Presented to Prof. K. Venkata raman.

With respectful regards. B. C. Subba Rao

30th Jan 1963.

SYNTHESES

USING

PHENOLIC COMPONENTS OF CASHEWNUT SHELL LIQUID

by

AMAR SINGH GULATI, M.Sc.

National Chemical Laboratory,
POONA 8
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A
THESIS
SUBMITTED TO
THE UNIVERSITY OF POONA
for
THE DEGREE OF
DOCTOR OF PHILOSOPHY
IN CHEMISTRY

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GENERAL INTRODUCTION

India is one of the major cashew (Anacardium occidentale) producing countries of the world. The production during 1960-61 was 73,000 tons and the production is expected to reach 1,50,000 tons by the end of 1965-66[1]. India meets over 90% of the total world demand for cashew kernels which are produced from the cashewnuts. Home production not being sufficient at present, India also imports raw cashewnuts from Mozambique and other countries and after processing here export[2] the kernels.

The cashew kernel is present in the kidney shaped nut or shell which is attached to the cashew apple. The nut contains the kernel inside, while the outside shell contains an acrid oily juice, having vesicant properties. For the production of kernels the cashewnuts are carefully roasted with constant stirring in shallow iron pans or perforated earthenware pans which are heated by direct fire. Under these conditions, most of the cashewnut shell liquid is lost. Some of the larger processing concerns use cylindrical rotary roasters whereby a large portion of the shell liquid is recovered. The latest trend, however, is to pass the nuts held in wire trays through a cashewnut shell liquid bath maintained at 188-193°C. at a uniform speed of fifteen feet in eighty to ninety seconds. Owing to the high temperature and the presence of moisture (7-8%) in the nuts, the honey combed

cells of the shell burst and the exuded liquid flows into the bath, at the same time roasting the kernels to the desired degree. The recovery of the cashewnut shell liquid (CNSL) by this process is much higher and only 10 to 15% residual oil is left in the broken shells[3] which can be further extracted by using superheated steam.[4] After the roasting operation, the nuts are carefully broken and shelled manually, to obtain the kernels. Latest trends are to open the nuts mechanically and remove the kernels which is roasted to the required degree. The empty shells are expressed in expellers to give a red coloured liquid. The higher cost of expression is well compensated by the higher returns for the better quality of kernels and shell liquid.

The kernel weighs about 30% of the weight of the cashewnut and the proportion of the shell liquid to kernel is approximately 1:1. According to this about 45000 tons of CNSL will be produced in 1965-66, provided all the shell liquid is recovered. However taking an average yield of 66% only, the CNSL available from the year 1965-66 onwards would be about 30,000 tons per annum, which is over four times the 1960-61 production.

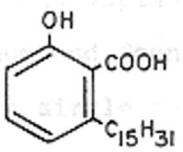
Cashewnut shell liquid is a black viscous corrosive liquid thus creating a disposal problem. Presently the major portion of the CNSL produced in India is being exported to U.S.A., U.K., Japan etc. where it is used in the

paint industry etc. Exports are declining[3] while production of CNSL is on the increase, practical methods have to be developed soon to utilise this large amount of the CNSL as raw material for the production of various types of chemicals, potentially useful in industry such as dyes, detergents and compounds of pharmaceutical value. This shows the magnitude of the problem of finding out new uses for this raw material.

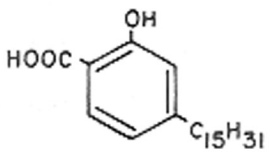
The chemistry of CNSL has been the subject of several investigators. Stadeler[5] investigating the ether extract of cashewnuts reported that 90% of it consisted of an acid (anacardic acid), the rest being a dihydroxy phenol (cardol). Later on, Ruhemann and Skinner[6] gave anacardic acid its present formula $C_{22}H_{32}O_3$ and suggested that it was probably a hydroxy carboxylic acid as they could prepare an acetyl derivative of its methyl ester. Smit[7] further showed it to be a homologue of salicylic acid having the unsaturated side chain $C_{15}H_{27}$ attached somewhere on the nucleus. Hydrogenated anacardic acid (tetrahydroanacardic acid, T.H.A.A.) gave violet colour with alcoholic ferric chloride and its methyl-ether-methyl-ester derivative on oxidation with chromic acid gave palmitic acid and by analogy of this acid with pelandjauic acid, Romburg et.al.[8] suggested that anacardic acid might be $C_6H_3(OH)(COOH)(C_{15}H_{27})$. Later on Pillay[9] studying the behaviour on

oxidation of anacardic acid, anacardol and their hydrogenated derivatives came to the conclusion that anacardic acid is an ortho-hydroxybenzoic acid with an unsaturated side chain $C_{15}H_{27}$.

The fact that anacardic acid and tetrahydroanacardic acid get decarboxylated to anacardol and tetrahydroanacardol respectively, and also that the phenyl-pentadecylate on Fries migration and subsequent reduction of the carbonyl group gives ortho- and para-pentadecyl phenols, none of which is dentical to tetrahydroanacardol led Gokhale, Patel and Shah[10] to conclude that tetrahydroanacardol is m-pentadecyl-phenol. They further substantiated it by showing that tetrahydroanacardol gave tribromo derivative whereas the o- and p-pentadecyl phenols gave only the dibromo derivatives and also that the methyl ether of anacardol on oxidation yielded m-methoxybenzoic acid. Hence tetrahydroanacardic acid could have either of the following structures:



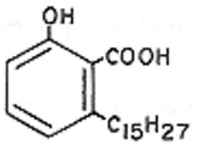
I



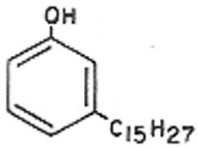
II

Backer and Haack[11] prepared an acid from tetrahydroanacardol by Kolbe's synthesis. On steric

considerations the acid formed was believed to be 2-hydroxy-4-pentadecyl benzoic acid (II) (m.p.98.5-99°C). Its mixed melting point with tetrahydroanacardic acid showed depression. Thus the structure of tetrahydroanacardic acid was finalised as 2-hydroxy-6-pentadecylbenzoic acid (I). Hence anacardic acid and its decarboxylated product anacardol would be III and IV respectively.



III



IV

Ittyerah et.al.[12] studied the properties of the oils obtained from cashewnut shells by solvent extraction and by roasting and observed that they were different, possibly because of some decarboxylation or polymerisation or both taking place during the roasting.[13]

Harvey and Caplan[14] distilled the commercial CNSL under vacuum and found that 70% of the total distillate was a single phenolic component with an unsaturated side chain in the meta position. This substance they termed as cardanol and concluded that this was presumably formed by the decarboxylation of anacardic acid.

Wasserman and Dawson[15] hydrogenated the mono-phenols obtained either by heat or solvent extraction. The hydrogenated product was the same in both cases, thus proving that the heat treatment did not alter the carbon skeleton. Further, investigations by Dawson and co-workers[16] established that neither anacardic acid nor cardanol was a homogenous compound. Chromatographic purification of anacardic acid and molecular still distillation of cardanol revealed that both of them were mixtures of several olefinic components possessing average unsaturation equivalent to about two double bonds.

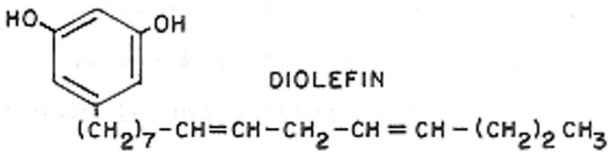
Symes and Dawson[17] obtained four pure components from the methyl ether of anacardol by chromatography. Their structures were elucidated by studying the products of ozonolysis and oxidative degradations. They reported the following compositions: (1) 3-pentadecyl anisole, 4.3%, (2) 3-(pentadecenyl-8')-anisole 45.1%, (3) 3-(pentadecadienyl-8',11') anisole 19.4% (4) 3-(pentadecatrienyl-8',11',14') anisole 31.2%.

Similarly, Paul and Yeddnappali[18] showed the heteroolefinic nature of anacardic acid by subjecting it to fractional crystallization at temperatures 0° to -80°. The composition reported by them is: saturated component, 4%; Mono-olefinic, 15%; Diolefinic, 44%; Triolefinic, 37%.

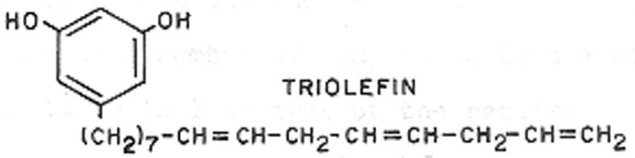
The diphenolic component present in CNSL and reponsible for the vesicant nature of it, is cardol, first isolated by Staddeler and assigned the molecular

formula $C_{21}H_{32}O_2$ by Becker and Haack[11]. The structure of cardol was finalised as 5-pentadecadienyl resorcinol by the investigations of Becker and Haack[11] and Paul and Seddnappalli[19] and confirmed by the synthesis of 5-pentadecyl resorcinol by Dawson and Wassermann.[15]

The positions of the olefinic linkages in the side chain of cardol were found to be similar to that in cardanol except that only diolefin and triolefin components have been isolated so far. The products of ozonolysis and oxidative degradations of these olefins were identified and the following structures were assigned to them (V and VI).



V



VI

Thus commercial cashewnut shell liquid is a mixture of a salicylic acid derivative and mono and dihydroxy phenols having a long unsaturated side chain. To make it a useful commodity it is necessary to take

advantage of these structural features and utilise them in the synthesis of various types of potentially useful chemicals.

Amongst the various uses so far proposed for CNSL, anacardol and its derivatives are: for the manufacture of insulating varnishes, typewriter rolls, oil and acid proof cold setting cements, automobile brake-lining, plasticisers, mosquito larvicides[20], detergents[21] etc. Many patents have been taken out for using CNSL for lacquers, baking enamels[22], water proof materials insulating and plastic compositions etc. Advantage of the presence of a phenolic hydroxyl group in the components has been taken in the preparation of 4-amino and 6-amino pentadecyl phenols, which are recommended as oil soluble antioxidants and gasoline gum inhibitors[23]. Tetrahydroanacardol has also been used for the preparation of azo dyes.[21,23,24] Kudva[25] patented the preparation of azo dyes from the cashewnut shell liquid, but the presence of a number of components in the oil made it difficult to isolate dyes of the required standard of purity. Tetrahydroanacardol has also been suggested for use as a perfume fixative and as a plasticizer for cellulose acetate lacquers.[14] Derivatives of tetrahydroanacardol are indicated to be useful as intermediates in the manufacture of heat reactive resin coatings.

The present investigation was started with a view to systematically explore the possibility of obtaining some useful pure chemical compounds from CNSL e.g. (a) quaternary ammonium compounds which can be used as industrial sanitizing agents or germicides, (b) azo dyes of proved structure and desirable properties and (c) special synthetic chemicals potentially useful in the pharmaceutical field.

In a study of this nature it is essential to start with pure components, so that the identity and the purity of the final products are beyond doubt. Hence the pure components of CNSL like tetrahydroanacardol (T.H.A.), tetrahydroanacardic acid (T.H.A.A.) and tetrahydrocardol have been used as the starting materials in the present investigation rather than crude CNSL or anacardol, anacardic acid and cardol which have been proved each to be mixture of two-three products by themselves.

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PART I
QUATERNARY GERMICIDES

INTRODUCTION:

Quaternary ammonium surface active antiseptics have secured a prominent and important place in the fields of medicinal and general disinfection during the past decade. These compounds are of particular interest in that, unlike most other disinfectants, they exhibit not only germicidal action but also surface active detergent and wetting properties.

Quaternary germicides may be defined as a group of bactericidal substances composed of quaternary compounds of nitrogen and to a lesser extent of phosphorus and arsenic. These elements are normally trivalent and when the tertiary amines (phosphines or arsines) are allowed to react with an alkylating agent; such as alkyl halide, quaternary salts are formed:

$$R_3N + R'X \longrightarrow R_3N\overset{+}{R'}X$$

Domagk's[1] pioneering work has clearly established the importance of the long alkyl chain and the quaternary nitrogen atom as fundamental units of structure for the activity of the quaternary nitrogen compounds.

Quaternary nitrogen compounds, being salts of strong acids and strong bases, are practically neutral in reaction and are not subject to hydrolysis in aqueous solutions.

Their stability, non-volatility, solubility in water, absence of odour and high activity have made them particularly attractive as germicides. It is for these reasons quaternary germicides are today considered to be the nearest in line to an 'ideal antiseptic' and as such they are being increasingly used in food industry, diary industry, eating and drinking establishments, medicinal and other fields as sanitizing agents, disinfectants and germicides. Their successful application in the field of sanitation has led to continuous research on properties and applications and to the synthesis of new types of quaternary compounds.

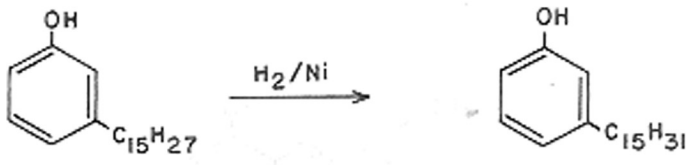
Quaternary nitrogen compounds ionise into two portions (i) the positively charged cation, representing the bulk of the compound in respect of molecular weight and germicidal activity, (ii) the negatively charged anion representing only a small portion of the molecular weight of the compound and exerting but little influence on the germicidal activity. Structurally the nitrogen of the quaternary compound can be derived from a tertiary amine or from part of heterocyclic ring such as pyridine quinoline etc. The activity of the germicide depends on the bulk and length of the alkyl chain attached to the nitrogen atom. The long alkyl chain R (1) may be directly linked to a quaternary nitrogen atom or 2) may form part of a substituted chain or 3) may be directly linked to an isocyclic ring or 4) may be directly linked to a carbon atom of nitrogenous hetrocycle etc. The object of present study

was to study the properties of quaternary nitrogen compounds derived from alkylated phenols[11] (class 3) specially the main phenolic component of cashewnut shell liquid (CNSL), m-pentadecadienyl phenol (anacardol). The crude CNSL itself is reported to have germicidal properties[2] and it was hoped that the quaternary compounds derived from it would have far more pronounced germicidal activity and might prove useful as industrial sanitizers.

Accordingly the main phenolic components of cold pressed CNSL, anacardic acid and the heat extracted CNSL, anacardol were isolated and hydrogenated to yield the corresponding saturated tetrahydroanacardic acid (6-pentadecylsalicylic acid, T.H.A.A.) and tetrahydroanacardol (m-pentadecylphenol, T.H.A.). Using these as starting materials quaternary ammonium, pyridinium and isoquinolinium compounds were prepared by various routes so that there were slight changes in the structure of the molecule, variations in linkages and presence of certain functional groups in the alkyl phenol moiety. By this it was hoped that certain useful conclusions could be drawn regarding the germicidal properties of quaternary compounds and the effect of certain functional groups or linkages present therein.

RESULTS AND DISCUSSION

The monophenolic component of the heat extracted CNSL, anacardol (I, m-pentadecadienyl phenol) obtained by vacuum distillation, on hydrogenation yielded tetrahydroanacardol (T.H.A. m-pentadecyl phenol III). Similarly the cold pressed CNSL by ion exchange method of Krishnaswamy et.al.[3] gave anacardic acid (II) which on hydrogenation yielded tetrahydroanacardic acid (T.H.A.A. IV)



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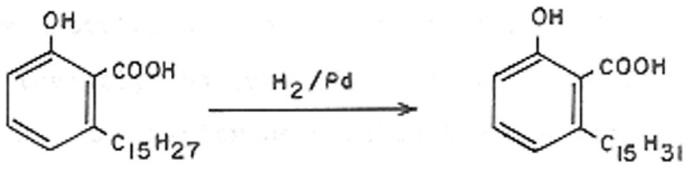
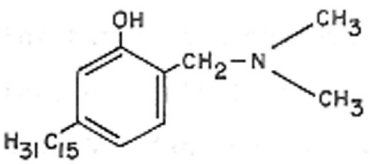


II IV

Quaternary compounds from T.H.A. (Type 1)

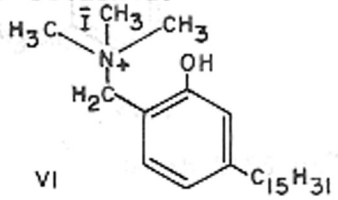
Baker[4] in 1942 and Quisno[5] in 1946 observed that the cationic surface active agents are bactericidal in low concentrations to a wide variety of gram positive and gram negative organisms. If the hydrophobic long alkyl chain present in T.H.A. is balanced by positively charged

hydrophilic group, quaternary ammonium, the resulting quaternary compound may be expected to give bactericidal surface active agent. With this in view Mannich reaction was carried out on T.H.A. using formaldehyde and dimethylamine and the Mannich base (V) was thus obtained. This Mannich base itself will be of further interest as an antimalarial compound. Compounds related to this (i.e. V) have been prepared by Burkhalter et.al.[6] and found to have appreciable activity.

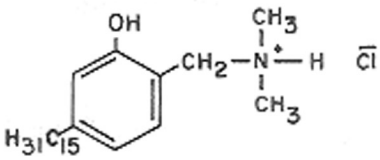


V

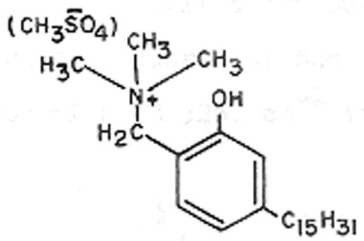
However, the activity of the Mannich base itself was not further investigated but it was reacted with CH_3I HCl, $(CH_3)_2SO_4$ and p-nitrobenzylchloride and the quaternary nitrogen compounds, VI, VII, VIII and IX were obtained.



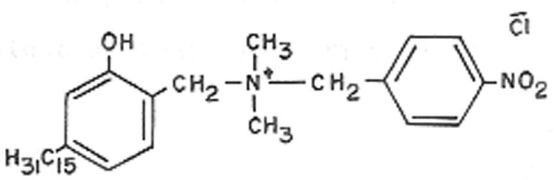
VI



VII



VIII

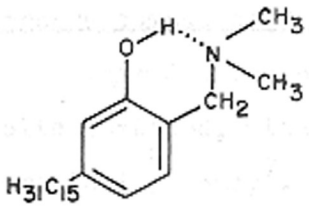


IX

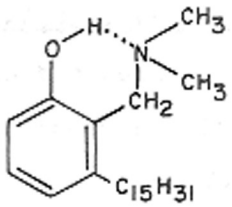
These quaternary compounds were found to be insoluble in water and hence were tested for their activity in 95% acetone solution. These were however found to be inactive upto a dilution of the order 1:5000. The activity at higher concentrations were not studied.

Position of $-CH_2-N(CH_3)_2$ group in the Mannich base (V)

Infrared spectrum of T.H.A. (III) has the following principal absorption bands, at 3220 cm^{-1} (-OH), at 1155 cm^{-1} (-OH, C-H, out of plane deformation), at 785 cm^{-1} (indicating three adjacent hydrogen atoms) and at 863 cm^{-1} (indicating a single free hydrogen atom). The infrared spectrum of the Mannich base (V) does not show any absorption at 3220 cm^{-1} region which can be attributed to chelation of -OH with >N- as shown in (V.A.) or (V.B.).



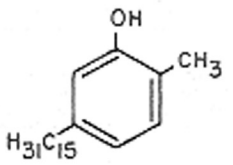
V.A.



V.B.

Bands at 1155 cm^{-1} and 863 cm^{-1} (single free hydrogen atom) were still there but 785 cm^{-1} band was absent. Infrared spectrum of the quaternary salt VI also has a -OH absorption at 3260 cm^{-1} (indicating that hydrogen bond is

broken because of quaternizing). Based on this and steric considerations, the sandwitched position (V.B.) was eliminated. This was further confirmed by reducing the Mannich base V to obtain o-methyl-T.H.A. (X) in the infrared spectrum of which a band at 3220 cm^{-1} indicating free -OH group reappeared. Thus Mannich base of T.H.A. was assigned structure V.



X

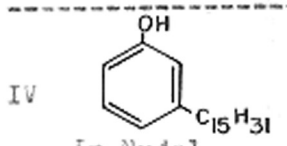
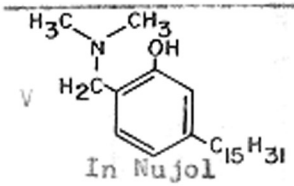
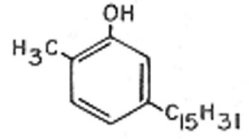
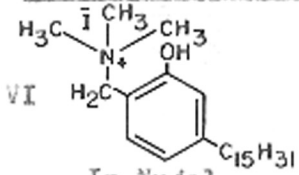
The infrared spectra were recorded in nujol on a Grubb Parson Double beam spectrophotometer using sodium chloride optics and the principal absorption bands are given in Table I.

Quaternary compounds from monochloro-T.H.A. (Type II)

Introduction of halogen into the nucleus of phenolic compound, without exception, increases its bactericidal potency[7]. This increase is less for ortho position than the para, perhaps owing to the inter-action between the hydroxyl group and the halogen atom[8]. Quaternary compounds containing chlorine in the nucleus have been prepared and found to possess greater activity than the corresponding unchlorinated quaternary salts.[9,10] Since the quaternary compounds of T.H.A. prepared through

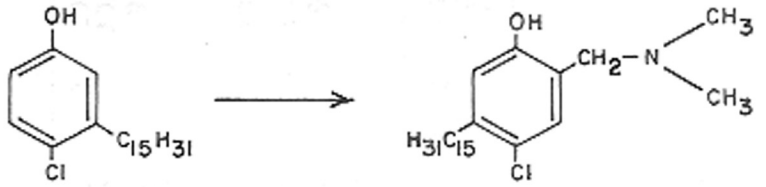
Table I

Principal Absorption Bands in Cm^{-1}

No.	Compound's structure	3650-2700	2700-2000	2000-1500	1500-1300	1300-1000		1100-900		900-650	
IV	 In Nujol	3220S		1589S	1304M	1282 1250 1265	1235 1155	1072 939 924		864 785 749 728	720 696
V	 In Nujol		2370VW	1613M 1579S 1511M	1429 1359 1330 1310	1288 1266 1248 1235 1210	1199 1183 1156 1120 1102	1045 1020 977 960 938	935	889 868 851 819 794	774 761 754 747 720
	 In Nujol	3220S		1647 1581 1501	1429 1323 1303	1284 1262 1242 1183	1152 1118	1040 1018 1003 981	941 923	863 807 764 748	723
VI	 In Nujol	3260S		1608M 1581S	1432S 1404S	1298 1272 1231 1155 1127	1108	1093 1014 993 975 951 928	913	886 868 834 804 770 751	721

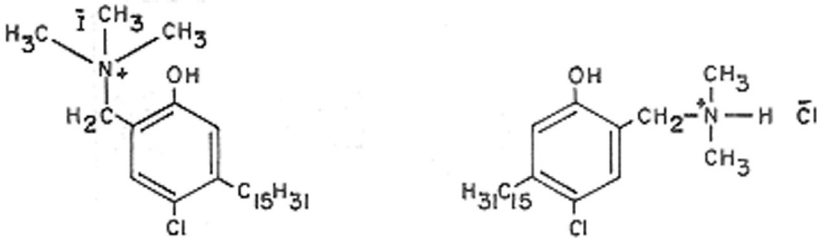
S=Strong; M=Medium; V=Very; W=Weak.

The Mannich base (V) were not very soluble and did not show much activity, the corresponding quaternary compounds were synthesised as before using p-chloro-T.H.A. instead of T.H.A. Para-chloro T.H.A. (XI) gave on treatment with formaldehyde and dimethylamine the Mannich base (XII).



XI XII

The Mannich base of mono-chloro-T.H.A. (XII) was quaternised by CH_3I and HCl to give quaternary salts XIII and XIV respectively.

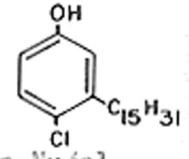
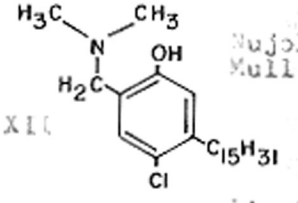
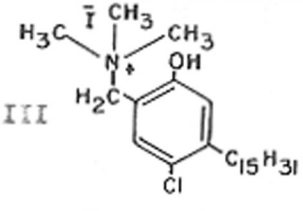


XIII XIV

Infrared absorption spectra of the Mannich base XII showed no absorption for -OH group in the region of 3300 to 3600 cm^{-1} whereas free -OH absorption around 3320 cm^{-1} appeared in the case of quaternary salt from it, where chelation is broken. This indirectly also confirms that chlorine is para to the hydroxyl group in the monochloro-T.H.A. and in the Mannich base XII. (Principal absorption bands are given in Table II).

Table II

Principal Absorption Bands in cm^{-1}

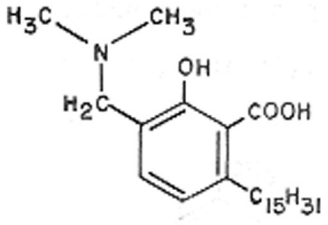
No.	Compound's structure	3650-2700	2700-2000	2000-1500	1500-1300	1300-1100	1100-900	900-650
XI	 In Nujol	3260 S	-	1608 1583	1357	1288 1276 1264 1242	1158 1138	1090 919 1049 975 953	868 790 845 779 825 810
XII	 Nujol Mull	2830 S	-	1608 1570	1486 1346 1467 1302 1424 1378	1261 1100 1242 1181 1163	1042 1021 976	885 803 871 755 845 722 810
	Liquid film	2860 S	-	1702 1608 1570	1481 1348 1442 1300 1463 1375	1257 1181 1161 1101	1040 1020 976	871 846 723 810
XIII	 In Nujol	3320 S	-	1611 1551	1481 1451 1410 1314	1294 1192 1266 1133 1235 1211 1171	1096 920 994 910 972 946	881 849 827 729 720

S = strong

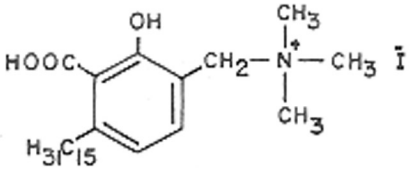
The quaternary salts thus obtained from this Mannich base were expected to have improved solubility and activity. Actually they were found to be soluble only in hot water and were inactive upto 1:5000 dilution in acetone solution.

Quaternary compounds from T.H.A.A. (Type III)

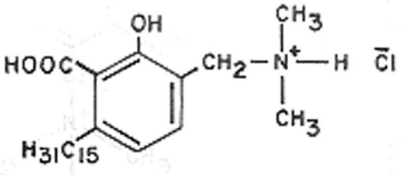
As the quaternary compounds from Mannich base of T.H.A.A. were insoluble in water, it was desired to introduce one more hydrophilic group in the nucleus. Fortunately T.H.A.A. contained carboxyl group and hence quaternary compounds XVI, XVII and XVIII were prepared through its Mannich base XV.



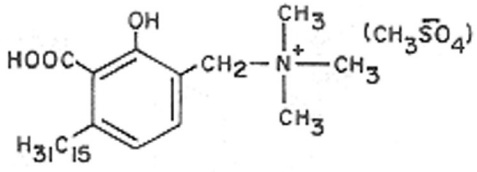
XV



XVI



XVII



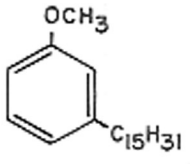
XVIII

These salts with free (-COOH) group were also found to be insoluble in water and inactive upto 1:5000 dilution in acetone medium.

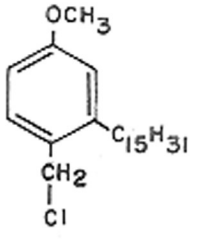
Infrared spectra of T.H.A.A. (IV) and Mannich base XV are recorded in Table III.

Quaternary compounds from methyl-ether of T.H.A. (Type IV)

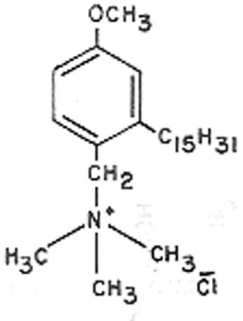
Isomeric para compounds of the type (I) were attempted by chloromethylation of T.H.A. which led to polymerisation. Chloromethylation was therefore carried with methyl-ether of T.H.A. (XIX) to give XX. This on quaternizing with trimethylamine, pyridine and isoquinoline gave the quaternary compounds XXI, XXII and XXIII respectively.



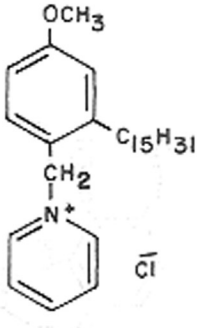
XIX



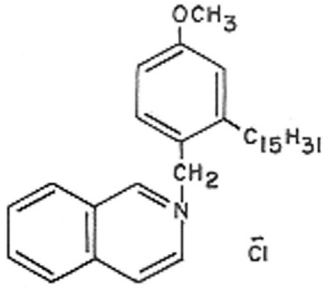
XX



XXI



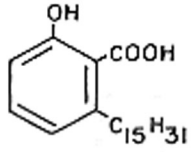
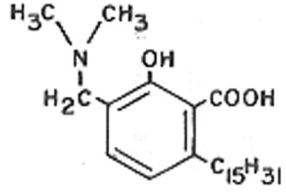
XXII



XXIII

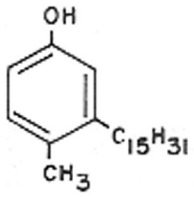
Table III

Principal absorption bands in cm^{-1}

No.	Compound's structure	3650-2700	2700-2000	2000-1500	1500-1300	1300-1100	1100-900	900-650
IV	 In Nujol	3000 Sh	2385W 2685Sh 2600Sh	1650S 1602S	1461Sh 1306S	1245 1209 1219 1168 1130		891 736 882 709 801 689 788 760
XV	 In Nujol		2420M	1598S 1568M	1483 1437 1467 1377 1354	1286 1131 1244 1217 1173	1059 909 1021 957 946	847 764 828 750 821 720 749

S=Strong; M=Medium; W=Weak; Sh=Shoulder.

