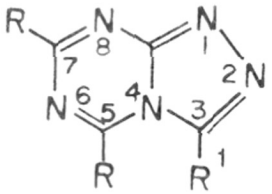
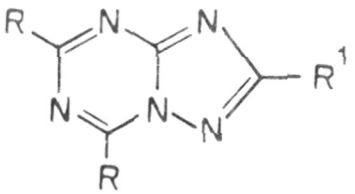


(18)



(19)



(20)

s-triazoles, building up the triazine portion from aliphatic precursors. M. Tisler *et al.* in 1966 have synthesised a few 3-phenyl-*s*-triazolo [4,3-a]-*s*-triazines by the oxidative ring closure of benzylidene-2-hydrazino-*s*-triazine with lead tetraacetate. The known representatives of *s*-triazolo[1,5-a]-*s*-triazine were prepared in 1970 by Bokaldere and Grinshteins from *s*-triazole derivatives.

Treatment of 2-hydrazino-*s*-triazines (17; R=NMe_2, ) with formic acid or acetic acid resulted in the formation of uncyclised acyl hydrazides (18; R^1 = H; Me) and not the bicyclic products (19; R^1 = H; Me), although the analogous 2-hydrazinopyrimidines undergo ring closure with extreme ease on treatment with carboxylic acids, anhydrides or esters. The exclusive formation of the uncyclised acyl intermediates (18) may be connected with the presence of the NR_2 substituents in the 4- and 6-positions of *s*-triazine. The reaction of 2-hydrazino-*s*-triazines (17) with an equimolar amount of benzoyl chloride also gave the benzoyl hydrazide (18; R^1 = Ph).

When the *N*-acetyl derivative (18; R=NMe_2; R^1 = Me) was refluxed in xylene with phosphorous

pentoxide and the product worked up under alkaline conditions (pH above 10), cyclisation to (19) is followed by isomerisation to 2-methyl-5,7-bis(dimethylamino)-s-triazolo[1,5-a]-s-triazine (20; R=NMe_2; R^1=Me) took place. When the pH is 6-7 during isolation a mixture of (19) and (20) is obtained. Using a modified procedure for cyclodehydration, it was possible to convert (18) into (19) or (20) exclusively. Products from (18), where R^1=H, are mostly of type (19). However, where R^1=Me or Ph, two products have been isolated and characterised as derivatives of (19) and (20). Isomerisation of type (19) to type (20) can be effected by acid, alkali or heat. P. Guerret et al. in 1971 reviewed similar isomerisations in other heterocyclic systems and termed these as Dimroth-type rearrangements.

Because of steric interaction between 3- and 5-substituents, the 3-methyl group in 3-methyl-s-triazolo[4,3-a]-s-triazine (19; R=NMe_2; R^1=Me) is deshielded by about 0.3 ppm in the NMR spectrum in comparison with the 2-methyl derivative (20; R=NMe_2; R^1=Me); the chemical shifts are 7.28 and 7.6 respectively. The chemical shift of the protons of 7-NMe_2 group was mainly constant in both the bicyclic systems (19) and (±20) irrespective of the substituent in the 3- or

the 2-position. The protons of the 5-NMe_2 group are slightly deshielded in both (19) and (20) where R^1 = H; but when R^1=Me or Ph, they are deshielded in (20), but shifted upfield in (19). The considerably highfield shift of the protons of the 5-NMe_2 group in (19) when R^1=Ph may be explained in terms of the nonplanar conformation into which the 3-phenyl group is forced by the neighbouring NMe_2 group. The protons of the 3-phenyl group (19; R^1=Ph) appear as a complex multiplet, whereas the protons of the 2-phenyl group in (20; R^1=Ph) are resolved into two multiplets; the o-protons are deshielded compared to the m- and p-protons. This can be explained by assuming that the 2-phenyl group exists in planar conformation with the bicyclic nucleus. The mass spectral fragmentation of the two systems (19) and (20) was also studied.

Mechanisms for the cyclodehydration of (18) to (19) and the thermal and base-catalysed rearrangement of (19) to (20) have been suggested.

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Jan. 1974.