Supramolecularity and Photodimerization of Isophorone: FTIR and Molecular Mechanics Studies

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The FTIR spectroscopic study of isophorone solvation in various media using the C═O group as the microenvironmental probe shows that in aprotic medium (cyclohexane) at least two forms are present, even at low concentrations: the monomolecular form and the aggregated forms (dimers and larger). In hydroxylated organic media (butanol), only monosolvated forms are present. In aqueous solutions, solvated species with various degrees of aggregation and hydration can be identified. Molecular mechanics studies show that isophorone, which is an α-enone, has a preference for an aggregated form over the monomolecular form. Further, the hydrogen atoms of a water molecule can take part in a stabilizing interaction with the carbonyl oxygen atoms of two isophorone molecules. The information on the solvation states (derived from FTIR spectroscopy) and on the nature of the supramolecular structures (calculated via molecular mechanics) have been correlated to the results of photodimerization. Finally, we propose a mechanism of photoreaction, based on the supramolecular structures which are flexible and therefore have a modifiable molecular structure and whose geometry is determined by the interactions with the medium.

Introduction

Molecules that bear an α-enone structure are of importance in biological phenomena involving photocycloaddition reactions.[1] To study their behavior in a biological environment, one can employ organized media such as micellar solutions or microemulsions, which serve as crude biomimetic models. The α-enone chosen for our study is 3,5,5-trimethyl-2-cyclohexenone (isophorone, **1**), whose reactivity is well-known.[2−5] Its irradiation in classical solvents results in three photodimers denoted as HT_s, HT_a and HH_a, based on head−tail (HT) or head−head (HH) conformation and syn (s) or anti (a) orientation (Scheme 1).

In previous studies,[6,7] we found that for a given concentration of isophorone the photodimerization in organized media is faster, the yield is better, and the reaction is more selective than in homogeneous nonaqueous solutions. We did not investigate the photodimerization in homogeneous aqueous solutions since isophorone was considered insoluble in water.[8] The high yields and regioselectivities observed in micellar media were attributed to an interfacial reactivity involving a combination of polarity effects, bringing substrate nearer one another and reorientation of substrate molecules.[9] It was proposed that isophorone would be concentrated continually at the interface, where it would react preferentialy.[6,7] Obviously no role was assigned to the aqueous phase. To fully understand the mecanism of photodimerization in organized media, it is necessary to determine the location of isophorone in the different microenvironments present in micellar and microemulsion systems and also study the reactivity in each of these environments. Of special importance is the fact that the solubility of isophorone in water measured in our laboratory is not insignificant but is 0.066 mol L^{-1}, which is sufficiently large to study the photodimerization even in homogeneous aqueous solution. Therefore, in this work, we conduct studies in cyclohexane, butanol, and water media, which are the constituents of the microemulsions and also reflective of the various microenvironments present in the organized media. Since isophorone has a carbonyl group, it can be used as a microenvironmental probe, by taking advantage of the hydrogen-bonding effects on the carbonyl vibrational frequency,[10] and IR spectroscopy can be fruitfully employed. The IR bands being very sensitive to microenvironments, frequency and intensity variations can be used to supply information on the system's various microphase structures.[11] We show in this study that FTIR allows us to identify different states of isophorone depending on the carbonyl group environment: monomer and aggregates of isophorone in cyclohexane, solvated isophorone molecular complexes in butanol, and isophorone hydrates in water. We have also conducted molecular mechanics studies to agree with the formation of the above kinds of supramolecular structures. We suggest that the results of photodimerization in the different media can be correlated to the supramolecular geometry of the structures present in those media.

Experimental Section

Reagents. The solvents for spectroscopy, cyclohexane, *n*-butanol, and methanol (Merck, spectroscopically pure), D_2O 99.8% (Spin et Techniques), were used as supplied. The water was distilled or double distilled. Isophorone, **1** (Aldrich), was distilled to purity as checked by gas chromatography (GC) and by ^1H NMR. Deuterated isophorone, **2**,[12] was prepared by isotope exchange using the method described in ref 15.

Photodimerization. The concentration of **1** in the reaction mixture was varied from 0.02 to 0.06 M in water; it was constant at 0.1 M in the other media. The reaction mix (after bubbling with nitrogen or argon for 30 min) was irradiated for 24 h (ambient temperature 25−30 °C) in quartz tubes in a RPR 100

[†] In memory of my mother.