Position of $-CH_2-Cl$ group: That the chloromethyl group has gone to the position indicated above (XX, para to $-OCH_3$) was established by reducing and demethylating (XX) to p-methyl-T.H.A. (XXIV). The other possible isomer, o-methyl-T.H.A. (X) was obtained by reducing the Mannich base of T.H.A. (V) and the two, on comparison, were found to be two distinct compounds.



XXIV

These quaternary compounds of Type IV were found to be soluble in water and also in 95% acetone. These compounds were found active both in water and in acetone solutions, as shown in the Table (V) their phenol coefficients were also determined.

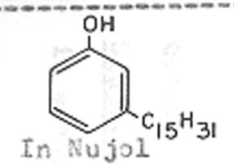
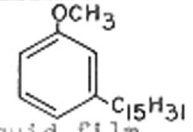
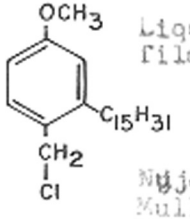
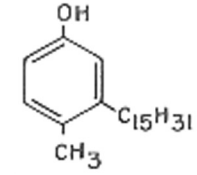
Infrared spectra of IV, XIX, XX and XXIV are recorded in Table IV.

Quaternary compounds from ω-Bromoethoxy-T.H.A. (Type V)

Encouraged with the results of compounds of Type IV and assuming that free phenolic -OH group masks the activity of quaternary compound, it was decided to eliminate the phenolic nature of the compound by blocking through an ethoxy bridge. Thus one mole of ethylene bromide was condensed

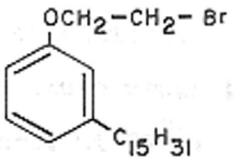
Table IV

Principal Absorption Bands in Cm^{-1}

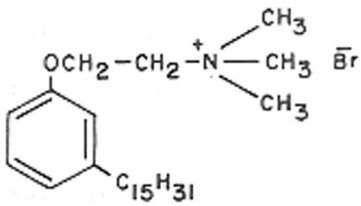
No.	Compound's Structure	3650-2700	2700-2000	2000-1500	1500-1300	1300-1100	1100-900	900-650
IV	 In Nujol	3220S	-	1589S	1304M	1282 1250 1155 1265 1235	1072 924 939	864 749 720 785 729 696
XIX	 Liquid film	2840S	-	1598S	1484 1440 1463 1311	1263 1163 1190 1154	1076 1046 996	870 775 722 846 740 692
XX	 Liquid film	2860S	-	1608 1583M 1501M	1478 1320 1360	1290 1209 1155 1258 1163 1119	1097 967 1042 938	870 813 851 724
	Nujol Mull	2830S	-	1602S 1579M	1492 1449 1372 1314	1292 1193 1162 1153 1101	1090 1040 940	898 864 852 813 787 722
XXIV	 In Nujol	3322S	-	1613 1587	1493 1379 1347 1303	1286 1250 1212 1194 1151 1124	1075 1033 997 946	867 823 806 786 740 725 697

S=Strong; M=Medium.

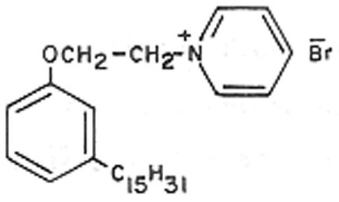
with T.M.A. to give XXV from which quaternary salts XXVI, XXVII and XXVIII were prepared.



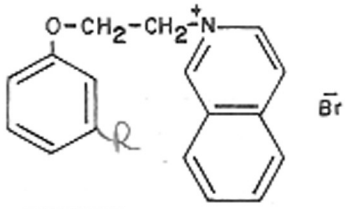
XXV



XXVI



XXVII



XXVIII

These compounds were also found to be water-soluble and active in accordance with our expectations except (XXVIII) as shown in Table (V).

Thus from the above results it is safe to conclude that phenolic -OH group masks the activity of quaternary nitrogen compounds to the extent that even the introduction of other activating groups like -Cl, -COOH etc. have very little effect on the activity of the resulting compound.

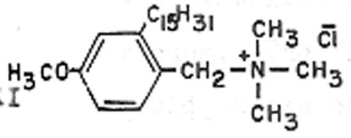
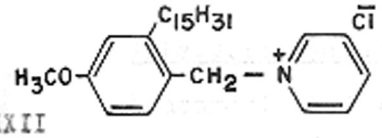
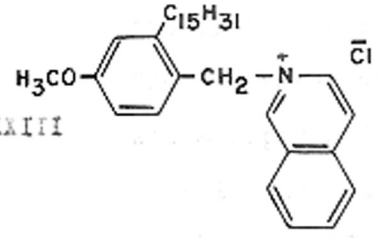
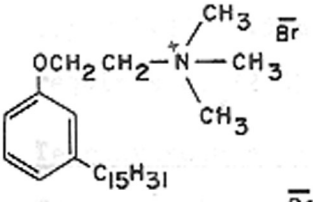
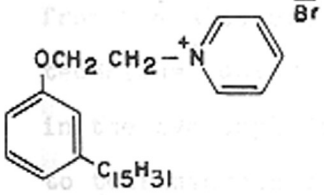
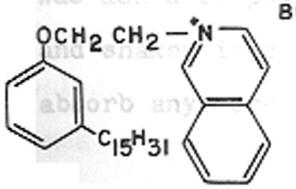
Method adopted for testing Biological activity

The activity of the various quaternary nitrogen compounds synthesised in this study were tested against Staphylococcus aureus 209 P. The compounds were dissolved in acetone (95%) or water depending upon their solubility

to a concentration of 0.5%. These solutions were added to sterile nutrient broth in serial dilutions under aseptic conditions. After seeding with 0.05 ml of a 24 hr. culture grown in nutrient broth at 37°C, incubated for 48 hrs. at 37°C. Visible growth was observed and observations recorded as shown in the Table V.

Phenol coefficients of the water soluble compounds were determined using Staphylococcus aureus A.T.C.C. 6538 as the test organism by the method given in "Methods of analysis" A.O.A.C. Eighth Edn. 88, (1955).

Table V

No.	Structure	Solubility behaviour	Active dilution against *Staphylococcus aureus*	Phenol Coeff.	Activity determined in solvent.
XXI		Soluble in water soluble in 95% acetone	100,000	80	Acetone & water
XXII		"	200,000	120	"
XXIII		"	100,000	60	"
XXVI		"	100,000	60	"
XXVII		"	50,000	60	"
XXVIII			++	60	"

++ Bacteria grows at 1:5000 dilution

EXPERIMENTAL

Distillation of commercial CNSL for obtaining Anacardol (I)

Commercial cashewnut shell liquid (heat extracted) 1 kg. was distilled from 2 litre round bottom flask under vacuum. The flask was heated slowly in the beginning to avoid excess of frothing. Anacardol, 450 g. a pale yellow liquid was collected between 195-200°C/2 mm. n_D^{30} 1.5080.

Catalytic hydrogenation of anacardol to tetrahydroanacardol (III)

Anacardol (300 g.) was hydrogenated (at 60°) in a Paar medium pressure autoclave using (W-7) Raney nickel (3 to 4 g.) as catalyst. Initial hydrogen pressure was 200 lbs./sq.in. When no more hydrogen absorption was noticed the hydrogenation was stopped and the product filtered and crystallized from petrol ether (40-60°). Tetrahydroanacardol (270 g.) was obtained in 90% yield as colourless needles. m.p.51-52°C. b.p.215-20°/3.5 mm. (Found, C, 82.5; H, 11.7; $C_{21}H_{36}O$ requires C, 82.83; H, 11.92%).

Tetrahydroanacardic acid (IV) Anacardic acid was obtained from the alcoholic extract of cashewnuts by the ion exchange technique[3] using anion-exchange resin Amberlite IRA-400 in the hydroxyl form. This was catalytically hydrogenated to tetrahydroanacardic acid. The acid (20 g.) in alcohol (60 ml.) was added to palladised charcoal suspended in alcohol (20 ml.) and shaken in a hydrogen atmosphere till it had ceased to absorb any more hydrogen. The catalyst was removed by

filteration, the filtrate diluted with water and cooled. The precipitated tetrahydroanacardic acid was then filtered and dried under suction. Two crystallizations from benzene-hexane mixture gave shining needles of T.H.A.A. (m.p.92-93°C. Found, C, 75.8; H, 10.4; $C_{22}H_{36}O_3$ requires C, 75.81; H, 10.41%).

Mannich base derived from T.H.A.(V) T.H.A. (15 g.) was dissolved in alcohol (100 ml.). The solution was cooled to -5°C, dimethylamine (10 ml, 30%) was added slowly with stirring (maintaining the temperature below 0°C). After the addition of dimethylamine, formaldehyde (5 ml.37%) was added. The reaction mixture was kept at 0°C for ½ an hour to one hour and then at room temperature for 18 hours. The crystalline mass was then separated by filteration, decolourised with active charcoal and recystallized from alcohol. Two further crystallizations gave the pure product (m.p.47°C; yield 13.0 g. 72.95%; Found, C, 79.9; H, 11.82; N, 3.7; $C_{24}H_{43}ON$ requires C 79.71; H, 11.9; N, 3.87%).

Quaternary salts derived from Mannich base of T.H.A.

Compound VI: To Mannich base of T.H.A. (V) (1.0 g.) methyl iodide (0.5 ml.) was added and the mixture warmed to get a homogenous solution. Immediately on cooling the solid separated out. Dry acetone was added and the reaction mixture cooled. The precipitate was filtered and washed four to five times with cold dry acetone to get the desired product VI.

(m.p.165°C yield 1.3 g. 93% Found: C, 59.64; H, 9.14; N, 2.8; I, 25.2; $C_{25}H_{46}ONI$ requires C, 59.12; H, 9.14; N, 3.0; I, 25.3%).

Compounds No.VII and VIII: Mannich base (V) was taken in dry ether and the requisite reagent was added to it with stirring. Quaternary salt immediately precipitated out. These were filtered and purified by dissolving in minimum quantity of alcohol and adding ether. On cooling, the crystals separating out of alcohol-ether solution, were washed with ether and dried. The yields of quaternary salts were invariably above 90%.

No.	Compound	Reagent for quaternization	m.p.	%N reqd.	%N found
VII	$C_{24}H_{44}ONCl$	HCl	130°C	3.52	3.24
VIII	$C_{26}H_{49}O_5NS$	$(CH_3)_2SO_4$	98°C	2.87	2.5

Compound No.IX: Mannich base (V) (1.0 g.) in toluene (10 ml.) was refluxed with p-nitrobenzyl chloride (0.5 g.) for two to three hours. Toluene was removed under reduced pressure and the quaternary salt was obtained by adding dry ether. Purification of the crude quaternary salt was effected by crystallization from alcohol and ether as in the preceeding preparation (yield 1.25 g. m.p.112°C. Found, N, 5.15; $C_{31}H_{49}O_3N_2Cl$ requires N, 5.3%).

Reduction of Mannich base of T.H.A. to obtain (X)

Mannich base of T.H.A.(V) (1.0 g.) was reduced in alcohol (25 ml.) medium at ordinary temperature and pressure by shaking it in hydrogen atmosphere, in the presence of Raney nickel (W-7) catalyst. When no further hydrogen absorption took place (64 ml.), the solution was filtered, concentrated and crystallized. Two more crystallizations from alcohol gave 3-pentadecyl-6-methylphenol (X) (m.p.57-58°C yield 0.6 g. 70%; Found: C, 82.9; H, 12.3; $C_{22}H_{38}O$ requires C, 82.95; H, 12.03%).

Monochloro tetrahydroanacardol (XI) T.H.A. (26 g.) was taken in dry ether (100 ml.) in a flask fitted with a condenser provided with a calcium chloride guard tube. The reaction mixture was cooled to 0°C. While stirring was in progress sulphuryl chloride (7 ml.) was slowly added, stirring was continued at this temperature for 1½ hours and then at room temperature for another two hours. The reaction mixture after keeping overnight was refluxed for ½ an hour, cooled and poured into water. Ether layer was separated, washed free of acid, dried over sodium sulphate and concentrated. The residue was crystallized from pet. ether (40-60°) when monochloro T.H.A. (16 g.) was obtained. (m.p.56°; Found C, 74.3; H, 10.4; Cl. 9.9; $C_{21}H_{35}OCl$ requires C, 74.40; H, 10.42; Cl, 10.23%).

Mannich base from monochloro T.H.A. (XII) Monochloro T.H.A. (XI) (4.0 g.) was dissolved in alcohol (50 ml.) cooled to -5°,

dimethylamine (5 ml. 30%) and formaldehyde (3 ml. 37%) were added with stirring. The reaction mixture was stirred for ½ an hour in the cold and then set aside at room temperature for seven days (no separate layer appeared nor did any solid separate out). Reaction mixture was diluted with water and then extracted with ether. The ether extract was washed till neutral. After removal of the solvent the residue was crystallized from alcohol (m.p.35-36°; yield 3.9 g. Found: C, 72.8; H, 10.5; N, 3.9; $C_{24}H_{42}ONCl$ requires C, 72.83; H, 10.62; N, 3.5%).

Quaternary salts derived from monochloro T.H.A.

Compound No.XIII: To the Mannich base (XII) (1.0 g.) was added methyl iodide (0.5 ml.) and allowed to stand overnight. The solid mass which separated was crystallized from alcohol and ether (m.p.155°, softens at 90°; yield 1 gm. Found: N, 2.7; I, 23.4; Cl, 6.5; $C_{25}H_{45}ONCl$ I requires N, 2.61; I, 23.6; Cl, 6.6%).

Compound No.XIV To the Mannich base (XII) (0.8 g.) was added concentrated hydrochloric acid (4 drops) and mixed well with a glass rod. The pasty mass thus obtained was crystallized from alcohol and ether (softens at 80°C, yield 0.7 g. Found: N, 3.3; $C_{24}H_{43}ONCl_2$ requires N, 3.24%).

Mannich base of Tetrahydroanacardic acid XV

Tetrahydroanacardic acid IV (7.0 g.) was taken in alcohol (60 ml.) and cooled to -10°C. Dimethylamine

(6 ml., 30%) and formaldehyde (3 ml. 37%) were slowly added with stirring maintaining the temperature below 5°C. After addition the reaction mixture was maintained at that temperature for one hour with occasional shaking, and then allowed to come to room temperature. After four days crystals separated. These were filtered and recrystallized from alcohol (m.p.175-6°; yield 6.5 g. Found: C, 74.2; H, 10.5; N, 3.3; $C_{25}H_{43}O_3N$ requires: C, 74.2; H, 10.5; N, 3.3%).

Quaternary salts derived from Mannich base of T.H.A.A.

Compounds No.XVI, XVII and XVIII: These compounds were prepared and crystallized in the same manner as the corresponding compounds of Mannich base of T.H.A. (V) their yields were almost quantitative and analysis were as follows:

No.	Compound	Reagent for quaternization	m.p. in °C.	% N	
				Reqd.	Found
XVI	$C_{26}H_{46}O_3NI$	CH_3I	95-97	2.56	2.6
XVII	$C_{25}H_{44}O_3NCl$	HCl	104-5	3.2	3.0
XVIII	$C_{27}H_{49}O_7NS$	$(CH_3)_2SO_4$	101-2	2.63	2.4

Methyl ether of T.H.A. XIX Tetrahydroanacardol (304 g. 1 mole) acetone (800 ml.), sodium hydroxide solution (310 g. in 400 ml. of water) were taken in a three necked flask fitted with a reflux condenser, a mercury seal stirrer and a dropping funnel. Dimethyl sulphate (168 g. 1.3 mole)

was added slowly with stirring and the reaction mixture was refluxed for 2 hours. The reflux condenser was replaced by a distillation condenser and most of the acetone recovered. The residue was cooled and enough water added to dissolve all the sodium sulphate formed, and the liquids transferred to a separating funnel. The lower aqueous layer was removed and extracted with petrol ether (40-60°) (3x150 ml.) and the combined extracts were added to the oily layer. This was then washed with aqueous alcohol (50%) to remove the unreacted sodium salt of tetrahydroanacardol, and then with water. The pet. ethere extract was dried over sodium sulphate (anhydrous), solvent recovered and the residue distilled under vacuum. Methyl ether of T.H.A. (300 g.) was obtained in 94% yield (b.p.180-2°/2 mm. n_D^{30} 1.4835, Found: C, 83.1; H, 12.2; $C_{22}H_{38}O$ requires C, 82.95; H, 12.03%).

Chloromethylation of Methyl ether of T.H.A. (XX)

Methyl ether of T.H.A. (40 g.), paraformaldehyde (4.0 g.) acetic acid glacial (100 ml.) and benzene (100 ml.) were taken in a three necked flask fitted with a slip seal stirrer, an inlet for hydrogen chloride and an outlet connected to a gas absorption system. Hydrogen chloride was passed till there was no more paraformaldehyde, maintaining the temperature of the reaction at 15° to 20°C by keeping the flask in ice bath. After saturation with hydrogen chloride the reaction mixture was poured on to crushed ice in a beaker. The oily layer with benzene was extracted with ether, washed till neutral, solvents recovered

and the residue vacuum distilled. The fraction distilling at 180-185°C/0.002 mm. was collected (5) g. 67% yield; n_D^{30} 1.4959). This product on crystallization from pet. ether (40-60°C) gave white crystals (m.p.38°C. Found: C, 75.2; H, 10.3; Cl, 9.2; $C_{23}H_{39}OCl$ requires: C, 75.3; H, 10.62; Cl. 9.68%).

Quaternary salts derived from methyl ether of T.H.A.

Compound No.XXI: Chloromethylation product (XX) (2.0 g.) in dry acetone (10 ml) was taken in a glass stoppered conical flask. On adding acetone solution of trimethylamine (in excess) and keeping for six to seven hours, crystals appeared. The flask was further cooled and crystals filtered. Recrystallization from alcohol-ether gave white shining crystals (m.p.168-170°C; yield 1.6.g. Found: N, 3.14; $C_{26}H_{48}ONCl$ requires: N, 3.37%).

Compound No.XXII: Compound (XX) (2.0 g.) and pyridine (1.0 g.) in anhydrous toluene (8 ml.) were refluxed for five hours. Toluene was removed under reduced pressure and the residue treated with dry ether. Pyridinium salt was obtained on cooling and was crystallized from alcohol and ether yield 2.0 g. (m.p.102-3°C; Found: N, 3.31; $C_{28}H_{44}ONCl$ requires: N, 3.29%).

Compound No.XXIII: Isoquinolinium compound was obtained as above in the pyridinium compound, by refluxing XX (2.0 g.) and isoquinolin (1.0 g.) in anhydrous toluene (8 ml.). The isoquinolinium salt thus obtained was a sticky mass but on

crystallization from alcohol and ether gave beautiful crystals (m.p.142-3°C; Yield 2.0 g.; Found N, 2.67; $C_{32}H_{46}ONCl$ requires: N, 2.82%).

Reduction and demethylation of chloromethylated methyl ether of T.H.A. to XXIV

Chloromethylated product (XX) (4.0 g.) was taken in dry ether (30 ml.) added $LiAlH_4$ (0.5 g.) and refluxed for four hours. The ether was distilled off and dry benzene (30 ml) and anhydrous aluminium chloride (4.0 g.) were added and again refluxed for 12 hours. The reaction mixture was cooled and poured into methanol (50 ml. 20%) containing concentrated sulphuric acid (5 ml.). Benzene layer was separated washed with methanol (20%), dried over sodium sulphate and finally solvent removed by distilling. The residue was crystallized from pet. ether (60-80°) (m.p.50-51°C; yield 2.1 g. 56.7%; Found C, 82.8; H, 12.3; $C_{22}H_{38}O$ requires C, 82.95; H, 12.03%). The compound exhibits green fluorescence in the ultraviolet light.

ω -Bromoethoxy T.H.A. XXV: T.H.A. (10.0 g.) in toluene (20 ml.) and aqueous sodium hydroxide (2.0 g. in 5 ml. water) were mixed. The sodium salt emulsion in toluene was refluxed with ethylene dibromide (10.0 g.) for eight hours. The reaction mixture was then diluted with water and extracted with butanol-toluene (1:1). The extract was washed twice with water, solvents removed under reduced pressure on water bath and the residue crystallized from pet. ether (40-60°) (m.p.38-39°. Yield 6.5 g.; Found: C, 67.3; H, 9.6; Br, 19.3;

$C_{23}H_{39}OBr$ requires C, 67.16; H, 9.59; Br, 19.46%).

Quaternary salts derived from ω-Bromoethoxy T.H.A.

Compound No.XXVI, XXVII and XXVIII: These compounds were prepared and crystallized in the same way as described under the corresponding compounds of XX. Their yields in general were over 80% and their analysis, m.p. and the quaternizing agent used in their preparations are given below:

No.	Compound	Reagent for quaternizing	m.p. in °C.	%N	
				Reqd.	Found
XXVI	$C_{26}H_{48}ONBr$	Trimethylamine	186°	2.98	2.9
XXVII	$C_{28}H_{44}ONBr$	Pyridine	180°	2.6	2.4
XXVIII	$C_{32}H_{46}ONBr$	Isoquinoline	69-70°	2.8	2.6

Testing Procedure for Determining Biological Activity:

Organism tested. Staphylococcus aureus 209P

Method: The quaternary compounds were dissolved in 95% acetone (containing 5% water) or water depending upon their solubility to a concentration of 0.5%. These solutions were added to sterile nutrient broth (Bacto Peptone, 1%; Difco Beef extract, 1%, sodium chloride 0.5%; pH 7.2-7.4 after autoclaving) in serial dilutions under aseptic conditions. 0.05 ml. of a 24 hours culture grown on nutrient broth at 37°C. was added to the solutions and the total volume made up to 10 ml. with water. The tubes were

incubated for 48 hours at 37°C. and visible growth observed. For those tubes which were opalascent, one loop from them was transferred on to fresh nutrient broth and visible growth observed after another 48 hours incubation.

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PART II

A. AZO DYES

RELATION BETWEEN STRUCTURE & CHROMATOGRAPHIC BEHAVIOUR

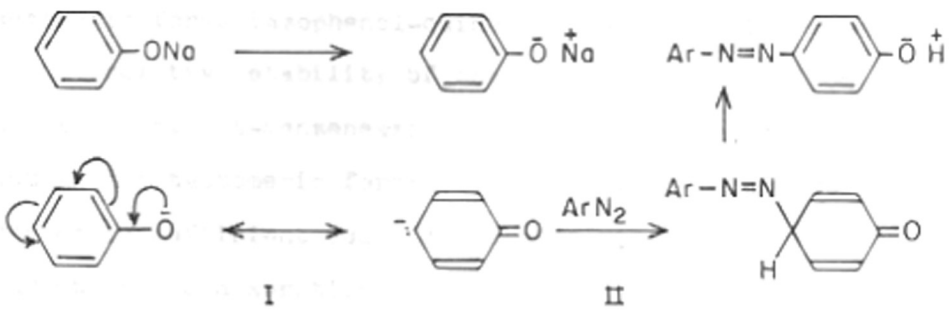
INTRODUCTION

Azo dyes of which the commercial representatives probably amount to over a thousand, inclusive of all types with the common feature of one or more azo groups, constitute numerically the most important class of synthetic colouring matters. They are all prepared by a common process involving two reactions a) diazotizing an aromatic primary amine and b) coupling the diazonium salt with a phenol or aromatic amine with a free ortho and/or para position, or with certain other components having reactive positions, such as β-ketonic acid arylamides.

The effective agent in a smooth and rapid diazonium coupling is the positively polarized diazonium radical ArN_2^+, which is strongly electrophilic and attacks anionoid or nucleophilic centres, such as the ortho- and para- positions in sodium phenolate ion or aniline. The mechanism of the reaction between diazonium salts and aromatic phenols or amines has not yet been completely elucidated and quantitative kinetic study has been made only in a few cases.[1,2]

Phenols are coupled in alkaline solution with diazonium salts. The alkaline reaction of aqueous solutions of the diazonium carbonates, the electrical conductivity of solutions of diazonium salts, and other properties have

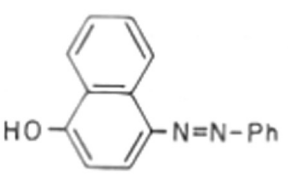
shown that diazonium compounds are ionized in aqueous solution. In the phenoxide ion (I) the 4-position is a site of high electron density and the diazonium coupling reaction consists essentially in the attack of this electronegative site by the positively polarised or cationoid diazonium radical. Elemination of a proton from the activated complex II then takes place and the formation of the azo compound is completed.



Although aromatic azo compounds have been known for over ninety years, their various chemical reactions and properties have not been examined widely or systematically and it was only relatively recently, in 1938, the cis-trans isomerization of azobenzene on irradiation was reported. Cook[3] has shown that a solution of irradiated azobenzene can be readily separated into cis and trans isomerides by preferential adsorption on active alumina following the observations of Hartley[4] and co-workers. The indefinite "tailing" of bands of 4-substituted azo dyes on column of alumina was also attributed to ineffective separation of isomerides. Generally the trans compounds are stable and can be isolated in pure solid state while the

solidification of pure cis-compounds have not yet been achieved. Cook and Jones[5] have examined the light absorption of cis and trans azobenzenes and they have observed that while there is little difference in wave length of absorption, the lower intensities of absorption of cis-compounds help to characterise them.

Azo phenols and azo naphthols can exist in tautomeric forms (azophenol-quinonehydrazone tautomerism) and the relative stability of the tautomers varies from case to case. 4-Benzeneazo-1-naphthol has been shown to contain the tautomeric forms (III) and (IV), which are present in sufficient quantity to give rise to characteristic absorption bands.



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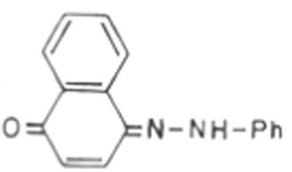
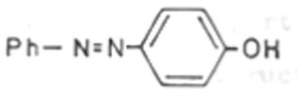
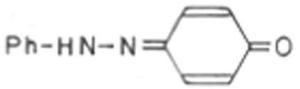


IV

The equilibrium between the two forms is dependent on the solvent.[6,7] The physical and chemical properties of p-hydroxyazobenzene indicate that it exists in the azophenol form V rather than the quinonehydrazone form VI.

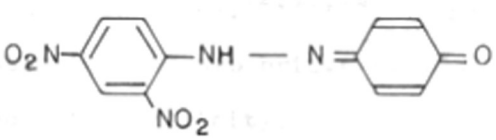


V



VI

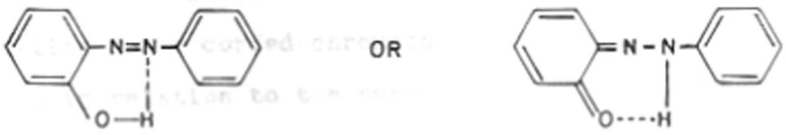
Branch and Calvin[8] have discussed the azophenol-quinonehydrazone tautomerism of p-benzeneazophenol (A) and other dyes and concluded that (A) is essentially in the azophenol form. Evidence of the quinonoid character of certain p-hydroxyazo compounds, such as VII is provided by their ability to undergo the Diels-Alder reaction; addition compounds have been obtained with cyclopentadiene. The extent of addition is influenced by the acidity of the medium and its occurrence is not a general property of the p-hydroxyazo compounds.[9] Further it is obvious that the strongly electronegative nitro groups in the benzene ring not carrying the hydroxyl group would tend to stabilize the hydrazone form.



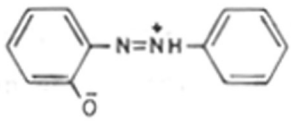
VII

Based on their study of infrared spectra of certain unsulphonated monoazo dyes, Bolinsky and Jones[10] have supported the zwitterion type of structure VIII for o-hydroxyazo compounds, first proposed by Kuhn.[11]

Ortho-hydroxyazobenzene differs from the p-isomer in its being volatile in steam, low melting point and formation of metal complex. These properties are attributed to the chelation or hydrogen bonded structure of the ortho-hydroxyazo compounds. Thus o-hydroxyazo compounds can exist in zwitterion type of structure VIII or azophenol-quinonehydrazone tautomerism each of which can further exist in chelate structure as shown in IX.



IX IX



VIII Zwitterion structure

Difficulty also has been encountered in analysing infrared spectra of azo dyes and this is attributed to the presence of hydrogen bond.[12,13,14]. So far, bands characteristic for the azo bridge (-N=N-) have not yet been demonstrated with certainity.[32]

Spectral studies of hydroxyazo compounds have been done by Taku Uemura et.al.[15] and the difference between the ortho and para isomers noticed. Brode[16] has done extensive studies on the absorption spectra and chemical

constitution of azo dyes. From investigations of the spectra of 2-phenylazophenols[17], it has been established that they are essentially true azo compounds. Hodgson and Rosenberg[18] have studied the influence of methyl group on the colour of substituted benzeneazo phenols.

Gore and Venkataraman[19] have studied chelation in azophenols in relation to chromatographic adsorbability and recorded chromatographic behaviour of azophenols in relation to the number and position of hydroxyl and azo groups.

Survey of the literature showed that systematic study of alkyl-phenol azo dyes with respect to their chromatographic behaviour, physical and chemical properties have not been attempted. However solubility and light fastness of certain phenylazo phenol dyes containing ortho and para substituents in the phenolic portion have been reported.[20] No work seems to have been done with dyes obtained from m-alkyl phenols. In view of this fact, it will be of interest to obtain further data on the coupling of m-alkyl substituted phenols with diazonium ions.

The present investigation deals with the coupling of various m-alkyl substituted phenols with diazonium ions and their systematic chromatographic separation into different isomeric products from the coupling reaction.

Several m-alkyl phenols, with varying chain length and branching of alkyl group were coupled with diazotised aniline and the crude coupled product was chromatographically separated into its various constituent azo derivatives. The phenolic components employed were phenol, m-cresol, m-ethyl phenol, m-n-propylphenol, m-n-butylphenol, m-pentadecylphenol, m-isopropylphenol and m-tertiary butyl phenol.

