STERIC FACTORS IN THERMOCHROMISM OF SPIROPYRANS AND IN REACTIVITIES OF CERTAIN METHYLENE GROUPS

C. F. KOELSCH

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Substances whose visible light absorption changes markedly with temperature are said to be thermochromic. Dinaphthospiropyran (I) is a typical thermochromic compound and a representative of a group in which thermochromism is common¹ (1). It forms colorless solutions in cold xylene, but when these solutions are heated to about 100°, they become purple, and the color deepens as the temperature is raised. The changes are reversible. The colored solutions are stable to air, to hydrogen, and to hydroquinone; but they are bleached by piperidine.



Color development, obviously not caused by formation of free radicals, was first ascribed to the development of a quinoid compound (II) (2), but now a zwitterion (III) (3) is usually preferred. Bleaching by piperidine has been used as evidence against the quinoid structure, because quinones are not ordinarily decolorized by piperidine. Apparent parallelism in base strengths and thermochromic tendencies in a series of spiropyrans was believed to indicate the zwitterionic structure (4). Some basis for the contrary view has been found in the discovery that dipole moments of thermochromic spiropyrans do not change significantly with temperature (5), but in the absence of information as to concentration of colored substance in hot solutions, it appears that deductions based on physical properties of such solutions are apt to be misleading.

It has been suggested (6) that resonance theory may "explain the stability of the zitterions", whereas "the lowered stability of the spirans (I) may be due to their non-planar configuration interfering with the development of resonance."

In the present paper the results of detailed applications of resonance theory to thermochromic spiropyrans are presented. With the aid of reasonable assumptions it is possible to account for otherwise puzzling effects brought about by

¹ Thermochromism in bianthrones was shown by Grubb and Kistiakowsky [J. Am. Chem. Soc., 72, 419 (1950)] to involve diradical formation in non-planar molecules, transition between singlet and triplet states requiring no detectable activation energy. The chemical evidence collected in the present paper indicates that in spiropyrans the phenomenon has a different cause.

substitution. Also it becomes apparent that base strength and tendency for a spiropyran to be thermochromic are affected by a common steric factor.

If a spiropyran molecule (I) suffers a properly oriented and sufficiently energetic collision, a twisting stress will be set up at the spiro atom. If there is a structure of not too different energy content that can be formed by not too improbable atomic motions, rearrangement to this structure may take place,² and the rearrangement will be reversible.

It may be assumed that a resonance hybrid of II and III (and other minor forms) is the structure that fulfils the requirements noted.³ Then, since formation of II or III alone requires more energy than formation of the hybrid, when hybridization is prevented, rearrangement is also prevented. Two factors which tend to prevent hybridization will be noted in the present discussion.

Resonance is hindered if the extreme contributing forms differ much in energy. Dibenzospiropyran (IV) is not thermochromic, for ring opening involving resonance structure V, would disturb the aromatic system of a benzene ring. Such



disturbance in benzene is effected with more difficulty than a similar disturbance in naphthalene, as evidenced by the oxidation potential of *o*-benzoquinone (0.833 v.) (7), and that of β -naphthoquinone (0.576 v.) (8), or by the relative ease of electrophilic attack on phenol and on β -naphthol. Benzonaphthospiropyran is thermochromic, and the present considerations indicate that the colored material in its hot solutions must be all naphthoquinoid (VI) and contain none of the benzoquinoid isomer (VII).

