A THEORETICAL INVESTIGATION OF THE MECHANISM
OF PHOTOCHROMISM OF CHROMENES AND SPIROPYRANS

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A semiempirical quantum chemical method was used to investigate changes in the electron structure of chromenes and the probable direction of displacement of atoms after excitation. The difference in participation of the singlet and triplet states in the photoreaction and the role played by excited states in bioanalogical processes occurring in natural chromenes are discussed.

The reversible photoactivated splitting of the CH_2—O bond in molecules with the pyran structure is known to occur in synthetic photochromic systems, such as spiropyrans (compounds containing the $2H$-pyran ring in which the C^2 carbon atom participates in the spiro bond), which are used in technical applications as filters or for recording information[1]. Also, many natural compounds containing the pyran ring, especially $2H$-chromenes and chromenocoumarins, participate in photoregulated processes which occur in the nature on the molecular level. The photochromic and luminescent properties of alloevodionol, evodionol, evodione, lapachenole, xanthyletin, and of other natural compounds with the chromene structure have been studied in a paper by Kolc and Becker[2], in which the participation of triplet states in the photochromic cycle was proved by photosensitization studies.

It is quite likely that especially the chemically more active open forms, which are formed after irradiation of the above compounds with UV light, participate in the photoregulation of biological processes in plants. However, open forms characterized by absorption in the visible region are not stable, returning back into closed forms after some time.

It is known that in the biosynthesis of $2H$-chromenes an important role is played by phenols with the o-(3-alkyl-2-propenyl) chain I (ref.[3,4]), which stand in close chemical connection with the open o-quinoid structures of chromenes. The synthesis of chromenes *in vitro*[5,6] confirms that the biosynthesis of numerous chromenes very likely proceeds by route of cyclodehydrogenation of o-(3-alkyl-2-propene)phenol through the quinoid structure.

On the other hand, Fourrey and coworkers[6] showed that the synthesis of the biogenetic type might be realized also by cyclization of allyl alcohol formed by oxidation of the side chain of the respective phenol. The oxidation may be enzymatic or may be photosensibilized. It has also been observed that phenol and allyl ethers are formed during the irradiation of chromenes in alcoholic solutions[7]. It seems quite obvious, therefore, that light conditions and acidity of the medium *in vivo* affect the biosynthesis or photoisomerization of chromenes.

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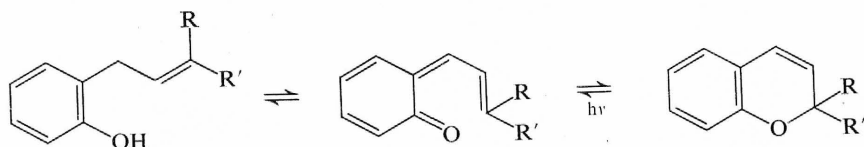
In this work we have investigated theoretically the primary photoinitiated process of formation of open coloured forms with the *o*-quinoid structure of 2*H*-chromenes. The effect of some substituents on the electron structure of chromenes has also been studied, and the different participation of the triplet and singlet excited states in the photochromic process has been examined.

THEORETICAL

In chromenes, relatively stable in their ground state, *i.e.* not exhibiting any observable thermochromism at low temperature, excited states are accompanied by adiabatic transition to geometrically different molecular conformations. A conclusive role in the prediction or interpretation of the process of photochemical reaction is played by a change in the electron structure of the molecule in the excited state. In this work, the electron structure of chromenes in excited states has been calculated using the CNDO/2S method[8,9]. The geometrical model of chromenes has been the same as in ref.[10], which is dealing with a theoretical investigation of the absorption and emission spectra of chromenes and spiropyrans. Atoms in the molecule of 2*H*-chromene are denoted in the usual manner; C^9 is the common carbon atom of condensed rings in the vicinity of the oxygen atom.