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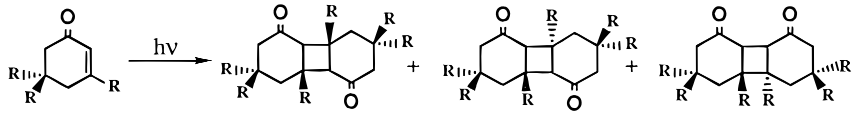
SCHEME 1



1
R = CH_3

HTs
Cis-syn-cis (Head to Tail)

HTa
HHa
Cis-anti-cis (Head to Tail and Head-Head)

Rayonet apparatus with 16 RPR lamps at 300 nm. The crystals that precipitated out during the reaction of **1** in water contained at least 90% of the HH_a photodimer. After elimination of the solvents from the reaction mixture, the residue was dissolved in $CDCl_3$ for gas chromatography analysis as well as their assay and that of the byproducts formed (Intermast IGC 112 chromatograph temperature programming from 100 to 220 °C; SE30 column). The GC identification of the products was done by comparison with the retention times of the pure photodimers.[6a,c] The percentage conversion of **1** was estimated using NMR by considering the integrated signal of the ethylenic proton with respect to that of all the other signals together. For the overall experimental conditions, the assays were accurate to within 5%.

FTIR Spectroscopy. The solutions of **1** and **2** in the various solvents were examined at thicknesses of 500, 100, and 50 μm (CaF_2 windows, one-piece cells) depending on the solute concentration and the band intensity. The spectra were obtained with a Brüker FTIR spectrometer (IFS 110) fitted with an MCT detector (mercury−cadmium telluride). The apparatus was continuously swept through with dry air, and the room temperature was maintained at 25 °C. Experimental resolution between 1710 and 1580 cm^{-1} was 2 cm^{-1}. Second-derivative spectra were obtained by applying the Deriv program twice consecutively to the original absorbance data. The spectra were recorded and the frequencies determined with a resolution of 0.5 cm^{-1}. An accumulation of 96 interferograms was apodized using the Happe Genzel function. Alternating recordings of the solvent and the solution data were made. This complemented the effect of the dry air sweep and gave spectra that were free of water vapor bands.

Molecular Mechanics. The molecular mechanics study of isophorone molecular association and of isophorone−water aggregates was performed by means of the MM2(87) and MM3(92) programs of Allinger et al.[16] Program MM2 enables the study of the relative positions of the two molecules or entities (not possible with MM3) but ignores the directional character of the hydrogen bonding, while the MM3 program takes it into account. The MM2 program includes two successive optimization methods: the simplex algorithm optimizes the orientation and the distance between the rigid molecules (or entities) taking into account only the intermolecular van der Waals energy and the electrostatic dipole−dipole interaction energy. Minimization is then pursued on the molecular geometries by letting the molecules (or entities) relax. The sequence simplex−molecular relaxation was then repeated a second time. The geometries obtained in this way were taken as the initial geometries, which were then optimized with the MM3 program. The final results are reported in this paper.

Results

I. Photodimerization. The generation of nπ* or $\pi\pi$* excited states by photolysis of isophorone solutions at 300 to 350 or 254 nm leads to mainly photodimers [2−4,6,7,17a,b,f] (Scheme 1) and a deconjugation product.[2b,5] If the conditions used for the photodimerization in organized media (24 h at $\lambda = 254$ nm) are employed, the irradiation of isophorone in cyclohexane, butanol, and water favors secondary reactions at the cost of photodimerization. But irradiation at 300 nm is less energetic and gives photodimers having the same HH/HT ratio (as at $\lambda = 254$ nm) while reducing secondary reactions.

TABLE 1: Isophorone Photodimerization in Various Media ($\lambda = 300$ nm)

medium	[Isophorone] (M)	% conversion[a]	% dimers[b]	HH/HT[c]
cyclohexane	0.1	40	25	30/70
butanol	0.1	5	70	70/30
H_2O	0.02	95	90	95/5
H_2O	0.06	90	85	90/10
H_2O[d]	0.02	100	100	99/1

[a] Conversion to photodimers and other byproducts after irradiation for 24 h at 300 nm, temperature 30 °C. [b] In relation to total products. [c] Ratio between HH and HT: cis-anti-cis photodimers. [d] Bubbled with argon.

The structures of isophorone photodimers have long been the object of discussion.[2b,3,4,17a−e] The structures have been identified as cis-anti-cis HH, cis-syn-cis HT, and cis-anti-cis HT, which are denoted, respectively, as HH_a, HT_s, and HT_a in Scheme 1. The fourth product, cis-syn-cis HH, has never been isolated, and its possible occurrence was attributed by default.[4a] In the present study, for all solvent media, on irradiation at 300 nm and at a temperature of 30 °C, we identified two photodimers HH_a and HT_a by gas chromatography. Near the HT_a signal, three other signals appeared as traces and can most probably be attributed to unidentified dimers.