Resonance in a conjugated system requires that all the atoms concerned be in a plane. In a system like Ia \rightleftharpoons IIa \leftrightarrow IIIa, any hindrance to complete planarity of the resonance hybrid is a hindrance to its formation and therefore a stabilizing factor for Ia. This explains the long-known lack of thermochromism in 3,3'-dialkylated dinaphthospiropyrans, VIII, (9) for in the related resonance

 2 Or, simply, in the proper substance, energy of activation for rearrangement will be low. An interesting demonstration that the reverse of the color developing change requires a small but appreciable activation energy may be made. About 20 mg. of paraffin wax and 2 mg. of dinaphthospiropyran are put into a long m.p. tube, heated to 200°, and mixed. The resulting deep purple solution fades to white when it is allowed to cool to room temperature, and no further change is seen when it is more strongly cooled. If, however, the hot tube is removed from its heating bath and quickly plunged into Dry Ice and acetone, it becomes pale blue. The blue color is stable at low temperature, but fades completely in about 30 seconds when the tube is brought to room temperature.

⁸ Visible light absorption by the colored compound is probably dependent on the resonance II \leftrightarrow III, but absorption spectra, which might give information on this point, have not yet been examined.

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hybrid, IX, crowding occurs not only between the two alkyl groups, but also between R' and quinoid oxygen. The approximate distance between C_{α} in R' (in IX) and O is 1.5 Å, whereas the usual closest approach of unbonded CH₃ and O is 3.4 Å (10). It may be objected that structures X or XI will be formed



rather than IX. Actually, however, X also represents a strained structure; and XI, also strained, can result from VII only by a sequence of complex and syn-



chronized, and therefore improbable motions.⁴ The steric requirements are diagrammed in structures VIIIa–XIa.

⁴ A substance of structure IX may exist in eight stereoisomeric planar forms, corresponding to two possible orientations about each of the three carbon-carbon bonds connecting the ring systems. The middle, single bond must be *trans* to avoid interference between the rings, thus inverted from VIII. Structures IX, X, and XI are then three of four possible forms, representing two types of interference between R' and the quinonoid ring. The improbability of XI presumably rests on the circumstance that the right-hand bond, leading to the naphthalene system, also is inverted from VIII.

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Such considerations are of interest also when applied to 3- and to 3'-methylbenzo- β -naphthospiropyrans, XII and XIV. The former is thermochromic, for its ring-opened form (XIII) is flat without strain; but the latter, XIV, is not thermochromic, for steric requirements of the methyl group prevent structure XV from forming.



Another interesting illustration of the necessity for planarity in the resonance hybrid is afforded by the diminishing tendency for thermochromism in the series XVI, n = 2,3,4 (4, 11, 12). Here the five-membered ring (XVII, n = 2) favors a flat structure⁵, whereas a puckered ring with more than five members (XVI, n = 3) hinders it (XVIa).



The necessity for planarity that influences thermochromism affects also the basicity of a spiropyran. The ion formed by combination of a spiropyran with a proton owes part of its stability to resonance as in XVIII, R = H, a resonance which requires the molecule to be flat. Highly hindered spiropyrans have not been observed to form salts at all (4, 13) and often such a spiropyran, for example the one corresponding to XVIII, $R = C_{s}H_{s}$, precipitates directly from a mixture of salicylaldehyde, ketone, and hydrochloric acid (14). Many non-thermochromic spiropyrans are such not because they are weakly basic, but rather they are at once weakly basic and non-thermochromic because of restrictions on planarity.

⁵ It is noteworthy that in XVIIa there evidently is little hindrance between the fivemembered ring (\mathbf{R}') and the quinonoid ring. Even XVI shows weak thermochromism.

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Ring opening when a dibenzospiropyran is converted into a salt does not, however, involve serious disturbance of a benzenoid system. And thus basicity and thermochromic tendency are not always directly related. A salt is not necessarily a protonated form of a *naphthoquinoid* structure, but may be related to an alternative *benzoquinoid* form. For instance, XIV is not thermochromic, but it appears to be just as basic, forming salt XIX, as its thermochromic isomer XII.



Experiments described in the present paper were designed to test the main assumption made above, that the tendency of a spiropyran to exist in a colored form is directly related to the ease with which the molecule can lie in a plane. In order that centers of undisputed classical basicity might be involved, quinoline derivatives were studied.