Basic information about the electron structure of the molecule is contained in the electron density matrix. A change in the density matrix caused by excitation corresponds to a change in the interatomic bonding indices, E_{AB}, expressed in Fischer and Kollmar's[11] partition scheme as the sum of contributions of the bonding resonance energy (E_{AB}^R), electron-core energy (E_{AB}^V), electron coulomb and exchange energy (E_{AB}^J, E_{AB}^K), and core-core repulsion (E_{AB}^N):

$$E_{AB} = E_{AB}^R + E_{AB}^V + E_{AB}^J + E_{AB}^K + E_{AB}^N . \qquad (1)$$

The total force acting on the atom A is then given as the vector sum

$$\mathbf{F}_A = - \sum_{B \neq A} \operatorname{grad} E_{AB} . \qquad (2)$$

Expressions for the interatomic bonding indices E_{AB} and for the force $\mathbf{F}_A$ are further used in the discussion of the photoreaction process in chromenes. Expression (2)

does not contain any information about the energy in the system, and cannot there-fore be thoroughly reliable in predicting the course of a thermodynamically controlled reaction, but it does provide information about the likely direction in which atoms are displaced by excitation. A similarly simplified procedure was employed in a paper by Labhart and coworkers[12], where however the two-centre energy (also denoted as E_{AB}) was approximated by a contribution from the resonance energy (E_{AB}^R), which predominates in expression (1) for the bonding index E_{AB}.

The interatomic bonding indices expressed by Eq. (1) are important in the qualita-tive characterization of the relative importance of excited singlet and triplet states for the process of photoreaction. In particular, it is important to know their relative magnitude with respect to the ground state. The weakening of a bond in excited states is quantitatively expressed by the lower absolute E_{AB} values in these states with respect to the ground state.

RESULTS AND DISCUSSION

Photochemical Activity in Various Excited States

The bonding indices E_{AB} of bonds directly participating in the photoinitiated ring--opening of pyran are given in Table I. Since in both benzochromenes and 6-methoxy--2H-chromene the electron transitions are basically of the same character as in un-substituted 2H-chromene[10], only interatomic indices in 2H-chromene are given.

Table I shows that excitation leads to a certain strengthening of the C^2—C^3 bond in all molecules, and in particular to an essential weakening of the C^3—C^4 bond, which has as a consequence breaking of the relatively weak bond O—C^2. This change in the electron structure is especially visible with the lowest triplet states of the type $^3(\pi\pi^*)$. Even in the lowest singlet states of the type $^1(\pi\pi^*)$ the weakening of the C^3—C^4 bond and strengthening of the C^2—C^3 bond are com-paratively important; moreover, the C^9—O bond is somewhat strengthened. On the other hand, if n- or π_0-nonbonding electrons localized on oxygen atoms of the pyran ring or on the aldehyde or nitro group as substituents are excited, there is virtually no change in the electron structure. We believe, therefore, that the photochemical reaction takes place either in singlet or in triplet states of the type $(\pi\pi^*)$. With the chromenes under study, photochemical reactions from the state $^1(\pi\pi^*)$ may be of importance only for unsubstituted chromene, 6-methoxychromene and benzo-chromenes. Photochromism of these compounds is weak, however. In accord with other authors[13], we are of the opinion that the extinction coefficient of open coloured forms of chromenes or spiropyrans is not too much affected by the substituents present, and that the weaker colourability is given by the low concentration of the coloured form.

The colouration of spiropyrans may be sensitized by donors of the triplet energy, which does not mean, however, that the triplet state participates directly in the photoreaction. In ref.[14] it was found that acceptors of the triplet energy, such as oxygen, did not inhibit formation of the open form of unsubstituted spiropyran. On the other hand, however, both sensitisation and suppression of formation of the coloured form by triplet energy donors or acceptors were observed[15] with 5,7-dichloro-6-nitro-1',3',3'-trimethylspiro-[2H-benzopyran-2,2'-indolin]. The presence of the triplet state as an intermediate state decomposing at the same rate at which the coloured form is formed has also been proved[16]; this is also corroborated by an investigation of the effect

TABLE I

Interatomic Indices, E_{AB}, in the Ground State and in the Lowest Excited States of Unsubstituted and Substituted 2H-chromene in Ohno Approximation of Coulomb Integrals