Purification And Preparation of Phenols

Various m-alkyl phenols used in this study were obtained by purification of commercial products or synthesised by known methods to obtain them in highly pure form free from their isomeric products.

m-Cresol: m-Cresol (Naarden Holland) after careful fractionation was found to give with benzenediazonium chloride a coupled product which contained azo derivatives of p-cresol as shown by chromatographic analysis. Purification of m-cresol was therefore effected by debromination of the tribromo derivative.

m-Ethylphenol: Acetophenone on nitration with nitrating mixture yielded 3-nitro-acetophenone[21] which on reduction with hydrazine hydrate in diethylene glycol[22] gave m-ethyl aniline. Diazotization followed by hydrolysis gave m-ethyl phenol in an overall yield of 44.15%. This method was preferred to the alternate method viz. hydrogenation of aromatic hydroxy carboxylic acids and their derivatives possessing the -CO group in an α -position to the aromatic ring at 210-320° over Mo_2S_2[23] because of its simplicity and satisfactory yields.

m-n-Propylphenol: Friedel-Crafts reaction between n-propionyl chloride and benzene gave propiophenone[24] which was converted to m-n-propylphenol by the same route as for m-ethylphenol in 28.14% yield.

m-n-Butylphenol: Based on n-butyrophenone the yield of m-n-butylphenol was 20.92%.

m-Pentadecylphenol (T.H.A.) Anacardol, obtained by vacuum distillation of cashewnut shell liquid, gave on catalytic hydrogenation m-pentadecylphenol in 90% yield.

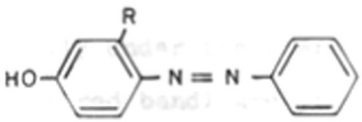
m-Isopropylphenol: Cumene was nitrated to p-nitrocumene. This was then reduced by hydrazine hydrate/Raney nickel to p-cumidine. p-Acetcumidide was converted to m-isopropyl phenol by slightly modifying Carpenters method[25], viz. effecting reduction of nitro to amino at room temperature, in ove all yield of 10.81%.

m-Tertiary-butylphenol: This phenol was obtained as a sample by the courtesy of Coalite and Chemical Products Ltd. Bolsover, Near Chesterfield.

COUPLING AND CHROMATOGRAPHIC EXAMINATION

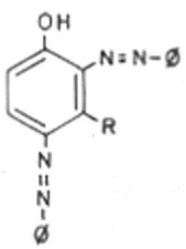
Aniline was diazotised and coupled with various phenols in alkaline medium and the dyes were precipitated by acidifying the solution to pH 2-3 with dilute hydrochloric acid. The solution of the crude dye in benzene or benzene-hexane (1:1) were adsorbed on the column of alumina and the chromatogram developed with the same solvent. Dyes from the lower bands were obtained by elution while the dyes from upper bands were obtained by extrusion and extraction. The dyes obtained from each band were then rechromatographed and the homogenous bands thus obtained were extruded, extracted and the dyes obtained on removal of the solvent were crystallized.

In all cases except m-cresol, three bands were obtained on the column; aniline→m-cresol gave four bands. The top most of the bands in all cases were orange yellow and were very strongly adsorbed. These have been shown to be monoazo compounds having azo group para to the hydroxyl group, by infrared spectra (band near 3600 cm^{-1} in chloroform solution) and in some cases (e.g. m-cresol and tetrahydroanacardol) by reducing them to corresponding known amines. The strong adsorption of these compounds on alumina can be explained, according to Gore and Venkataraman[19] by the fact that the two strong polar groups (-OH and -N=N-) in them are free. Hence these compounds have the structure I.



(I) where R = alkyl groups of various lengths and branching.

The second band from the top in all cases was a red band. However, only in the case of products formed from phenol, m-tertiary butyl phenol, m-cresol and m-ethylphenol this red band was somewhat larger and the dye from these could be crystallized. These crystalline dyes analysed correctly for disazo compounds and hence may have the structure II, III or IV.



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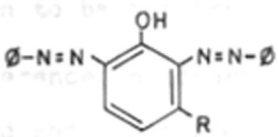

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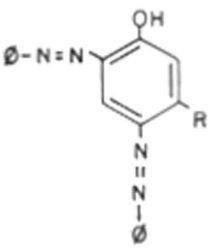


IV

As can be seen from the above structures, in each case one of the azo grouping is present in the position ortho to the hydroxyl and this leads to the formation of hydrogen bonding and hence renders the hydroxyl and one azo grouping ineffective for adsorption on alumina. This leaves only one effective azo group for adsorption and hence these compounds are comparatively less adsorbed and more easily eluted than the monoazo of the topmost band.

Normally under the present coupling conditions these dyes (from red band) are obtained in small quantities (less than 1%) but in the case of the dye from m-tertiary butyl phenol, it is the only disazo compound isolated and is present in relatively large amounts (6 to 7%).

The third band from the top was yellow in colour and the dyes obtained from it, in all the cases except phenol and m-tertiary-butyl phenol, analysed for disazo compound. In the case of phenol the dye obtained from this band has been shown to be ortho-hydroxyazobenzene. The corresponding dye was also obtained from m-tertiary butyl phenol and is shown to be the ortho monoazo dye.

The difference in adsorbability of the disazo dyes from this band and those from the red bands cannot be easily explained on the above lines, however for the monoazo dyes from this band the absence of any effective polar group explains its low adsorbability.

In the case of azo dyes from m-cresol a fourth band, brown in colour, could be obtained at the lower end of the column. The crystalline dye from this band analysed for a disazo compound.

In the preparation of azo dyes, coupling though normally carried out in aqueous sodium hydroxide medium, sometimes the alkali is replaced by sodium carbonate and even pyridine when it is deemed necessary to use pH 8-9 or 7

respectively. In the present case also, coupling has been carried out in pyridine, in sodium carbonate and sodium hydroxide solutions, at least in the case of certain selected phenols to see if variation of pH of the coupling medium has any effect on the course or products of coupling. Accordingly the following selected phenols- phenol, m-cresol, m-tertiary-butylphenol were coupled with diazotised aniline in pyridine (pH 7), in sodium carbonate (pH 8-9) and sodium hydroxide (pH 10) and the coupled products carefully examined, particularly aniline → m-cresol for the presence of ortho monoazo dye. It is clear from the results (see Table I) that there is no indication of the formation of ortho monoazo compound in the case of aniline → m-cresol. Varying pH of the coupling medium had however significant effect on the yields of the different dyes formed as is indicated in the Table (I). Reaction product of aniline → phenol in sodium hydroxide, however, showed quite a number of additional bands on the column of alumina but the dyes from these could not be obtained in crystalline form (bands might have appeared due to side products). Orthohydroxy azo benzene was also not isolable in this case. The yields of the disazo dye and the monoazo dye were however noted.

Table I

Aniline → Phenol

Order of Elution	Melting point °C.	Analysed for	Yields using NaOH pH 10 Recovery:	Yields using Na_2CO_3 pH 8 to 10 Recovery 84.65%	Yields using pyridine pH 7 Recovery: 76.95%
1	82	Monoazo		1.639	1.519
2	131	Disazo	-	1.228	0.072
3	155	Monoazo	-	97.14	98.4
		Aniline → m-Cresol	Recovery: 83.92%	Recovery: 82.52%	Recovery: 85.67%
1	177	Disazo	1.989	0.03	0.583
2	148-49	Disazo	8.141	12.12	2.277
3	179-80	Disazo	0.536	2.48	0.029
4	107	Monoazo	89.35	85.39	97.16
		Aniline → m-tertiary butylphenol	Recovery: 97.7%	Recovery 86.94%	Recovery: 91.87%
1	60	Monoazo	0.012	13.43	0.14
2	137	Disazo	4.99	28.17	0.91
3	108.9	Monoazo	94.88	58.39	98.93

INFRARED SPECTRA OF PHENOLS AND AZO COMPOUNDS

The infrared spectra of various phenols and their coupled products were determined as Nujol mulls and in chloroform solution using Perkin-Elmer Model 201 instrument with sodium chloride optics and the rlevant data are discussed here.

-OH Stretching vibrations

The infrared spectra of various m-alkyl substituted phenols[26] show a marked similarity in their absorption pattern. The strong absorption observed around 3300 cm^{-1} in their spectra is due to intermolecular hydrogen bonding of the free -OH groups and they break down to reveal the free -OH stretching vibrations around 3600 cm^{-1} when their spectra are determined in chloroform solutions. With 4-substituted monoazo dyes from various phenols the free -OH vibrations are not noticeable (except in those from m-pentadecylphenol around 3300 cm^{-1}, m-tertiary butylphenol and m-isopropylphenol around 3150 cm^{-1}) when spectra are determined in Nujol mulls but the absorption around 3600 cm^{-1} become apparent in chloroform solutions. The existence of some p-hydroxyazo compounds in their hydrazone form has been reported by earlier workers.[9] However in the compounds under study the absence of ketone absorption (above 1610 cm^{-1}) clearly indicates that they exist mainly as azophenols.[12] This is confirmed by the absence of any peak at 3100 cm^{-1} corresponding to -NH stretching.

However in the case of monoazo dye (m.p.60°) from aniline → m-tertiary butylphenol a strong band was obtained in the 1620 cm^{-1} regions indicating that the compound may exist in quinone-hydrazone form. But this frequency is rather low even for a hydrogen bonded quinone. Moreover the expected -NH band is also absent. The -NH band (around 3100 cm^{-1}) would be expected to have a very low intensity, it is therefore probable that this compound may exist in quinone hydrazone form. With further substitution of another azo group in the p-hydroxyazo compounds the free -OH bands entirely disappear as they enter into hydrogen bonding with the ortho substituted azo linkage. As in the monoazo dyes, there was no ketone absorption peak in the disazo dyes prepared from various phenols indicating their existence in the azo phenol form, rather than the hydrazone form. The only absorption that can be observed around 2900 cm^{-1} region is that due to the -CH stretching vibrations.

<u>C-CH_3 absorption</u>:

In all the alkyl substituted phenols the C-CH_3 absorption was located around 2960 cm^{-1} as strong absorptions (liquid films) which become weaker in chloroform solution due to dilution. In the corresponding azo dyes C-CH_3 absorption were difficult to locate in Nujol mulls but could be identified with difficulty as weak absorptions

when taken in chloroform solutions. The strong absorption at 2933 cm^{-1} observed in the spectrum of m-pentadecyl phenol in chloroform is due to CH_2 vibrations of the long alkyl chain.

Aromatic vibrations

In most of the phenols medium to strong absorptions around 3030 cm^{-1} due to ≡C-H stretching modes can be readily located especially in liquid film spectra. With, m-pentadecyl phenol, however, they appear to be masked although the C=C skeletal in plane vibrations around 1590 cm^{-1} and C-C skeletal vibrations around 1460 cm^{-1} are clear. In various other phenols the C=C vibrations are seen at 1610 cm^{-1} and 1587 cm^{-1} and are unaffected in chloroform solution or as liquid film except for intensity variations.

The ≡C-H stretching vibrations of the monoazo dyes examined are not easily located even when the spectra were taken in chloroform solution but the C=C skeletal vibrations appear in the 1597 cm^{-1} — 1608 cm^{-1} region and 1575 cm^{-1} — 1582 cm^{-1}. With disazo derivatives a strong absorption around 1587 cm^{-1} is seen in all alkyl substituted compounds, however in the m-tertiary-bisazophenol, the 1613 cm^{-1} and 1570 cm^{-1} bands appear strongly.

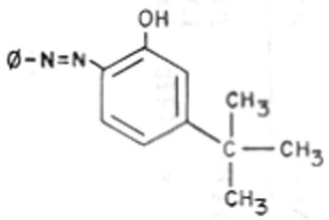
-N=N-Linkage: The absorption due to -N=N-linkage is expected to appear around 1600 cm^{-1} by analogy with -C=N- and -C=C- absorptions and therefore in the case of aromatic compounds their identification and allocation become increasingly difficult. The strong absorption around 1430 ± 10 cm^{-1} are probably due to -N=N- vibrations as they appear in all the azo dyes examined. The interference of aromatic vibrations with azo vibrations limit the use of infrared spectroscopy for identification of aromatic azo compounds.

Region 1500-650 cm^{-1}

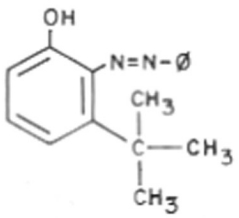
In this region very definite allocations could not be made due to the large number of absorbing groups present although differences in the absorption pattern could be easily recognised from compound to compound. The aromatic substitution patterns are also difficult to recognise with certainity in the case of azo dyes due to the presence of two or more benzene rings in the molecule.

An allocation can however be made in the case of monoazo dye m.p.60°C. from aniline → m-tertiary butylphenol; this compound shows a prominent band at 823 cm^{-1} which may be assigned for 1,2,4 trisubstituted benzene. The absence of any band in 725 cm^{-1} region rules out the possibility of 1,2,3 substituted benzene. The formation of 1,2,4 compound is also expected on the basis of steric hinderance.

This compound can therefore be assigned the structure VI in preference to the structure V.



VI



V

Complete absorption bands (in cm^{-1}) of different phenols, their monoazo and disazo derivatives are given in Table II, III and IV respectively.

Table II

Complete Absorption Bands of m-alkyl phenols in Cm^{-1}

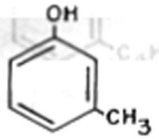
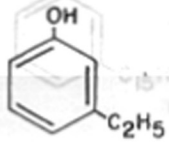
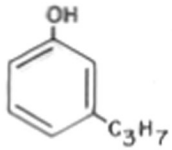
Compound's structure		3650-2700	2700-2000	2000-1500	1500-1300	1300-1100	1100-900	900-650
	Liquid film	3306S 3030M 2915M		1610 1587S	1487S 1331MB 1460S 1437Sh	1279S 1264S 1152S	1081M 925S 1035WB 1003M	877M 731M 852M 687S 772S
	Chloro-form	3597S 2915W 3420W 2857W 3008W		1610S 1587S	1487S 1379W 1458S 1309S 1437MB	1279S 1151S 1267S 1183S	1081W 1000W 1040WB 925S 1010WB	877W
	Liquid film	3311S 2861Sh 3035M 2967S		1587S 1613Sh	1487S 1320MB 1453S 1346MB	1253SB 1153S	1090W 923M 1050W 905S 999W	860MB 691S 780SB 725M
	Chloro-form	3603S 2967M 2861Sh		1587S 1613Sh	1484M 1307MB 1453S 1373W	1272M 1181M 1151S	1087W 906S 1050W 1000W 983M	875WB 855WB
	Liquid film	3311S 2874S 3040S 2941S		1612Sh 1590S	1486SB 1340S 1451S 1377SB	1287S 1245SB 1152S	1094M 1063M 1003W 946SB	872S 748S 850SB 692S 797Sh 777SB
	Chloro-form	3597S 3367WB 2941S 2857M		1610Sh 1587S	1481M 1340Sh 1451S 1307MB 1377W	1269S 1180S 1152S	1097W 946M 1062W 1043WB 999W	876M

Table II (continued)

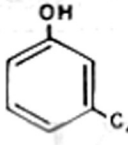
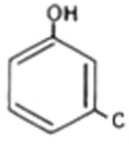
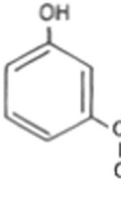
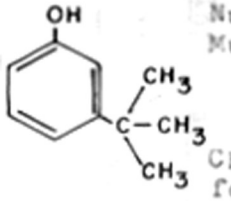
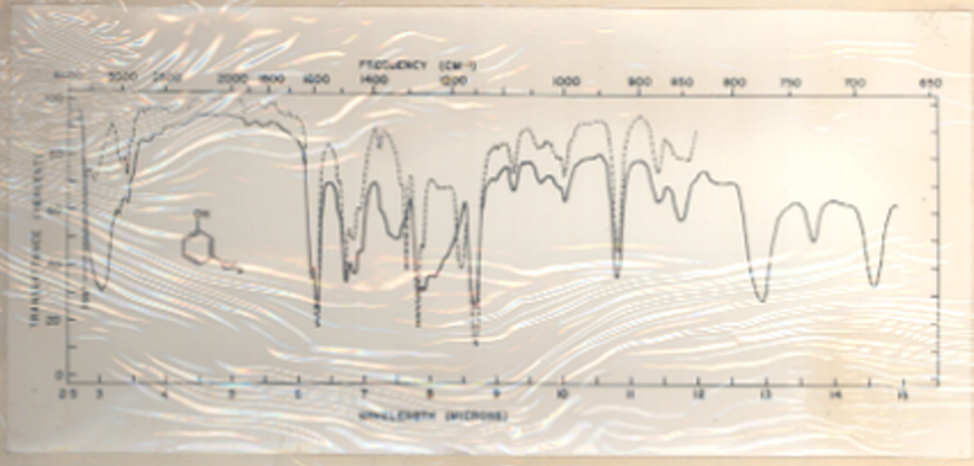
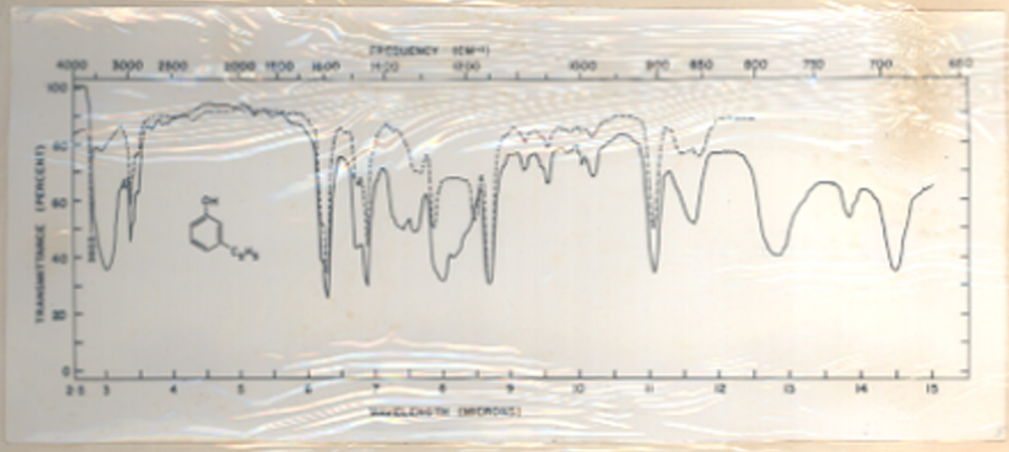
Compound's structure		3650-2700	2700-2000	2000-1500	1500-1300	1300-1100	1100-900	900-650
	Liquid film	3333S 2859S 3333M 2933S		1610Sh 1590S	1481SB 1453S 1376W	1270S 1242SB 1153S	1067M 945M 1000M 921MB 973WB	778S 875M 749S 857M 692S
	Chloro-form	3603S 2924S 2857M		1610Sh 1590S	1481MB 1453S 1379W	1180M 1104S 1180M 1153S	1067M 920MB 1000W 945M	875MB 854MB
	Nujol Mull	3311S 2924SB 2857S		1610Sh 1590S	1460S 1376S 1300W	1282M 1231M 1262S 1214MB 1250S 1153S	1072WB 942M 928W	865M 748M 847WB 727M 790S 718M 784S 698S
	Chloro-form	3603M 2933S 2857S		1590M 1610Sh	1484W 1453M	1271M 1180W	1000W	876W
	Liquid film	3306S 2967S 2178S		1592S	1484Sh 1451S 1384S 1384S 1361	1258SB 1235SB 1179S 1157S 1133M	1090WB 1072 1047M 1000W 933S	865S 858Sh 781S 697S
	Chloro-form	3628S 3333M 2967S 2878M		1592S	1484S 1451S 1384S 1364M 1348M	1294S 1270MB 1170S 1157S 1134M	1089WB 1070W 1045W 1000M 928M	865M 955M

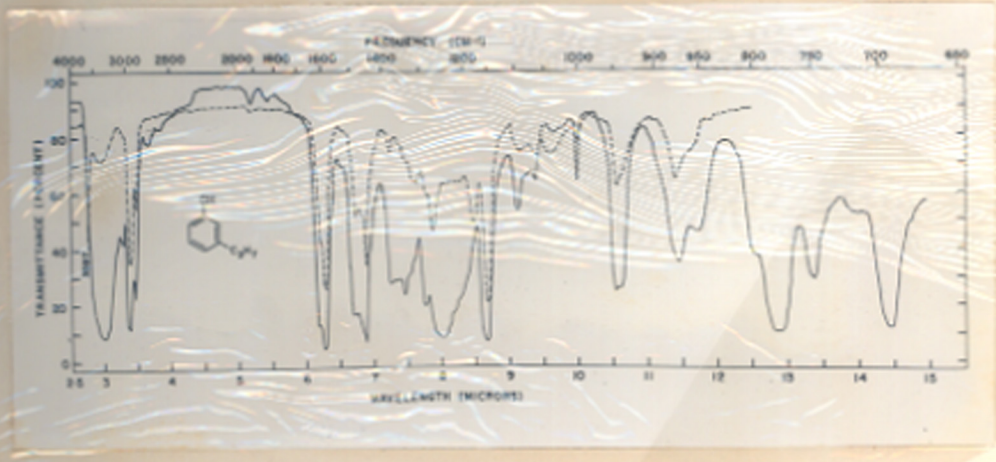
Table II (continued)

Compound's structure		3650-2700	2700-2000	2000-1500	1500-1300	1300-1100	1100-900	900-650
	Nujol Mull	3226S 2924S 2857S		1613Sh 1585S	1485SB 1365S 1449S	1278S 1166M 1220S 1114M 1201S	1079W 913S 1021WB 1000W	877WB 782S 860M 698S 815M
	Chloroform	3610S 3390WB 2972S		1613M 1587S	1485M 1366M 1449M 1304M 1397M	1284S 1114M 1183S 1163S	1079WB 1021WB 1000W 915S	875W 857W

S=Strong; M=Medium; W=Weak, Sh=Shoulder, B=Broad.



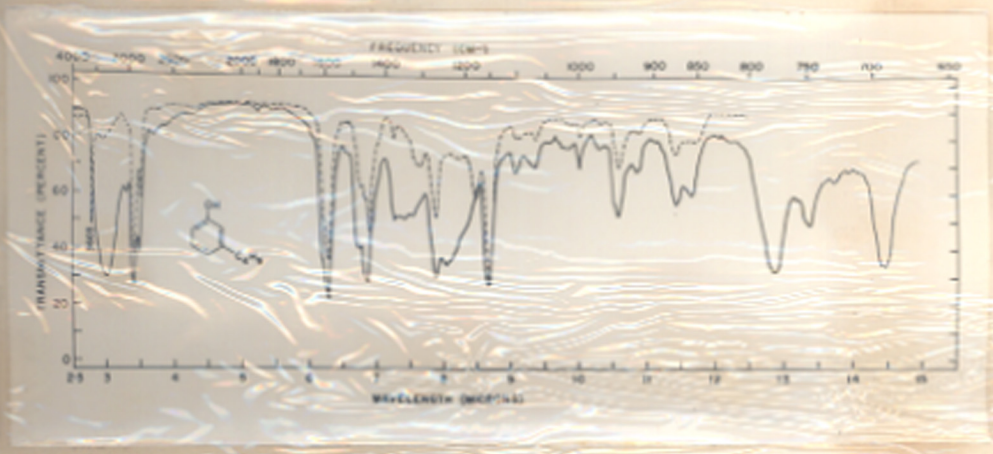


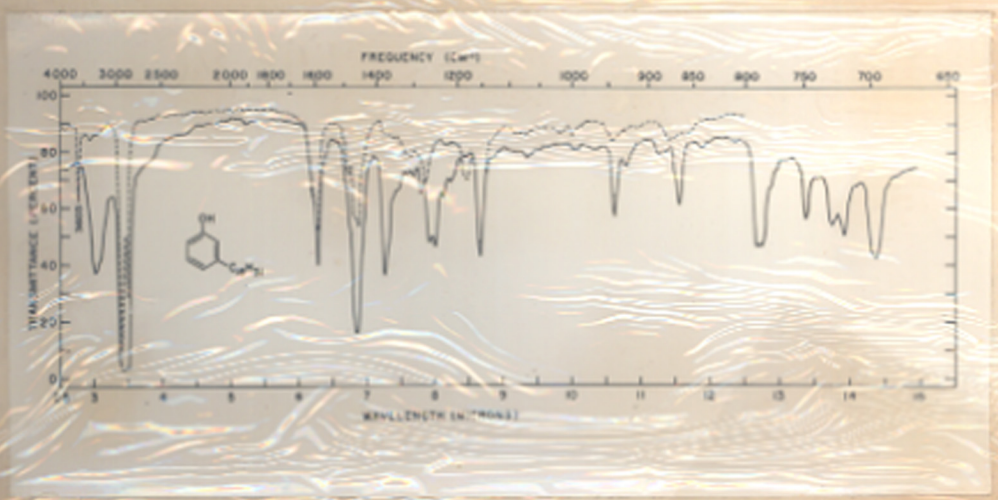


Infrared Absorption Spectra Of m-Alkyl-phenols

..... Chloroform solution

_____ Nujol Mull OR LIQUID FILM



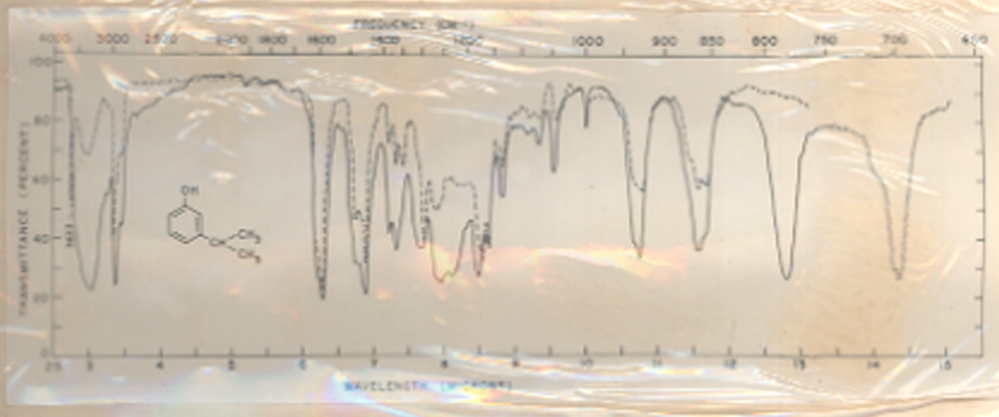


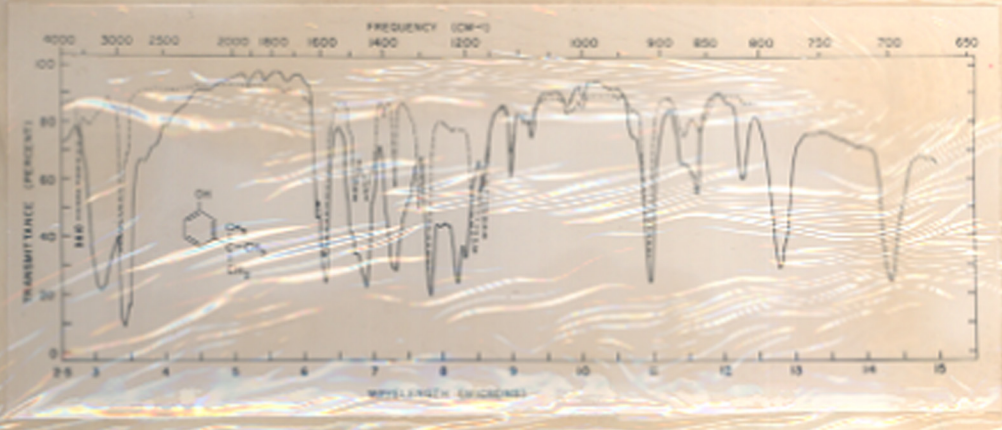
Infrared Absorption Spectra Of m-Alkyl-phenols

(continued)

..... Chloroform solution

_____ Nujol Mull or Liquid Film





Infrared Absorption Spectra Of m-Alkyl-phenols

(continued)