When the preparations of the desired compounds were being carried out, a new type of steric inhibition of resonance was encountered. Quinaldine methochloride reacted readily with salicylaldehyde to form the expected product, XX, but 2ethyl-3-methyl-, and 2-benzyl-3-phenyl-quinoline methochlorides, XXI, were



completely inactive towards salicyaldehyde. Resonance XXII \leftrightarrow XXIII is inhibited when R is larger than hydrogen, because the lateral substituent R has insufficient room⁶ to enter the plane containing the nuclear substituents R and CH₃.

The same steric inhibition of methylene activity affects the behaviors of cycyclopentenoquinoline—and tetrahydroacridine methochlorides. The former, XXIV, with its normally flat five-membered ring, yields XXV readily, and is therefore very reactive towards salicylaldehyde. The latter, XXVI, with its normally puckered six-membered hydroaromatic ring, yields XXVII with diffi-

⁶ The unreactivity of the quinolinium salts (XXI) depends on the presence of substituents at both the 1 and 3-positions, so that the 2-group has no way to turn. The parent bases hence undergo condensation. However, if the 2-substituent is attached by a secondary carbon atom, hindrance obtains in the base also [Koenigs, *Ber.*, **34**, 4322 (1901)]. culty, and therefore requires vigorous conditions in its reaction with salicylal-dehyde.⁷

In spite of the apparently close similarity in the structures of the two compounds, the salicylal derivatives of the last two quinolines show a remarkable difference in behavior towards base. This difference is explicable on the basis of the steric considerations developed for the spiropyrans.



Salicylalcyclopentenoquinoline methochloride (XXVIII) yields a betaine when it is treated with ammonia. This betaine, bronze needles with a blue streak, m.p. 175° dec., is nearly insoluble in benzene. Its solution in chloroform is deep green, in alcohol deep purple. Such properties demonstrate that it has the structure assigned, XXIX.



Salicylaltetrahydroacridine methochloride, XXX, yields a red-purple precipitate with dilute ammonia, but this precipitate becomes colorless during two hours at room temperature in contact with its mother liquor, or at once when it is moistened with an organic solvent. The product, transparent colorless prisms, m.p. 150°, is easily soluble in benzene, and its solutions are colorless. The properties of this substance indicate that it has structure XXXI. It is non-polar because it contains a puckered ring, whereas its homolog, XXIX, is polar because it is flat.

EXPERIMENTAL

2,5-Disubstituted quinolines were prepared through the Pfitzinger synthesis. A mixture of 40 g. of isatin, 56 g. of dibenzyl ketone, 15 g. of sodium hydroxide, and 180 ml. of 50%

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⁷ The qualitative unreactivity of methyltetrahydroacridinium salts compared to methylcyclopentenoquinolinium salts has been remarked previously [Petrow, J. Chem. Soc., 18 (1945); Lal and Petrow, J. Chem. Soc., 1895 (1948)].

alcohol boiled five hours, gave 78 g. of 2-benzyl-3-phenylcinchoninic acid (16). When 66 g. of the acid was melted with 1 g. of copper acetate and distilled at 30 mm., a crude base was formed whose picrate (53 g.), purified by crystallization from alcohol, furnished 27 g. of nearly colorless 2-benzyl-3-phenylquinoline. This was converted into 2-benzyl-1-methyl-3-phenylquinolinium methosulfate by warming it with 13 g. of methyl sulfate in 50 ml. of benzene; yield 30 g.; 78%; m.p. 193-195°.

Anal. Cale'd for C24H28NO4S: C, 68.4; H, 5.5.

Found: C, 68.7; H, 5.8.

The bromide, obtained from the methosulfate by precipitation with potassium bromide formed fine needles from ether-alcohol, m.p. 201° dec. Concordant analytical figures were not obtained, because the crystals were solvated, and complete removal of solvent left a partly decomposed hygroscopic residue. The bromide, however, yielded pure 2-benzyl-1methyl-3-phenylquinolinium picrate, yellow needles from dilute alcohol, m.p. 142-143°.