λ_{obs} [a]	λ_{calc}	State (transition)	E_{AB}			
	nm		C^2—C^3	C^3—C^4	O—C^2	C^9—O
			2H-chromene			
		ground	−27·42	−39·89	−38·57	−43·63
310	308	$^1(\pi\pi^*)$	−27·60	−37·52	−38·71	−44·10
	450	$^3(\pi\pi^*)$	−27·73	−34·39	−38·71	−43·74
	358	$^3(\pi\pi^*)$	−27·50	−38·03	−38·61	−43·81
	330	$^3(\pi\pi^*)$	−27·51	−37·67	−38·55	−44·59
			6-Formyl-2H-chromene			
		ground	−27·42	−39·90	−38·54	−43·79
(350)	367	$^1(n\pi^*)$[b]	−27·41	−39·90	−38·55	−43·69
328	304	$^1(\pi\pi^*)$	−27·59	−37·61	−38·68	−44·13
	420	$^3(\pi\pi^*)$	−27·72	−35·59	−38·73	−43·86
			6-Nitro-2H-chromene			
		ground	−27·41	−39·91	−38·51	−43·93
373	331 (417[c])	$^1(n\pi^*)$[b]	−27·41	−39·90	−38·51	−43·87
345	314 (391[c])	$^1(n\pi^*)$[b]	−27·41	−39·90	−38·51	−43·88
(295)	293 (297[c])	$^1(\pi\pi^*)$	−27·60	−37·49	−38·68	−44·18
	375 (472[c])	$^3(\pi\pi^*)$	−27·62	−37·23	−38·70	−43·84
	366 (627[c])	$^3(\pi_0\pi^*)$[d]	−27·41	−39·90	−38·51	−43·88
	333 (385[c])	$^3(\pi\pi^*)$	−27·56	−38·16	−38·65	−44·42

[a] Ref.[10]; [b] If monocentric integrals are neglected, the singlet-triplet splitting for $(n\pi^*)$ transitions is zero. *i.e.* $^3(n\pi^*) = {}^1(n\pi^*)$; [c] The Mataga–Nishimoto approximation of coulomb integrals. [d] π_0 denotes the non-bonding π orbital localized on oxygen atoms of the nitro group.

of high pressure on colour formation[17] and by the EPR signal corresponding to the triplet species[18,19]. It seems very likely, therefore, that photoinitiated splitting occurs mainly in the triplet state of the type $(\pi\pi^*)$, with molecules bearing electronacceptor substituents in position 6, for which the probability of population of the triplet states is raised by the effective intersystem crossing $^3(\pi\pi^*) \leftarrow {}^1(n\pi^*)$. In the case of 6-methoxychromene, the lowest triplet state is photochemically the most active one, while the active state of 6-nitrochromene is the second lowest triplet state, situated somewhat above the state $^3(\pi_0\pi^*)$. The state $^3(\pi_0\pi^*)$ is not photochemically active, but phosphorescence from this state can be observed[10]. The photochemically active triplet state situated higher (275 kJ/mol) than the phosphorescent triplet state (250 kJ/mol) was observed in the photosensibilization of photochromism of 6-nitro-1',3',3'-trimethylspiro-[2H--benzopyran-2,2'-indolin] in a polar medium[20].

Although participation of the triplet states during the photochromic cycle has been proved, it is still not clear to what extent the triplet states take part in direct excitation. Ref.[15] reports an experimental investigation of the triplet states in the photolysis of 5,7-dichloro-6-nitro--1', 3',3'-trimethylspiro-[2H-benzopyran-2,2'-indolin]; it was found that these were singlet states which predominate in direct photolysis. Also the fact that oxygen does not inhibit photochromism of unsubstituted spiropyran[14] indicates the predominant participation of singlet states.

