

FIXATION OF AROMATIC DOUBLE BONDS

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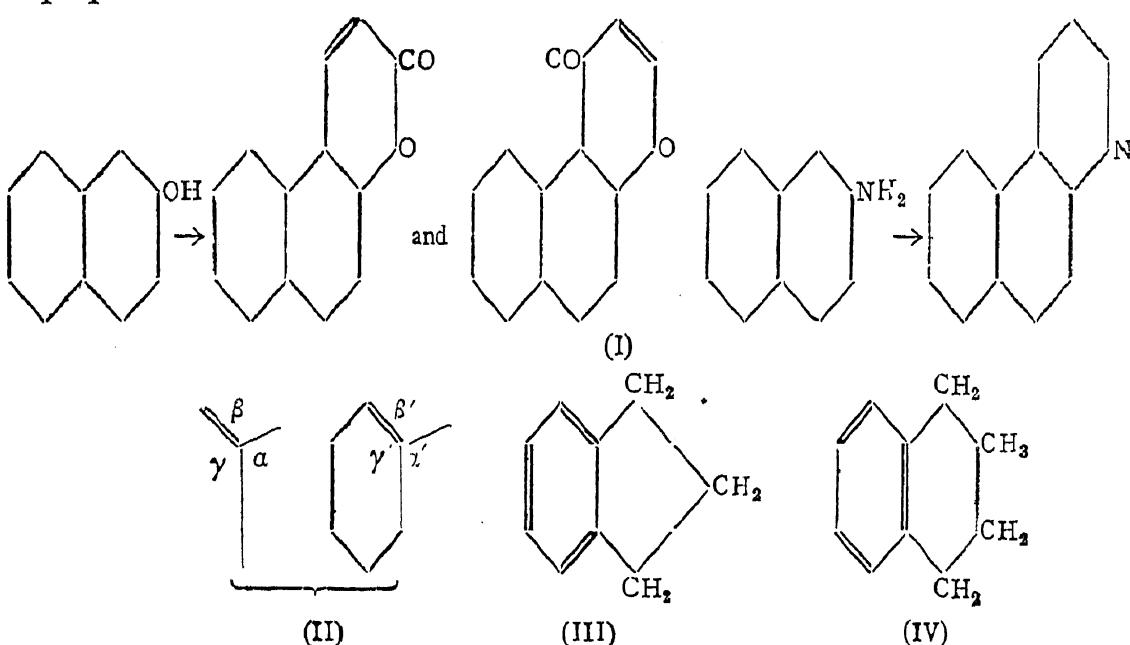
Introduction

THE essential feature of the theory of Kekule relating to the structure of the benzene ring is the existence of oscillating double bonds. Consequently they should have no fixed positions. Based upon this idea the properties and reactions of the compounds of the aromatic series were considered to be satisfactorily explained. When therefore the possibility of the fixation of these bonds in certain favoured positions was announced, it attracted considerable attention and a great deal of work has been done with a view to get clear information of the behaviour of aromatic ring systems.

Work carried out towards the end of the last century and the beginning of this century with reference to derivatives of naphthalene and anthracene indicated the existence of certain select active positions. Fresh rings when formed tended to be of the angular type and not of the linear, as for instance, β -naphthol and β -naphthylamine formed rings (α - and γ -pyrone and pyridine rings) involving the 2:1 positions and not the 2:3 as shown in (I). The same phenomenon was noticed in the case of β -substituted anthracenes and anthraquinones. A similar preferential activity was noticed in other reactions such as bromination, nitration, aldehyde formation, etc. But the first to develop a theory on the fixation of aromatic double bonds were Mills and Nixon and the phenomenon is sometimes called the Mills-Nixon effect. If in a doubly bound carbon atom the angle α between the two single bonds is the same as that between the valencies of the carbon atom in methane ($109^\circ 5$) then the angles β and γ which the single bonds make with the plane of the double bond would be each equal to one half of ($360^\circ - 109^\circ 5$) or $125^\circ 25$; i.e., β is equal to γ and is greater than α (*vide II*). In the benzene ring each internal angle is 120° , i.e., γ' is 5° less than γ . If this reduction of 5° in the value of γ' brings about proportionate increases in the values of α' and β' then the difference between these latter (α' and β') will be slightly more than that between α and β . In other words, in the benzene nucleus constituted in accordance with the Kekule formula, the angle which each of the external valencies makes with the intranuclear single bond on

the one side of it is less than that which it makes with the plane of the double bond on the other side, these being roughly in the ratio of $109^\circ : 125^\circ$.

On this hypothesis Mills and Nixon argued that the stable form of a compound in which the benzene ring is fused with a 5-atom ring (internal angle 108°) must be that in which the linking common to the two rings consists of a single bond since such a configuration produces little distortion in the normal directions of the external valencies. Similarly the stable form of a compound in which the benzene ring is fused with a 6-atom ring (internal angle 120°) must be that in which the common link is a double bond. Thus hydrindene should consist of an equilibrium mixture in which the form with the common single bond (III) preponderates, and tetralin of a mixture in which the form with the common double bond (IV) is preponderant.



The effects of fixation are also brought about by fusion with other aromatic rings just as in naphthalene, anthracene, phenanthrene, etc. Carbocyclic rings having five atoms as in fluorene have a similar influence. Fusion with heterocyclic rings such as pyrones, furans, pyridine, etc., have also been studied. It is interesting to record that even such unstable rings as are found in chelate structures have a tendency to bring about fixation of the aromatic double bonds.

The Methods Employed

As already mentioned data obtained from the direction of closing up of fresh rings starting from hydroxy and amino compounds gave valuable indications. Substitution reactions such as bromination and nitration, entry of aldehyde and ketone groups and formation of quinones and acids

in the case of isomeric hydroxy and amino compounds were subsequently utilised. Ingenious methods involving reactivity of methyl groups and of halogens in alternative positions have been employed by Mills and collaborators. Probably the most sensitive of all these methods is the formation of azo-dyes by the action of certain reactive diazonium salts. This has been very largely used by Fieser who has been also responsible for introducing what is known as the blocking technique. If the orientation of the newly entrant groups is dependent upon the presence of a double bond between the carbon atom having a hydroxylic or amino substituent and its neighbour all these methods are capable of locating the position of the double bond. But, as has been frequently realised it is probably more correct to say that there is quantitative difference in reactivity rather than any essential difference in the quality of the neighbouring positions. Fieser's technique of blocking one of the alternative positions with an alkyl group comes in very useful in this connection, since competition between two alternative positions is eliminated (examples are given in detail in subsequent pages). Combining with the blocking technique the very sensitive method of azo-dye formation, he claimed to have in certain cases proved the existence of rigid fixation of aromatic double bonds (naphthalene, anthracene and hydrindene). Another satisfactory method that has been employed to a large extent by Baker in studying the effect of chelate rings was the migration of groups like allyl (Claisen) and acetyl (Fries) from oxygen to carbon. A combination of this procedure along with the blocking method has been employed by Rangaswami and Seshadri in the case of coumarins and chromones with very definite results.

The above chemical methods suffer from certain inherent difficulties since in a number of cases the treatment is not simple. Physical methods have the advantage that they do not disturb the condition of the molecules. The most valuable of these is the determination of dipole moments. The dissociation constants of isomeric acids and phenols have been employed in certain cases and so also the oxidation-reduction potentials of certain quinones. Evidences from Raman spectra, infra-red spectra, absorption and X-ray spectra have also been obtained in a few cases. The lowering of the melting point under water has found application in special cases where chelate ring structures are involved.

For an explanation of the terms 'reactive methyl' and 'reactive halogen' reference may be made to the article on the 'principle of vinylogy' by Fuson.¹ A reactive methyl group is generally identified by its capacity to react with aromatic aldehydes and less frequently with phthalic anhydride

or *p*-nitrosodimethylaniline while a reactive halogen is characterised by its replaceability with hydrogen on treatment with reducing agents like phosphorus and hydriodic acid or acid stannous chloride and with other groups on treatment with bases like alcoholic ammonia, aromatic amines, alkali hydroxides or piperidine.