Anal. Calc'd for C29H22N4O7: C, 64.9; H, 4.1.

Found: C, 65.1; H, 4.3.

2-Ethyl-3-methylcinchoninic acid, from diethyl ketone and isatin in 35% yield (17), gave 2-ethyl-3-methyl-quinoline; yield 80%. Five grams of this was converted to a methosulfate, which was dissolved in water and treated with ether and sodium hydroxide. The ether solution of the yellow oily pseudo-base was separated and extracted with dil. hydrochloric acid; the resulting 2-ethyl-1,3-dimethylquinolinium chloride formed colorless crystals (3.4 g.) from alcohol-ether, m.p. 195° dec., but it was solvated and gave no significant analytical figures. Precipitation of an aqueous solution of the chloride with ammonium picrate gave 2-ethyl-1,3-dimethylquinolinium picrate, yellow needles from dil. alcohol, m.p. 131-132°.

Anal. Cale'd for C19H18N4O7: C, 55.2; H, 4.4.

Found: C, 55.6; H, 4.6.

2,3-Cyclopentenocinchoninic acid, from cyclopentanone in 80% yield (18), gave a 60% yield of 2,3-cyclopentenoquinoline. Five grams of the latter gave a methyl sulfate addition product that was converted through the pseudo-base (yellow crystals that blacken rapidly in air) into 1-methyl-2,3-cyclopentenoquinolinium chloride, solvated grey needles that sintered at 140°; m.p. ca. 170° dec. Again satisfactory analytical figures were obtained only from the corresponding 1-methyl-2,3-cyclopentenoquinolinium picrate, yellow-green needles, m.p. 143-145°.

Anal. Calc'd for C₁₉H₁₆N₄O₇: C, 55.4; H, 3.9.

Found: C, 55.9; H, 4.1.

1,2,3,4-Tetrahydroacridine-9-carboxylic acid, from cyclohexanone in 85% yield (19), gave a 66% yield of 1,2,3,4-tetrahydroacridine. Through the methyl sulfate addition product and the yellow crystalline pseudo base, there was obtained a yield of 68% of 9-methyl-1,2,3,4-tetrahydro acridinium chloride, solvated crystals, m.p. 135–140°, that did not give a satisfactory analysis. The quaternary picrate formed yellow needles, m.p. 135–137°.

Anal. Cale'd for C20H18N4O7: C, 56.4; H, 4.2.

Found: C, 56.6; H, 4.4.

Salicylalquinaldine methochloride and the related betaine. A solution of 0.5 g. of 1-methylquinaldinium chloride, 0.4 g. of salicylaldehyde, and 0.1 g. of piperidine 5 in ml. of alcohol was boiled for five minutes, made slightly acid with alcoholic hydrogen chloride, and mixed with ether. The crystalline precipitate was recrystallized from dilute hydrochloric acid, giving 0.6 g. of orange-brown prisms, m.p. 236-237° with darkening and gas evolution. The salt did not appear to change when it was dried at 100°. [Compare (15)].

Anal. Cale'd for C₁₈H₁₆ClNO: C, 72.6; H, 5.4.

Found: C, 72.7; H, 5.7.

A dilute aqueous solution of the salt was yellow-brown; it became reddish purple with ammonia. A solution of 1.5 g, of the salt in 20 ml, of water gave a bulky precipitate of purple-bronze needles when it was treated with ammonium hydroxide. This was washed well with water and dried for two weeks at 20° over sulfuric acid. The betaine sintered at 150° and

melted at about 165° ; it was insoluble in water or benzene, but gave a blue solution in chloroform.

Anal. Calc'd for $C_{18}H_{15}NO + H_2O: C, 77.5; H, 6.1.$

Found: C, 77.9; H, 5.9.