..... Chloroform solution

_____ Nujol Mull or Liquid Film

Table III

Complete Absorption Bands of Monoazo dyes in Cm^{-1}

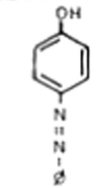
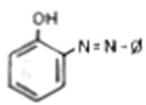
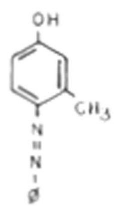
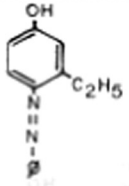
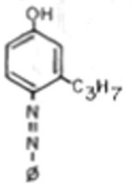
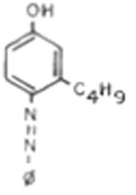
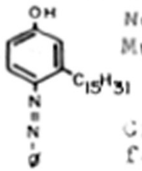
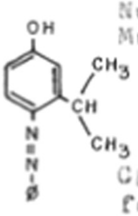
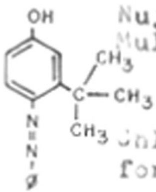
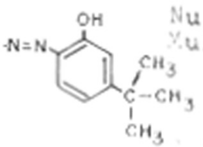
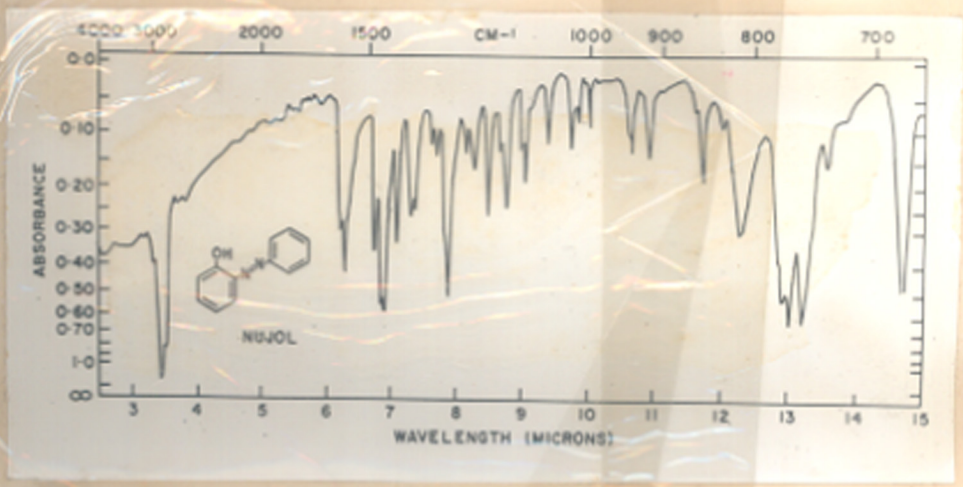
Compound's structure		3650-2700	2700-2000	2000-1500	1500-1300	1300-1100	1000-900	900-650
	Nujol Mull	2907S 2850S		1608Sh 1587S	1500M 1377S 1460S 1314W 1414M	1274S 1236S 1220S 1143S	1075W 1000W 920	840S 683M 809W 794W 769M 721M
	Nujol Mull	2907S 2847S		1601M 1597S	1488S 1370M 1468S 1361M 1451S 1310W 1412S 1300W	1271S 1144M 1232W 1115 1212W 1110W 1183M 1156M	1068W 741W 1030 917 1017 1000W	854M 737 816S 6[illegible] 775S 769S 758S
	Nujol Mull	2920S 2855S		1607M 1572S	1481S 1376S 1456S 1347MB 1431S	1299S 1183M 1263M 1157M 1222S 1103S	1072W 920WB 1038WB 1021W 950WB	872W 722 818 690W 774M
	Chloroform	3603M 3300 B 2924W 2850W		1600 1587S 1558W	1487 1376W 1471M 1451W 1429WB	1293S 1176SB 1250S 1156M 1205SB 1100B	1070 920WB 1038WB 948W	864B 854B

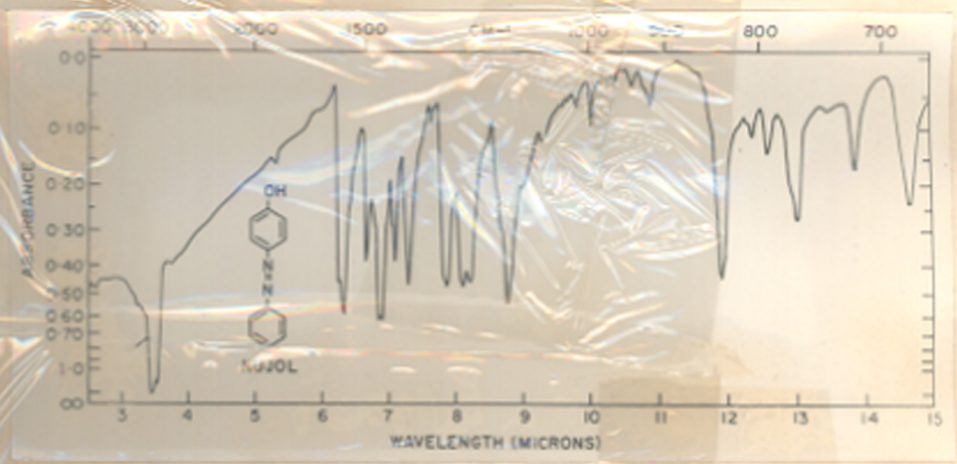
Table III (continued)

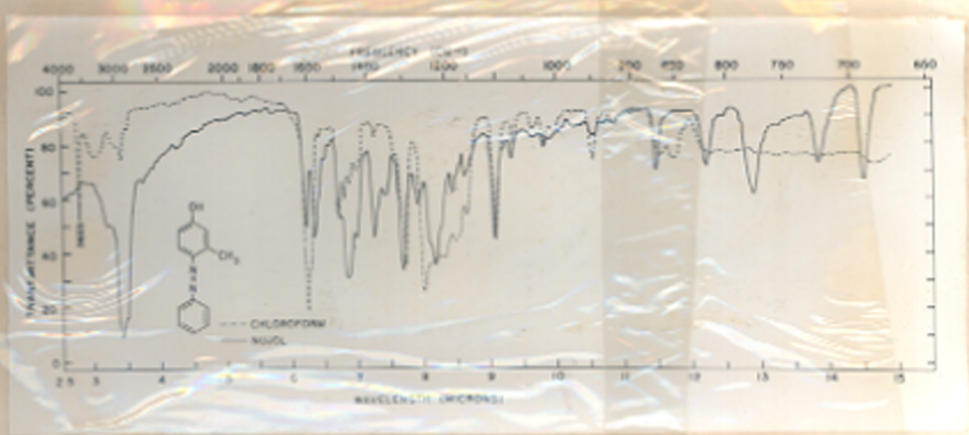
Compound's Structure		3650-2700	2700-2000	2000-1500	1500-1300		1300-1100		1100-900		900-650	
	Nujol Mull	2915S 2857		1610S 1580S	1481Sh 1460S 1430M 1376M	1327M	1299S 1263S 1230S	1252M 1108M	1068W 1052W 1023WB 917Sh	908W	873W 815W 767M 738W	719W 679
	Chloro-form	3597M 3279WB 2967W		1600S 1582S	1481M 1471M 1449M	1433Sh 1326W	1292M 1261M 1173S	1156M 1104M	1069W 1052W 1019W	918W 912W	874W 857W	
	Nujol Mull	3111Sh 2915S 2852S		1608S 1575S	1484Sh 1462S 1429S 1377S	1307S	1245S 1227S 1209S	1188W 1153M 1110S	1093W 1073W 1026W	961W 948W 912W	866W 822Sh 813M 765M	753W 723W 680S
	Chloro-form	3597M 3279M 2967W 2871W		1600S 1582S	1484M 1471M 1379W		1299WB 1247M 1173M	1150W 1106M	1068W 1034WB 1019W 953WB		866WB 850WB	
	Nujol Mull	2920S 2857S		1608S 1575S	1481S 1460S 1427S	1379S 1330	1299S 1242S 1228S	1194M 1183M 1152M 1109S	1072W 1024W 967WB 948W	909W	899W 825Sh 813W 800	765M 757W 727 679S
	Chloro-form	3597M 3297M 2924M 2857M		1600S 1581S	1481M 1468S 1449M 1432M	1379W 1330M	1292M 1242SB 1208SB 1176SB	1153M 1108W	1072W 1036W 1018W	953WB	855WB 820WB	

Compound's structure		3650–2700	2700–2000	2000–1500	1500–1300		1300–1000		1000–900		900–650	
	Nujol Mull	3367S 2920S 2955S		1600S 1582S	1431Sh 1466S 1377S	1351M 132[illegible]M 1304M	1298S 1276W 1223S	1181WB 1152M 1110M	1078M 1018M 967WB	950M 922W	859M 814S 757M 753M	828M 719W 685S
	Chloroform	3600M 3289WB 2933S 2557S		1600S 1582S	1483M 1466M 1333W		1298M 1171MB 1155W	1115W	1096W 1035W 1018W	952W	855WB	
	Nujol Mull	3150Sh 2890S		1594S	1460S 1378S 1331M 1303M		1239S 1212S 1176S 1152M 1133M 1110MB		1064M 1021W 998W 944W 916W		871Sh 863M 803M 768S 682S	
	Chloroform	3601M 3279WB 2967W		1602S 1582M	1481M 1449M 1429W 1379W 1365W		1290M 1235MB 1212MB 1167S 1136W	1110	1069W 1039W 1017W 941W		871W	
	Nujol Mull	3101SB 2907S 2849S		1590S	1465S 1442S 1377S 1359Sh	1303S	1256S 1238S 1198S 1178M	1156M 1126M	1072M 1021W 1000W 965W	947M 937WB 922W 915W	862S 839M 823M 800W	769S 733VB 694[illegible]
	Chloroform	3603S 3289WB 2955M		1597S 1575S	1477S 1445M 1393W 1359M		1290S 1257S 1172S 1126M		1075M 1021W 1000W 937M		876W 859W	
	Nujol Mull	2950S 2850S		1620S 1570M	1460S 1395S 1370S	1305M	1280M 1224M 1185M 1155W 1135M		1090M 1070W 960M 923W		878W 820S 800M 770M 687S	
	Chloroform	2950S		1620S 1580S 1570S	1490M 1480M 1460S 1395S 1362S	1315M	1280S 1230S 1185S 1155S 1135S		1090S 1070W 1020W 1000W	960S 923M	878M 823S 687S	

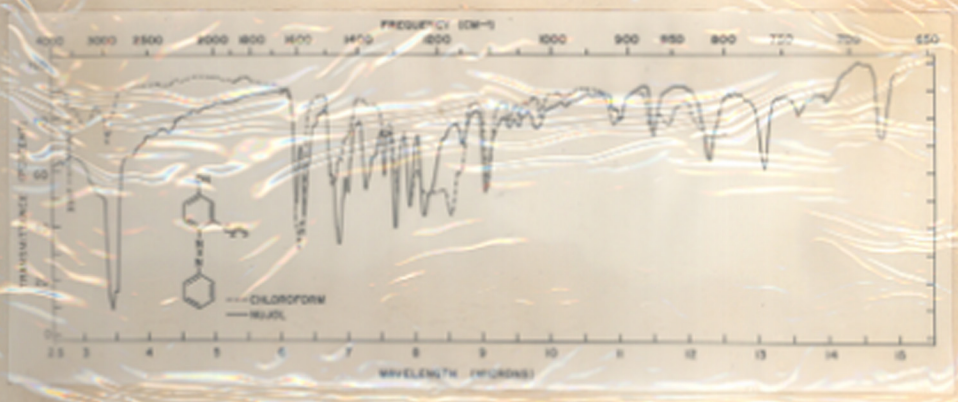
[illegible]

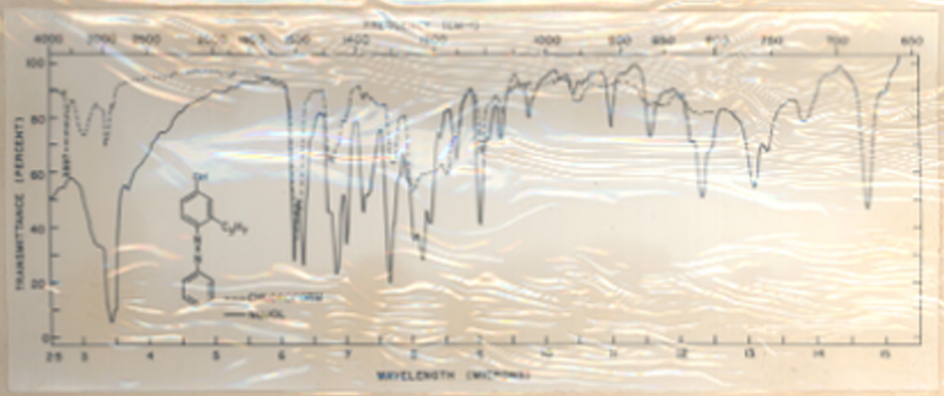


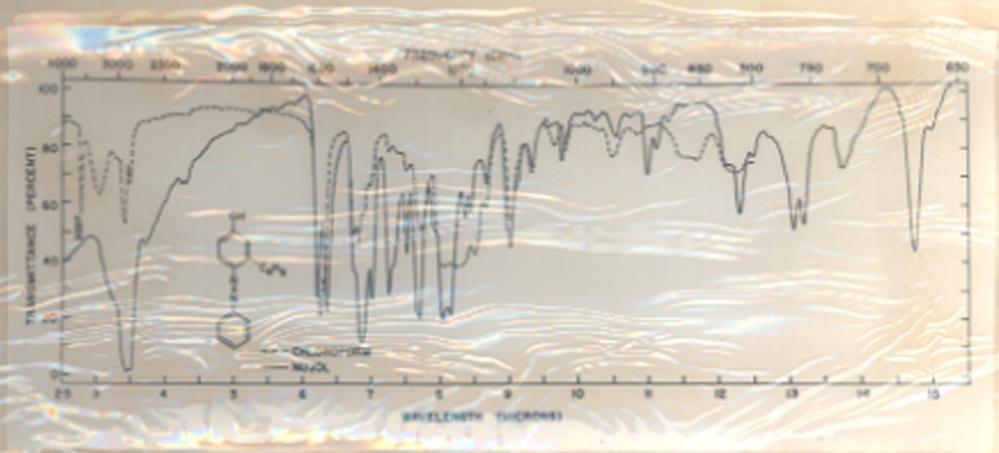




Infrared Absorption Spectra Of Monoazo Dyes

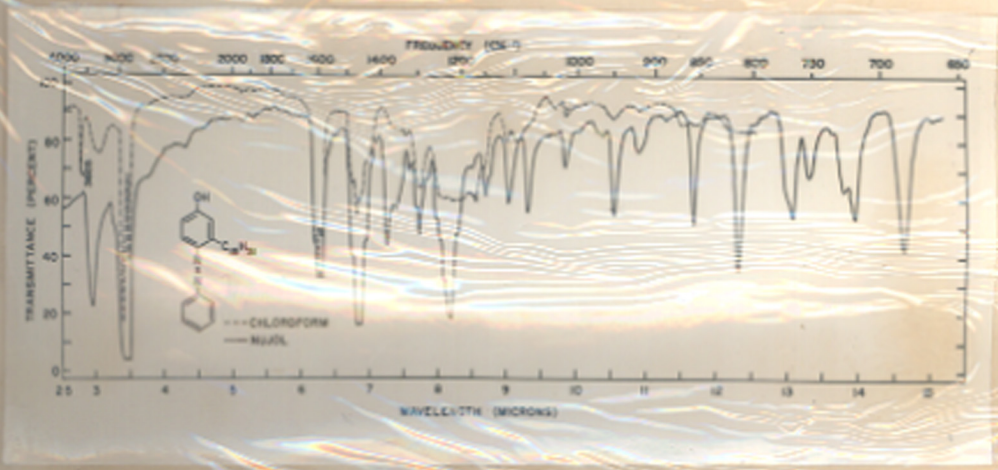


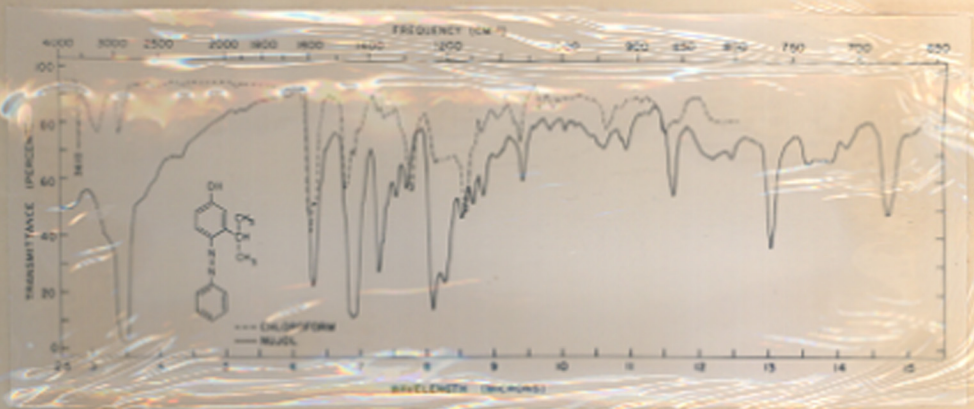




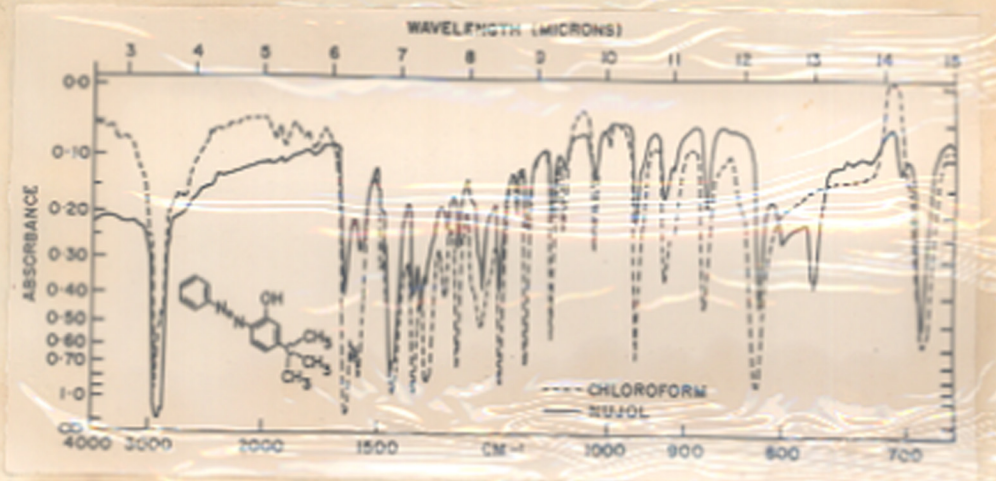
Infrared Absorption Spectra Of Monoazo Dyes

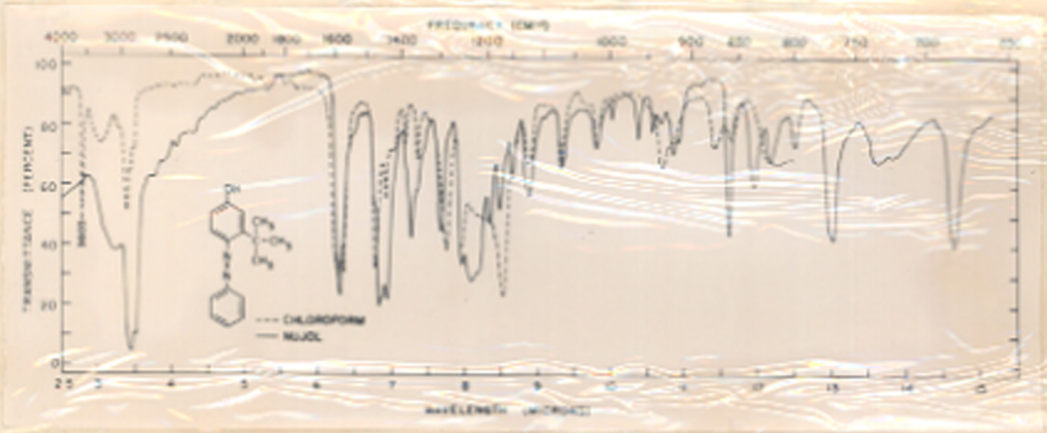
(continued)





Infrared Absorption Spectra Of Monoazo Dyes
(continued)





Infrared Absorption Spectra Of Monoazo Dyes
(continued)

Table IV

Complete Absorption Bands of Disazo dyes in Cm^{-1}

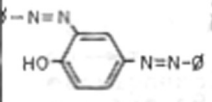
Compound		3650-2700	2700-2000	2000-1500	1500-1300	1300-1100	1100-900	900-650
	Nujol Mull	2910S 2857S		1600S	1493S 1462S 1404M 1372S	1276S 1149M 1205M 1130M 1181M 1161M	1099S 960W 1067M 922W 1018W 900W 1000W	893W 773S 845W 737M 827M 702W 800W 682S
Disazo from An→m-Cresol m.p.149°	Nujol Mull	2841S		1575S	1453S 1320S 1416S 1370S 1351Sh	1277S 1227S 1183S 1156S	1070S 962WB 1044M 917S 1020M 997WB	843Sh 769S 834M 748S 818S 727WB 790M 678S
	Chloro-form	3088S 2632M		1594S	1479S 1378M 1460S 1355M 1461M 1315M	1286S 1185WB 1156M	1071W 919W 1044M 1020M 1000W	828SB
Disazo from An→m--cresol m.p.177°	Nujol Mull	2920S		1581S	1467S 1379S 1456S 1311S 1418S	1285S 1194M 1160M 1150M	1092S 914M 1070M 902M 1020M 998M	877SB 719WB 828W 681S 773S 754S
	Chloro-form	2920W		1587S	1471S 1416S 1460S 1383M 1441S 1374M 1412M 1355M	1285S 1153W	1092M 919W 1072M 1020M 998WB	850WB
Disazo from An→m-Cresol m.p.180°	Nujol Mull	2900S 2803S		1600S 1562M	1481M 1461S 1393W 1370M 1350M 1300	1268W 1232W 1203M 1159W 1100M	1068W 1020W 920W 909W	840M 823M 768S 734W 690M 685M

Table IV (continued)

Compound		3650-2700	2700-2000	2000-1500	1500-1300		1300-1100	1100-900		900-650	
Disazo from An→m-ethylphenol m.p.138.5°	Nujol Mull	2899S		1587S	1456S 1429S 1414S 1376S	1364S 1316W	1279S 1223S 1185M 1157M	1066M 1042M 1018W 1000W	963M 919M 901W	866M 826S 785W 777WB	756S 723W 681S
	Chloroform	2963W 2861W		1587S	1477S 1455M 1433M 1414M	1366M 1312W	1287S 1185WB 1155M	1066M 1042M 1018W 1000W	920W	888W 827M	
Disazo from An→m-ethylphenol m.p.137°	Nujol Mull	2900S 2830S		1610M 1580	1482W 1460S 1400W 1371M 1322M 1300W		1275W 1260W 1205W 1182W 1155W 1145W 1108W	1070W 1054W 1020W 922M 915Sh		870W 820M 770M 740M 730W 685S	
Disazo from An→m-n-propylphenol	Nujol Mull	2901S 2850S		1590S	1480M 1460S 1430M 1410M 1370M 1360M	1310W	1285M 1225M 1187W 1155W	1065W 1050W 1030W 1020W 1000W 922W		865WB 843W 825S 787W 763S 687S	
	Chloroform	3311 2959 2874		1590	1477 1454 1414 1362	1314	1284 1183 1157	1099 1070 1050 1018	1000	829	

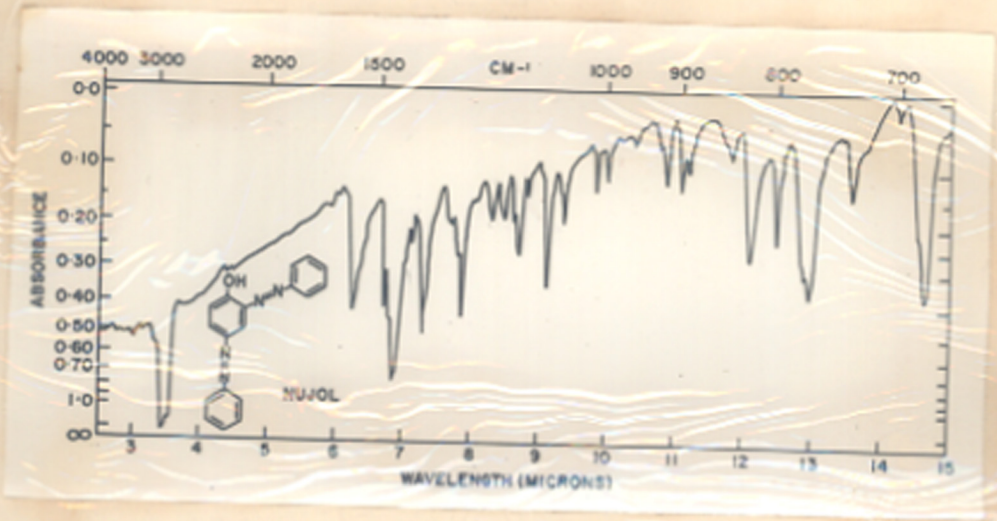
Table IV (Continued)

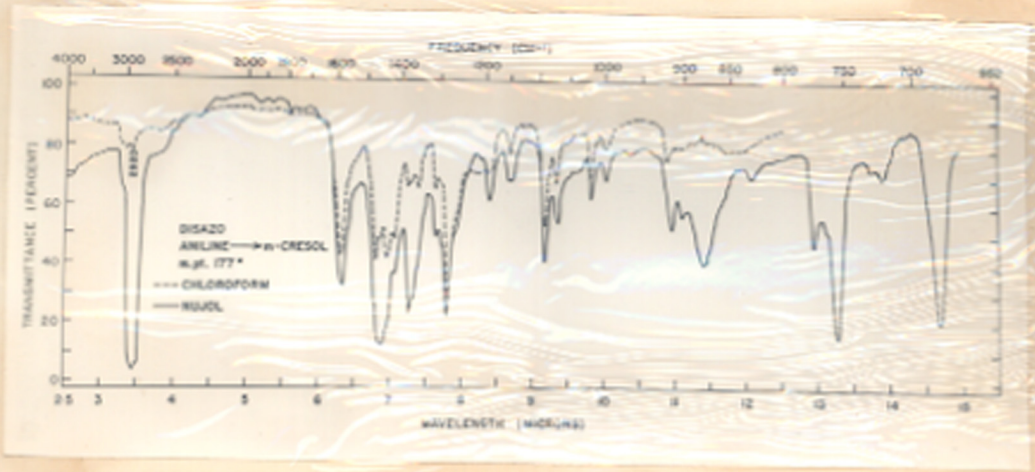
Compound		3650-2700	2700-2000	2000-1500	1500-1300	1300-1100	1100-900	900-650
Disazo from An→m-n-Butyl phenol	Nujol Mull	2900 2820		1580	1475Sh 1460S 1410M 1370M 1310W	1280S 1225M 1180M 1155M	1095W 1065W 1042M 1018W 1000W 918W	858W 824S 787W 762S 687S
	Chloroform	3279 2924 2857		1587	1475 1313 1455 1414 1366	1285 1182 1155	1093 920 1068 1045 1018	826
Disazo from An→m-penta-decyl phenol	Nujol Mull	2915S 2852S		1587S	1479Sh 1318W 1458S 1412S 1365S	1278S 1104WB 1226S 1183S 1153M	1067Sh 963W 1053S 920M 1018M 1000W	867WB 759S 818S 719M 787M 683S 777M
	Chloroform	2924S 2849S		1587S	1475S 1453M 1413WB 1364M	1284M 1155M	1067M 1045W 1018W 920WB	828M
Disazo from An→m-Isopropyl phenol	Nujol Mull	2924S		1580S	1468Sh 1377M 1453S 1312W 1408M	1282M 1131W 1220W 1170M 1153W	1087W 1070W 1017M 917WB	827M 790W 762W 687M
	Chloroform	2915W		1580S	1468M 1443M 1408M 1377W 1312W	1282M 1220WB 1170M 1153W 1131W	1087W 1070W 1017M 917W	830M

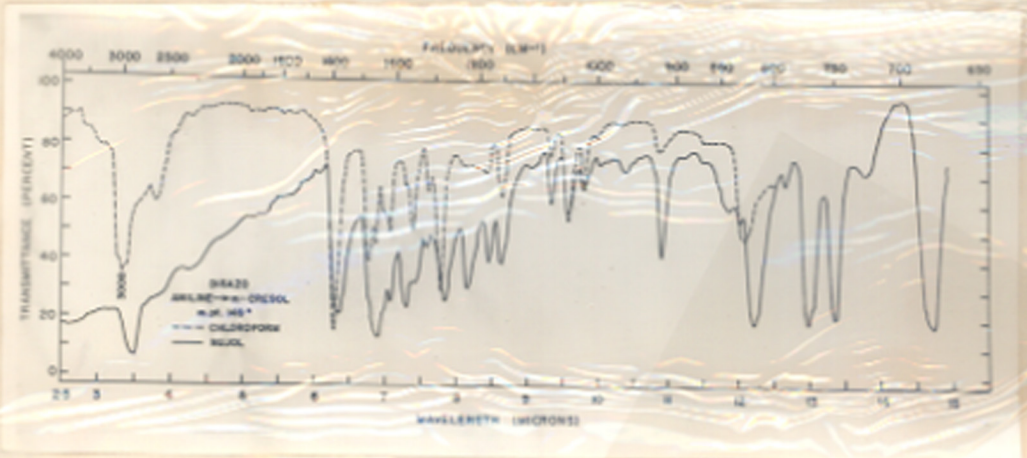
Table IV (continued)

Compound		3650-2700	2700-2000	2000-1500	1500-1300	1300-1100	1100-900		900-650
Disazo from An→m-t-butylphenol	Nujol Mull	2878S		1613S 1570S	1460S 1397Sh 1377S 1359S	1314M 1278M 1179M 1303M 1232S 1153M 1208MB 1143M 1193M 1130S	1070M 918S 1053M 1020M 934W		867M 789S 848M 764S 831M 737M 810Sh 712MB 679S
	Chloro-form	2967M		1613S 1592S 1569S	1465S 1449M 1401M 1350M	1316M 1299M 1131M 1278M 1179M	1073M 922MB 1055M 1021M		876W

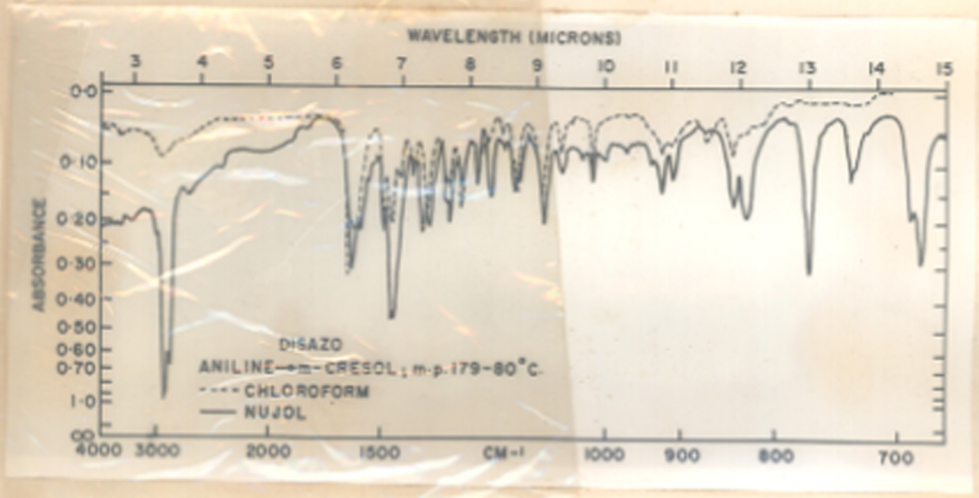
S=Stron ; M=Medium; W=Weak; Sh=Sho lder, B=Broad.