Quantitative information about the tendency of atoms to change their position in singlet and triplet excited states with respect to the position of atoms in the ground state may be provided by the vector of force $\boldsymbol{F}_A$ acting on the atom A expressed by Eq. (2). The direction of displacement of atoms is shown graphically in Fig. 1. A comparison of the graphic representation of forces $\boldsymbol{F}_A = \sum\limits_{B \neq A} \mathrm{grad}\, E_{AB}$ with a change in the two-centre index E_{AB} with respect to the ground state indicates a quantitative and qualitative agreement between the two approaches. It also follows from Fig. 1, Table I, that from the viewpoint of the change in the electron structure there is no reason why even the lowest singlet states of the type $(\pi\pi^*)$ should not participate in photochromic changes in the direct photoreaction. We believe, therefore, that in the case where the lowest singlet excited state is of the type $(\pi\pi^*)$ the singlet states participate in the photolysis, while in molecules with an effective intersystem crossing of the type $^1(\pi\pi^*) \rightarrow {}^3(n\pi^*)$ or $^1(n\pi^*) \rightarrow {}^3(\pi\pi^*)$ also the triplet states take part in it. Since no fluorescence from the state $^1(\pi\pi^*)$ has been observed with chromenes and spiropyrans, a pronounced nonradiative degradation probably occurs from this state into the ground state, and photolysis from the singlet state overlaps that proceeding *via* the triplet state. The relatively weak colourability of chromenes and spiropyrans unsubstituted or carrying electrondonor groups, and the pronounced colourability and phosphorescence of molecules carrying electronacceptor groups, especially —NO_2 group, are in agreement with the suggested mechanism.

Degradation of Spiropyrans

In ref.[21] a hypothesis has been forwarded about the importance of polarity of the $O—C_{\mathrm{spiro}}$ bond in the photochromism and stability of indolin-2'-spiropyrans. If the

TABLE II

Bonding Index (E_{AB}) and the Polarity of the O—C^2 Bond of Substituted 2H-Chromenes and the Rate of Photodegradation of Derived Spiropyrans. V number of flashes[21], σ Hammett's constant[13].

Substituent in position 6	E (C^2—O)	Charge density		V	σ
		C^2	O		
—NO$_2$	— 38·513	0·1261	— 0·2166	100	0·78
—CHO	— 38·549	0·1280	— 0·2259	950	0·55
—H	— 38·577	0·1292	— 0·2292	9 000	0·00
—OCH$_3$	— 38·616	0·1299	— 0·2340	8 000	— 0·76

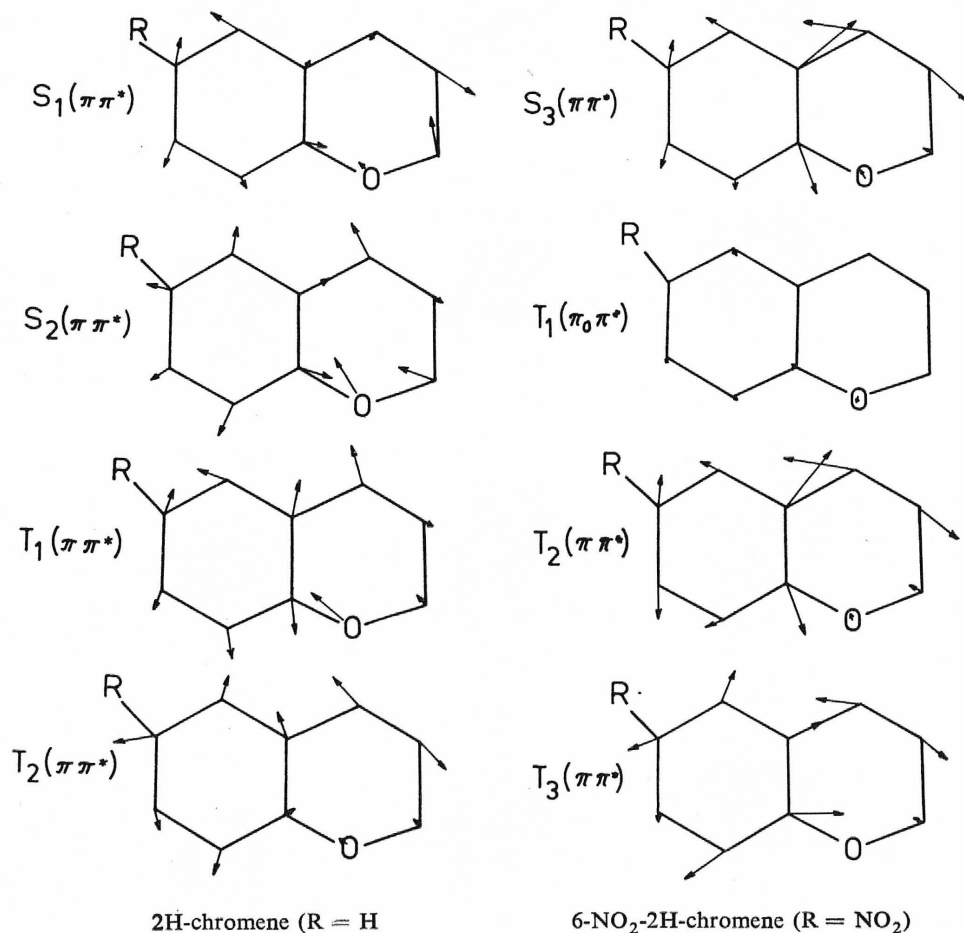2H-chromene (R = H   6-NO$_2$-2H-chromene (R = NO$_2$)