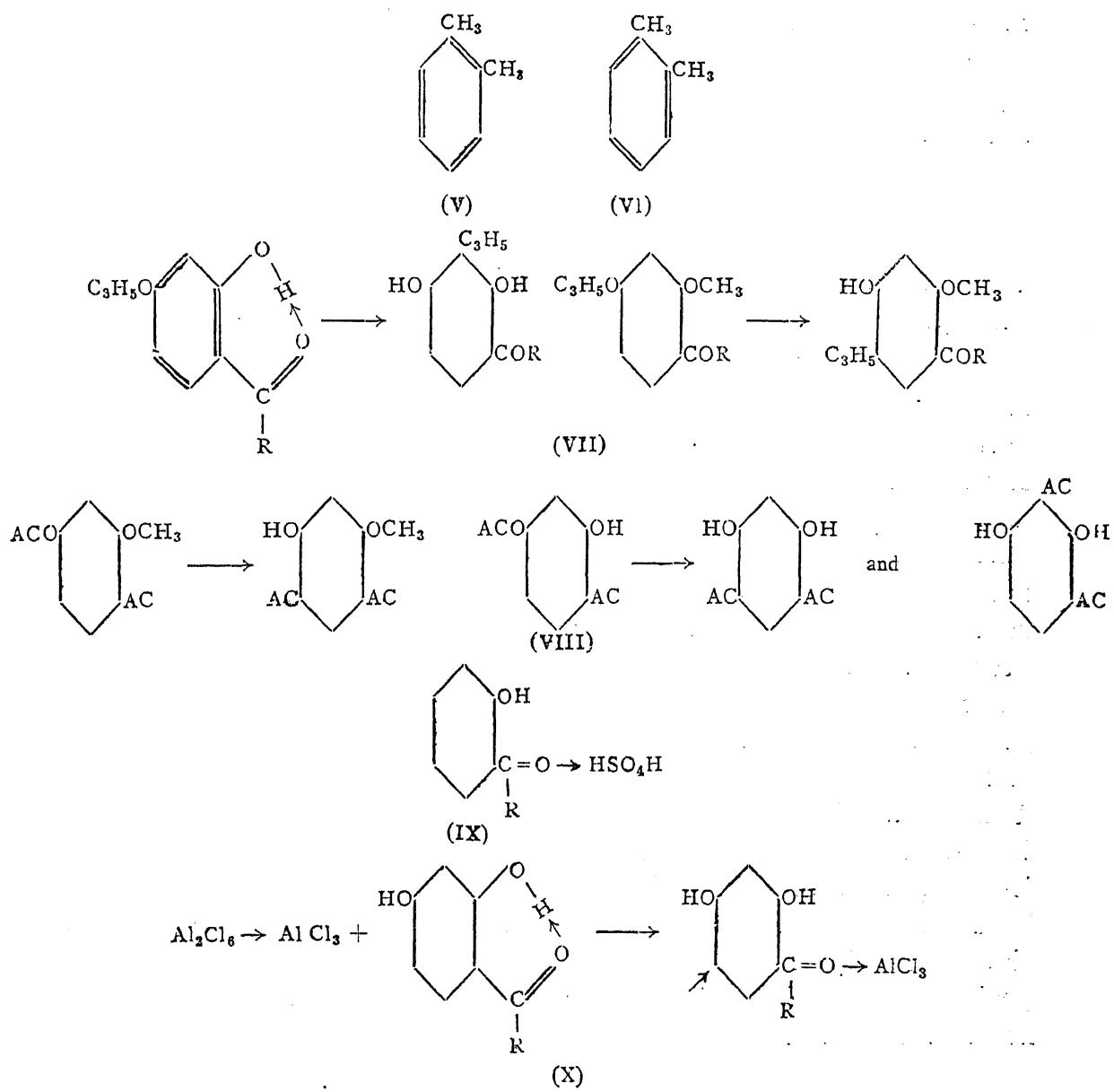
Details of the application of the above methods are given in the following pages where the examples of the important types are dealt with.

Benzene.—Considerable amount of work has been done in regard to the structure of this fundamental hydrocarbon molecule using delicate physical methods. All the results indicate that it has a plane symmetrical structure. Of the several chemical experiments made to determine the disposition of single and double bonds in benzene, that of Levine and Cole² deserves special mention here. As the result of ozonisation of *o*-xylene they obtained three products, *viz.*, glyoxal, methyl-glyoxal and diacetyl. Neither form of the xylene can yield all the three oxidation products and hence the hydrocarbon should consist of an equilibrium mixture of the two Kekule forms (V) and (VI):

While this gives one side of the picture the work of Baker and others shows that fixation is possible under certain circumstances even in the simple benzene system. Baker and Lothian³ found that 4-O-allylresacetophenone undergoes the Claisen transformation to produce mostly 3-allylresacetophenone though its methyl ether gives 5-allyl-2-O-methyl-resacetophenone under the same conditions (*vide* VII). Baker and Lothian explain these reactions by assuming that in the former case the existence of chelation between the adjacent hydroxyl and acetyl groups fixes one of the nuclear double bonds between the carbon atoms carrying these groups and the other two double bonds are in appropriate positions as shown in (VII). Hence the migration of the allyl group which involves the participation of a double bond is directed to the 3-position. When chelation is prevented as in the methyl ether then migration tends to produce a symmetrically substituted molecule.

Observations which support the above view have been made in connection with other types of reactions as well. Baker⁴ found that though 2-methoxy-4-acetoxy-acetophenone gave 2-4:-diacetyl-5-methoxy-phenol when subjected to the conditions of Fries migration, 4-O-acetylresacetophenone gave a mixture of 2:4- and 4:6-diacetylresorcinols under the same conditions owing to the operation of the forces of chelation in this case (*vide* VIII). Perkin⁵ found that the methylation of β -resorcylic ester using methyl iodide and methyl alcoholic potash introduced a methyl group into the nuclear

position 3. Using ethyl iodide instead of methyl iodide Robinson and Shah⁶ obtained similar ethylation in the same nuclear position. More recently Rangaswami and Seshadri⁷ have found that under a similar treatment resacetophenone and ω -methoxyresacetophenone produce 3-C-methyl derivatives. Again Shah and others^{8,9} have found that resorcylic ester and resacetophenone undergo the modified Gattermann reaction to give the 3-aldehydes. All these are in conformity with the hypothesis that chelation between the hydroxyl and the carbonyl in the *o*-position does involve a fixed nuclear carbon-carbon double bond. But at the same time the evidences accumulated by a number of workers go to show that this fixation is not very rigid and does not operate under all conditions. For example Baker *et al.* (*loc. cit.*) themselves conclude from the behaviour of resacetophenone



derivatives that 'fixation by chelation of the Kekulé forms in *o*-hydroxy-acetophenones is not rigidly complete' though such fixation occurs 'to a considerable extent'. Similar conclusions can be arrived at from the nature of certain coumarin condensations as reported by Sethna *et al.*¹⁰ These authors noted that whereas methyl β -resorcylate and aceto-acetic ester give methyl 4-methyl-5-hydroxycoumarin-6-carboxylate with aluminium chloride as the condensing agent, sulphuric acid produces 4-methyl-6-carbomethoxy-7-hydroxycoumarin; in the first case the γ -position of β -resorcyclic ester is the reactive one whereas in the latter it is the free β -position.

The above irregularities are obviously due to the effect of reagents and temperature. Chelation is a special case of the wider phenomenon of hydrogen bond formation. From evidence accumulated in our laboratories chelate bonds seem to be some of the strongest of the type. Still they are not as strong as the ordinary covalent bonds and are possibly ruptured by such reagents as sulphuric acid which have the capacity of co-ordination to a high degree (IX). Regarding the influence of aluminium chloride somewhat contradictory results have been reported. Its behaviour probably varies considerably with the conditions and their effect on the changes represented in (X). It may also be mentioned here that chelation between a hydroxyl and a nitro group in the *o*-position does not seem to involve the participation of a nuclear double bond.

Naphthalene.—The structure of naphthalene is probably one of the most thoroughly investigated. A large number of methods have been employed to study the disposition of the nuclear bonds in one half of the molecule and also simultaneously in both the halves. Of the numerous canonical structures only the three represented in (XI), (XII) and (XIII) are important since they are the most stable valence bond structures and make the maximum contribution to the resonance energy of the naphthalene molecule. Among these three since (XII) and (XIII) are equivalent only structures (XI) and (XII) need be considered here. The symmetrical formula (XI) due to Erlenmeyer represents the molecule as being on the whole more aromatic than (XII) and hence would be the more plausible. Kohlrausch¹¹ has reported that the unsymmetrical formula for naphthalene is inconsistent with the Raman and infra-red spectra of the hydrocarbon though the data do not distinguish between the various symmetrical formulæ. Chemical evidence favouring the idea of a double bond between positions 1 and 2 and of a single bond between 2 and 3 is abundant. Thus β -naphthol couples with diazonium salts at C₁ whereas 1-methyl- and 1-allyl-2-naphthols do not couple.^{12,13} Again in the formation of naphthapyrones from β -naphthol it is the 1-position that is involved.^{14,15} β -Naphthol allyl ether rearranges to give 1-allyl-