The photodimerization results are summarized in Table 1, where the percent conversion of isophorone to photodimers and byproducts, percent of products that are photodimers, and the ratio between HH and HT photodimers are listed. The results show that the formation of HH photodimers is favored over HT photodimers with increasing polarity of the medium, in good accordance with the literature.[2b,3]

In cyclohexane, the HT_a photodimer is favored over the HH_a photodimer, but the yield of dimers is low (25%) because of the high formation of secondary products, essentially from the photodeconjugation of isophorone. In butanol, we obtain 70% yield of the photodimers preferentially containing the HH_a photodimer. However, only 5% of isophorone was transformed after 24 h irradiation, indicating the high photostability of isophorone in butanol. In water, the conversion of isophorone is nearly complete, and the photodimerization yield is at least 85% for solutions that are almost saturated with isophorone. Both photodimers with anti configuration have been obtained with a ratio HH_a/HT_a of 95/5. This high level of selectivity indicates that the molecules are “trapped” in the aqueous medium and forced into a configuration that leads to mainly HH_a.

II. Infrared Spectroscopy. The stretching band ($\nu_{C=O}$) of isophorone was found to be intense and asymmetrical in cyclohexane and water but symmetrical in butanol. Since the absorbance band is the sum of the absorbance contributions of several species,[18] the accuracy of the FTIR data enabled the decomposition of the vibrational spectrum into the contributions of distinct species. Fourier second-derivative [19] technique was

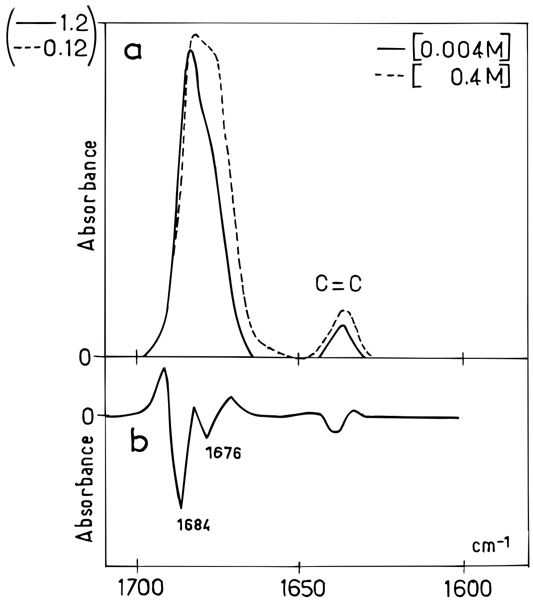


Figure 1. Spectra (a) and their second (b) derivative for different concentrations of isophorone **1**, in cyclohexane solution (---) 0.4 M, thickness 50 μm; (—) 0.004 M, thickness 500 μm.

employed for detailed analysis of the elementary band superimposition to give the carbonyl band.

1. Cyclohexane (Figure 1). Because cyclohexane is apolar and not polarizable, the solute−solvent interactions are limited to the van der Waals weak interactions. For concentrations of the substrate between 0.004 and 0.4 M, the C═O band is never perfectly symmetric. It shows a shoulder at the low frequencies, and from the second derivative one can identify two bands at 1676 and 1684 cm^{-1} (Figure 1b). The lower frequency of 1676 cm^{-1} is near that of the pure liquid state of the isophorone, 1664 cm^{-1}. Therefore, this lower frequency can be attributed to the aggregated forms. The frequency at 1684 cm^{-1} can thus be attributed to the carbonyl vibrator, which is relatively free from the influence of other molecules.

2. Protic Media. Hydrogen bond formation on the carbonyl oxygen elongates the C═O bond. This lowers the frequency depending on the magnitude of the hydrogen bond formation energy. With conjugated C═C−C═O systems, the bond occurs in the plane of the system and the stereochemistry is determined by the covalent contribution, which favors an angular arrangement (in the direction of a lone pair), compared to the electrostatic contribution, which rather favors a linear arrangement (along the axis of the carbonyl band). With isophorone the bond occurs in the direction of a free pair.[20a]

In butanol, we observe only a single band at 1655 cm^{-1}. This implies that irrespective of its monomeric and/or aggregated state, all the isophorone molecules must be complexed with butanol (so that the carbonyl group has the same environment and the hydrogen bonding lowers the frequency). In water (Figure 2) three elementary bands are observed with a maximum respectively at 1624, 1630 and 1636 cm^{-1}, their relative importance varying with the isophorone concentration.

The intensity of the spectral envelope of these elementary bands is not proportional to the solute concentration. Specially the intensity at 0.06 M is lower than twice the intensity at 0.03 M (Figure 2a). Spectral changes in the carbonyl stretching region can be attributed to aggregates with various degrees of aggregation and hydration.[20b] The maximum at 1624 cm^{-1} essentially appeared in the most diluted solution and the maximum at 1636 cm^{-1} in the most concentrated solution. We may consider that maxima at 1624, 1630, and 1636 cm^{-1} show the aggregates' size increasing when isophorone concentration increases in aqueous solutions from 0.03 to 0.06 M.