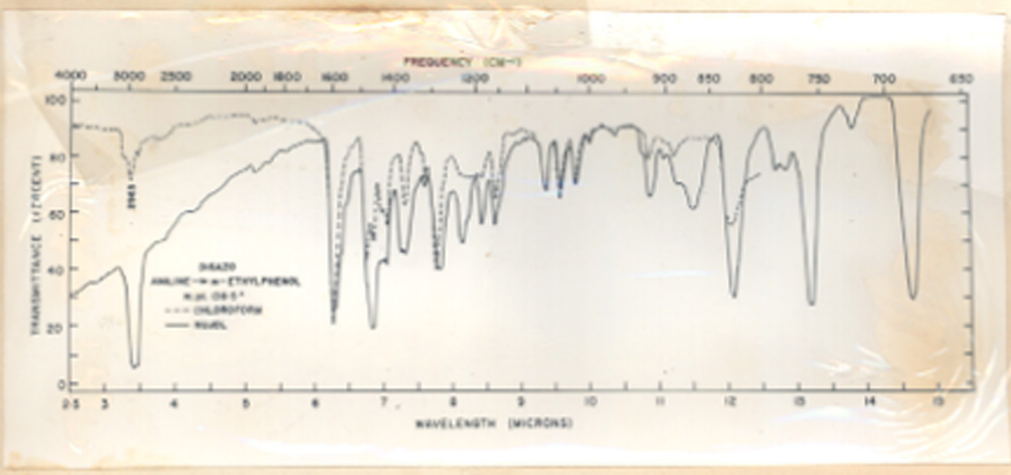


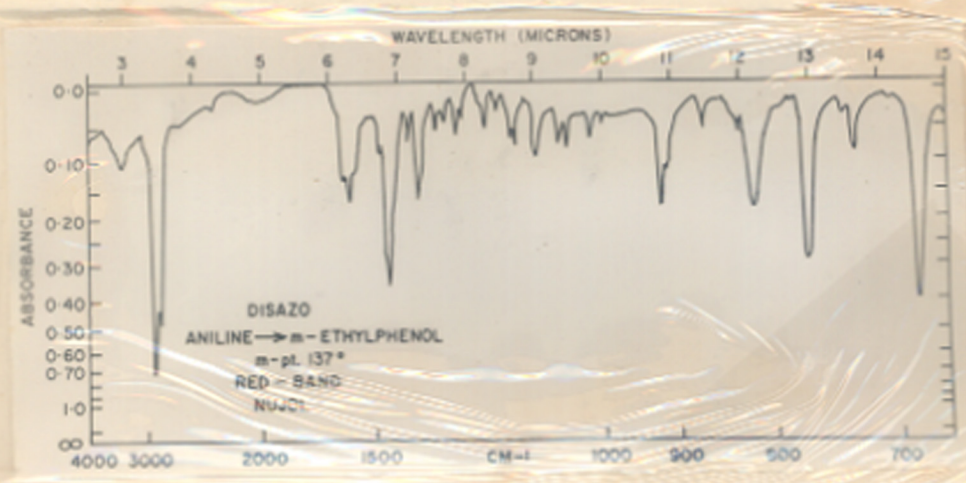




Infrared Absorption Spectra Of Disazo Dyes

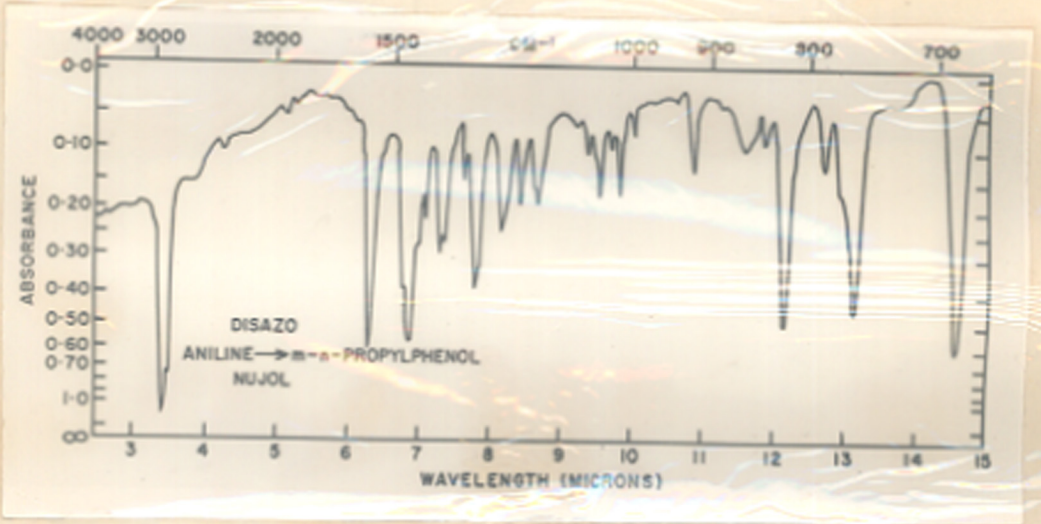


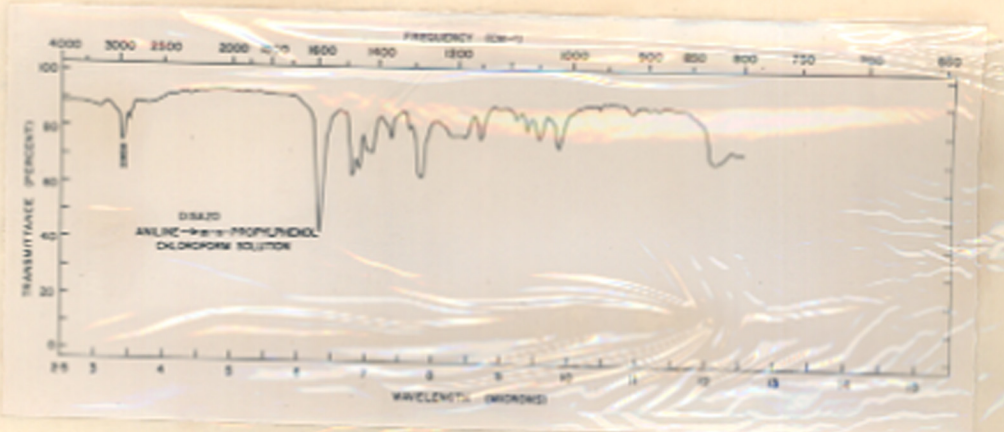




Infrared Absorption Spectra Of Disazo Dyes

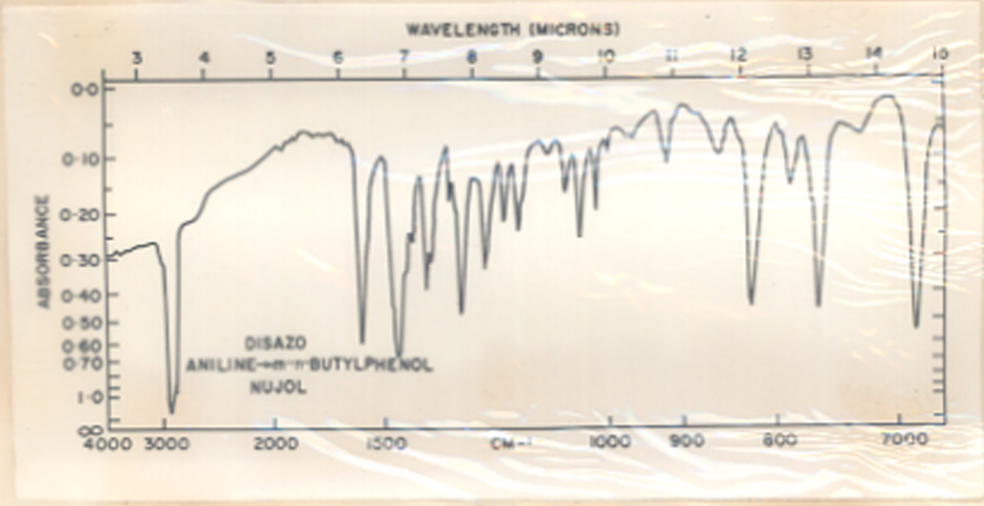
(continued)

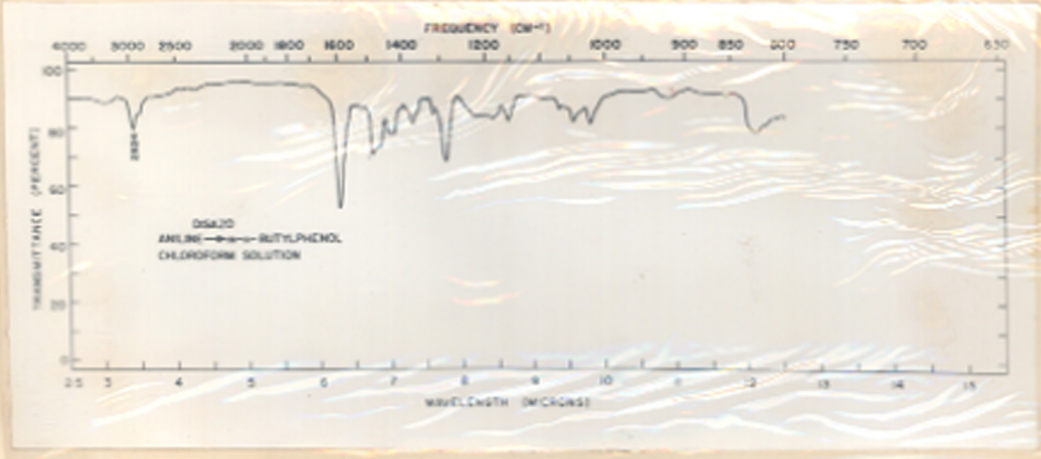




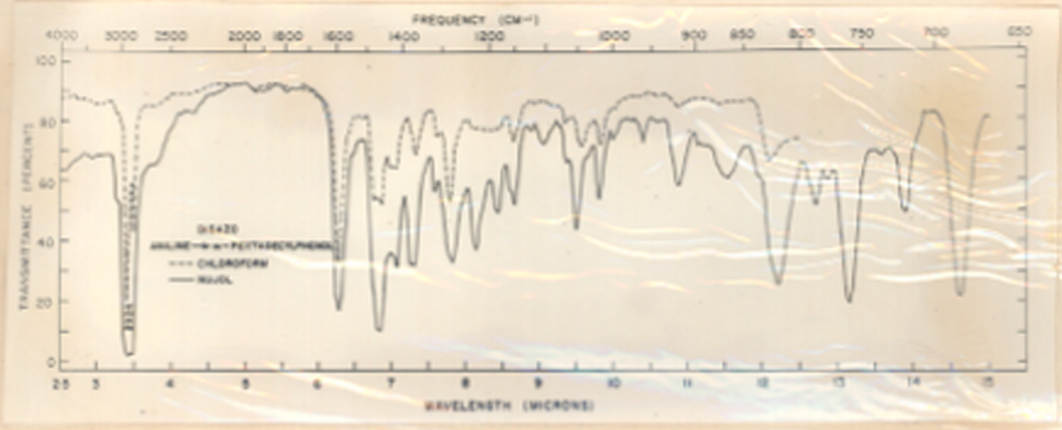
Infrared Absorption Spectra Of Disazo Dyes

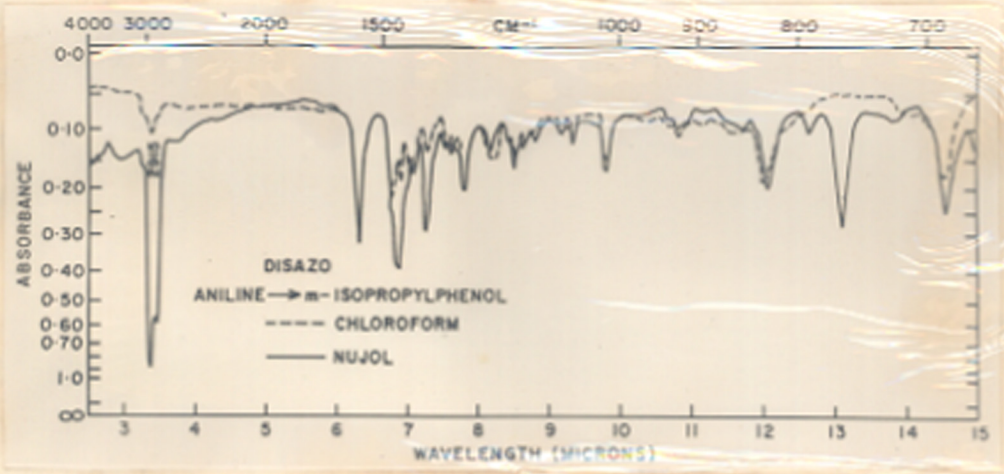
(continued)

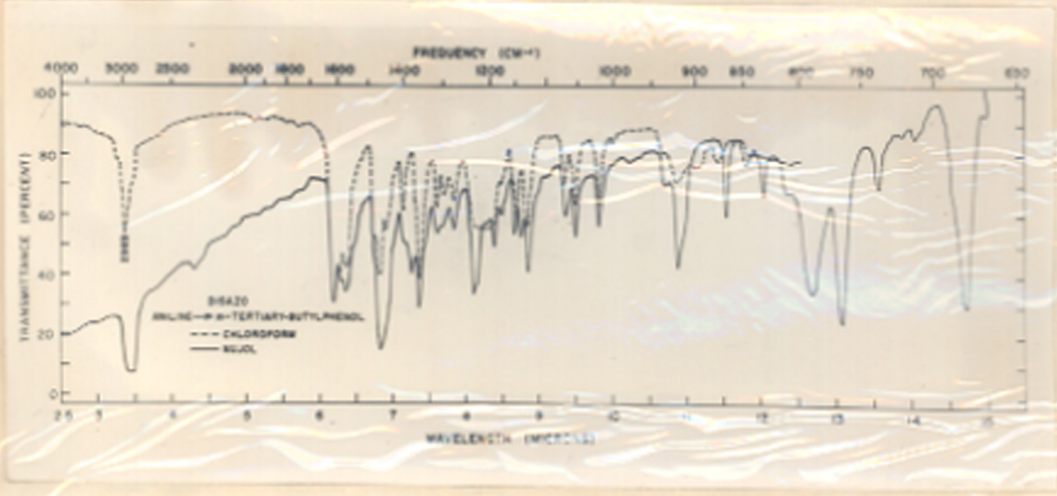




Infrared Absorption Spectra Of Disazo Dyes
(continued)







Infrared Absorption Spectra Of Disazo Dyes

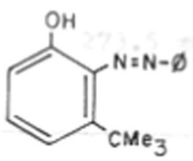
(continued)

U.V. AND VISIBLE SPECTRA OF PHENOLS AND AZO COMPOUNDS.

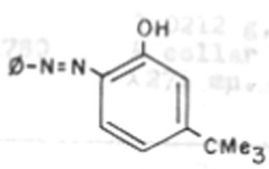
The electronic spectra of the various phenols and their coupled products were determined in alcoholic solution on a Beckmann DK II automatic recording spectrometer. All the phenols absorb around 272-274 mμ and their extinction coefficients are recorded in the Table V. The length or branching of the meta substituted alkyl chain has very little effect on the maxima of the absorption of the phenols as can be observed from the Table V.

The absorption maxima of the monoazo and disazo derivatives prepared from the various phenols are given in Table VI and VII respectively. It can be seen that the spectral pattern of monoazo and disazo dyes are very similar to one another. The introduction of an azo chromophor into the phenols produces a marked change in the spectra. All the para substituted monoazo phenols show three bands[27], near 237 mμ (benzene band 'B'), 356 mμ (K band) and 45) mμ (R band). Brode et.al.[28] have shown that p-phenylazophenol has a K band at 348 mμ. The shift towards the higher wave length in the alkyl azophenols may be due to alkyl group in ortho position. Brode et.al.[24] have also shown that orthophenylazophenol has a K-band at 323 mμ. In the present study it has been observed that the dye from the lower most band of the

chromatogram from aniline → m-tertiary-butylphenol (viz the first eluted dye) shows an absorption maximum for the K band at 328 mμ which is in good agreement with the expected higher frequency of the alkyl substituted azophenol. On the basis of this evidence, substantiated by colour (orange yellow), melting point (60°), low solubility in alcohol and dilute sodium hydroxide solution structure V or VI can be assigned to this dye.



V



VI

Due to the greater steric hinderance in V the structure VI is more probable and is supported by infrared spectra.

The introduction of second azo group does not cause a marked change in the B band but K band is shifted towards lower wave length (348 mμ), the shift is greater (334 mμ) in the case of disazo dyes obtained from red band. However in the case of the dye from m-cresol (m.p.177°) there is hardly any shift (354 mμ). In all the disazo compounds the R band is masked.

Table V

U.V. and Visible Spectra of some m-alkyl phenols in ethanol

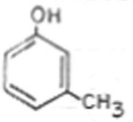
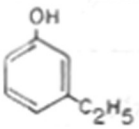
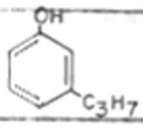
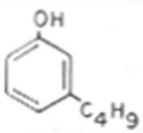
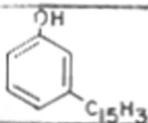
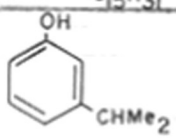
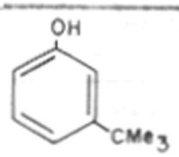
Compound	λ max in mμ	ε	Concentration and remarks.
	274 mμ	1678	0.0222 g./litre A collar is observed at λ 280 mμ.
	273.5 mμ	1780	0.0212 g./litre A collar is observed at λ 274 mμ.
	273.5 mμ	1859	0.0278 g./litre A collar is observed at λ 280 mμ.
	272 mμ	1445	0.028 g./litre A collar is observed at λ 279 mμ.
	273 mμ	2213	0.0224 g./litre A collar is observed at λ 280 mμ.
	272 mμ	1590	0.0338 g./litre A collar is observed at λ 290 mμ.
	272.5 mμ	1900	0.0304 g./litre A collar is observed at λ 290 mμ.

Table VI

U.V. and Visible Spectra of Monoazo dyes in ethanol

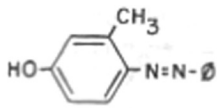
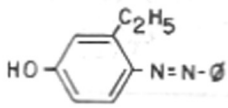
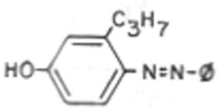
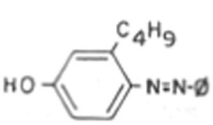
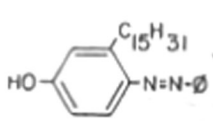
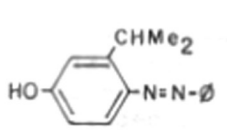
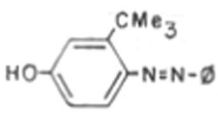
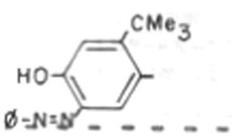
Compound	max in mμ		Concentration and remarks
	237 356 450	10190 23290 1359	0.0078 g./litre Bands at 237 and 450 are very broad.
	237 354 450	11430 22390 2287	0.0084 g./litre. Bands at 237 and 450 are very broad.
	238 356 440	11140 25050 1990	0.0064 g./litre. Bands at 238 and 440 are very broad.
	238 356 445	8582 19830 1067	0.0088 g./litre. Bands at 238 and 445 are very broad.
	236 356 450	13760 19740 3091	0.0066 g./litre. Bands at 238 and 450 are very broad.
	240 356 450	20000 28960 2400	0.0075 g./litre. Bands at 240 and 450 are very broad.
	250 358 450	10570 23310 1980	0.0068 g./litre. Bands at 250 and 450 are broad.
	244 328 374	8769 19293 11619	0.0232 g./litre. Absorption at 374 mμ is as a shoulder.

Table VII

U.V. and Visible Spectra of Disazo Dyes in ethanol

Compound	λ max in mμ	ε	Concentration and remarks.
Disazo from Aniline→m-Cresol m.p.149°	348 245	46510 17780	0.0032 g./litre Band at 245 mμ is very broad.
Disazo from Aniline→m-Cresol m.p.177°	354 235	37660 11410	0.0036 g./litre Band at 235 is very broad.
Disazo from Aniline→m-Cresol m.p.180°	334 230	43970 17580	0.0036 g./litre Band at 240 is very broad.
Disazo from Aniline→m-Ethylphenol m.p.138-5	348 230	36280	0.0035 g./litre Bands at lower or higher wave length were not well defined.
Disazo from Aniline→m-n-Propylphenol	348 230	43080	0.0039 g./litre Bands at lower and higher wave length were not well defined.
Disazo from Aniline→m-n-Butylphenol	348 230	42070	0.004 g./litre. Bands at lower and higher wave length were not well defined.
Disazo from Aniline→m--Pentadecylphenol	350 240	43520	0.003 g./litre Bands at lower and higher wave length were not well defined.
Disazo from Aniline→m--Isopropylphenol	348 230	51650	0.0039 g./litre Bands at lower and higher length were not well defined.
Disazo from Aniline→m-tertiary--butylphenol	334 230	36990 14910	0.0036 g./litre Band at 230 is very broad.

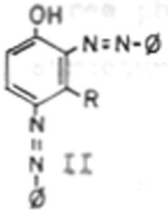
Difficulties in assigning a definite structure to disazo dyes:

i) All the disazo compounds that could be isolated in the reaction product were in very small quantities. In the case of m-cresol, the disazo dye (m.p.148°) which was obtained in somewhat larger quantity reduction was attempted to the corresponding known amine. However the amine could not be isolated in pure crystalline form as it spontaneously decomposed (indicated by change in colour).

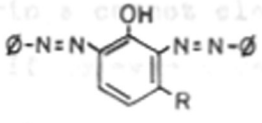
ii) On the basis of the greater reactivity of the para position it would be quite reasonable to expect that the para position to the phenolic -OH must bear an azo group in the disazo compounds. Also on the basis of the greater steric hinderence of the 2,6-disazo alkylphenol (III), this structure seems improbable. However the presence of three disazo compounds in the case of aniline ⟶ m-cresol suggest that this structure may be possible.

iii) If for the moment structure III is neglected, then II and IV are the probable disazo structures. Examination of the formulae shows that the structure II is sterically hindered and naturally lesser quantities of dyes are expected to correspond to structure II. If this is the case, then dyes obtained from the red band (λ max 334 mμ) should have

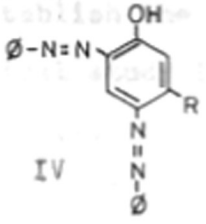
structure II. In the case of disazo dye obtained from m-tertiary butylphenol one would expect an even lower yield of dye corresponding to structure II. However, the disazo dye isolated (λ max 334 mμ) is from the red band and is in appreciable quantity. Moreover it is the only disazo dye isolated. Hence if we assign structure IV to this dye, lower yields in the cases of other phenol dyes cannot be explained.



II



III



IV

iv) It is probable that the dyes may exist in cis-trans forms. If this is the case then two paramonoazo dyes should be isolated but even though large quantities of para monoazo dyes were isolated no trace of second para azo compound could be isolated. These para monoazo compounds have been shown to be homogenous by repeated chromatography on alumina. Moreover in no case the number of the bands obtained on the column corresponded or even approached the theoretically possible number of isomers. Quinone-hydrazone structure in the case of dyes was ruled out on the basis of infrared spectra.

v) The substitution pattern cannot be definitely pin pointed because of the following reasons:

(a) structures II and III correspond to 1,2,3,4 tetra substituted benzene and cannot be differentiated by infrared spectra.

(b) Though it is apparently possible to distinguish between IV and II or III, the large number of bands in 900 to 650 region due to presence of three phenyl rings cannot clearly establish the structure. If however a very critical study is made all compounds correspond more to 1,2,3,4 tetra substituted benzene. This is however not expected.

It is because of these reasons that definite structures have not been assigned to the disazo compounds.

EXPERIMENTAL

Purification of m-cresol

Tribromo-m-cresol: m-Cresol (108 g.; 1 mole) dissolved in glacial acetic acid (400 ml.) was cooled to 0°C and bromine (480 g.; 3 mole) was added to it drop by drop with constant stirring. Stirring was continued for ½ an hour at 0°C. and then for 2 hrs. at room temperature, after the completion of addition of bromine. The reaction mixture was poured on crushed ice with stirring, the precipitated tribromo-m-cresol was filtered, washed with cold water and dried by suction. It was crystallized from alcohol and then from petroleum ether (40-60), into white needles (m.p.81°C; yield, 250 g. 73.7%).

Debromination of tribromo-m-cresol: Tribromo-m-cresol (34.5 g.) dissolved in alcohol (80 ml.) was taken in a hydrogenation bottle and to it was added Raney-nickel (20 g.) and sodium hydroxide (12 g. dissolved in 20 ml. of water). The reaction mixture was agitated in an atmosphere of hydrogen (70 p.s.i.) in a Paar Hydrogenation apparatus. When there was no more absorption of hydrogen the reaction mixture was acidified with hydrochloric acid (3 N) and the spent catalyst removed by filteration. The solvent was removed by distillation and the residue was fractionated to obtain pure m-cresol. (b.p.198°C. yield 9 g.; 83.3%). This pure m-cresol was used for the preparation of azo dyes.

1. m-Ethylphenol

m-Nitroacetophenone: To a cooled and stirred solution of sulphuric acid (d, 1.84; 150 ml.) acetophenone (60 g. 0.5 mol.) was added dropwise at such a rate that the reaction temperature did not rise above 0°. After the addition was complete the contents of the flask were cooled to -10°C. by the addition of solid carbon dioxide. Previously cooled nitrating mixture (40 ml. HNO_3, d.1.42 and 60 ml. H_2SO_4 d. 1.84) was added as quickly as possible (20 to 30 minutes), maintaining the temperature below -5°C. After stirring for 10 minutes it was poured on crushed ice, the flocculent precipitate was collected on a filter, washed and dried by suction. It crystallized from alcohol in cream coloured needles. (m.p.78°; yield 60.0 g. 70%).

m-Aminoethylbenzene: A solution of m-nitroacetophenone (12 g. 0.072 mole) in diethylene glycol (75 ml.) was refluxed for one hour with 100% hydrazine hydrate (12 g. 0.24 mole) cooled and potassium hydroxide pellets (2 g.) were carefully added, refluxed for another thirty minutes. After distilling the fraction boiling below 190° the contents of the flask were maintained at this temperature for eight hours. The reaction mixture was cooled and steam distilled. Steam distillate was extracted with ether, the ether extracts dried and then after the removal of the solvent the residue (7.5 g.) was distilled using a small

fractionating column (b.p.210-215°; yield 7.0 g. 80.4%).

m-Ethylphenol: m-Aminoethylbenzene (26 g. 0.215 mole) was dissolved in concentrated hydrochloric acid (80 ml.) diluted with water (150 ml.) and cooled under stirring to -5°. Sodium nitrite (14.83, 0.215 mole) was added in small portions at a time maintaining the reaction temperature below 0° and stirring continued for another thirty minutes. A vigorous current of steam was passed into 500 g. of 15% sulphuric acid and the cold diazonium solution gradually was added and the steaming continued until no more oil distilled over. The steam distillate was extracted with ether and the extract dried over sodium sulphate. After removing the solvent the residue was distilled at 126-7° at 45 mm. of Hg. (75°/1 mm.) to yield m-ethylphenol (20.0 g. n_D^{27} 1.5310; 76.1%).

2. m-n-Propylphenol:

Propiophenone: A mixture of propionyl chloride (46 g. 0.5 mole) and sodium dried, thiophene free benzene (85 g.) was added to a vigorously stirred suspension of aluminium chloride (50 g.) in dry carbon disulphide (100 ml.). Stirred for fifteen minutes more after the whole mixture had been added. More aluminium chloride (about 10 g.) was then added in small portions till no more hydrogen chloride was evolved. Stirring was continued for two more hours and then the reaction mixture was poured on crushed ice. Upper layer was separated, water layer extracted with ether, ether extract and upper layer were mixed and washed with sodium hydroxide solution (10%; three times)

and then with brine (4 times). Ethereal solution was dried over sodium sulphate, ether removed and the residue distilled. (b.p.210-11°; 58.73 g.; 89.5%).

m-Nitropropiophenone: Fuming nitric acid (33 g. d^{15} 1.5) was cooled and acetic anhydride (33 g.) added slowly below 15°C. The mixture was cooled under stirring to -10°C. Propiophenone (5 g. 0.037 mole) was added dropwise maintaining the temperature below 0°C. and stirred at this temperature for 45 minutes. The reaction mixture was poured on crushed ice and the flocculent precipitate collected on a filter, washed and dried. It crystallized from alcohol in cream coloured needles, m.p.100°C. (3.44 g. 52% of theoretical yield).

m-n-Propylaniline: A solution of m-nitropropiophenone (50 g. 0.28 mole) in diethylene glycol (200 ml.) was reduced to m-n-propylaniline, by using 100% hydrazine hydrate (50 g. 1 mole) as described under m-ethyl aniline (yield 28 g. 74.29%).

m-n-Propylphenol: m-n-Propyl aniline (28 g. 0.207 mole) in hydrochloric acid (100 ml. in 300 ml. water) was diazotised at -5° with sodium nitrite (14 g.). Hydrolysis of this diazotised solution as in m-ethylphenol gave m-n-propylphenol (b.p.133°/25 mm. n_D^{28} 1.5230; yield 20.74, 74.1%).