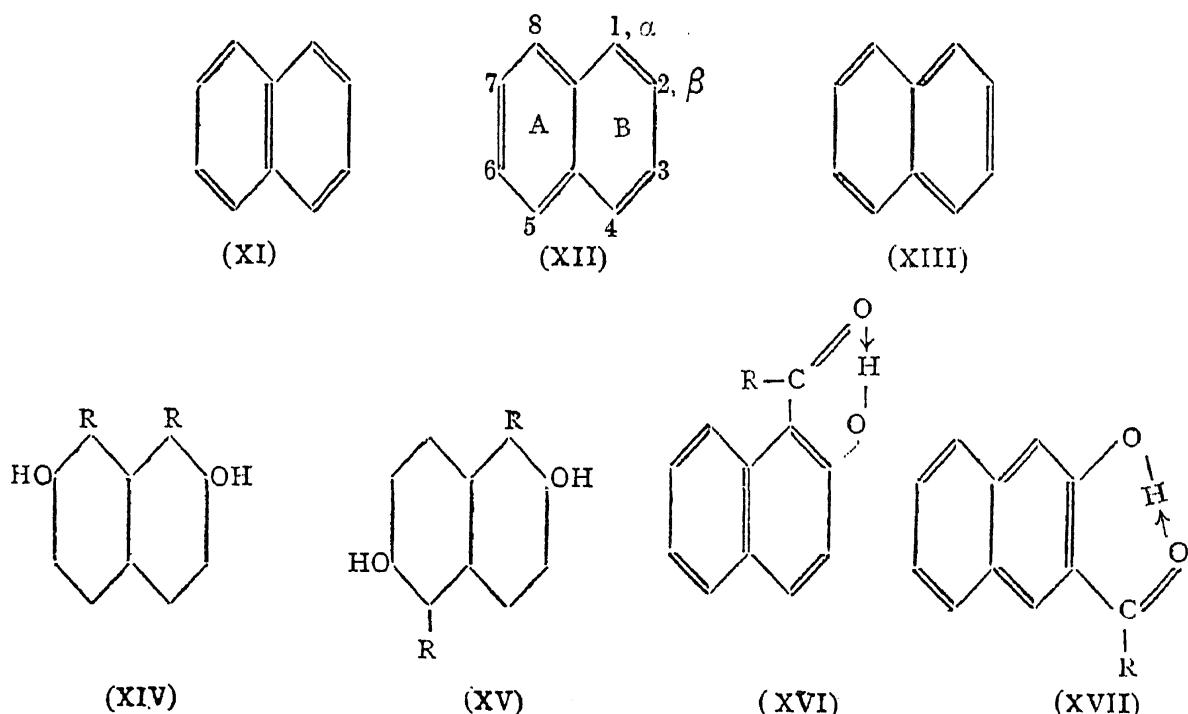
2-naphthol but 1-allyl-2-naphtholallyl ether does not rearrange (Claisen¹³). Again β -naphthylamine couples at C₁ to form azo-dyes and undergoes the Skraup reaction by ring closure involving position 1 (Marckwald¹⁶). The failure of 2:3-dihydroxynaphthalene to form a quinone (Marckward¹⁷) is definite proof that the HO-C-C-OH system here does not function as a single unit as it would do if the C atoms were connected by a double bond. Further evidence for the Erlenmeyer structure can be obtained from the reactivity (*i.e.*, elimination) of the halogen in chloro- and bromonitronaphthalenes (McLeish and Campbell¹⁸), bromo-aminonaphthalenes (Sandin and Evans¹⁹) and bromonaphthols (Franzen and Straube²⁰). Again Hodgson and Elliot²¹ found evidence for the symmetrical structure in the behaviour of halogeno-naphthylamines during acylation, nitration and hydrochloride formation while Bergmann and Hirschberg²² concluded from the dissociation constants of *o*-chloronaphthoic acids that in naphthalene the single and double bonds have a fixed disposition as depicted by Erlenmeyer and do not undergo any rearrangement.

Strictly speaking all the above chemical evidence proves the disposition of bonds only in one part of the molecule. They do not necessarily indicate a symmetrical structure for the entire molecule and can be explained even on the structure (XII) if B is the nucleus carrying the substituents. Even the diazocoupling of 2:7-dihydroxynaphthalene at positions 1 and 8 (Ruggli and Courtin²³) is not incompatible with the structure (XII) if it be assumed that substitution first occurs at C₁ and then following a rearrangement to the alternative unsymmetrical structure at C₈. Hence Fieser and Lothrop²⁴ studied the behaviour of 1:8-dialkyl-2:7-dihydroxynaphthalene (XIV) and 1:5-dialkyl-2:6-dihydroxynaphthalene (XV) and found that they do not couple and that their allyl ethers do not rearrange. This furnishes conclusive proof regarding the distribution of bonds in the entire molecule. They are arranged as in Erlenmeyer's representation and do not change under the above conditions.

Thus far all the observations have gone to support the idea of the symmetrical structure (XI). The study of the dipole moments of some chlorinated naphthalenes by Hampson and Weissberger,²⁵ however, cast the first doubt on the above conclusion. According to them "each C-Cl bond in the chloronaphthalenes is directed as from the centre of the ring; if there is any fixation of single and double bonds in naphthalene it is not revealed in the direction of the substituents". Further evidence on the same lines was forthcoming from the work of Arnold and Sprung²⁶ who concluded from the values of the ionisation constants of isomeric *o*-hydroxy-naphthaldehydes that while a double bond was largely present between C₁ and C₂,

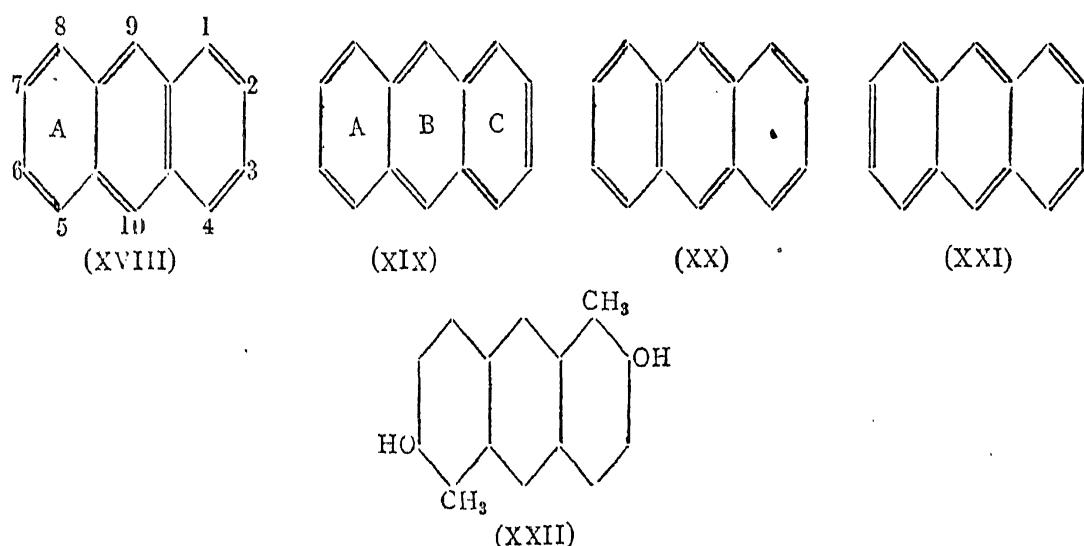
the presence of valence isomers with a double bond between C_2 and C_3 was also indicated. Also Baker and Carruthers²⁷ found a high degree of chelation not only in 2-acetyl-1-naphthol and 1-acetyl-2-naphthol (XVI) but also in 3-acetyl-2-naphthol (XVII). In the last compound the structure is definitely unsymmetrical with a double bond between C_2 and C_3 . In the case of these hydroxy-aldehydes and ketones the change is probably brought about as the result of chelation. Purely chemical evidence for the presence of a double bond between C_2 and C_3 are the conversion of sodium β -naphthoxide to the 3-carboxylic acid (Schmitt and Burkard²⁸) and the bromination of 1-bromo-*p*-toluenesulphon-2-naphthalide in the 3-position in pyridine solution (Bell²⁹). The formation of 3-iodo-1-nitronaphthalene indirectly from 1-nitro-2-naphthyl-amine (Hodgson and Elliot³⁰) is also another instance of the reactivity of the 3-position in a 2-substituted naphthalene.

From the comprehensive data presented above regarding the behaviour of naphthalene derivatives it is clear that though the double bonds exhibit very marked tendency to be located as in the symmetrical Erlenmeyer formula the alternative positions are not altogether excluded. The characteristic properties of fixation are noticed in this ring system far more prominently than with the simpler benzene derivatives.



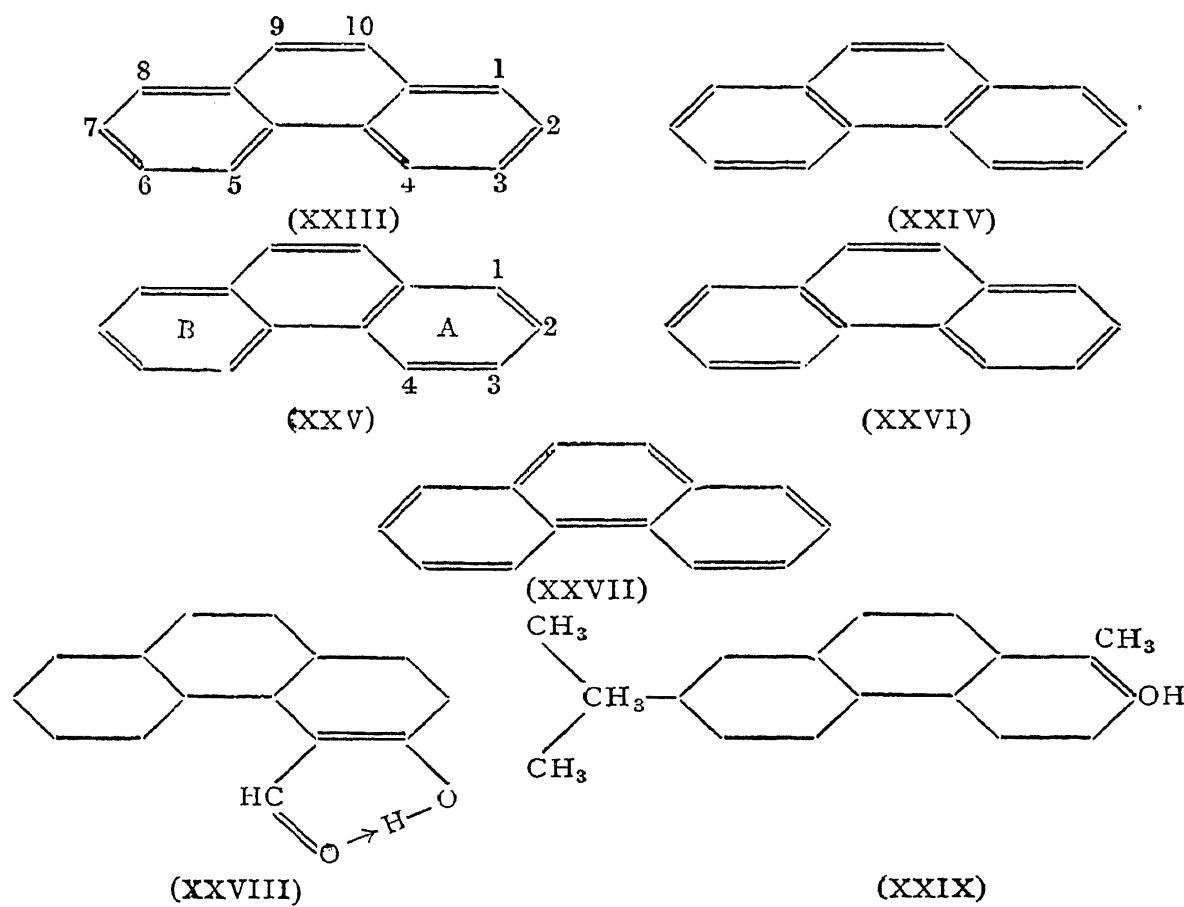
Anthracene.—Not much critical work has been done on polynuclear condensed ring systems. It was Armstrong who first put forward the view that in anthracene there is present at least one ring (A) which contains only two double bonds and which together with the ethylenic linkages extending into the central nucleus constitutes an *o*-quinonoid or dihydrobenzenoid