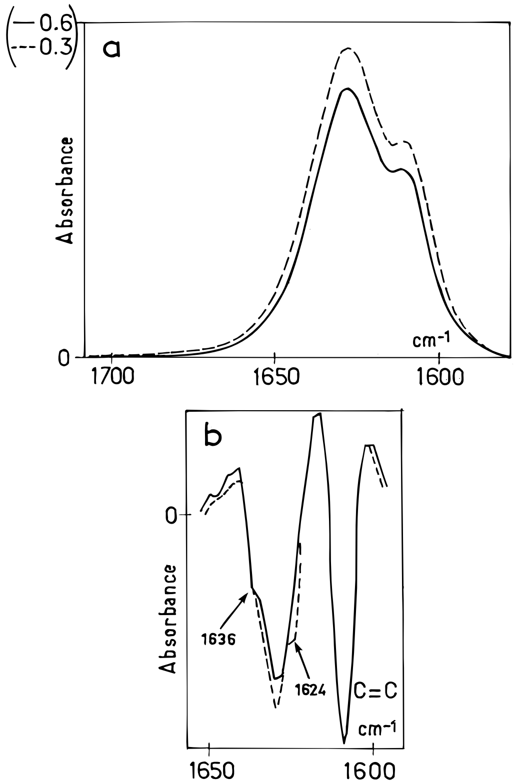


Figure 2. Spectra (a) and their second (b) derivative for different concentrations of isophorone **2**, in aqueous solutions (D_2O) (---) 0.03 M; (—) 0.06 M.

Water is a solvent that has the capacity to promote solute self-organization,[21a,b] given its characteristics (cohesion, polarity, supplier of hydrogen bonds). The solubility of isophorone in water is primarily the consequence of carbonyl group water solvation, with states having a high dipole moment being strongly solvated.[21c] Therefore, isophorone tends to aggregate in such a way as to decrease the contact between its hydrophobic regions and the neighboring water molecules. Further, the electrostatic repulsions will be attenuated by solvation related to bridging water microstructures, the specific water−solute interaction stabilizing the two converging carbonyl sites.[21d,22a,b] In view of both these factors, one may anticipate that the aggregate in water will be of the HH type rather than the HT type.

To summarize, FTIR spectroscopy has revealed different isophorone states depending on the microenvironment of the carbonyl group: monomer state (1684 cm^{-1}); aggregated state (1676 cm^{-1}); isophorone-butanol monomolecular complex (1655 cm^{-1}) involving monomers or aggregates of isophorone; and isophorone hydrates (1624, 1630, 1636 cm^{-1}) involving monomers or aggregates of isophorone with various degrees of aggregation and hydration.

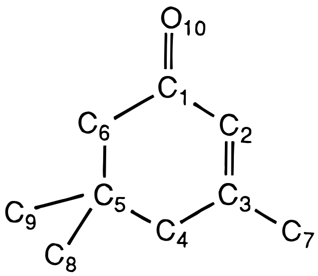
III. Molecular Mechanics. *1. Conformation of Monomolecular Isophorone.* For this study, we have numbered the heavy atoms as shown in Scheme 2. All the starting geometries (ring in the sofa conformation with the point of the back being C_4, C_5, or C_6, half-chair, or boat) converged to give a single sofa form where the point of the back is occupied by carbon C_5 (which bears two CH_3 groups) with a dihedral angle $C_2-C_3-C_4-C_5$ of 25° for both isophorone (whatever the dielectric constant of the medium) and deuterated isophorone. The calculated dipolar moment is 3.5 D.