3. m-n-Butylphenol:

Butyrophenone: A mixture of butyryl chloride (53 g. 0.5 mole) and sodium dried thiophene free benzene (100 g.) was added to vigorously stirred suspension of aluminium chloride (50 g.) in dry carbon disulphide (100 ml.) as in propiophenone and the reaction mixture, on working up, gave butyrophenone (b.p. 222-24°C; yield 70.66 g. 93.7%).

n-Nitrobutyrophenone: Butyrophenone (90 g. 0.608 mole) was nitrated at 0° by the nitrating mixture formed from nitric acid (d. 1.5, 330 ml.) and acetic anhydride (550 ml.). Crystallization from alcohol yielded m-nitrobutyrophenone m.p.61°C. (55 g.46.8%).

m-n-Butylaniline: m-Nitrobutyrophenone (20 g. 0.104 mole) was reduced to m-n-butylaniline by 100% hydrazine hydrate (25 g. 0.5 mole) as described under m-ethylaniline (yield 10 g. 64.77%).

m-n-Butylphenol: m-n-Butylaniline (10 g. 0.067 mole) in hydrochloric acid (40 ml. in 100 ml. water) was diazotised by using sodium nitrite (5 g. 0.07 mole) at -5 to 0°C. Diazonium chloride solution was hydrolysed using 15% boiling sulphuric acid as in the previous experiments. m-n-Butylphenol was distilled at 156°/25 mm. (6.94 g.; 68.9%; n_D^{28} 1.5159).

4. m-Isopropylphenol

p-Nitrocumene: To a cooled solution of sulphuric acid (d, 1.84; 225 ml.) isopropyl benzene (80 g. 0.667 mole) was added dropwise and under stirring below 0°C. After the addition was complete the contents of the flask were cooled to -10° by the addition of solid carbon dioxide. Previously cooled nitrating mixture (60 ml. HNO_3, d, 1.42 and 90 ml. H_2SO_4 d, 1.84) was added in shortest possible time maintaining the temperature below 0°C. After stirring for ten minutes it was poured on crushed ice. After ice had melted the reaction mixture was extracted with ether, ether extract was washed with water and dried over anhydrous sodium sulphate. Removal of solvent gave a residue which was distilled under vacuum at a constant temperature (b.pt. 100°/6-8 mm.; 63 g. 57.2%).

p-Cumidine: To a solution of p-nitrocumene (63 g. 0.382 mole) in ethyl alcohol (175 ml.) was added 100% hydrazine hydrate (60 ml. 1.2 mole) and a pinch of Raney nickel. The reaction started immediately and after the initial frothing subsided, a little more Raney nickel was added and the reaction mixture was warmed on water bath. After half an hour it was filtered and alcohol removed under reduced pressure. The residue was distilled at 220-225° (44.74 g.; 86.6%).

p-Acetcumidide: Acetic anhydride (34 g. 0.34 mole) was added gradually to p-cumidine (44.7 g. 0.331 mole) and freshly fused sodium acetate (4 g.), the solution refluxed for one hour. The reaction mixture was poured into water, the precipitated acetcumidide collected on buchner funnel and pressed to dryness. It crystallized from petroleum ether (40-60°) as waxy plates (m.pt. 104-105°; yield 53 g. 90.3%).

3-Nitro-4-acetaminocumene: Nitric acid (d. 1.50; 31.6 mole) was added to a solution of acetic acid (100 mole) and acetic anhydride (122.4 ml.), keeping the temperature below 20°. Nitrating mixture was further cooled to -10° by keeing in ice-salt mixture bath under constant stirring. p-Acetcumidide (53.0 g. 0.299 mole) dissolved in acetic acid (44 ml.) was added dropwise maintaining the temperature below 0°C. After stirring for 45 minutes at 0° the reaction mixture was poured on crushed ice and the product taken up in benzene, washed till neutral first with water, then with 5%. sodium hydroxide and again with water. The benzene solution was dried over sodium sulphate, benzene removed and the residue crystallized from dilute alcohol and then from benzene-nexane (m.p. 80°C. yield 45.26 g. 68.1%).

3-Nitro-4-aminocumene: Potassium hydroxide (30.0 g. of 50% solution) was added to a refluxing solution of 3-nitro-4-acetaminocumene (45.26 g. 0.203 mole) in ethanol (50 ml.). After 15 minutes of refluxing, the solution was

poured into water, the oil taken up in ether, dried over sodium sulphate and ether was removed to obtain 3-nitro-4-aminocumene (35.22 g. 97.1%).

m-Nitrocumene: 3-Nitro-4-aminocumene (35.2 g. 0.195 mole) was dissolved in ethanol (180 ml.) and hydrochloric acid (78.0 g. 31%) refluxed, and a solution of sodium nitrite (27.5 g. in 50 ml. water) was added during a an hour. The mixture was steam distilled. Steam distillate was extracted with ether, dried, and after removing the solvent the residue was distilled (b.p.89-91/3-5 mm. 17.6 g. 54.5%).

m-Cumidine: To A solution of m-nitrocumene (17.6 g. 0.105 mole) in ethyl alcohol (100 ml.) was reduced by using hydrazine hydrate (30.0 g. 100%, 0.6 mole) and Raney nickel as in p-cumidine. After removing alcohol under reduced pressure the residue was distilled under vacuum at 75°/2.5 mm. (12.9 g. 90%).

m-Isopropylphenol: m-Cumidine (12.9 g. 0.095 mole) in sulphuric acid (50 ml. d. 1.84 in 200 ml. water) was diazotised by using sodium nitrite (6.9 g. 0.1 mole) at -5 to 0°. Diazonium solution was hydrolysed using 15% sulphuric acid in a current of steam. Steam distillate yielded m-isopropylphenol (b.pt. 75°/1.5 mm., 9.8 g. 75.19%).

COUPLING AND CHROMATOGRAPHIC EXAMINATION:

Aniline → Phenol: Aniline (4.65 g. 0.05 mole), concentrated hydrochloric acid (16 ml.) and water (50 ml.) were stirred to obtain a clear solution. It was cooled to -5°. Sodium nitrite (3.2 g.) was added in small portions maintaining the temperature below 0°C. Stirring was continued for another 30 minutes to complete the diazotisation.

To a solution of phenol (4.7 g.) in aqueous sodium carbonate (10%; 200 ml.) was added diazonium chloride solution slowly at 0° with stirring. The reaction mixture was stirred for 30 minutes at 0° and then for one hour at room temperature, acidified and the yellow dye filtered, washed and dried (8.7 g.).

Chromatographic examination: A column (2.2 x 70 cm.) was packed uniformly with alumina (150.0 g. Gr.II) in benzene. A solution of the crude dye (4.5 g.) in benzene (100 ml.) on chromatographing and developing with benzene three bands appeared, an orange-yellow band at the top, a red orange band in the middle and a yellow band at the bottom. On eluting the chromatogram with benzene the bottom band was eluted and the dye obtained (0.0624 g.) crystallized from alcohol as orange needles m.pt. 82-83°. This has been characterised as ortho-hydroxyazobenzene. By extruding the column and separating the reddish orange layer of alumina from the middle band and extracting the alumina with boiling

alcohol, the dye thus obtained (0.0468 g.) has been characterised as 2:4-bisbenzeneazophenol m.pt. 131°C. By separating the orange layer of alumina from the orange yellow band at the top, and boiling with alcohol, a yellow dye was obtained (0.7 g.) which crystallized as yellow crystals from benzene-hexane m.p.155°. This has been characterised as p-hydroxyazobenzene. Thus the order of decreasing adsorbability was p-hydroxyazobenzene, 2:4-bisbenzeneazophenol and o-hydroxyazobenzene.

Aniline → Phenol: (Pyridine coupling pH 7)
Aniline (0.93 g. 0.01 mole) concentrated hydrochloric acid (4 ml.) and water (20 ml.) were stirred to obtain a clear solution and the solution was cooled with stirring to -5°C. Sodium nitrite (0.69 g.) was added in small portions maintaining the temperature below 0°C. Stirred for further ½ an hour to complete the diazotisation.

To a solution of phenol (0.94 g.) in pyridine (30 ml.) diluted with water (20 ml.) diazonium chloride solution was added slowly at 0° with stirring. The reaction mixture was stirred for 30 minutes at 0° and then for four hours at room temperature, acidified and the oily dye was taken up in ether. After drying and removing the ether the crude dye weighed 1.8 g.

Chromatographic examination: A solution of the crude dye showed the same three bands, orange yellow at the top, a red orange band in the middle and a yellow band at the bottom. The dyes obtained from different bands were same as mentioned in carbonate coupling. The following are the yields of the dyes obtained from different bands:

1. Yellow band (lower most) 0.021 g.
2. Red orange band (middle) 0.001 g.
3. Orange yellow band (top) 1.36 g.

Aniline → Phenol: (Sodium hydroxide coupling pH 7 10.5) Diazonium chloride solution prepared as above from aniline (0.93 g.) was coupled with phenol (0.94 g.) dissolved in 50 ml. of 10% sodium hydroxide at 0°. After the coupling was complete the reaction mixture acidified and worked up as in the previous experiment. Crude dye weighed 1.85 g.

Chromatographic examination: Many bands appeared on the column of alumina, the individual dyes from which could not be isolated. The top most band however yielded p-hydroxyazobenzene (0.85 g.) and a dye from the red band was identified as 4:6 bisbenzeneazophenol (0.009 g.).

Aniline → m-cresol (NaOH coupling pH 7 10.5) Aniline (1.86 g. N/50 mole) was diazotised at -5° by means of hydrochloric acid (9 ml.). Water (50 ml.) and sodium nitrite (1.4 g. N/50 mole). The diazonium solution was added to a mechanically stirred solution of m-cresol (2.16 g.

N/50 mole) in aqueous sodium hydroxide solution (20%; 50 ml.) cooled with ice and salt. The reaction mixture was stirred at 0° for 30 minutes and then for one hour at room temperature. The solution was acidified with dilute hydrochloric acid (1:1) and the precipitated dye was taken up in benzene. After drying and removing the benzene the dye weighed 4.140 g.

Chromatographic examination: A solution of the crude dye (4.0 g.) in benzene-hexane (1:1, 25 ml.) was chromatographed on a column (2.2 x 70 cm.) of alumina (150.0 g. Gr.II). The column was prepared and developed with benzene-hexane (1:1) mixture. Four bands appeared: a deep orange band at the top, a very narrow red band, an orange brown band and a brownish band. On eluting the chromatogram with benzene-hexane (1:1) mixture the lower most band gave a brown crystalline substance (0.0668 g.) from the percolate. It was crystallized from alcohol (m.p. 177°) and analysed for disazo compounds (Found, C, 72.2; H, 5.3; N, 17.8; $C_{19}H_{16}ON_4$ requires C, 72.13; H, 5.1); N, 17.71%).

Further elution of the column with benzene the orange band was eluted next and the eluent yielded a brown crystalline dye (0.273 g.). It was crystallized from alcohol (m.p.149° reported 148° [30]) and analysed for disazo dye. (Found, C, 72.6; H, 5.1; N, 17.2; $C_{19}H_{16}ON_4$ requires C, 72.13; H, 5.1; N, 17.71%).

By extruding the column and separating the red layer of alumina from the red band and extracting the alumina with boiling alcohol the dye obtained (0.018 g.) was crystallized from alcohol (m.p.180°) in brown needles and analysed for disazo dye.(Found N, 17.4; $C_{19}H_{16}ON_4$ requires N, 17.71%).

The deep orange layer of alumina from the top band on extraction with boiling alcohol gave a dye (3.0 g.) which was crystallized from benzene-hexane (1:10) to give the known monoazo dye (m.p.107°C. reported 107°C [31]). Found: C, 73.6; H, 5.4; N, 13.5; $C_{13}H_{12}ON_2$ requires C, 73.56; H, 5.7; N, 13.2%).

Aniline → m-Cresol: (Pyridine coupling pH 7)
Diazonium chloride solution from aniline (0.3 g.) was added to a solution of m-cresol (1.08 g.) in pyridine (30 ml.) diluted with water (20 ml.) slowly at 0° with stirring. The reaction mixture was stirred for an hour at 0° and then for four to five hours at room temperature. The oily dye obtained on acidification was taken up in ether. Removal of the solvent yielded 2.05 g. of the crude dye.

Chromatographic examination: Four bands as obtained in sodium hydroxide coupling (pH above 10.5) were also seen here and the dyes obtained from different bands in the order of elution were as follows:

Order of elution	Colour of bands	m.pt.	Yield
1	Brown	177°C	0.010 g.
2	Orange	148°C	0.039 g.
3	Red	180°C	less than 0.001 g.
4	Deep orange	107°C	1.66 g.

The four dyes obtained by coupling at pH 7 were identical with the dyes obtained by coupling at higher pH.

Aniline → m-Cresol: (Sodium carbonate coupling pH 8-9) Diazonium chloride solution from aniline (0.93 g.) was coupled with m-cresol (1.08 g.) in sodium carbonate solution (10%; 100 ml.). The crude dye after removal of the solvent weighed 2.070 g.

Chromatographic examination: 2.0 g. of the crude dye on chromatography gave four dyes as in the previous experiments.

Order of elution	Colour of bands	m.pt.	Yield
1	Brown	177°C	less than 0.001 g.
2	Orange	148°C	0.200 g.
3	Red	179-80°C	0.041 g.
4	Deep orange	107°C	1.409 g.

Aniline → m-Ethylphenol: A mixture of aniline (0.93 g. 0.01 mole) concentrated hydrochloric acid (4 ml.) and water (30 ml.) was diazotised by using sodium nitrite

(0.69 g. 0.01 mole) at -5° to 0° and the diazonium solution was coupled with m-ethylphenol (1.22 g. 0.01 mole) dissolved in aqueous sodium hydroxide (20%; 25 ml.) After stirring for one hour the solution was acidified with dilute hydrochloric acid (1:1). The oily dye after working up weighed (2.1 g.).

Chromatographic examination: A solution of the crude dye (2 g.) in benzene-hexane (1:1, 25 ml.) was chromatographed on a column (2.2 x70 cm.) of alumina (100 g. Gr.II), and developed with the same solvent. Three bands appeared: an orange yellow band at the top, a red band in the middle and a yellow band at the bottom. The bottom yellow band was completely eluted with benzene and the dye obtained (0.068 g.) was crystallized from alcohol (m.p. 138.5°) in dark brown needles, analysing for disazo dye. (Found C, 73.0; H, 5.6; N, 16.9; $C_{20}H_{18}ON_4$ requires C, 72.7; H, 5.49; N, 16.96).

The reddish layer of alumina was separated from the red band and the dye extracted with hot alcohol. Solvent was removed and the dye (0.005 g.) was crystallized from benzene-petroleum ether (40-60°). (m.p.137°C.).

Extrusion and extraction with hot alcohol of the orange yellow top band gave a dye (1.60 g.) which was crystallized from hexane (m.p. 93°C.) and analysed for

monoazo. (Found: C, 74.3; H, 6.5; N, 12.8; $C_{14}H_{14}ON_2$ requires C, 74.31; H, 6.24; N, 12.38%.)

Aniline → m-n-Propylphenol: A mixture of aniline (0.93 g. 0.01 mole) concentrated hydrochloric acid (4 ml.) and water (30 ml.) was diazotised using sodium nitrite (0.69 g. 0.01 mole) at -5° to 0°C. The diazonium solution was coupled with m-n-propylphenol (1.36 g. 0.01 mole) dissolved in dilute alcohol (30 ml. 50%) containing aqueous sodium hydroxide (20%; 25 ml.) at 0°C. The reaction mixture was stirred for two hours, acidified with hydrochloric acid (1:1) and the dye was taken up in benzene. Working up as usual gave 2.3 g. of the crude dye.

Chromatographic examinations: A solution of the crude dye (2.0 g.) in benzene-hexane (1:1, 25 ml.) was chromatographed on a column (2.2 x 70 cm.) of alumina (100.0 g. Gr.II) prepared in benzene-hexane (1:1). Three bands appeared: an orange yellow band at the top, a red band in the middle and a yellow band at the bottom. The bottom yellow band was eluted completely with benzene and the upper bands were extruded and extracted. The dye obtained from lower band (0.02 g.) was crystallized from alcohol (m.p. 87-88°) as dark brown needles and analysed for disazo. (Found: C, 73.5; H, 5.6; N, 16.3; $C_{21}H_{20}ON_4$ requires C, 73.23; H, 5.86; N, 16.27%.)

Pure dye from the red band could not be isolated in quantities sufficient for further examination.

Extrusion and extraction with hot alcohol of the top orange yellow band gave a dye (1.85 g.) which was crystallized from hexane (m.p. 107-8°C.) and analysed for monoazo dye. (Found: C, 75.0; H, 6.5; N, 11.6; $C_{15}H_{16}ON_2$ requires C, 74.97; H, 6.71; N, 11.66%).

Aniline → m-n-Butylphenol: Aniline (0.93 g. 0.01 mole) was diazotised with concentrated hydrochloric acid (4 ml.), water (30 ml.) and sodium nitrite (0.69 g. 0.01 mole) at -5° to 0°. The diazonium chloride solution was coupled with a solution of m-n-butylphenol (1.5 g. 0.01 mole) in aqueous alcohol (30 ml. 50%) containing aqueous sodium hydroxide (20%, 25 ml.) at 0°C. The oily dye obtained on acidification was taken up in benzene which on working up gave a semi-solid crude dye (2.5 g.).

Chromatographic examination: Crude dye (2.5 g.) when chromatographed on a column (2.2 x 70 cm.) of alumina (100 g. Gr.II) gave three bands, an orange yellow band at the top, a red band in the middle and a yellow band at the bottom. The lower band was completely eluted with benzene and the upper bands were extruded and extracted with hot alcohol. The dye obtained from the lower bands (0.02 g.) was crystallized from alcohol (m.p. 107-8°C.) as dark brown needles, analysing for disazo. (Found: C, 75.6; H, 6.2;

N, 15.72; $C_{22}H_{22}ON_4$ requires C, 73.72; H, 6.19; N, 15.63%).

Pure dye from the red band could not be isolated in sufficient quantity for further examination.

Extraction of the top orange yellow band gave a dye (2.0 g.) which was crystallized from hexane (m.p. 88°C) and analysed for monoazo (Found: C, 75.9; H, 7.2; N, 11.3; $C_{16}H_{18}ON_2$ requires C, 75.56; H, 7.13; N, 11.02%).

Aniline → m-Pentadecylphenol (T.H.A.): Diazonium chloride solution prepared from aniline (0.93 g. 0.01 mole) by using concentrated hydrochloric acid (4 ml. in 30 ml. water) and sodium nitrite (0.69 g. 0.01 mole) at 0° to -5°C was coupled with a solution of m-pentadecylphenol (3.04 g. 0.01 mole) in aqueous alcohol (80 ml. 50%) containing aqueous sodium hydroxide (20% 25 ml.). The oily dye thus obtained was taken up in benzene and on working up 4.0 g. of the crude dye was obtained.

Chromatographic examination: This crude dye (4.0 g.) when chromatographed on a column (2.2 x 70 cm.) of alumina (150 g. Gr.II) gave four bands, an orange band at the top, a very pale narrow red band, an orange band and lower most pale yellow very narrow diffused band. This last band on elution with benzene-hexane (1:1) mixture gave no crystalline dye. The next orange band on elution with benzene gave a brown dye (0.10 g.) which was crystallized from alcohol (m.p. 74°C.) as brown needles and analysed for disazo. (Found: C, 77.25;

H, 8.6; N, 10.6; $C_{33}H_{44}ON_4$ requires C, 77.30; H, 8.65; N, 10.93%). No pure dye from the red band could be isolated. Extrusion with hot alcohol of the top band (orange brown) gave a dye (3.2 g.) which was crystallized from acetic acid-water (m.p.66°) and analysed for monoazo. (Found: C, 79.1; H, 9.6; N, 6.47; $C_{27}H_{40}ON_2$ requires C, 79.36; H, 9.87; N, 6.86%).

Aniline → m-Isopropylphenol: Diazonium chloride solution of aniline (0.93 g., 0.01 mole) obtained by diazotising in hydrochloric acid (4 ml. in 30 ml. water) with sodium nitrite (0.69 g. 0.01 mole) at 0°-5°C. was coupled with a solution of m-isopropyl phenol (1.36 g. 0.01 mole) in dilute alcohol (80 ml. 50%) containing aqueous sodium hydroxide (20% 25 ml.) at 0°. The oily dye on working up gave a crude dye (2.4 g.).

Chromatographic examination: Crude dye (2.4 g.) when chromatographed on a column (2.2 x 70 cm.) of alumina (100 g. Gr.II) gave three distinct bands: an orange yellow band at the top, a red (very narrow) band in the middle and a yellow band at the bottom. The lower band was eluted completely with benzene and the upper bands were extruded and extracted with hot alcohol. The dye obtained from the lower band (0.03 g.) was crystallized from alcohol (m.p. 109-110°C.) as dark brown needles and analysed for disazo. (Found: N, 16.21; $C_{21}H_{20}ON_4$ requires N, 16.27%). Pure dye from red band could not be isolated. Top orange band gave a dye (2 g.) which was crystallized from hexane

(m.p.95°C.) and analysed for monoazo. (Found: C, 75.0; H, 6.9; N, 11.78; $C_{15}H_{16}ON_2$ requires C, 74.97; H, 6.71; N, 11.65%).

Aniline→m-Tertiary butylphenol (Sodiumhydroxide coupling pH 7 10.5). Aniline (1.86 g. 0.02 mole) was diazotised by using hydrochloric acid (9 ml in 60 ml. water) and sodium nitrite (1.38 g. 0.02 mole) at 0° to -5°C. The diazonium solution was coupled with a solution of m-tertiary butylphenol (3 g. 0.02 mole) in aqueous sodium hydroxide (20%, 60 ml.) at 0°C. in the usual way. The sticky dye obtained on acidification was taken up in benzene and on working up gave 4.5 g. of the crude solid dye.

Chromatographic examination: Crude dye (4.5 g.) when chromatographed on a column (2.2 x 70 cm.) of alumina (150 g. Gr.II) in the usual way gave three bands an orange band at the top, a middle red band and a yellow band at the bottom. The bottom yellow band was eluted with benzene-hexane (1:1) and a dye (0.006 g.) was recovered from the percolate. It crystallized from petroleum ether (40-60°) (m.p.60°) as orange yellow rectangular crystals. (Found: N, 10.4; $C_{16}H_{18}ON_2$ requires N, 11.02). The middle red band was completely eluted with benzene and a dye (0.20 g.) was obtained from the eluent. It crystallized from alcohol (m.p.137°) as brown needles and analysed for disazo. (Found: C, 73.8; H, 6.1; N, 15.2; $C_{22}H_{22}ON_4$ requires C, 73.72; H, 6.19; N, 15.63%). The top orange band was eluted with chloroform

and finally with ethyl acetate. The dye obtained (3.9 g.) from the percolate was crystallized from hexane (m.p.108-9°C.) and analysed for monoazo. (Found: C, 75.5; H, 7.1; N, 11.4; $C_{16}H_{18}ON_2$ requires C, 75.56; H, 7.13; N, 11.02%).

Aniline → m-tertiary-butylphenol: (Pyridine coupling pH 7) Diazonium chloride solution from aniline (0.93 g.) was coupled with m-tertiary butylphenol (1.5 g.) in pyridine solution (60 ml. 50%). On working up 2.4 g. of crude dye was obtained.

Chromatographic examination: Same three bands as obtained in sodium hydroxide coupling (pH above 10.5) were also seen here and the dyes obtained from the different bands in the order of elution are:

Order of elution	Colour of band	m.pt.	Yield
1	Yellow	60°C	0.004 g.
2	Red	137°C	0.020 g.
3	Orange	108°C	2.181 g.

These dyes were identical with the dyes obtained at higher pH coupling.

Aniline → m-tertiary-butylphenol (Sodium carbonate coupling pH 8-9). Diazonium chloride solution from aniline (0.93 g.) was coupled with m-tertiary butylphenol (1.5 g.) in sodium carbonate solution (10%, 100 ml.). The crude dye after removing the solvent weighed 2.45 g.

Chromatographic examination: Same three dyes were obtained as above with following yields:

Order of elution	Colour of band	m.pt.	Yield
1	Yellow	60°C	0.286 g.
2	Red	137°C	0.600 g.
3	Orange	108°C.	1.244 g.

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PART II

A NEW DYES FROM [illegible]

PART II

B. NEW DYES FROM C.N.S.L.

INTRODUCTION.

The processes for the preparation of azo dyes from cashewnut shell liquid[1] and from its saturated monophenolic component, 3-pentadecylphenol[2,3] have been patented. Pansare[4] has prepared some dyes by coupling different amines with tetrahydroanacardol and one amine with tetrahydrocardol. Since the alkyl groups increase the oil solubility of azo dyes[5] and further the dyes having nuclear alkyl substituent are applicable by metachrome process and have good fastness to potting,[6] it was thought that azo dyes, with long alkyl chain in the molcule, would be of greater use in leather industry.

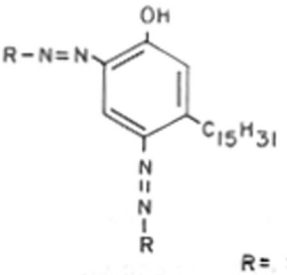
Pansare's method of fractional crystallization gave him mostly the monoazo dyes and in a few cases disazo dyes along with them. During the present studies (Part II A) it was observed that disazo dye is formed exclusively in all cases when different phenols were coupled with diazotised aniline. Thus preparation of pure azo dyes were undertaken in view of the fact that single dyes are preferred to mixtures in order to obtain good level dyeing.[7] Different aromatic amines were diazotised and coupled with tetrahydroanacardol which was obtained by hydrogenation of anacardol, the major component of cashewnut shell liquid. The coupled products were chromatographed on a column of alumina and the dyes separated. Disazo dyes were eluted first and the monoazo dyes last, as expected. A central red

band appeared in all cases but no dye could be isolated in any case. The crystalline dyes were characterised as monoazo or disazo on the basis of elemental analysis and their ultraviolet and visible spectra are recorded in Table I. Spectra were obtained using Perkin Elmer 350 spectrophotometer in 95% ethanol solution.

Table I

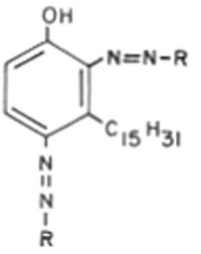
Coupling of	Dye characterised as	λmax in U.V. and visible in mμ		ε value
Anisidine → T.H.A.	Monoazo	368 246		20078 9968
	Disazo	378 242		35084 17184
Anisidine → T.H.A.	Monoazo	360 246		28083 12621
	Disazo	370 284 252		44795 13952 18358
Nitroaniline → T.H.A.	Monoazo	369 233 256	Shoulders	17718 10985 9936
	Disazo	356 230	Shoulders	40682 23354
Nitroaniline → T.H.A.	Monoazo	388 264		19697 7460
	Disazo	465 366 266		12197 40180 10782
Chloroaniline → T.H.A.	Monoazo	356 240		20527 11186
	Disazo	356 240		44856 14865

The disazo dyes may have the structure I or II though I is more likely on steric considerations.



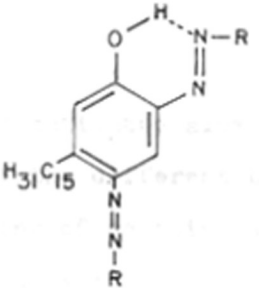
R= Substituted aromatic nucleus

I



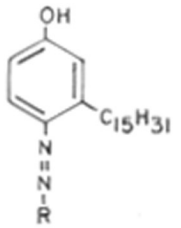
II

In the infrared spectra of disazo dyes, free -OH vibration (around 3400) cm^{-1}) is absent, which may be due to the presence of hydrogen bonding between azo and the hydroxyl group as shown in III.



III

Structure of the monoazo dyes was finalised as IV on the basis of infrared spectra which shows free -OH vibration (around 3400 cm^{-1}). This is also in conformity with its chromatographic behaviour.



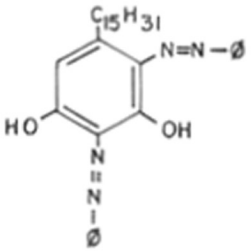
IV

There was no indication of the presence of any ortho-monoazo dye under these conditions.

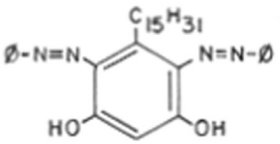
No attempt was made to improve the yields of various dyes by varying the conditions of the coupling.

Tetrahydrocardol obtained by hydrogenation of cardol (another phenolic component of CNSL) was coupled with diazotised aniline using sodium hydroxide (pH 10) and sodium acetate (pH 7 to 8) as buffers. Coupled products were chromatographed on activated alumina. There was no clear cut separation of the different bands on the column, due to indefinite tailing of certain bands and also due to the probable existence of various possible isomers of the same dye. However one disazo and two monoazo dyes were isolated which were checked and found to give homogenous bands on the chromatographic column.

The disazo dye may have the structure V. or V.A.



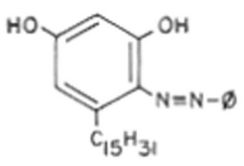
V.
2:4 Disazo



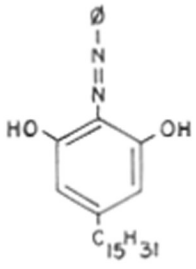
V.A.
4:6 Disazo

In the visible and ultraviolet spectra of the disazo dye obtained, the following peaks were observed, λ430 mμ ($\epsilon\sim$42068), and λ251 mμ ($\epsilon\sim$11938). This is analogous to 2:4-disazo resorcinol[8] which shows the absorptions at λ415 mμ ($\epsilon\sim$60,000) and λ253 mμ ($\epsilon\sim$40000) rather than 4:6 isomer which shows three absorption bands at λ445 mμ ($\epsilon\sim$33500), λ375 mμ ($\epsilon\sim$40,000) and λ260 mμ ($\epsilon\sim$17,740). Hence based on this analogy the structure assigned to the disazo dye was V.