system of linkages. All the four stable valence bond structures (XVIII, XIX, XX and XXI) for anthracene are expressive of this idea. But (XVIII) and its counterpart (XX) are more plausible since these structures are on the whole more aromatic than (XIX) and its counterpart (XXI). With a view to test this, Fries *et al.*³¹ studied the bromination of 2: 6-dihydroxy-anthracene and obtained the 1: 5-dibromo derivative; but though this result supports formula (XVIII) it is not incompatible with (XIX) if we assume that after substitution in one ring (A) the bonds undergo a rearrangement so as to confer on ring (C) the same structure as is initially present in (A) and *vice versa*. Hence Fieser and Lothrop³² sought unequivocal evidence by studying the properties of 1: 5-dimethyl-2: 6-dihydroxy-anthracene (XXII). The failure of this compound to couple with diazotised amines definitely proved that in the anthracene structure the bonds are distributed as in (XVIII) and that the arrangement is immobile.



Phenanthrene.—Five stable valence bond structures are possible for phenanthrene as in (XXIII–XXVII) of which (XXV) and (XXVI) are equivalent. Mere inspection reveals that all the three rings tend to approach the ideal aromatic condition only according to the second representation (XXIV). The logical consequence would be that this structure would make a greater contribution to the resonance energy of the hydrocarbon than the others and the reactions and other behaviour of phenanthrene would be more in accord with it than with any of the other structures. Critical evidence which can throw light on this problem is neither exhaustive nor even adequate. The great ease with which the 9:10 quinones are formed from phenanthrene and its derivatives indicates the presence of a double bond between these positions and thus definitely eliminates formula (XXVII). Smith³³ observed that 3-phenanthrol-4-aldehyde did not couple with diazotised amines simulating the behaviour of 1-methyl-2-naphthol; the evidence

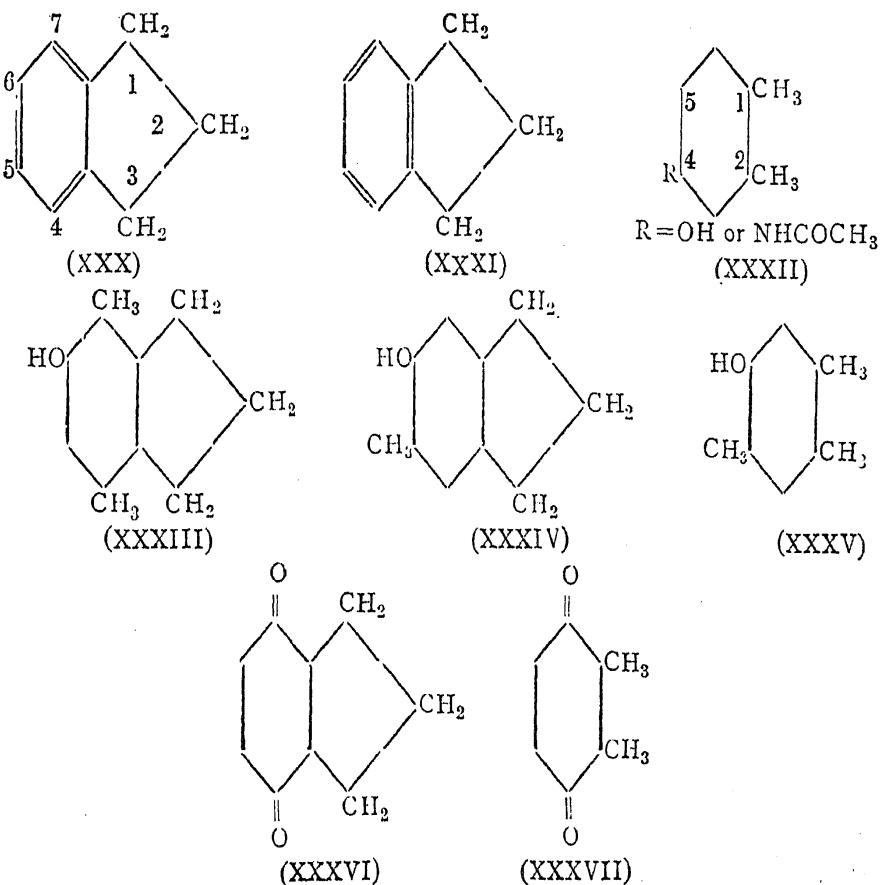
in this case is complicated by the existence of chelation as shown in (XXVIII). Recently Fieser, Young and Newman³⁴ have found that the allyl ethers of 2- and 3-phenanthrols undergo the Claisen transformation smoothly but the transformation products (obviously 1-allyl-2-phenanthrol and 4-allyl-3-phenanthrol) do not couple with diazotised amines and the allyl ether of the former does not again rearrange on heating. These evidences show that in phenanthrene the bonds are located as in (XXIV) or (XXV) [in the latter case if the substituents mentioned above are attached to ring (A) and not to ring (B)] and that structure (XXIII) is incompatible with these reactions. Though the behaviour of phenanthrene derivatives containing substituents in both the end nuclei does not seem to have been recorded, considerations of symmetry would dictate that (XXIV) is probably the nearest approach to the true configuration of phenanthrene rather than (XXV) or (XXVI). In fact belief in the rigid and unalterable distribution of the bonds of phenanthrene as in (XXIV) and in the infallibility of the diazo-coupling method for the location of double bonds has become so strong that this procedure has been employed by Fieser *et al.*³⁴ to assign the constitution of 2-retinol (XXIX) to the compound previously known as A-retinol. This compound had been prepared by Komppa and Wahlforss³⁵ and the chief argument in support of the constitution assigned by Fieser *et al.* was its inability to couple with diazotised amines.



Hydrindene.—The earlier evidence on hydrindene seemed to favour the idea that it has a rigidly fixed bond structure with a single bond common to the two rings but more recently this has not been found to hold good in all cases of hydrindene derivatives. From theoretical considerations Mills and Nixon³⁶ concluded that in hydrindene the form with a common single bond (XXX) should be the more favoured structure and in support of this they showed that in 5-hydroxyhydrindene and 5-acetamidohydrindene it is the 6th position that is reactive to the almost complete exclusion of the 4th. Similar results had been obtained even as early as 1926 by Borsche and Bodenstein.³⁷ They found that 5-acetamidohydrindene gave the 6-nitro and 6-bromo derivatives on nitration and bromination respectively. These evidences, however, lose much of their significance when the behaviour of 4-hydroxy-1: 2-dimethylbenzene and 4-acetamido-1: 2-dimethylbenzene (XXXII) is considered. These compounds are reactive only in position 5^{38,36} so that even in the 5-substituted hydrindene derivatives mentioned above the mere chemical effect of the methylene groups may be enough to explain adequately the formation of 6-substituted hydrindenes without any help from steric effects consequent on the fusion of the benzene ring with the 5-atom ring. Unambiguous evidence was therefore sought in the value of the dipole moment of 5: 6-dibromohydrindene by Sidgwick and Springall.³⁹ They found for the Br·C·C·Br system of this compound a smaller value of the dipole moment than for the same system in *o*-dibromobenzene or in dibromo-*o*-xylene, thus proving definitely that there is no free resonance in hydrindene and that the rings have a common single bond. The same conclusion was arrived at by the application of the rigid chemical method developed by Fieser.⁴⁰ 6-Hydroxy-4: 7-dimethylhydrindene (XXXIII) gave azo-dyes with diazotised amines but not 6-hydroxy-5-methylhydrindene (XXXIV). On the other hand pseudocuminal (XXXV) was able to couple with diazonium salts. Since chemically (XXXIV) and (XXXV) are similar the difference in the coupling capacity of the two compounds should be attributed to stereochemical effects. Obviously, owing to the fusion of the benzene ring with the polymethylene ring in (XXXIV), the C₆·C₇ link cannot behave like a double bond; in other words, the bonds of hydrindene are arranged as in (XXX) and this arrangement is unalterable. Further support to this conclusion was afforded by the results obtained by Arnold and Evans.⁴¹ By the ozonisation of hydrindene followed by catalytic hydrogenolysis of the ozonide they obtained glyoxal and succinic acid (obviously from cyclopentane-1: 2-dione). This indicates that hydrindene exists mostly as (XXX). The alternative structure (XXXI) would have given glyoxal and α - α' -diketopimelic aldehyde or its oxidation products, none of which were detected in the final mixture.