TABLE 2: Structural Parameters of Dimeric Aggregates

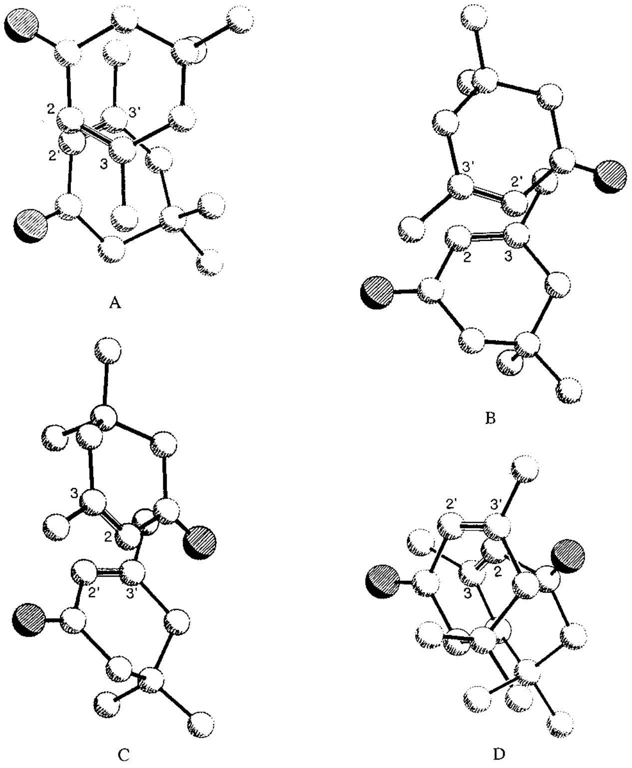
parameter	A	B	C	D
total energy lowering (kJ mol^{-1})	−14.6	−14.2	−10.9	−10.4
dipole moment (D)	5.07	1.37	2.19	1.89
type of association	HH	HT	HT	HT
expected photodimer[a]	HH_a	HT_a	HT_a	HT_s
d^b (Å)	4.33	3.90	4.98	5.03
distances (Å) 2−2′	3.57	3.77	4.25	4.10
3−3′	4.81	4.42	5.89	6.10
2−3′	4.46	4.04	4.92	4.88
3−2′	4.10	3.76	5.07	5.21
dihedral angles (deg) 2−3−2′−3′	123	−19	−43	−35
2−3−3′−2′	−51	159	128	130
angle between double-bond planes (deg)	60	31	27	31

[a] For HH type 2−3′ and 3−2′ bonds are not possible, whereas for HT type 2−2′ and 3−3′ are not possible, consistent with cyclobutane structures. [b] Distance between the double-bond centers.

SCHEME 2



SCHEME 3



2. *Study of Dimeric Isophorone Aggregates.* We studied the superimposition of two isophorone molecules, starting from the calculated conformation of each molecule in the isolated state. For 65 starting geometries, the calculations performed using the Simplex MM2 algorithm always led to structures with a total energy that was lower than twice the energy of an isolated isophorone molecule calculated by the same program. The association of two molecules, therefore, has a stabilizing effect.

We used MM3 to process the geometries obtained with MM2 for the two dimeric aggregates with the lowest energies produced by superimposing the rings (denoted A and B) and for the two dimeric aggregates of lowest energy obtained by superimposing the C=O groups (denoted C and D). The geometries resulting from the optimization using MM3 are only slightly different from those obtained by using MM2.

The lowering of the total energy with respect to the energy of two isolated isophorone molecules and the structural parameters obtained for these four dimeric aggregates are reported in Table 2. Scheme 3 illustrates these four dimeric aggregates (H atoms are omitted in all schemes). As this investigation was carried out with the aim of studying the photodimerization reaction of isophorone, Table 2 also presents the type of photodimer predicted (see, for example, photodimer HH_a[23] in Scheme 6) based on the geometry of the aggregates in the ground state.

3. *Study of Tetrameric Isophorone Aggregates.* From the four dimeric aggregates A, B, C, and D that we selected for study, we investigated 10 possibilities of two-by-two stacking, yielding tetrameric aggregates denoted E to N. For optimization with the simplex algorithm, the association between molecules denoted I and II made up the first dimer and the association between molecules III and IV made up the second dimer. One may note that, for a set of two molecules, the carbon atoms of the double bond are numbered 2 and 3 for the molecule denoted by the smaller roman numeral and 2′ and 3′ for the other. Schemes 4 and 5 visualize two of these tetramers (G and I). Table 3 summarizes the structural characteristics for the 10 different tetrameric aggregates considered. Also indicated are the types of photodimers predicted on the basis of the geometry of the tetrameric aggregates. Again, it is found that the total energy calculated for the stacking of four isophorone molecules is always lower than four times the energy of the isolated molecule, suggesting that the formation of tetrameric aggregates has a stabilizing effect.

4. *Study of Isophorone Interaction with One or Two Water Molecules.* In a molecular dynamics study about polyammonium host molecules, Wipff et al. showed that "although hydration cannot be attributed to a few water molecules, specific water-solute interactions stabilize convergent ammonium sites in the absence of counter ions and thus participate to preorganization of the host molecules".[22a] Moreover, a similar work about crown ethers, cryptands, and cryptates led these authors to the same result: "the role of bridging water molecules is again crucial, as in the stabilization of like charged ion pairs".[22c,d]

So we tried to show the existence of such microstructures between one (or two) water molecule and the A, B, C, or D dimeric aggregates. In the case of B, C, and D dimers (HT type), a water molecule may interact with only one C=O group. The calculations indicate the formation of hydrogen bond of length 2.07 Å and energy −16.8 kJ mol^{-1}. On the other hand, for the A dimer (HH type), optimizations lead to structures in which two hydrogen bonds (of the same energies) keep a water molecule bridging the two isophorone molecules. This result is obtained even if, for a starting geometry involving two water molecules, each water molecule is near a C=O group on the opposite side of the other isophorone molecule. Structural parameters of such association designated (P) (Scheme 6) are reported in Table 4.