Monoazo dyes may have the structure VI and VII.



VI



VII

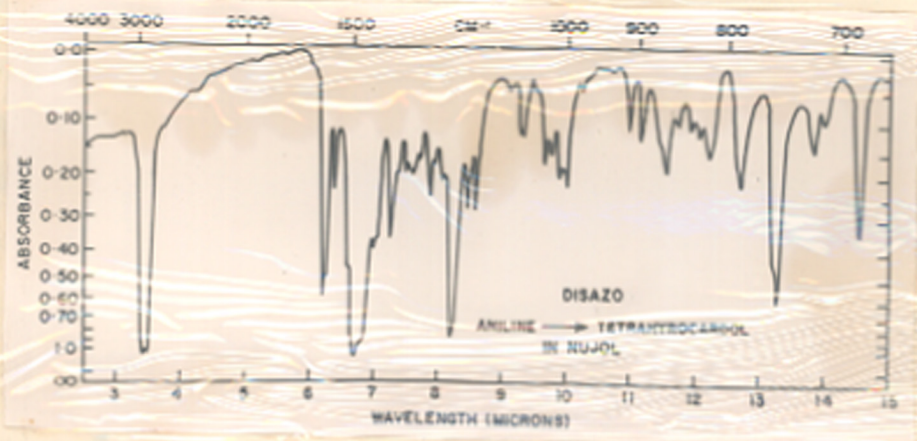
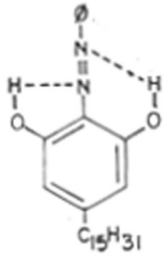
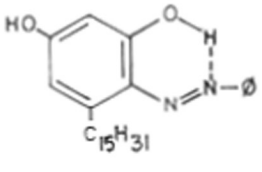


Fig.1. 2:4-Phenylazo 5-pentadecyl resorcinol

The monoazo dye obtained using sodium hydroxide as coupling medium has m.p.101° and is only slightly soluble in alcohol whereas the dye obtained using sodium acetate as buffer has m.p.86°C. and is quite soluble in alcohol.
On chromatography of the two isomers the higher melting dye comes out first from the column and the lower melting one much later. The higher melting isomer may thus be assumed to have the structure VII in which both the -OH groups may be supposed to go under chelation with -N=N-group (VIII), and hence no effective polar group is left for adsorption on alumina. The lower melting isomer should then have the structure VI, because only one -OH group is involved in chelation (IX) leaving the other -OH group free for effective adsorption on alumina, and is therefore eluted later.



VIII



IX

Infrared spectra of the two dyes were determined in Nujol and in chloroform solutions. In the case of the higher melting isomer there was no free -OH absorption seen in the region of 3300 to 3600 cm^{-1} whereas in the lower melting isomer free hydroxyl absorption (around 3300 cm^{-1}

in Nujol mull and around 3600 cm^{-1} in chloroform solution) was clear. Hence the lower melting isomer is confirmed to have the structure VI and the higher melting isomer, structure VII. (Infrared spectra are shown in Fig. 1, 2, 3).

Ultraviolet and visible spectra of these dyes were determined in alcoholic solution and they showed the following absorptions bands:

Lower melting m.p. 86°	λ 384 mμ	ε ~ 22863
	λ 252 mμ shoulder	ε ~ 7757
Higher melting m.p. 101°	λ 400 mμ	ε ~ 20968
	λ 252 mμ shoulder	ε ~ 6747

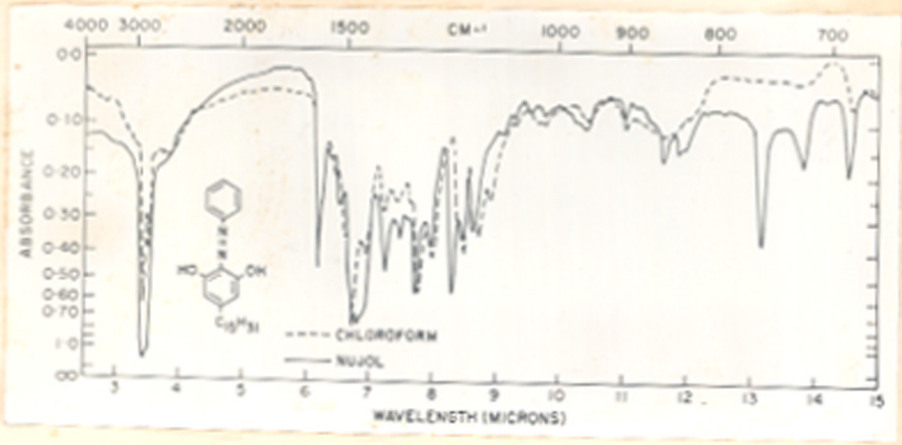


Fig. 2

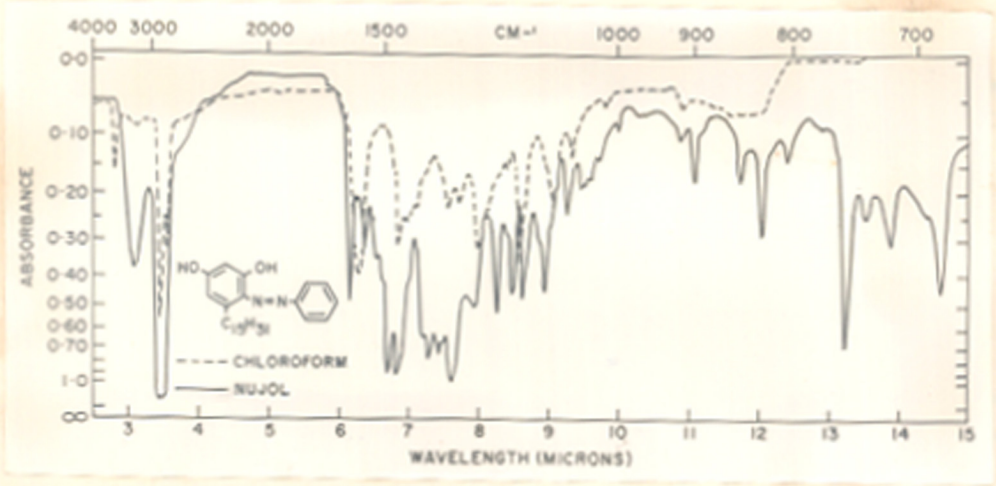


Fig. 3.

Infrared Absorption Spectra Of Monoazo Dyes from Aniline → Tetrahydrocardol

EXPERIMENTAL

o-Anisidine → T.H.A.

Ortho-anisidine (3.69 g. 0.03 mole) dissolved in dilute hydrochloric acid (16 ml. in 100 ml. water) was diazotised by using sodium nitrite (2.07 g. 0.03 mole) at -5 to 0°C. The diazonium chloride solution was coupled with a solution of m-pentadecylphenol (T.H.A.) (8.04 g. 0.01 mole) in dilute alcohol (100 ml. 50%) containing aqueous sodium hydroxide (15.0 g. in 40 ml.). Stirring was continued for one hour in the cold and then for three hours at room temperature to complete the coupling. The solution was then acidified with dilute hydrochloric acid (10%) and the precipitated dye was taken up in benzene. After drying over anhydrous sodium sulphate the dye solution was concentrated (4.01 g.) and chromatographed.

Chromatography: The crude dye was chromatographed on a column (2.2 x 70 cm.) of alumina (120 g. of Gr.II). The dye solution was added on the top and developed with benzene. The column was eluted with benzene, benzene-chloroform (with varying proportions of chloroform), chloroform and finally with alcohol. Four bands appeared on the column which were successively eluted.

1st band: Pale brown, very narrow, diffused band from which no dye could be isolated.

2nd band: Brown coloured band, eluted completely with benzene. Dye obtained was crystallized from alcohol and analysed for disazo (m.p.105-6°C. Yield 0.16) g. Found: C, 73.2; H, 8.4; N, 9.3; $C_{35}H_{48}N_4O_3$ requires C, 73.39; H, 8.45; N, 9.78%).

3rd band: Very narrow red band. No dye could be isolated from this band.

4th band: Orange brown band. Eluted with chloroform. The dye obtained was crystallized from alcohol-water and then from benzene-hexane. It corresponded to the reported monoazo dye (m.p.100° reported[4] 100-101°C. Found: N, 6.2. $C_{28}H_{42}N_2O_2$ requires N, 6.39%).

p-Anisidine → T.H.A.: The diazonium chloride solution from p-anisidine (0.69 g. 0.03 mole) was coupled with alkaline alcoholic solution of T.H.A. (3.04 g. 0.01 mole) as above. On working up, 4.2 g. of the crude dye was obtained which was chromatographed on alumina.

Chromatographic behaviour of the dye was the same as noticed in the case of o-anisidine. Two dyes could be separated and identified as follows:

1. The dye which eluted first was crystallized from benzene-pet.ether (40-60°) and was analysed for disazo (m.p.75-76°C. Yield 0.150 g.). Found: C, 73.5; H, 8.2; N, 9.6; $C_{35}H_{48}N_4O_3$ requires C, 73.39; H, 8.45; N, 9.78%).

2. The dye which eluted last was crystallized from acetic acid-water and corresponded to the known monoazo dye (m.p.59-60°, reported[4], 59-60°; Yield 2.1 g. Found: N, 6.6; $C_{28}H_{42}N_2O_2$ requires: N, 6.39%).

<u>o-Nitroaniline → T.H.A.</u> The diazonium chloride solution from ortho-nitroaniline (4.14 g. 0.03 mole) was coupled with T.H.A. in alcoholic solution containing aqueous sodium hydroxide. The dye after working up (4.0 g.) was chromatographed on the column of alumina. Dye which eluted first was crystallized from alcohol and was analysed for disazo (m.p.100°C. Yield 0.61 g.). Found: C, 65.75; H, 6.97; N, 14.4; $C_{33}H_{42}O_5N_6$ requires C, 65.76; H, 7.02; N, 13.95%).

The last eluted dye was crystallized from alcohol and characterised as monoazo dye (m.p.& 97°, reported[4], 96-97°C; Yield 1.96 g. Found: N, 9.4; $C_{27}H_{39}N_3O_3$ requires N, 9.26%).

<u>p-Nitroaniline → T.H.A.</u> Para-nitroaniline (4.14 g. 0.03 mole) was diazotised by using hydrochloric acid (16 ml. in 100 ml. water) and sodium nitrite (2.07 g. 0.03 mole) at 0 to -5°C. and the diazonium chloride solution was coupled with alcoholic solution of T.H.A. (3.04 g.) containing aqueous sodium hydroxide. The crude dye (3.97 g.) obtained on working up, was chromatographed on the column of alumina. Dye which eluted first was crystallized

from alcohol in black crystals (violet alcoholic solution) and analysed for disazo (m.p.112°C. Yield 1.3 g.) Found: C, 65.5; H, 6.7; N, 13.55; $C_{33}H_{42}N_6O_5$ requires C, 65.76; H, 7.02; N, 13.95%).

The dye which eluted last was crystallized from acetic acid water into orange coloured crystals and characterised as monoazo dye (m.p.81°C. reported[4] 80-81°C. Yield 1.5 g. Found: N, 9.3; $C_{29}H_{39}N_3O_3$ requires N, 9.26%).

<u>p-Toluidine → T.H.A.</u>: Diazonium chloride solution from p-toluidine (1.07 g. 0.01 mole) was coupled with T.H.A. (3.04 g. 0.01 mole) in alcoholic sodium hydroxide solution as above. The crude dye (4.1 g.) on chromatography gave i) disazo dye which eluted first (m.p.84-85° reported[4] 85-86°C. Yield 0.56 g. Found N, 9.9; $C_{35}H_{48}N_4O$ requires N, 10.36%).

ii) Monoazo dye, which eluted last (m.p.45-46°C. yield 1.5 g. Found: C, 80.0; H, 9.7; N, 6.8; $C_{28}H_{42}N_2O_2$ requires C, 79.57; H, 10.02; N, 6.63%).

<u>Aniline → Tetrahydrocardol</u>: (Sodium hydroxide coupling pH 7 10). Aniline (0.93 g. 0.01 mole) was diazotised by using hydrochloric acid (4 ml. in 20 ml. water) and sodium nitrite (0.69 g.) at 0 to -5°. The diazonium chloride solution was coupled (at 0°C.) with 5-pentadecyl resorcinol (tetrahydrocardol) (3.2 g. 0.01 mole) dissolved in dilute alcohol (100 ml. 50%) containing aqueous sodium hydroxide (6.0 g. in 10 ml. water). After four hours of stirring at

room temperature the reaction mixture was acidified with dilute hydrochloric acid (1%) and the precipitated dye filtered, washed and dried by suction (4.2 g.). The dye was dissolved in 100 ml. of chloroform and chromatographed on the column of alumina (150 g. Gr.I). Many bands appeared on the column as red, yellow, reddish orange, black (very narrow) brown etc. The percolate which eluted first was concentrated and rechromatographed. The dye collected from homogenous band was crystallised from benzene hexane to give 2:4-disazo dye (2:4 dis(phenyl) azo-5-pentadecyl resorcinol). (Yield 0.56 g. m.p.127-8°; Found: C, 74.8; H, 8.4; N, 10.5; $C_{33}H_{44}N_4O_2$ requires: C, 74.96; H, 8.39; N, 10.6%). Reddish orange band was further eluted with chloroform and afte rechromatography, and crystallization from alcohol and ether, yielded 0.8 g. of the dye characterised as 2-phenylazo-5-pentadecyl resorcinol (m.p.101-2°C. Found: C, 76.4; H, 9.5; N, 6.48; $C_{27}H_{40}N_2O_2$ requires C, 76.37; H, 9.5; N, 6.6%). Dyes other than these could not be definitely characterised.

Aniline → tetrahydrocardol: (Sodium acetate coupling pH 7-8). The diazonium chloride solution from aniline (0.93 g. 0.01 mole) was coupled with solution of 5-pentadecyl resorcinol (3.2 g. 0.01 mole) in alcohol (25 ml.) containing aqueous sodium acetate (10.0 g. in 25 ml.). After six hours of stirring the solution was acidified with dilute hydrochloric acid (10%) and the precipitated dye filtered, washed and dried by suction (4.1 g.). On chromatography over alumina, in the beginning, three bands appeared

i) red, ii) reddish orange, iii) brown, in the ascending order. The first band was eluted completely with chloroform and on rechromatography and crystallization gave 2:4-diphenylazo-5-pentadecyl resorcinol, m.p.128°.

There was no depression of the mixed melting point with the dye obtained under higher pH coupling. The dye from the reddish orange band was obtained by extrusion and extraction with alcohol. Crystallization from acetic acid yielded 1.2 g. of the dye which was characterised as 4-phenyl azo-5-pentadecyl resorcinol (m.p.86°. Found: C, 76.3; H, 9.48; N, 6.6; $C_{27}H_{40}N_2O_2$ requires C, 76.37; H, 9.5; N, 6.6%). Dyes from other bands could not be characterised definitely.

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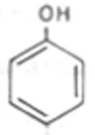
PART III
POTENTIAL DRUGS

INTRODUCTION

Various phenolic compounds have had a wide vogue as medical and sanitary germicides, since the time Lister[1] used phenol in the early days of antiseptic surgery. Phenol itself is rarely used these days as a medical germicide because of its irritating action on the skin when used in effective concentrations and other harmful side effects, like causing gangrene on prolonged application. Cresols, o-, m- and p-methylphenols, on the other hand are germicidally more active and less caustic. It is generally known that substitutions of halogens or of hydrocarbon side chains on the benzene rings of phenols increase the anti-bacterial or fungicidal activity.[1] This is true in both alkyl phenols and alkyl resorcinols as is borne out by the following figures of phenol coefficients, of certain selected alkyl phenols and alkyl resorcinols, obtained by testing the compounds against Eberthella typhi in the absence of organic matter.[2]



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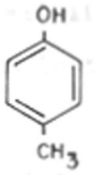

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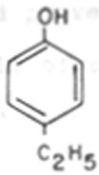

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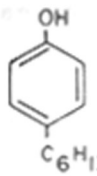

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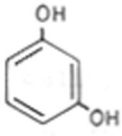

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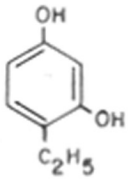

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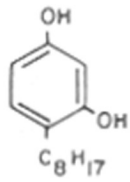


400

Resorcinol and alkyl resorcinols in general are relatively less active than the corresponding phenol but they are also less toxic and hence are widely in use today. Thus hexylresorcinol[3], 1,3-dihydroxy-4-n-hexyl benzene, $C_6H_{13}C_6H_3(OH)_2$, is a commercially available patent drug (Caprokol) used internally as a urinary antiseptic[4] and to a greater extent in dentifrices, since the low surface tension of its solution gives it a considerable penetrating power. But its most important use today is as an anthelmintic.[5]

The introduction of an alkyl chain in the phenol or resorcinol ring though beneficial from the point of —— increased activity, has however certain disadvantages. Thus as the length of the alkyl chain increases the activity increases but the solubility in water decreases, thus limiting its applications. However, in the special cases where water solubility is not a criterian these are highly valuable. Tetrahydroanacardol (m-pentadecylphenol) and tetrahydrocardol (5-pentadecyl resorcinol), both derived from cashewnut shell liquid should prove of great use as starting materials in the synthesis of certain special chemicals, analogues of which, are known to be useful in the pharmaceutical field. These should prove more beneficial and less toxic than their analogues currently being used as drugs.

Salicylic acid, phenolic carboxylic acid is similarly employed in drug industry in an ever increasing manner.

Sodium salicylate and other derivatives of salicylic acid such as acetyl salicylic acid (aspirin) are some of the simplest known drugs and are extensively used in the pharmaceutical field as antipyretic,[6] analgesic[7,8], antirheumatic[9] etc. Free salicylic acid as such or in ointment form is also widely used for treating ringworm and athlete's foot, curing partly by its fungistatic[10] action and partly due to the peeling off of the affected skin. Para-aminosalicylic acid has been used in the treatment of human tuberculosis since Lehmann's[11] observation that it possesses bacteriostatic activity against tubercle bacilli. Though reports on the use of alkyl phenols and alkyl resorcinols in medicinal chemistry are available, similar reports on the use of alkyl salicylic acid and its derivatives are lacking. Tetrahydroanacardic acid is an alkyl salicylic acid with a long alkyl chain ($C_{15}H_{31}$), present in the cashewnut shell liquid. It is reasonable to hope that tetrahydroanacardic acid derivatives should have activity similar to that of salicylic acid derivatives and should prove less toxic and more fat soluble because of the presence of long alkyl chain.

To explore the potentiality of certain compounds (mainly derived from cashewnut shell liquid) in the field of drugs and medicinal chemistry, a few selected analogues of wellknown chemicals currently being used as drugs have been synthesised using (A) Tetrahydroanacardic acid, (T.H.A.A.), (B) tetrahydroanacardol (T.H.A.) and (C) tetrahydrocardol as starting materials.

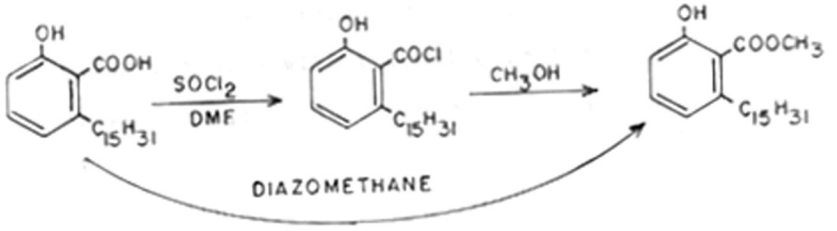
PRESENT WORK

A. Compounds derived from T.H.A.A.

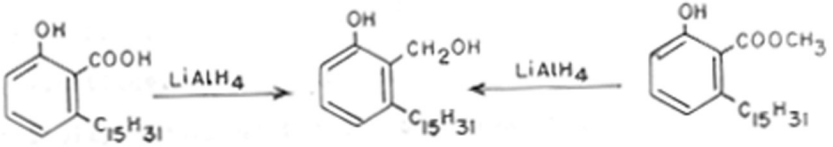
1) Saligenin analogue (I) Salicyl alcohol, sold under the trade name 'Saligenin' has been used medicinally as an antipyretic and tonic.[12] It is practically non-toxic and possesses marked local anaesthetic powers[13] and has been used with good results. It is prepared by reducing salicyl aldehyde with sodium amalgam[14] or by catalytic hydrogenation.[15]

The CNSL derived, Saligenin analogue (I), 2-pentadecyl-6-hydroxy-benzyl alcohol, has been prepared by a two step process. i) Preparation of the methyl ester of tetrahydroanacardic acid, ii) reduction of the ester with lithium aluminium hydride.

The preparation of the methyl ester of tetrahydroanacardic acid through the silver salt has been reported.[16] However, in the present study, the ester of the tetrahydroanacardic acid has been prepared by two simple and straight-forward methods a) preparing tetrahydroanacardic acid chloride by reacting with thionyl chloride in the presence of catalytic amounts of dimethyl formamide and reacting the acid chloride with anhydrous methanol, b) by reacting tetrahydroanacardic acid with diazomethane.



The methyl ester of tetrahydroanacardic acid thus obtained was reduced in almost quantitative yields with $LiAlH_4$, to give the corresponding alcohol, saligenin analogue (I). This could also be obtained in somewhat lower yields, by the direct reduction of tetrahydroanacardic acid with $LiAlH_4$.

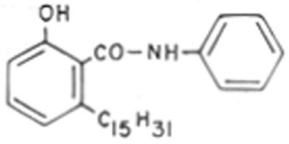


2. Salicylanilide analogue II and its bromo derivative (III)

Salicylanilide, long used as a fungicide in textiles, is an antifungal agent useful in the treatment of tineacapitis.[17] The use of salicylanilide is restricted to the treatment of ringworms of the scalp, as solutions having concentrations of above 5% are irritating to the skin.

Salicylanilide is usually prepared by heating salicylic acid and aniline in the presence of PCl_3.

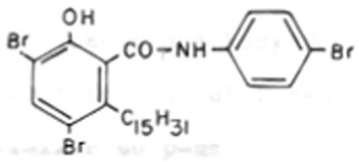
The anilide of tetrahydroanacardic acid has been prepared by two methods: (a) preparing first, the acid chloride by reacting the acid with thionyl chloride in the presence of dimethyl formamide, followed by its reaction with aniline; (b) first preparing phosphazoanilide[18] and then refluxing it with the acid to obtain the analogue II.



II

Halogenated salicylanilides are reported to have enhanced fungistatic activity[19] than the parent compound, salicylanilide. Hence with a view of getting the potentially highly active bromo derivative, the anilide of tetrahydroanacardic acid was subjected to the action of bromine. The product of bromination was however found to be a mixture of bromo compounds having varying bromine contents. In order to obtain a single product of a fixed bromine content, the anilide of T.H.A.A. was treated with excess of bromine. The crystalline compound thus obtained was found to be a tribromo derivative. On the basis of the availability of various reactive centres in salicylanilide as reported by Lemaire and Cahn[20], the tribromo derivative of tetrahydroanacardic acid anilide is expected to have

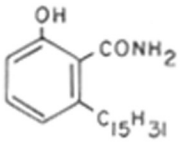
the structure III.



III

3) Salicylamide analogue IV: Salicylamide is currently widely used as it possesses outstanding analgesic properties.[21] It is reported to be less toxic than aspirin and in addition has no upsetting or untoward action on stomach. It is extensively used as an antipyretic, sedative, antispasmodic and anti-rheumatic.

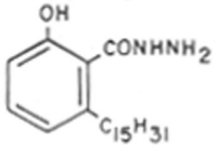
Though the amides are usually prepared by reacting the corresponding ester with liquor ammonia, heating of the methyl ester of tetrahydroanacardic acid with liquor ammonia resulted in the hydrolysis of the ester group and yielded back tetrahydroanacardic acid. The amide was therefore prepared by reacting the acid chloride of T.H.A.A. with liquid ammonia.



IV

4. Salicyloyl hydrazide analogue V: Salicyloyl hydrazide is reported[22] to be of great use in the identification of oxosteroids in the tissues and body fluids. It is also valuable as a reagent for the differentiation of aldehydes from ketones. Similar to p-amino salicylic acid it may be expected to possess antitubercular activity.

Tetrahydroanacardic acid hydrazide was prepared by the usual method of reacting the ester with hydrazine hydrate.

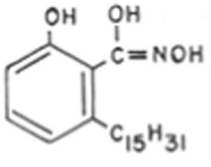


V

5. Salicylhydroxamic acid analogue VI: Salicylhydroxamic acid is reported to be effective in vitro and vivo, also confirmed by clinical tests, against tuberculosis bacillie.[23] Hydroxamic acids are normally prepared by the action of an aqueous alkaline solution of hydroxylamine on the sodium salt of the ester of salicylic acid.[23,24] The percentage of the alkali solution used in the preparation, however, seems to play a critical role, a 1% solution has been found to yield the desired product in high yields.

When attempts were made to prepare the salicyl hydroxamic acid analogue (VI) from T.H.A.A. methyl ester and hydroxylamine solution, in the presence of 10% alkali solution, the desired product was not obtained. When alkali

concentration was below 10% the unreacted material was recovered, while concentrations higher than 10% resulted in the hydrolysis of the ester to give T.H.A. Attempts to prepare the hydroxamic acid analogue in absolute ethanol, using sodium ethoxide as base, also resulted in failure. As T.H.A.A. is a hindered acid, it was felt that the use of more forcing conditions in the total absence of extraneous alkali, may lead to the formation of the desired product. Accordingly T.H.A.A. methyl ester was treated with a large excess of anhydrous hydroxylamine generated in anhydrous ether by the reaction of sodium metal with hydroxylamine hydrochloride. The reaction was carried out for prolonged times (72 hours) but the ester was recovered unchanged.



VI

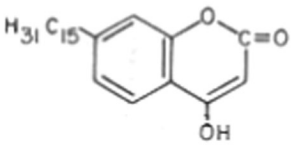
B. Compounds derived from T.H.A.

1. Warfarin analogue and its sodium derivative

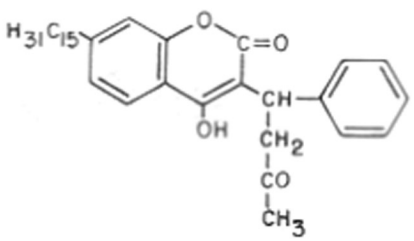
The use of warfarin (3-(α-acetonyl benzyl)-4-hydroxycoumarin) as a powerful rodenticide is dependent on the fact that it inhibits the formation of prothorombin by the liver in animals. The water soluble sodium derivative, sodium warfarin, is a potent anticoagulant used in prophylasis and treatment of thromboembolic disorders.[25]

It is normally prepared by the condensation of benzalacetone with 4-hydroxycoumarin.[26]

Hence before proceeding with the preparation of warfarin and sodium warfarin analogues, it was essential to first prepare the 4-hydroxycoumarin analogue VII (7-pentadecyl-4-hydroxycoumarin) from T.H.A. This (VII) was prepared by the condensation of malonic acid with tetrahydroanacardol using phosphorus oxychloride-zinc chloride as condensing agents.[27] Identity and purity of the 4-hydroxycoumarin analogue thus obtained was first confirmed by analysis and infrared spectra (Fig. 1) and then condensed with benzal acetone to obtain the warfarin analogue VIII, the infrared spectrum of which is shown in Fig. 2.



VII



VIII

The sodium warfarin analogue VIII.A. was obtained by careful neutralization, with dilute sodium hydroxide, of the phenolic hydroxy group present in the warfarin analogue. However, unlike the sodium warfarin, the sodium derivative of warfarin analogue (VIII A) was only sparingly soluble in water presumably because of the long alkyl chain in the

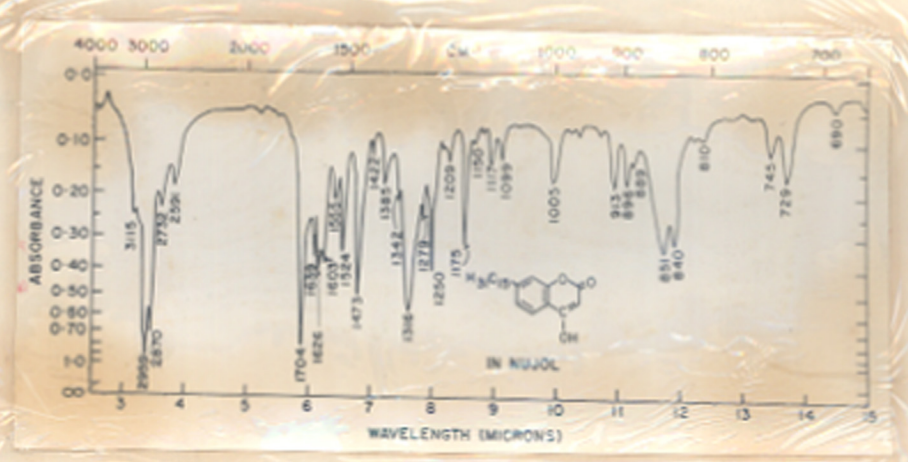


Fig. 1. 4-Hydroxy-7-pentadecyl coumarin

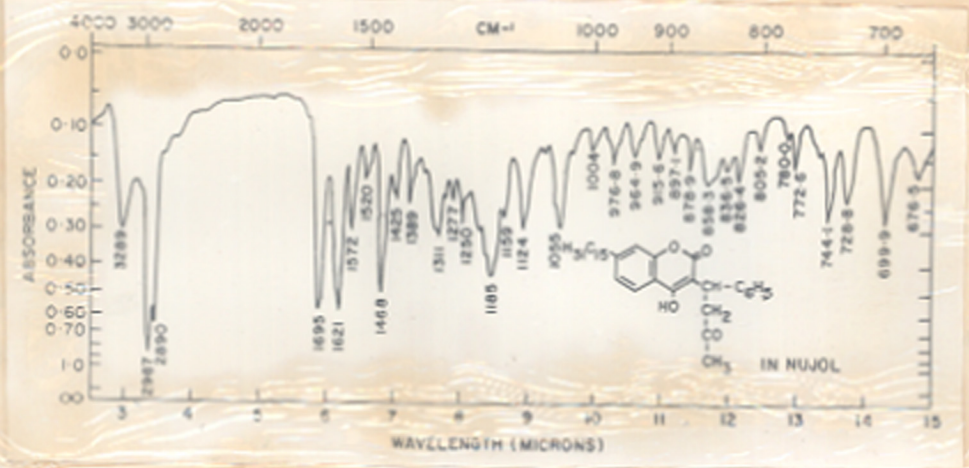
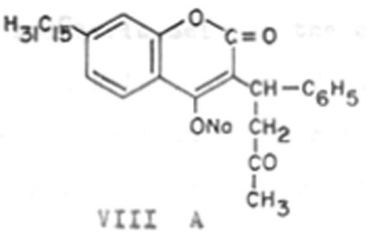


Fig. 2. (3-(α-Acetonylbenzyl)-4-hydroxy-7-pentadecyl coumarin

molecule. On warming with water a turbid solution with some frothing is observed. However perfectly clear solution of sodium warfarin analogue could be obtained by dissolving it in dilute aqueous alcohol.