Results not entirely supporting the rigid structure given above were first obtained by McLeish and Campbell.¹⁸ Besides finding that the bromine atom in 6-bromo-5-nitrohydrindene was highly reactive as mentioned above they noticed that the 4-bromo isomer also exhibited a feeble reactivity indicating a common double bond between the two rings (type XXXI). This was subsequently confirmed by Sandin and Evans¹⁹ who, working mainly with 5-amino-hydrindenes with bromine atoms in the *o*-positions, found both the 6- and 4-bromine atoms reactive though to varying degrees. These authors however added that any inference that might be drawn was in favour of (XXX) being the favoured structure. A similar conclusion was drawn by Arnold and Zaugg⁴² who found a higher oxidation-reduction potential for 4:7-hydrindenequinone (XXXVI) than for *o*-xyloquinone (XXXVII). This was attributed by these authors to a "positive Mills-Nixon type of partial double bond stabilisation" though the reasons for the use of the term "partial" are not clear. More definite evidence pointing to structure (XXXI) for hydrindene was furnished by the experiments of Fieser and Lothrop⁴³ who found that 5-hydroxy-6-methylhydrindene could form azo-dyes under certain carefully controlled conditions. A quantitative study of the diazo-coupling reaction led the latter author⁴⁴ to the conclusion that hydrindene derivatives were inferior to β -naphthol in coupling capacity and more comparable to 2:4-dimethylphenol. The smooth Claisen rearrangement of 5-allyloxyhydrindene when the 4- and 6-positions were separately blocked by methyl groups also lent support to the conclusion that the bond fixation in hydrindene derivatives is not very rigid.⁴⁴ The formation of 4:6-dibromo-5-amino-hydrindene by direct bromination of 5-aminohydrindene (Borsche and Bodenstein³⁷) and the comparative values of the dissociation constants of 5-hydroxy-6-nitrohydrindene and of 2-nitrophenols (Arnold and Evans⁴⁵) also show non-stabilization of double bonds as a result of ring fusion. Again from a study of the depression in melting point on wetting Baker⁴⁶ found that both 5-acetyl-6-hydroxy- and 5-acetyl-4-hydroxy-hydrindenes are chelated though to varying degrees. These compounds can exhibit chelation only if a single and a double bond respectively can be brought into being in common between the two rings in accordance with structures (XXX) and (XXXI) thereby enabling the chelate ring to possess a double bond. It may therefore be concluded that in hydrindene the structure with a common single bond is the more favoured though the other alternative is not excluded.

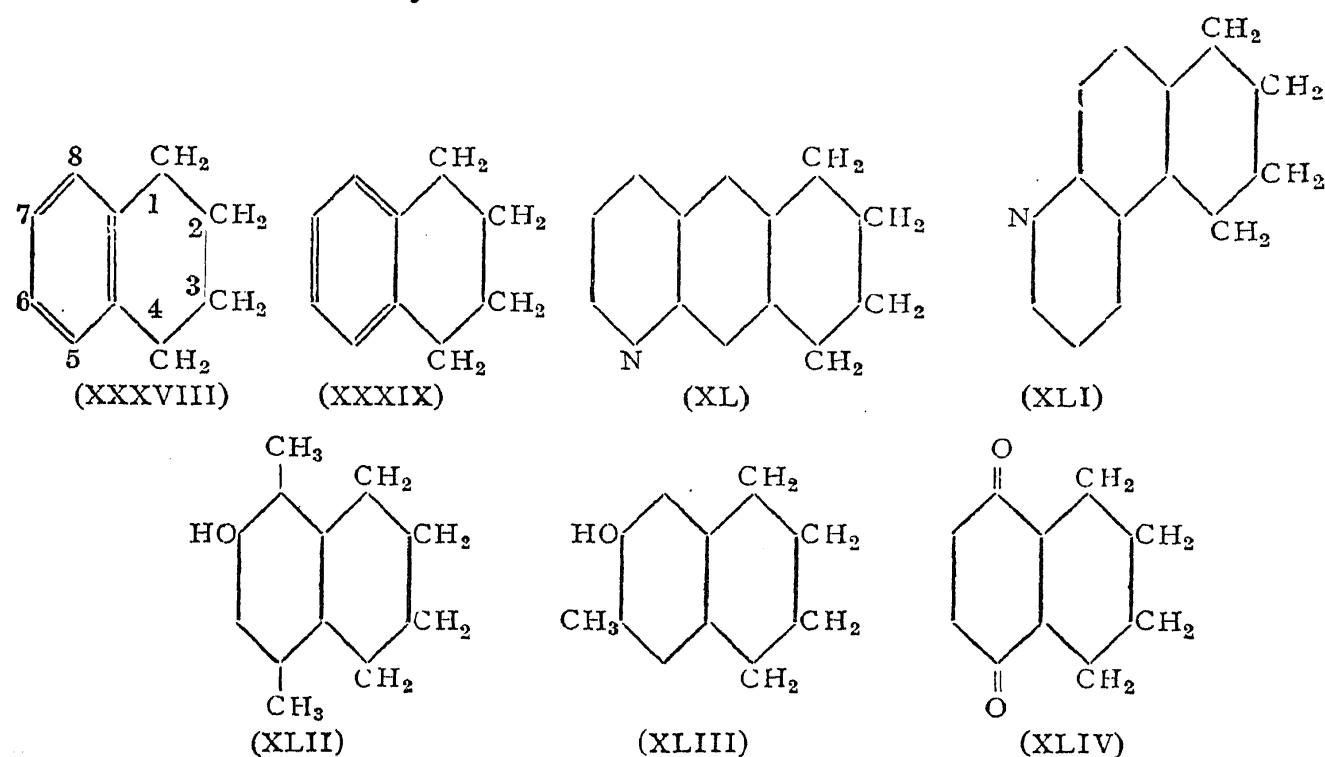
Tetralin.—According to the theoretical considerations developed by Mills and Nixon³⁶ tetralin should have a predominant structure in which a double bond is common to the two rings (XXXVIII). In support of their



conclusion these authors quoted the previous findings of Schroeter⁴⁷ and of Smith⁴⁸ that 6-hydroxy- and 6-acetamidotetralin gave 5-substituted compounds in bromination and diazo-coupling experiments. Another evidence favouring this idea is the presence of a positive bromine atom in 5-bromo-6-aminotetralin (Sandin and Evans¹⁹) and in 5-bromo-6-hydroxy-7-amino-tetralin (Schroeter⁴⁷). This method however does not seem to be altogether satisfactory and consistent, since McLeish and Campbell¹⁸ found proof for the alternative conclusion (common single bond, type XXXIX) in the behaviour of 6-bromo-5-nitrotetralin (unreactive) and 6-bromo-7-nitrotetralin (reactive). A result which is in conformity with the latter observation is the formation of 6-hydroxy-7-nitrotetralin from 6-hydroxy-tetralin (Thomas and Kross⁴⁹). Thus tetralin seems to be capable of reacting in the alternative structural form (XXXIX) with equal facility.

That tetralin is really to be considered as made up of a mixture represented by the two structures was evident from the work of V. Braun and Grüber⁵⁰ who subjected 6-amino-tetralin to the Skraup reaction and obtained a mixture of the linear and angular varieties of the tricyclic compound (XL and XLI). The more subtle methods of investigation are also largely in favour of the idea that in tetralin there is no fixation of the double bonds and that there is resonance in the purely aromatic sense. Thus, Sidgwick and Springall³⁹ found that the $\text{Br}\cdot\text{C}\cdot\text{C}\cdot\text{Br}$ system in 6:7-dibromotetralin

had a value for the dipole moment equal to that in *o*-dibromobenzene and dibromo-*o*-xylene. Fieser and Lothrop⁴⁰ found that both 7-hydroxy-5:8-dimethyltetralin (XLII) and 7-hydroxy-6-methyltetralin (XLIII) could couple with diazotised amines, while in quantitative experiments using the method of diazo-coupling tetralin derivatives were less reactive than β -naphthol and more akin to 2:4-dimethyl-phenol (Lothrop⁴⁴). Further Arnold and co-workers found 6-hydroxy-7-nitrotetralin and *o*-nitrophenols to have the same value for the dissociation constant⁴⁵ and 1,-2,-3,-4-tetrahydronaphtho-5:8-quinone (XLIV) and *o*-xyloquinone (XXXVII) to have nearly equal oxidation-reduction potentials⁴² showing non-stabilisation of the double bonds in the tetralin system.