Salicylalcyclopentenoquinoline methochloride and the related betaine. A solution of 0.5 g. of cyclopentenoquinoline methochloride, 0.4 g. of salicylaldehyde, and 0.1 g. of piperidine in 5 ml. of alcohol was boiled for five minutes, acidified with hydrochloric acid, and treated with ether. The black oily product crystallized during three days, and then formed orangebrown prisms (0.4 g.). The salt tended to separate as an oil, but slow cooling of its solution in dil. hydrochloric acid gave brown prisms that darkened at 215°; m.p. ca. 223° dec. It was dried at 100° and 20 mm. for six hours.

Anal. Calc'd for C₂₀H₁₈ClNO: C, 74.2; H, 5.6.

Found: C, 74.0; H, 5.9.

A solution of 0.27 g. of the methochloride in 5 ml. of warm water was treated with an excess of ammonium hydroxide. The resulting precipitate, bronze-purple needles and plates, was washed well with water, acetone, ether, and benzene, and dried over sulfuric acid at room temperature. The product had the appearance of red phosphorus, and melted immediately with decomposition when it was put in a bath at 140°. For analysis it was dried two hours at 100° and 20 mm. Its appearance was then unchanged, but it had m.p. ca. 175° dec. It was slightly soluble in acetone, giving a green solution, easily soluble in chloroform or alcohol, giving deep blue-green and deep red-purple solutions respectively.

Anal. Cale'd for C₂₀H₁₇NO: C, 83.6; H, 5.9.

Found: C, 83.3; H, 5.9.

Salicylaltetrahydroacridine methochloride and the related spiro compound. A solution of 0.5 g. of tetrahydroacridine methochloride, 0.8 g. of salicylaldehyde, 0.2 g. of piperidine, and 0.1 g. of acetic acid in 5 ml. of dry butyl alcohol was boiled for three hours, then acidified and steam-distilled. Cooling the residual solution gave 0.02–0.13 g. of the desired product, yellow crystals, and from the mother liquor much unchanged tetrahydroacridine methochloride was recovered. The salicylal derivative formed fine yellow needles from dil. hydrochloric acid, m.p. 222–226° dec. It was dried for eight hours at 100° and 20 mm.

Anal. Cale'd for C₂₁H₂₀ClNO: C, 74.7; H, 5.9.

Found: C, 74.7; H, 6.1.

A solution of 0.1 g. of the salicylal derivative in 2 ml. of water gave a red-purple crystalline precipitate with dilute ammonia. A portion became nearly white when it was left for two hours; another gave a colorless solution immediately in benzene. Two crystallizations from benzene-ligroin gave 60 mg. of silver-grey prisms, m.p. 148–150°; the spiran was taken up by alumina as a dark red complex, but it was partly decomposed in this process and partly held too firmly to be eluted with acetic acid. Completely colorless prisms, m.p. 150° to a faintly yellow liquid, were obtained by treating a benzene solution of the compound with a small amount of charcoal. It was dried at room temperature over sulfuric acid.

Anal. Calc'd for C₂₁H₁₉NO: C, 83.8; H, 6.3.

Found: C, 83.9; H, 6.6.

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SUMMARY

Thermochromism, the reversible development of color which occurs when certain compounds are heated, appears to be caused in spiropyrans by partial ring opening. The colored substance derived from a spiropyran is a resonance hybrid of a quinoid and a zwitterionic form. Such thermochromism is inhibited by structural factors that diminish hybridization, steric hindrance to planarity, and disparity in energies of the canonical forms.

Methylene activity in quinaldinium derivatives requires that any substituent on the α -methyl group be able to enter the plane of the quinaldine ring. Examples supporting this view are presented.

Striking differences between the salicylal derivatives of cyclopenteno- and cyclohexeno-quinoline methochlorides are ascribed to the tendency of a fivemembered ring to be flat, and of a six-membered ring to be puckered.

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