FIG. 1

The Directions of Atoms Displacement in Chromenes

O—C$_{spiro}$ bond is more polarized in the ground state, the heterolytic process of splitting prevails over the homolytic one. The homolytic splitting results in the formation of side products, and spiropyran undergoes photodegradation. From this standpoint it can be explained why photodegradation increases with increasing electronacceptor character of the substituent in position 6 (Table II).

The considerable polarity of the C^2—O bond in the ground state corresponds to the heterolytic splitting. Electrondonor substituents, which reduce the polarity of the O—C$_{spiro}$ bond, contribute to a higher light instability of spiropyran and to a lower so-called "fatigue" of the material with respect to the undesirable process of oxidation by the radical mechanism.

Photochromism of Natural Chromenes

The application of chromenes as triplet photosensibilizers in the inhibition of insecticide activity and in regulating other biological reactions indicates the considerable importance which triplet states may have for processes occurring on the molecular level. The energy of the photochemically active triplet state of natural chromenes lies[2,22] near 250 kJ/mol. Triplet energies determined from sensitization studies lie approximately at the same level.

The structure of chromenes investigated in this work is very similar to some natural chromenes; for instance, 6-methoxy-2H-chromene is very close to lapachenole, which is photochromic also at room temperature, and to ageratochromene. The character of electron spectra of these compounds is very similar (lapachenole, λ_{max} = = 357, 273 and 220 nm, ageratochromene λ_{max} = 322 and 278 nm). It may be expected, therefore, that the mechanism of photochromism in natural chromenes is similar to that of model chromenes.

The different properties of closed and open forms of natural compounds with the pyran structure may be reflected in a photoregulated control of the conformation of biomolecules and of the ability to catalyze some biochemical reactions, due to the fact that the affinity towards the proton exhibited by closed and open forms is completely different, thus affecting the acidity of the medium. The electrocyclic splitting of the pyran ring is analogous to the photosynthesis of praecarcipherol, a vitamin D$_2$ precursor, from ergosterol[23]; it may be expected, therefore, that natural chromenes participate directly also in the photosynthesis of more complex molecules.

One of the possibilities of application of photochromism consists in the regulation of biological processes. Some progress in this respect is suggested by papers dealing with the activity of enzymes[24–26] photoregulated through photochromic inhibitors. Chromenes and spiropyrans investigated in this work are particularly suited for this puprose, since during the photochromic cycle they exist as different geometrical isomers and may affect the activity of enzymes, either stereospecifically or owing to conversion between the hydrophilic coloured form and the hydrophobic closed form. In this way, the system enzyme–photochromic compound may serve as a model of similar phenomena observed in the nature, especially photoperiodic rhythms of higher plants

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