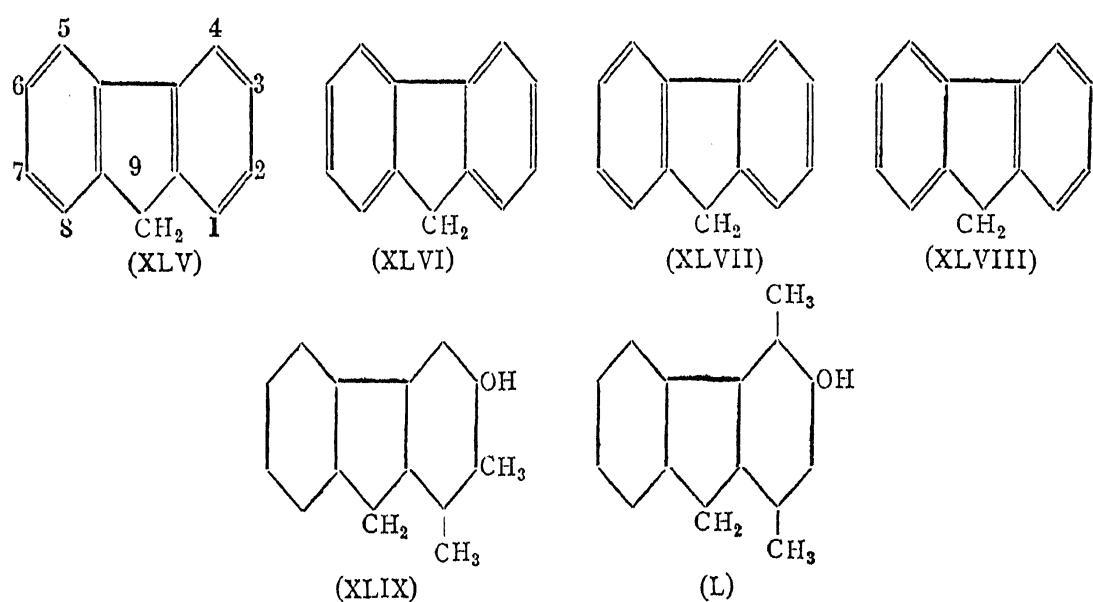


Fluorene.—There are four important structures that can be formulated for fluorene. Of these the symmetrical ones (XLV) and (XLVI) would be the more plausible though the unsymmetrical ones (LXVII) and (LXVIII) cannot be altogether ignored in the absence of positive evidence in favour of such elimination. (XLV) represents the fluorene molecule as essentially derived from cyclopentadiene while (XLVI) looks more like a cyclopentane compound. Both of them contain an unbroken chain of conjugated double bonds and would have considerable stability.

On the basis of refractivity studies Auwers *et al.*^{51,52} concluded that the aromatic rings in fluorene must be classed as similar to naphthalene and anthracene at least qualitatively. From nitration experiments Ananthakrishnan and Hughes⁵³ obtained evidence for considering fluorene as dibenzocyclopentadiene. Subsequently Hughes, LeFevre and LeFevre⁵⁴ concluded

from studies of dipole moments that their data did not point to any specific configuration for fluorene whose structures may be flat degenerate forms between (XLV) and (XLVI).

On the chemical side the evidence which is incomplete, inasmuch as it refers to only one of the benzene rings and not simultaneously to both, does not point to any rigid structure represented by either (XLV) or (XLVI). Thus γ -2-fluorene-butyric acid and *o*-2-fluorenebenzoic acid close up rings in such a way that the 3-position is involved.^{55,56} These point to structure (XLVI) for fluorene. On the other hand 2-acetoxyfluorene and 2-acetoxyfluorenone undergo the Fries migration to give 1-acetyl-2-hydroxy compounds⁵⁷ thus pointing to structure (XLV). However, a great many fluorene derivatives behave as though there is no fixation of the double bonds in any position. Thus, Lothrop⁵⁸ found that 2-allyloxyfluorene underwent the Claisen transformation to give a mixture of isomers supposed to be the 1- and 3-allyl-2-hydroxyfluorenes; both 1:2-dimethyl-3-hydroxyfluorene (XLIX) and 1:4-dimethyl-3-hydroxyfluorene (L) coupled with diazotised amines and their allyl ethers smoothly underwent the Claisen transformation thus showing that either of the *o*-positions of 3-hydroxyfluorene can behave as a reactive centre in these reactions. Again 2-allyloxyfluorenone behaved just like 2-allyloxyfluorene in the Claisen transformation giving a mixture of isomeric products,⁵⁷ and the Kolbe's reaction with 2-hydroxyfluorene gave two isomeric acids (obviously the 1- and 3-carboxylic compounds).⁵⁹ Thus the balance of evidence seems to be in favour of the idea that in fluorene there is little fixation of the nuclear bonds just as in diphenyl.

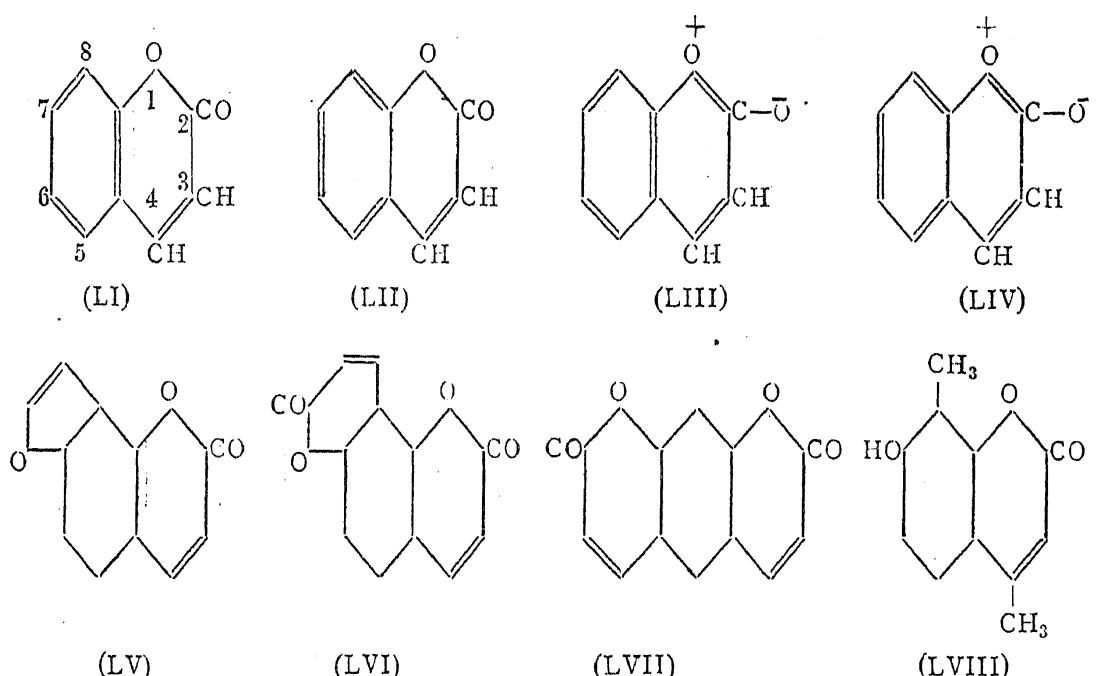


Coumarin and Chromone.—Though in coumarin itself substitution invariably takes place in the 6th position, in 7-hydroxycoumarins it is exclusively in the 8th position. When attempts are made to build up fresh rings

starting from 7-hydroxy-coumarins, it is the 8th position that is involved in the ring-formation. Thus employing 7-hydroxycoumarin and bromo-acetal Späth⁶⁰ obtained angelicin (LV). Rangaswami and Seshadri⁶¹ similarly found that the Pechmann condensation between 7-hydroxycoumarins and malic acid or acetoacetic ester gave mostly the angular coumarino- α -pyrones (type LVI). Again attempts to introduce an aldehyde group into 7-hydroxycoumarins gave the 8-aldehydes.^{61,62} All these show that 7-hydroxycoumarins react in the form (LI). The most reliable evidence for this structure, however, comes from the work of Baker and Lothian³ who found that 7-allyloxy-4-methylcoumarin undergoes the Claisen transformation to give 7-hydroxy-8-allyl-4-methylcoumarin thus proving conclusively that there exists a double bond between the 7- and 8-positions.