To summarize, molecular mechanics agrees that isophorone is aggregated in the ground state. It shows the existence of

TABLE 3: Structural Parameters of Tetrameric Aggregates

parameter	E A and A	F B and B	G C and C	H D and D	I A and B	J C and A	K C and B	L C and D	M D and A	N D and B
total energy lowering (kJ mol$^{-1)}$)	−52.3	−45.6	−38.0	−35.1	−46.0	−41.4	−46.0	−37.2	−42.2	−37.6
dipole moment (D)	0.66	2.33	3.96	2.90	4.65	5.53	2.82	2.82	5.19	2.91
dimerization between mol. I and II (*I and III) and photodimer	HH$_a$	*HH$_s$	anc.HH +rot.[a]	anc.HH +rot.	HH$_a$	anc.HH +rot.	anc.HH +rot.	anc.HH +rot.	anc.HH +rot.	anc.HH +rot.
d^b(Å)	4.06	4.15	4.96	5.06	4.10	4.92	4.80	4.90	5.03	5.06
distances (Å) 2−2′	3.45	3.87	4.15	4.07	3.51	4.12	4.06	4.12	4.10	4.08
3−3′	4.74	4.43			4.76					
2−3′	4.38	4.91			4.41					
3−2′	3.99	3.71			4.04					
dihedral angles (deg) 2−3−2′−3′	124	179	−42	−37	124	−44	−47	−45	−36	−38
2−3−3′−2′	−50	−1	130	130	−50	127	125	125	129	129
angle between double-bond planes (deg)	55	53			81					
dimerization between mol. III and IV (*III and II) and photodimer	HH$_a$	*HT$_a$	anc.HH +rot.	anc.HH +rot.	HT$_a$	HH$_a$	HT$_a$	anc.HH +rot.	HH$_a$	HT$_a$
d (Å)	4.06	3.71	4.90	5.00	3.88	4.09	3.87	5.02	4.13	3.89
distances (Å) 2−2′	3.47	3.40	4.12	4.02	3.76	3.52	3.73	4.07	3.56	3.77
3−3′	4.73	4.42			4.42	4.74	4.42		4.79	4.42
2−3′	4.37	3.56			4.04	4.33	3.99		4.44	4.03
3−2′	4.01	3.87			3.74	4.10	3.76		4.08	3.76
dihedral angles (deg) 2−3−2′−3′	123	−16	−45	−42	−19	120	−18	−36	123	−19
2−3−3′−2′	−50	160	124	123	159	−52	160	129	−50	159
angle between double-bond planes (deg)	53	38			27	62	37		70	31
other ability for dimerization, no. of molecules and photodimer	II and IV HT$_s$	II and IV HH$_s$	II and III HT$_a$			II and III HH$_a$				
d (Å)	3.41	4.15	5.46			4.37				
distances (Å) 2−2′	3.34	3.97	4.48			3.84				
3−3′	3.90	4.34	6.55			4.91				
2−3′	3.43	3.61	5.32			4.12				
3−2′	3.47	4.99	5.60			4.92				
dihedral angles (deg) 2−3−2′−3′	45	−174	−4			179				
2−3−3′−2′	−129	4	174			−1				
angle between double-bond planes (deg)	10	30	22			40				

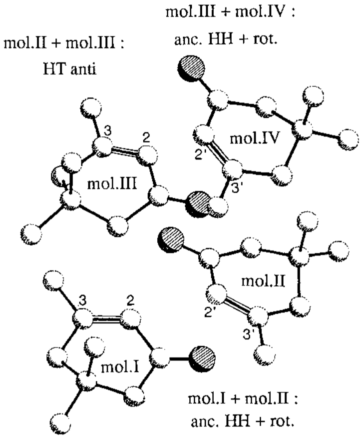
[a] Anchorage head−head + rotation. [b] Distance between the double-bond centers.

TABLE 4: Structural Parameters of P Association

H-bond[a] length (Å)		H-bond energy (kJ mol^{-1})		interatomic distances (Å)					dihedral angles (deg)		
$O_{10}\cdots H_a$	$O_{10'}\cdots H_b$	$O_{10}\cdots H_a$	$O_{10'}\cdots H_b$	2−2′	3−3′	2−3′	3−2′	d^b(Å)	2−3−2′−3′	2−3−3′−2′	Θ^c (deg)
2.07		−16.8		3.74	5.04	4.59	4.45	4.38	146	−29	56

[a] H_a and H_b refer to two hydrogen atoms of water which bond with the oxygen atoms of isophorone (Scheme 6). [b] Distance between the double-bond centers. [c] Angle between the conjugated bond planes.