VIII A

2. Phenolphthalein analogue IX

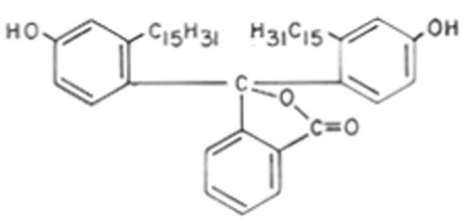
Phenolphthalein was introduced as a laxative as early as 1902 by Vamossy.[28] Its cathartic properties were discovered by chance, while investigating its application as a harmless denaturant of artificial wines. Being odourless, tasteless, and stable, it may be incorporated in any pleasant tasting vehicle and mineral oil emulsion. These properties have led to the extensive popularity of phenolphthalein as a drug, so that it has become probably the most frequently used organic laxative.[29]

Phenolphthalein is usually prepared by heating a mixture of phenol and phthalic anhydride in the presence of sulphuric acid. Many other condensing agents such as zinc chloride, aluminium chloride, stannous or stannic chloride, borontrifluoride or aromatic sulphonic acids are used in place of sulphuric acid. However in the commercial preparation of phenolphthalein, combinations of zinc chloride

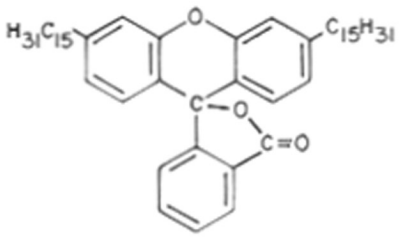
and sulphuric acid or p-toluene sulphonic acid[30,31] are employed.

When attempts were made to prepare the phenolphthalein analogue by reacting T.H.A. and phthalic anhydride with sulphuric acid as the condensing agent, it was noticed that sulphonation of T.H.A. took place in preference to the condensation reaction. When anhydrous zinc chloride was used as the condensing agent, the condensation proceeded smoothly (though in somewhat low yields) giving a product which was subsequently characterised as 3,6-dipentadecyl fluorane (X) based on analysis and infrared spectra. In the infrared spectrum of (X), hydroxyl absorption (in the region 3300 to 3600 cm^{-1}) was absent, the presence of lactone (1750 cm^{-1}) and ether linkage (1240 cm^{-1}) were clear (Fig. 3).

The formation of fluorane analogue looks analogus to the formation of 2,7-dimethylfluorane by the condensation of p-cresol with phthalic anhydride using zinc chloride or sulphuric acid as condensing agent.



IX



X

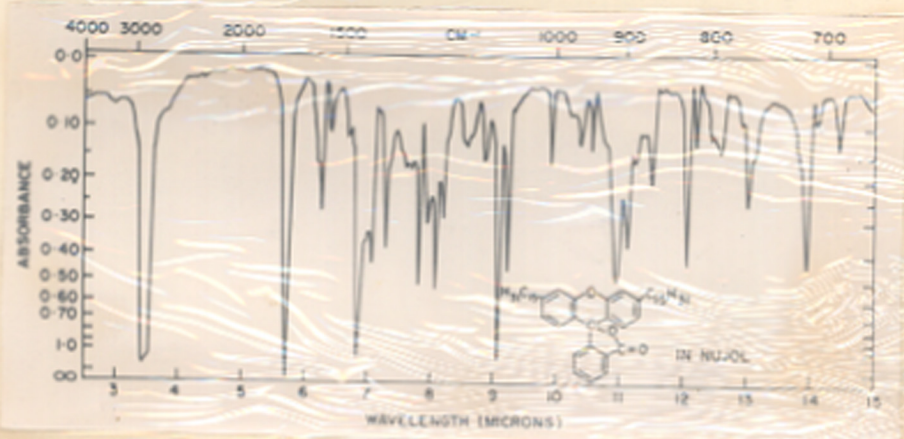
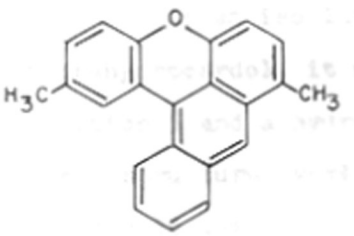
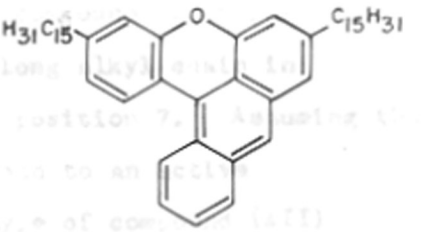


Fig. 3. 3,6-Pentadecyl fluorene

The fluorane analogue X cannot apparently be used as a drug since none of the fluorane derivatives are known to be used as drugs. However 2,7-dimethylfluorane is known to be a valuable intermediate in the preparation of fluoral 5G (XI A) used in the study of ocean bed currents. Since the fluorane analogue X obtained has two $C_{15}H_{31}$ alkyl chains, the resulting fluoral analogue (XI B) can be expected to be an even better water repellent, or water resistant chemical for the preparation of fluorescent sand. This type of compound is normally prepared by treating the dialkylfluorane with 24% oleum, and subsequent reduction with zinc and sodium hydroxide. However all attempts to prepare the fluorol analogue resulted in failure, the material being recovered unchanged under mild conditions or charred when forcing conditions were employed.



XI A



XI B

C. Compounds derived from Tetrahydrocardol

1. Isoflavone analogue XIII

The estrogenic activity of certain isoflavones and their derivatives have been reported by Bradbury and White.[32] They found that though 7:4' dimethoxy isoflav-3-en, itself was inactive, introduction of a methyl group in the 4-position rendered it the estrogenic activity. Introduction of methyl group in position 2 and ethyl group in position 4 seemed to make it more potent. (five times as potent as 4-methyl compound). Lawson[33] described 4-ethyl-7-4'-dimethoxy 2-methyl isoflav-3-en and 7:4' dimethoxy-4-phenyl isoflavan-4-ol and showed them to be oestrogenic. Recently Nilsson et.al.[34] have reported the preparation of estrogenically active isoflavone 5,7-dihydroxy-4'-methoxy isoflavone.

If an isoflavone type of compound is prepared from tetrahydrocardol, it will have a long alkyl chain in position 5 and a hydroxy group in position 7. Assuming that these structural variations may lead to an active estrogenic compound, isoflavone type of compound (XII) was prepared starting from tetrahydrocardol. This was effected by condensing tetrahydrocardol with phenylacetic acid to obtain the ketone (2-4-dihydroxy-6-pentadecylphenyl benzyl ketone XII,(Fig. 4) which on further reaction with ethylorthoformate in the presence of piperidine gave the desired isoflavone analogue (5-pentadecyl-7-hydroxyisoflavone XIII,(Fig.5).

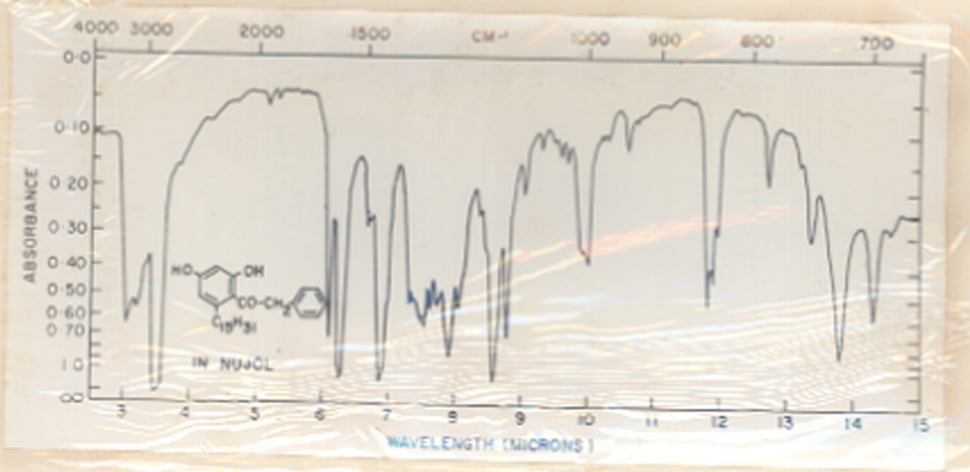


Fig.4. 2-4-Dihydroxy-6-pentadecylphenyl benzyl ketone

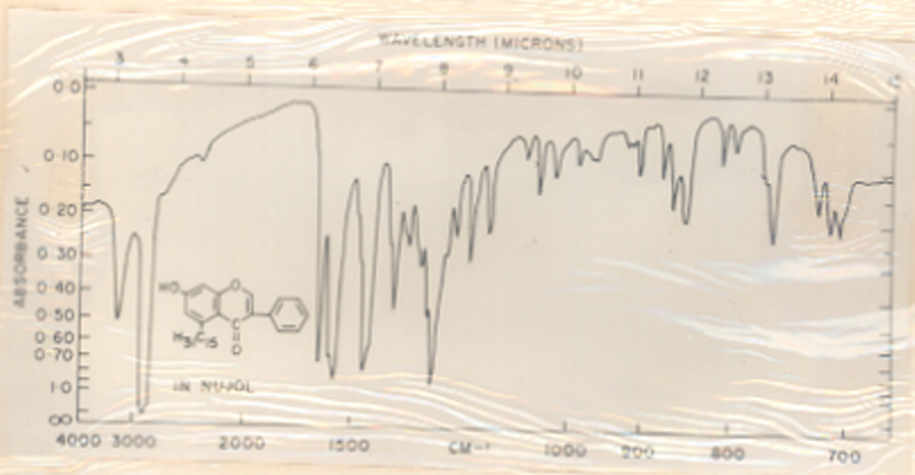
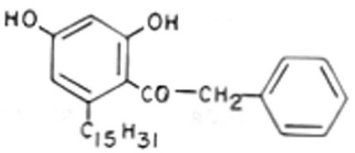
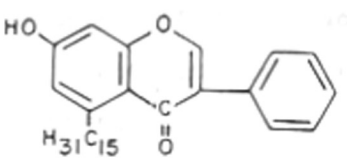


Fig.5. 5-Pentadecyl-7-hydroxy isoflavone



XII



XIII

Since no testing facility was available at the National Chemical Laboratory the activity of these compounds have to be tested elsewhere. Hence samples have been sent out to various centres for evaluation of their properties and the report on them are not yet available.

EXPERIMENTAL

Tetrahydroanacardic acid (T.H.A.A.). Anacardic acid was separated from solvent extracted cashewnut shell liquid and hydrogenated catalytically to tetrahydroanacardic acid as detailed in Part I.

Tetrahydrocardol[35] : Commercial cashewnut shell liquid (heat extracted) was vacuum distilled and the distillate was hydrogenated under pressure using Raney nickel catalyst. Hydrogenated product was then fractionally distilled to separate lower boiling tetrahydroanacardol and higher boiling tetrahydrocardol. Higher boiling fraction after repeated crystallizations and charcoal treatment gave pure tetrahydrocardol m.p.95°C.

Tetrahydroanacardic acid methyl ester (via. acid chloride) method (a): T.H.A.A. (1.0 g.) was taken in dry ether in a three necked flask fitted with a condenser, a mercury seal stirrer and a dropping funnel. Thionyl chloride (1.0 ml.) was then added with stirring. After five minutes, dimethylformamide (0.5 ml.) was added. When crystalline acid chloride appeared in the flask, anhydrous methyl alcohol (10 ml.) was added and the stirring continued for fifteen minutes. Excess solvent was distilled off and the residue on crystallization from alcohol gave methyl ester of T.H.A.A. (m.p.46°, reported[16], 49°C. yield 0.572 g. 55%). It gave no colour with ferric chloride solution.

Tetrahydroanacardic acid methyl ester: method (B):

A solution of tetrahydroanacardic acid (5.0 g.) in dry ether (50 ml.) was treated with an ethereal solution of diazomethane obtained from nitrosomethyl urea at 0° (excess of diazomethane solution was used). The reaction mixture was left overnight and then washed with sodium bicarbonate solution to remove any unreacted acid. Ether solution was dried, ether removed and the residue crystallized from alcohol (m.p.46° yield 4.6 g. 90.5%).

Saligenin analogue I: Methyl ester of T.H.A.A. (0.5 g.) dissolved in dry ether (10 ml.) was added to a cooled (0 to 10°C.) stirred suspension of $LiAlH_4$ (0.3 g.) in dry ether. Stirring was continued for one hour in the cold and then the reaction mixture was kept overnight at room temperature. Excess hydride was destroyed and the reaction mixture then poured into sulphuric acid (10%, 25 ml.), to break the ether complex. Ether layer was separated, washed repeatedly with water and then dried over sodium sulphate. After removal of the solvent, the residue was crystallized from hexane (m.p.66-66.5°; yield 0.3 g. 65.03%). (Found: C, 78.8; H, 11.52; $C_{22}H_{38}O_2$ requires C, 78.98; H, 11.54%).

Similarly when the reduction was repeated using T.H.A.A. in large amount of solvent, saligenin was obtained in somewhat lower yields (5%).

Salicylanilide analogue II: Method (A): Acid chloride of T.H.A.A. (1.0 g.) was formed by reacting it with thionyl chloride (1.0 ml.) and dimethyl formamide (0.5 ml.) as in the case of T.H.A.A. ester. To the ether suspension of the acid chloride, aniline (3 ml. in 5 ml. ether) was added immediately. The reaction mixture was stirred for a an hour and then poured into water. Ether layer was separated, washed with cold water and dried over anhydrous sodium sulphate. Removal of the ether and crystallization of the residue from benzene-hexane gave T.H.A.A. anilide (m.p.78°C. yield 0.458 g., 42.92%; Found: C, 79.2; H, 9.9; N, 3.1; $C_{28}H_{41}O_2N$ requires C, 79.38; H, 9.76; N, 3.31%). It gave very faint colour with ferric chloride solution.

Method (B): T.H.A.A. (3.0 g.) in toluene (250 ml.) and phosphazoanilide (2.5 g.) were refluxed for three hours, cooled and then poured into water (300 ml.). Toluene was removed under reduced pressure and the residue extracted with ether (brine solution was used to render the extraction easy). Ether extract was dried over anhydrous sodium sulphate, ether removed and the residue crystallized from benzene-hexane to give T.H.A.A. anilide (II) (m.p.78°; yield 5.09 g. 58.42%, Found N, 3.2; $C_{28}H_{41}O_2N$ requires N, 3.31%). Mixed melting point of it with the product obtained by procedure (A) showed no depression.

Phosphazoanilide[18] : Phosphazoanilide was prepared by reaction of aniline (186.0 g.) with phosphorus trichloride (55.0 g.) in toluene. Removal of aniline hydrochloride from the reaction mixture and recovering the solvent gave phosphazo compound (20.0 g.) which was washed with alcohol, dried by suction and used in the above experiment.

Tribromo derivative of T.H.A.A. anilide (III):

Tetrahydroanacardic acid anilide (1.0 g.) was dissolved in carbon tetrachloride and liquid bromine added to it drop by drop till red colour persisted. The reaction mixture was warmed for sometime on a water bath and left overnight. It was then poured into water, solvent and water removed under reduced pressure and the residue crystallized from alcohol (m.p.105°C; yield 1.1 g. Found: C, 51.2; H, 5.8; N, 1.93; Br, 36.2; $C_{28}H_{38}O_2NBr_3$ requires C, 50.75; H, 6.04; N, 2.1; Br.36.24%).

Salicylamide analogue (IV): Into a cooled (-5 to 0°C) suspension of acid chloride of T.H.A.A. (10.0 g.) in ether, obtained by reacting it with thionyl chloride (10 ml.) and dimethylformamide (5 ml.), was passed liquid ammonia till the white fumes ceased to come. The reaction mixture was poured on to crushed ice and extracted with benzene. Drying the extract over sodium sulphate and removing the benzene left a residue which on crystallisation from hexane gave IV m.p.80° as white crystalline needles (yield, 2.0 g. 25% Found: C, 76.5; H, 10.4; N, 3.9; $C_{22}H_{37}O_2N$ requires C, 76.03; H, 10.73; N, 4.03%).

Salicyloyl hydrazide analogue (V): Methyl ester of T.H.A.A. (1.) g.) and hydrazine hydrate (0.5 ml.; 100%) were heated for two minutes. Ethyl alcohol (10-15 ml.) was then added and the reaction mixture refluxed for three hours. On cooling a solid separated out which was crystallized from alcohol to give (V). m.p.135°C. (yield 0.52 g. 52%; Found: C, 72.9; H, 10.4; N, 7.74; $C_{22}H_{38}O_2N_2$ requires C, 72.88; H, 10.57; N, 7.73%).

Attempts to prepare salicylhydroxamic acid analogue (VI):

Hydroxylamine hydrochloride was treated with sodium hydroxide solution and to this alkaline solution of hydroxylamine, methyl ester of tetrahydroanacardic acid was added as such (in solid state) or as alcoholic solution of its sodium salt. The reaction mixture was shaken occasionally or continuously and acidified with dilute hydrochloric acid after 12 or 24 hours. The precipitated material was collected and crystallized. In cases where concentration of sodium hydroxide was 5% or below, methyl ester of T.H.A.A. was recovered unchanged whereas in the cases where higher concentrations of alkali (10% or above) was employed the material was characterised as T.H.A.A.

Hydroxylamine was generated in absolute ethanol by adding just sufficient or excess solution of sodium ethoxide in absolute ethanol and to these solutions were added

alcoholic solution of methyl ester of T.H.A.A. at 0° or at room temperature. After 12 hours precipitated products were filtered and acidified with dilute acetic acid or dilute hydrochloric acid. After crystallization the products were characterised as T.H.A.A.

Hydroxylamine was generated by reacting hydroxylamine hydrochloride with metallic sodium in dry ether. Ether solution of hydroxylamine was then reacted with ethereal solution of methyl ester of T.H.A.A. Removal of the ether after 72 hours gave the unreacted ester back.

4-Hydroxycoumarin analogue (VII): A mixture of tetrahydroanacardol (38.0 g.) anhydrous malonic acid (13.0 g.) freshly fused and powdered zinc chloride (56.0 g.) and phosphorus oxychloride (38 ml.) were taken together in a three necked flask fitted with an efficient stirring arrangement (mercury seal), a calcium chloride guard tube and a stopper. The reaction flask was heated in an oil bath maintained at 75 to 80°C. As the reaction proceeded there was free evolution of hydrogen chloride and the reaction mixture gradually thickened and turned from pale yellow to dark brown in colour. Stirring could not be continued after ten hours as the reaction mixture became very viscous. Heating was continued for another ten hours. The mixture was then carefully decomposed with ice and water, warming towards the end. The crude product was

collected on a buchner funnel and washed with cold water and pressed to dryness (32.0 g. 69%). The crude material was crystallized twice from alcohol and then three times from benzene-petroleum ether (40-60°) to a constant m.p.134°C. (Found: C, 77.3; H, 9.6; $C_{24}H_{36}O_3$ requires C, 77.37; H, 9.74%). Infrared spectrum shows the principal absorption bands at cm^{-1}, when taken in Nujol Mull: 3115, 2870, 2732, 2591, 1704, 1639, 1626, 1603, 1524, 1473, 1316, 1250, 1175, 1099, 1005, 913, 896, 851, 840, 729.

Warfarin analogue (VIII): A solution of 4-hydroxycoumarin analogue (1.0 g.) in dioxane (20 ml.) benzal acetone (0.5 g.) and piperidine (3 drops) were refluxed for six hours. The reaction mixture was cooled and poured on water. The product was extracted with ether, combined ether extracts dried over anhydrous sodium sulphate and then ether removed. The gummy residue was distilled under reduced pressure (1.9×10^{-3} mm.) using mercury diffusion pump and the product was then crystallized from benzene-hexane (m.p.110°C. yield 0.70 g. 50%; Found: C, 78.6; H, 9.1; $C_{34}H_{46}O_4$ requires: C, 78.72; H, 8.94%). The infrared spectrum shows the following principal absorption bands in cm^{-1} when taken in nujol mull. 3289, 1695, 1621, 1572, 1468, 1425, 1389, 1311, 1185, 1124, 1055, 1004, 977, 947, 858, 826, 772, 744, 728, 699, 676.

Sodium derivative of warfarin analogue (VIII A):

Warfarin analogue (0.5 g.) in alcohol (2 ml.) was treated

with sodium hydroxide solution (1 ml. 5%) and the reaction mixture left for two hours. The reaction mixture after adding 10 ml. of water was cooled in ice. The precipitated sodium salt was filtered and washed with cold water. It was crystallized from alcohol and water into white crystals (yield, 0.5 g.).

3,6 Dipentadecylfluorane (X): Tetrahydroanacardol (15.0 g.), phthalic anhydride (4.0 g.) and zinc chloride (6.0 g.) were heated, with stirring, at 120° to 125° in an oil-bath for 33 hours. The reaction mixture was poured in water (300 ml.) containing hydrochloric acid (30 ml.) and extracted with ether. Ether extract washed free of acid and ether removed. The gummy viscous residue (showing green fluorescence) was distilled under reduced pressure (0.002 mm.) using bulb tube. After the low boiling fraction (6.3 g. unreacted tetrahydroanacardol) was removed, the high boiling (air bath temperature 355-360°C) fraction was collected as a very viscous yellowish brown liquid (8.8 g.) which turned dark on keeping. It was crystallized from alcohol-ether mixture m.p. 58-59° (Found: C, 83.4; H, 10.2; $C_{50}H_{72}O_3$ requires: C, 83.28; H, 11.06%). Crystals as well as its alcoholic solution show intense green fluorescence in ultraviolet light.

Isoflavone analogue (XIII):

i) 2-4-Dihydroxy-6-pentadecylphenyl benzyl ketone (XII): Phenyl acetic acid (40.0 g.) was dissolved in dry chloroform (80 ml.) and stream of borontrifluoride was passed into the solution cooled to 10-15°C. After the separation of the phenylacetic acid trifluoride complex, 5 pentadecyl resorcinol (tetrahydrocardol) (10.0 g.) was added. BF_3 was again passed for ½ an hour (till no further absorption took place) and the reaction mixture left overnight at room temperature (25-28°C). The reaction mixture was poured on to ice and left for three hours. It was then extracted with ether and the ether chloroform extract, washed with sodium bicarbonate solution and then with water, dried over anhydrous sodium sulphate and the solvent removed by distillation. The residue (13.0 g.) was taken up in benzene-hexane (1:1) and cooled. The solid separated, was filtered and then crystallized from benzene-hexane at room temperature (m.p.117-118°, yield 4.08 g. Found: C, 79.7; H, 9.2; $C_{29}H_{42}O_3$ requires C, 79.4; H, 9.6%).

ii) 5-Pentadecyl-7-hydroxy isoflavone (XIII): The ketone (XII) (1.0 g.) was dissolved in ethyl orthoformate (12 ml.) and dry piperidine (6 drops) added to it. The mixture was refluxed for 12 hours, cooled, poured over ice and hydrochloric acid and left for four hours. The precipitated solid (1.0 g.) was collected and crystallized from alcohol m.p. 114-115°C. (Found: C, 80.4; H, 8.9; $C_{30}H_{40}O_3$ requires C, 80.31; H, 8.99%).

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SUMMARY

Part I. Quaternary Germicides.

Part II.

A. Azo Dyes: Relation Between Structure And Chromatographic Behaviour.

B. New Dyes From C.N.S.L.

Part III. Potential Drugs.

PART I. QUATERNARY GERMICIDES.

Crude cashewnut shell liquid itself is reported to have some anti-bacterial properties, presumably because of the presence of the phenolic components present therein. The present study was undertaken to isolate the individual phenolic components of CNSL in pure form and convert them into the more powerful quaternary nitrogen compounds by suitable changes in the structure of the phenol moiety. An attempt has been made here to draw a relationship between the structural features of the phenolic component and the bactericidal activity of the resulting quaternary nitrogen compounds as well as to synthesise some powerful germicides.

With this in view, the following phenolic components of CNSL have been isolated - anacardol (m-pentadecadienyl phenol), cardol (5-pentadecadienyl resorcinol)

anacardic acid (6-pentadecadienyl salicylic acid). In order to avoid complications, these components, by themselves mixtures of two or three isomers, were catalytically hydrogenated to obtain their saturated derivatives, tetrahydroanacardol, tetrahydrocardol and tetrahydroanacardic acid in pure form. Using these as starting materials, several quaternary nitrogen compounds - ammonium, pyridinium and isoquinolinium - have been prepared through their Mannich bases, chloromethyl derivatives or ω-bromo-ethoxy derivatives and their bactericidal properties are determined. The presence of groups like - -OH, $-OCH_3$, -Cl, -COOH and $-(OCH_2CH_2)-$ in the quaternary nitrogen compound and their effect on the activity has been studied. Preliminary biochemical tests have revealed that the presence of free -OH group adversely affects their bactericidal properties masking the otherwise beneficial effects of substituents like -Cl and COOH. Blocking the hydroxy group by converting it to an ether or introducing an ethoxy bridge, however, enhances the bactericidal properties of the resulting quaternary nitrogen compound.

Though several of the quaternary nitrogen compounds prepared in the present study were found to be water insoluble, a water soluble compound possessing unusually high activity (active 1 part in 2 lacs) viz. 2'-pentadecyl-4'-methoxybenzyl-pyridinium chloride has been reported here. Several other water soluble compounds,

active to a lesser extent have also resulted from the present study.

PART II.

A. AZO DYES: RELATION BETWEEN STRUCTURE AND CHROMATOGRAPHIC BEHAVIOUR.

Comprehensive survey of literature revealed that no systematic study has been made to determine how the properties such as colour, chromatographic behaviour, adsorbability etc. of azo dyes vary with the alteration of structure in the alkyl phenol moiety of the azo dye. A study of this nature was essential to examine the cause for the poor tinctorial properties of azo dyes derived from tetrahydroanacardol. Hence a few other m-alkyl phenols having varying chain length or branching were synthesised and coupled with diazotised aniline. The crude dyes, thus obtained, were systematically examined regarding their properties and chromatographic behaviour.

Despite varying the structure of the phenolic component from m-cresol, through m-ethylphenol, m-n-propylphenol, m-isopropyl phenol, m-n-butylphenol, m-tert.-butylphenol to m-pentadecylphenol all the dyes thus obtained showed marked similarity in their chromatographic behaviour and spectral absorptions.

All the monoazo and disazo dyes obtained from the various m-alkylphenols (except m-cresol) listed above have been reported here for the first time, complete with the

figures of their infrared spectra. Their spectral absorptions - I.R., Visible, U.V. are also presented in tabular form. In addition, two new dyes from aniline → m-cresol have also been reported.

B. NEW DYES FROM C.N.S.L.

Five new azo dyes derived from tetrahydroanacardol and o- and p-anisidine, o- and p-nitroaniline and p-toluidine have been reported. Three new dyes from aniline → tetrahydrocardol have also been reported, with the figures of their infrared spectra. The dyes were characterised and their structures finalised by means of infrared and electronic spectral studies.

All these new dyes reported here are oil soluble and as such are likely to be of great use in leather and other industries where oil soluble dyes are needed.

PART III. POTENTIAL DRUGS.

Several important compounds derived from salicylic acid, phenol and resorcinol are widely in use today in pharmaceutical field - from the simple analgesic aspirin to the anti-tubercular p-aminosalicylic acid. The presence of a long alkyl chain ($C_{15}H_{31}$) in tetrahydroanacardol, tetrahydrocardol and tetrahydroanacardic acid render them fat soluble and as such it was expected that using these as raw materials in place of phenol,

resorcinol and salicylic acid respectively, several new compounds - analogues of known and widely used drugs - could be prepared and these might prove more beneficial and less toxic than their analogues.

With this in view the analogues of some of the better known drugs were prepared. The compound, its analogue currently in use and the field/s of application are indicated below:

Compound	Analogue	Field/s of application
1. 2-Pentadecyl-6-hydroxy benzyl alcohol	Saligenin	Anti-pyretic and tonic
2. Anilide of tetrahydro-anacardic acid and its tribromo derivative	Salicylanilide and bromo derivatives	Anti-fungal
3. Amide of tetrahydroanacardic acid	Salicylamide	Anti-spasmodic and anti-rheumatic
4. Hydrazide of tetrahydroanacardic acid	Salicyl hydrazide	Anti-tubercular
5. Hydroxamic acid of tetrahydroanacardic acid	Salicyl-hydroxamic acid	-do-
6. 3-(α-acetonyl benzyl) 4-hydroxy, 7-pentadecyl coumarin and sodio derivative	Warfarin and Sodium warfarin	Rodenticide Anticoagulant
7. 3,6-Dipentadecyl fluorane	Phenolphthalein	Organic laxative
8. 5-Pentadecyl-7-hydroxy isoflavone	Isoflavone, isoflavonol and isoflavene	Estrogenic

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