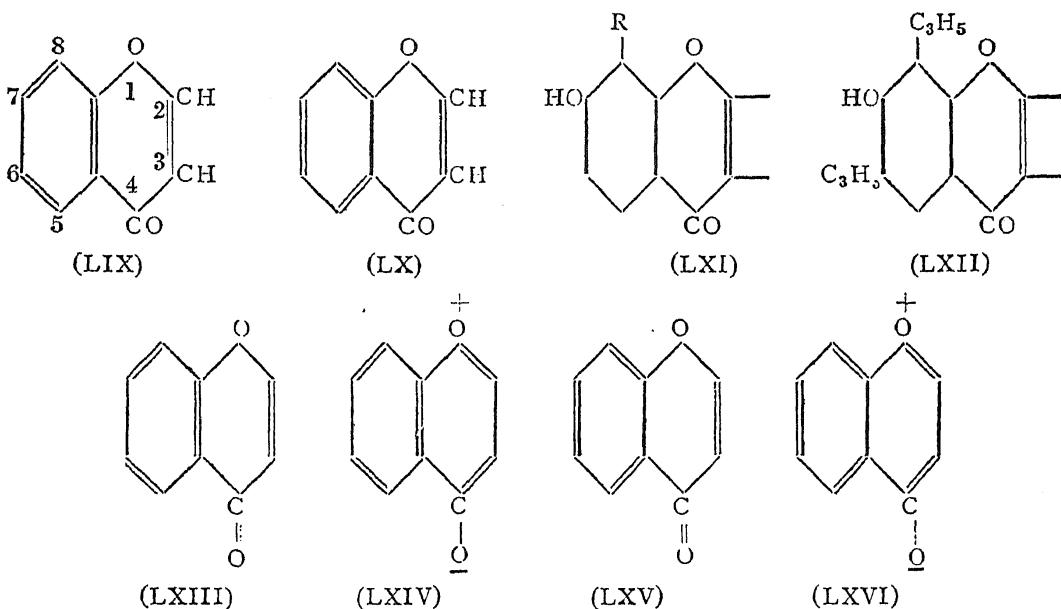
Evidence which does not fall into line with the above was first obtained by Limaye.⁶³ He found that when 4-methyl-7-acetoxycoumarin was subjected to Fries migration, the 8-acetyl-7-hydroxy compound which was the major product was accompanied by a small quantity of the 6-acetyl-isomer. The simultaneous formation of the angular coumarino- α -pyrone (LVI major product) and the linear isomer (LVII, minor product) from the Pechmann condensation using umbelliferone and malic acid (Rangaswami and Seshadri⁶¹) corroborates the above observation and shows the slight but significant reactivity of the 6th position in umbelliferone. The last-mentioned authors have applied Fieser's technique to the coumarin ring system and obtained unequivocal evidence on the distribution of the single and double bonds.⁶⁴ They have found that 7-hydroxy-4:8-dimethylcoumarin (LVIII) couples with diazotised *p*-nitraniline and forms with mercuric acetate a mercury derivative which contains 2-acetoxy-mercuri groups replaceable by bromine atoms. The allyl ether and acetyl derivative also smoothly undergo the Claisen transformation and Fries migration respectively. All these reactions can be explained only on the assumption of a reactive 6-position which is possible only if the bonds can take up positions as depicted in (LII). Thus in coumarins while the normal structure corresponds to (LI) the other is not precluded.

From a study of dipole moments Rau⁶⁵ concluded that coumarin exists in the excited state mainly as (LIII). Besides many others the alternative structure (LIV) (not mentioned by this author) is also possible in which the situation in the lactonic part is the same. A comparison of the two forms clearly shows that on the whole (LIII) represents a more aromatic structure than (LIV) and will tend to be the more important of the two forms in entire agreement with results deduced from chemical reactivity.



The theoretical considerations of the structure of chromones and flavones (benzo- γ -pyrones) and the experimental study follow on lines closely similar to those applied to the coumarins (benzo- α -pyrones). The great reactivity of the 8th position in 7-hydroxy-chromones is evident from the formation of the 8-aldehyde from 7-hydroxy-3-methoxyflavone by the action of formylating agents (Rangaswami and Seshadri⁶⁶). Again it is the 8th position that is involved in the Fries migration of 7-acetoxy-2-methylchromone (Wittig, *et al.*⁶⁷) or its 3-acetyl derivative (Baker⁶⁸) and in the Claisen transformation of the allyl ethers of 7-hydroxyflavone and 7-hydroxy-2-methyl-3-methoxychromone (Rangaswami and Seshadri⁶⁹). These suggest a fixation of the double bonds as in (LIX). But the 8-allyl-7-hydroxy-compounds (LXI, R = allyl) obtained from the above Claisen transformations give allyl ethers which are capable of undergoing further Claisen rearrangement to give rise to the 6:8-diallyl-7-hydroxy-chromones and flavones (LXII).⁶⁹ This indicates that the nuclear bonds are capable of redistribution as in type (LX). Further support for this conclusion is afforded by the capacity of 8-methyl-7-hydroxyflavone and its 3-methoxy derivative (LXI, R = methyl) and of 8-allyl-7-hydroxyflavone and 8-allyl-7-hydroxy-2-methyl-3-methoxy chromone (LXI, R = allyl) to couple with diazotised *p*-nitraniline.⁶⁹ Thus the initial distribution and realignment of bonds in chromones are quite analogous to the case of coumarins.

A close examination of the formulæ (LXIII) to (LXVI) leads us to the same conclusion. (LXIV) represents the reactive or excited state of the molecule and it exhibits the maximum aromatic characteristics. (LXIII) corresponds to a *p*-quinone structure. In both these there exists a double



bond in common between the two rings and as a consequence the disposition of the other bonds in the benzene part is fixed. Structures (LXV) and (LXVI) represent other possibilities and have a single bond in common between the rings; but these are obviously less stable structures devoid of the maximum conjugation and their contribution to the behaviour of the molecule will be small. Though small it seems to be appreciable and definite as indicated by the experimental results recorded above.

The simultaneous reactivity of the 6- and 8-positions in the coumarins and chromones indicating the occurrence of the two alternative positions of the double bonds has been to some extent indicated by recent experiments. The formation of 6:8-disubstituted derivatives from 7-hydroxy-coumarin during mercuration, bromination and nitration using excess of the reagents does not really have much significance in this connection; it is possible to explain these reactions by assuming that first the attack is initiated at position 8 of the form (LI), the product subsequently changes into the form (LII) and then reacts with more of the reagent in position 6 to give the 6:8-disubstituted compounds, provided of course that the physical conditions are not adverse to the progress of this second stage of the reaction (*vide* Rao, Sastri and Seshadri⁷⁰). On the other hand the simultaneous formation of the 8- and 6-acetyl-7-hydroxy compounds by the Fries migration of 7-acetoxy-4-methylcoumarin (Limaye⁶³), and of the angular and linear coumarino- α -pyrones by the Pechmann condensation of 7-hydroxycoumarin and malic acid (LVI and LVII⁶¹), show that the 8- and 6-positions can be simultaneously reactive in these compounds. In support of this there is the evidence of Rangaswami and Seshadri⁷¹ who have carried out quantitative diazo-

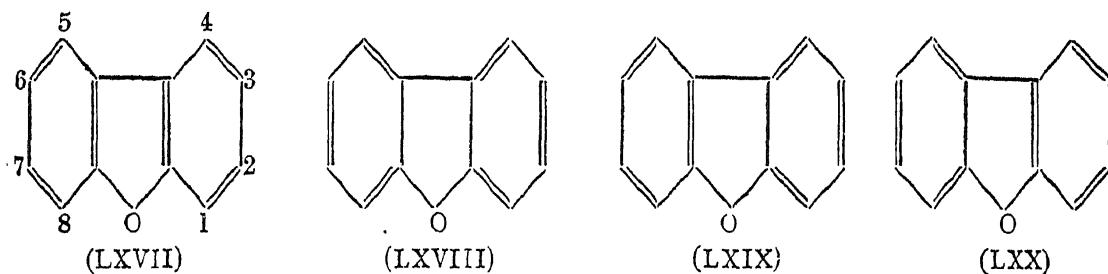
coupling experiments to study this question. Starting with 7-hydroxy-4-methylcoumarin and 7-hydroxy-2-methyl-3-methoxychromone and employing just one molecular proportion of diazonium salts they have obtained dyes whose compositions show that bis-azo-dye formation has taken place. This is not possible if the 6th position can become reactive only after the 8th has completely reacted, since in such a case the quantity of reagent used would have been completely used up by the 8th position. The fact that bis-azo-dyes were not formed in the case of all the coumarins and chromones studied under the influence of only one molecular proportion of the reagent does not invalidate the above conclusion regarding the simultaneous reactivity of the 6- and 8-positions. Obviously the substituent groups in these compounds are not altogether without an effect on the mobility of the nuclear bonds. This statement receives support from similar observations by the same authors in other types of reactions as well. Thus though umbelliferone and malic acid gave a mixture of coumarino-pyrone under the conditions of the Pechmann condensation only the angular compounds (reactive 8-position) were formed from 4-methyl-umbelliferone and malic acid or ethyl acetoacetate.⁶¹

Dibenzofuran

Four structures (LXVII to LXX) are important for dibenzofuran. LXIX and LXX which are equivalent among themselves are not likely to be as important as the other two inasmuch as they assume that the molecule is unsymmetrical. As between LXVII and LXVIII the former represents the hydrocarbon as a furan derivative, the latter as a dihydrofuran derivative. For maximum stability each component ring should have the maximum aromatic configuration and hence (LXVII) would represent the most important canonical structure. At the same time we find a high degree of conjugation even in (LXVIII) and hence the contribution of this form to the resonance energy would certainly come next in importance to that of (LXVII). Thus we seem to be having here a case similar to fluorene; the bonds can take up either of the alternative positions with equal ease.