SCHEME 4



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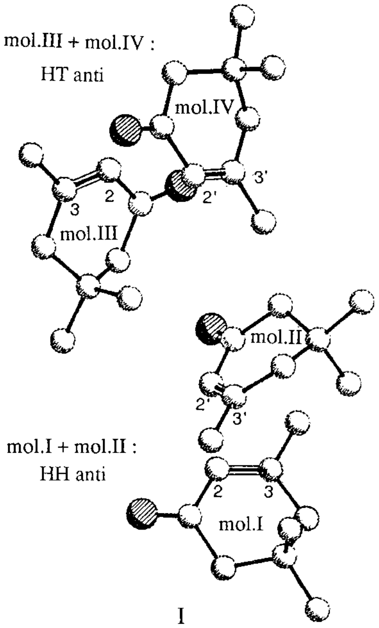
supramolecular structures characterized by the spatial arrangement of the isophorone molecules and by the nature of their interactions.[24] The possible occurrence of supramolecular structure, consisting of a water molecule bridging the two carbonyls of a HH isophorone dimer is also demonstrated.

SCHEME 5



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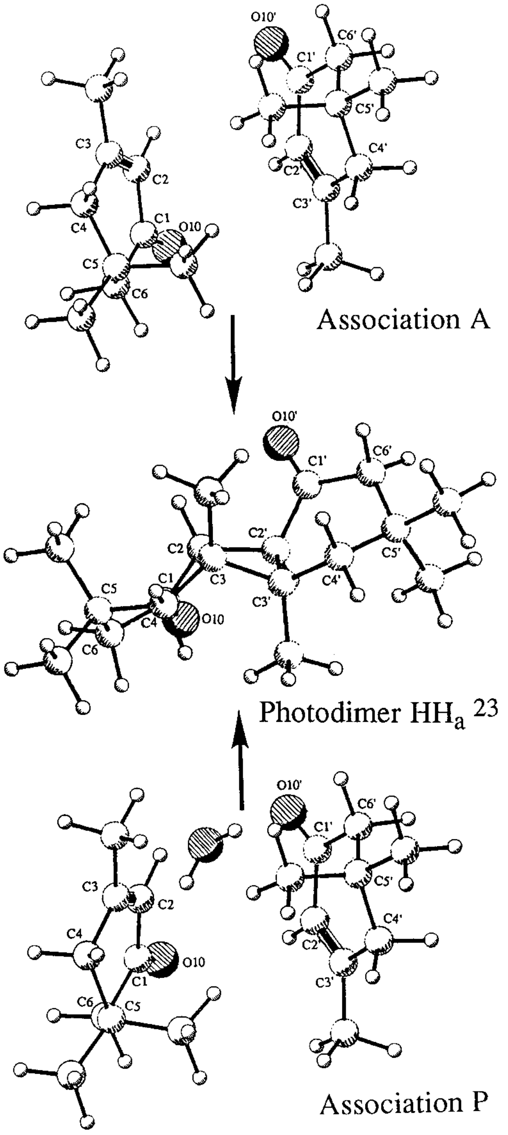
SCHEME 6



Discussion

It has been shown in the literature, for the case of the uracil derivatives, that the efficiency of the photodimerization is related to the presence of aggregates in the ground state. Also the multiplicity of the spin state depends on the nature of the solvent, the substituents, and the extent of aggregation in the ground state.[25] Since this important feature of aggregation is present in the case of isophorone, for which supramolecular structures have been identified, irrespective of the medium, we will use this as the fundamental information in order to explain the photodimerization results.[26] The key results (Table 1) are that the HH_a photodimer is clearly preponderant in polar medium. In contrast the HT photodimer is the dominant product in nonpolar solvents. The HT photodimer also forms in reduced proportion in polar solvents and in organized media.[6a,c] Further, in the case of HT photodimers, the HT_a type is always preferred over the HT_s photodimer at 30 °C.