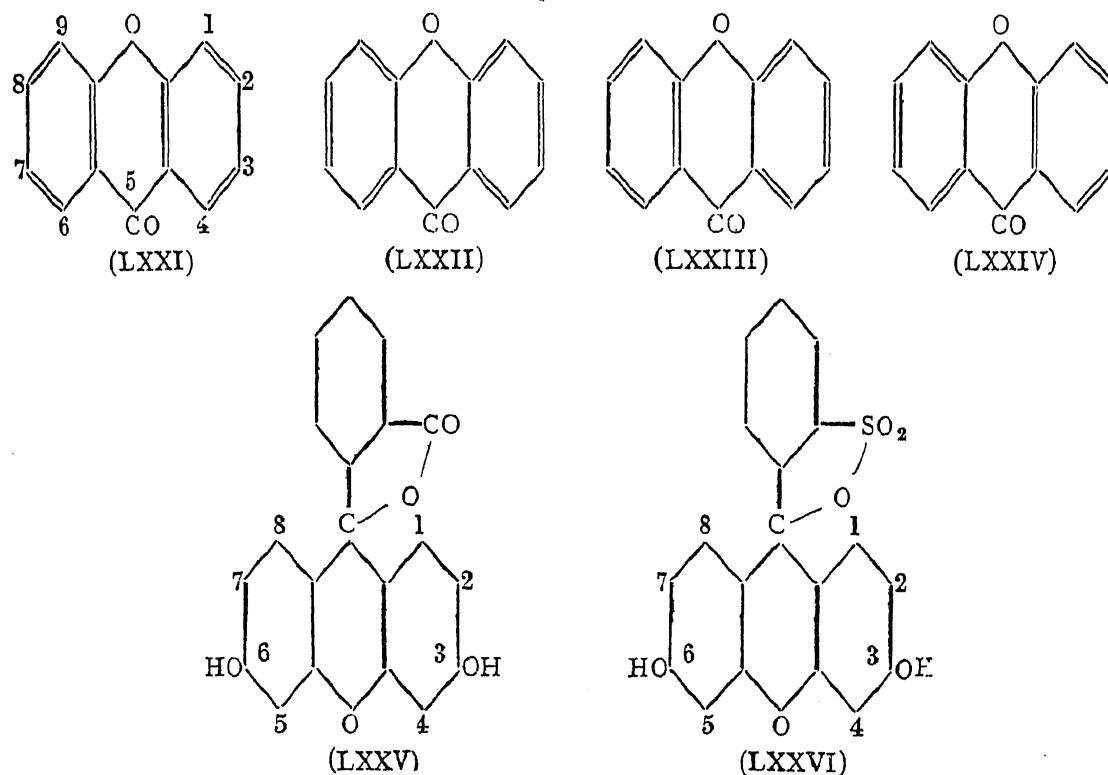
A complete chemical investigation of this question would involve the study of substitution not only in one part of the molecule but simultaneously in both the end rings. Such definite proof, however, seems to be lacking. The available evidence, mostly the work of Gilman and his school, shows that there is no specially favoured disposition for the bonds, though it refers only to one of the benzene rings. The bromination and nitration of hydroxy-, methoxy- and acetamido-dibenzofurans⁷² and the diazo-coupling of 2-hydroxy-, 3-hydroxy- and 4-hydroxy-dibenzofurans⁷³ give results some

of which are in accord with formula (LXVII) while the rest are expressive of formula (LXVIII).



Xanthone and Xanthene

Four important structures (LXXI to LXXIV) are possible for xanthone of which, by analogy with chromones, the first would be expected to be the nearest approach to the true structure of the molecule. LeFevre⁷⁴ found that the dipole moments of 2:7-dibromo- and dinitroxanthones are in good agreement with the structure (LXXI) and further that the bonds are almost completely fixed as depicted in that formula. If fluorescein (LXXV) can be considered as a xanthene derivative then valuable information can be gathered regarding the distribution of bonds in this system from the reactivity of the dye as pointed out by Sandin, *et al.*⁷⁵ The data available regarding this compound have one welcome feature; derivatives containing substituents in both the benzene rings are easily available and are amenable to experimental study so that it is possible to get a complete picture of the entire molecule. Sandin and co-workers thus found that bromination of fluorescein and sulphone-fluorescein (LXXVI) produced 4:5-disubstituted

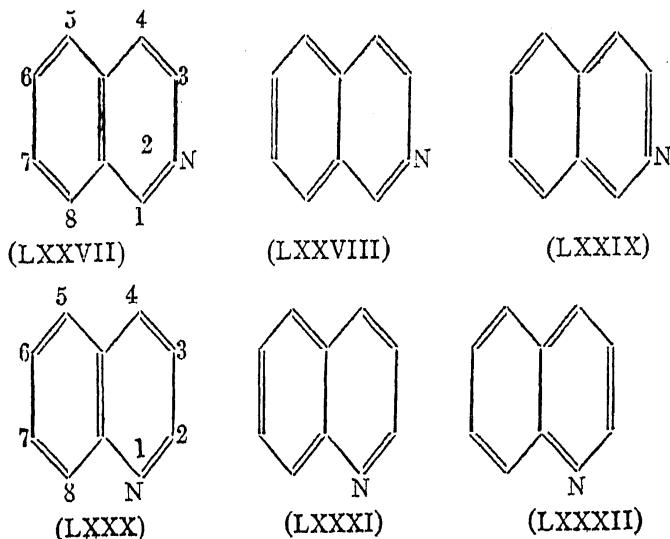


compounds (Orndorff, *et al.*⁷⁶; Sandin *et al.*⁷⁵) Further in tetrabromo-fluorescein and 4:5-dibromo-2:7-dichlorofluorescein, the 4 and 5 bromine atoms alone were found to be reactive (Sandin, *et al.*⁷⁵). The dinitration of fluorescein again yielded the 4:5-dinitro compounds (Hewitt, *et al.*⁷⁷) and the formation of bis-azo-dyes from fluorescein involved the same two positions (Irgraffia⁷⁸). All these suggest structures rigidly fixed as shown in (LXXI) for the xanthone system.

Quinoline and Isoquinoline

Chemical work relating to these systems was done as early as 1922. Three structures are possible for iso-quinoline (LXXVII to LXXIX). The work of Mills and Smith⁷⁹ showed that the methyl group in 1-methyl-iso-quinoline was reactive but not the methyl in 3-methyl-iso-quinoline. Similarly a chlorine atom in the 1-position was easily replaced by hydrogen on treatment with red phosphorus and hydriodic acid but not when it was present in the 3-position. These prove the existence of a double bond between positions 1 and 2 in isoquinoline and of another double bond between 3 and 4. Regarding the nature of the common link and of the bonds in the benzene part in iso-quinoline positive evidence is lacking, but it may probably be safe to assume that (LXXVII) is the closest approximation to the true structure of the molecule.

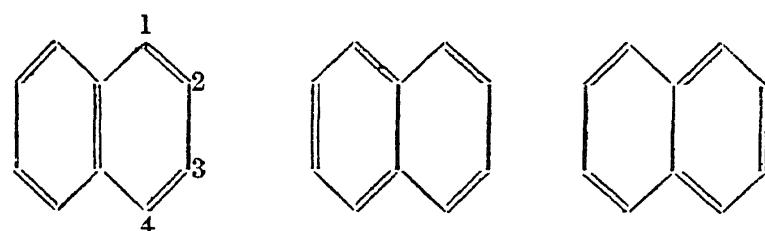
Mills and Smith⁷⁹ were of the opinion that in quinoline also the distribution of bonds should be just as in iso-quinoline, capable of representation by formula (LXXX). The theoretical structures are also of the same type as in iso-quinoline and their relative importance would be of approximately the same order of magnitude. Definite evidence was obtained by LeFevre and LeFevre⁸⁰ who concluded from the study of dipole moments of quinoline derivatives that the mobilities of the single and double bonds in quinoline derivatives are so diminished by ring fusion that the skeleton is best



formulated as (LXXX) and this statement seems to hold good except when dynamic isomerism is rendered possible as in the case of 2-methylquinoiline.

Discussion of Results and Conclusion

From the results presented in the foregoing pages it is clear that there has been a large amount of data of a chemical as well as physical nature relating to the question of the fixation of aromatic double bonds. It is possible that some of them might undergo modifications as a result of careful revision. This is due to the inherent difficulties of experimental technique in this line of work. Taking into consideration all factors there appears to be sufficient justification for concluding in favour of fixation of the double bonds. This fixation seems to be of varying degrees, being (1) very weak when chelate rings are the cause of fixation, (2) more prominent when heterocyclic rings are involved and (3) more or less rigid in polynuclear aromatic structures such as naphthalene, anthracene, etc. Apparently these statements may be objectionable from the physicist's point of view since it may be considered not to be in consonance with the discoveries that benzene and naphthalene are absolutely plane symmetrical structures. But the theory of resonance which has been developed and employed successfully during recent years seems to eliminate all difficulties. These ideas have been very adequately summed up by Pauling in his well-known recent book "*The Nature of the Chemical Bond*" (1st edition, pages 131-35). It has been shown that the stability and characteristic aromatic properties of benzene can be attributed to resonance of the molecule between two Kekulé structures, each of the six bonds in the ring acquiring half a double bond character. For naphthalene three stable valence bond structures can be formulated as below:



As a consequence there is brought about considerable difference between the characteristics of the different bonds. Thus the bond between 1- and 2-positions has $\frac{2}{3}$ double bond character whereas the one between 2- and 3-positions has only $\frac{1}{3}$ double bond character with the result the former behaves very much like a double bond whereas the latter has very little double bond characteristics. This results in an enormous difference in reactivity giving rise to the well-known phenomenon which has been described as 'fixation'. In the case of anthracene and phenanthrene the differences

between the bonds are even greater owing to the existence of larger numbers of valence bond structures. No correct prediction has obviously been attempted of the nature of the bonds when substituents which can produce powerful electromeric effects such as the hydroxyl, amino, bromo and nitro are introduced in these aromatic structures. It may however be expected that the differences between the bonds will be further accentuated. Similar explanations can be given of the effect of heterocyclic rings and of chelate rings. But this fixation can never be absolutely rigid since the other bonds also have very small but still appreciable double bond characteristics. And when the more reactive positions are protected, the feebler reactivity of the others is exhibited especially with powerful reagents and under favourable conditions.

The above remarks hold good even in the case of what is known as the "Mills-Nixon effect" where saturated carbon rings, attached to two ortho positions of a benzene ring, make it react as though the double bonds were fixed in one or the other of the alternative positions.

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