I. Topochemical Control of Photodimerization. In an earlier molecular mechanics study,[23,27] we compared the relative stabilities and conformations of isophorone photodimers. The highest energies were observed for the HH photodimers. Further, the steric repulsion of the two methyl groups at position 5 (Scheme 2) leads to the strain energy of the HH_s derivative being 7.4 kJ mol^{-1} greater than that of the HH_a photodimer, explaining why the HH_s adduct has never been isolated. Therefore, if the reaction is controlled by the stability of photodimers, the isophorone photodimerization would have to give a mixture of HT_s and HT_a photodimers, HT_s being the most abundant, and not the HH_a photodimer. This theoretical prediction based on the stability of photodimers is clearly contradicted by the experimental results summarized above. This suggests that, irrespective of the reaction medium, the photodimerization is not controlled by the stability of photoproducts but must be kinetically controlled.[23]

One may notice that selectivity and stereospecificity of this photoreaction lead to photodimers HH_a and HT_a of dipolar moment respectively 5.08 and 1.03 D,[3] close to those of isophorone dimeric aggregates A and B, respectively 5.07 and 1.37 D (Table 2). Structural and topological factors are similar to those characterizing the solid-state photodimerization.[28] "The topochemical principle is a very useful tool for the solid state chemistry and it is capable of application in a variety of situations." [28e]

If we consider a kinetically controlled reaction, one can imagine topochemical control. For this to occur, the possibility of suitable orbital overlap must exist. The topochemistry principle in the solid state presupposes a "minimum movement" for the molecules or atoms.[9a,28a−c] The term "minimum movement" can be applied only to the displacements of the reacting atoms; movements for the rest of the molecule can be larger. The reaction can take place even when the double bonds are not perfectly parallell[28d] provided the distance *d* between the centers of the double bonds is between 4.2 and 4.7 Å.[28e] For nonplanar molecules, accommodation can occur through a change of conformation. This concept of dynamic preformation[28f] explains the photoreactivity of coumarin derivatives, which otherwise should have been photostable on the basis of the double-bond characteristics ($d > 4.2$ Å; angle 65°).[28g]

If we apply the above concepts to the four isophorone dimers (A, B, C, D; Scheme 3, Table 2), the orientation of the double bonds not being parallel, only the dimers A and B have a distance *d*, smaller than 4.7 Å and possess a reaction site (or even two) favorable for the HH_a (2−2′) and HT_a (3−2′ or 2−3′) photodimers, respectively. If we compare the geometry of monosolvated species P (Table 4, Scheme 6) with that of the dimer A, which anticipates HH_a (Table 3), we note that the distance, *d*, is slightly greater in the P complex but always lower than 4.7 Å. The C═C double bonds [dihedra (2−3•2′−3′) and (2−3•3′−2′)] take up the most favorable position for HH dimerization, and the reaction can always occur at the 2−2′ site. Thus, one can conclude that if the reaction is under topochemical control, either HH_a or HT_a photodimers will be formed.[29] Indeed this was observed in our experiments, confirming the topochemical control of photodimerization.

II. Role of Aggregation. In organic solvents, the interaction strengths of van der Waals associations in the ground state are weak, and therefore the aggregates can be destroyed. In cyclohexane, we have found (from FTIR) that the monomer form is always predominant. The photodeconjugation reaction, which is a unimolecular reaction,[5] is therefore favored in the apolar medium[2b,30] where the monomers are preponderant. This explains the low yield of photodimers in this medium (25%). In butanol, the specific solvation of the carbonyl group by hydrogen bonding stabilizes the monomers and inhibits the photodeconjugation reaction (Table 1).

In the aqueous medium, the supramolecular structure of isophorone with a bridging water molecule (aggregate P) determines the reaction selectivity. The trapped molecules in water medium must take a configuration leading essentially to HH_a (95%). As the isophorone concentration rises from 0.02 to 0.06 M, the percentage conversion of isophorone and the yield of dimers both slightly decrease and the formation of HT_a dimer slightly increases (Table 1). In this case, the compactness of the aggregates increases and the mobility of groups trapped inside the clusters is more and more reduced. Therefore, if we look at the model of tetrameric aggregates which can exist in a concentrated medium, these tetramers are precursors not only of HH but also of HT photodimers (Table 3 and, for example, Schemes 4 and 5). We can expect that the choice between a HH anchoring point followed by a rotation or a translation leading to HT is in favor of HT formation (e.g., Scheme 4). The intermediate excited states that could lead to HH (after rotation of one molecule with respect to the other around the 2−2′ axis) would become deactivated to return to the enone ground state. The intermediate excited states that could lead to HT would increase the proportion of HT or would themselves become deactivated. Therefore as the concentration of isophorone increases, the conversion of isophorone in 24 h and the HH/HT ratio should both decrease, as was indeed observed (Table 1).

III. Photodimerization Mechanism. The photodimerization of cyclic enones is very interesting owing to the complexity of its mechanistic potential.[1−3,31] The reaction mechanism may involve, in general, both triplet and singlet states, the lifetime of the singlet state being very short. When the molecule exists in aggregated forms, the proximity between two molecules permits photodimerization involving even the singlet states of short lifetimes. If, however, the molecule is nonaggregated, the probability of contact and photodimerization is small on the basis of the singlet states of the molecules, and hence only the triplet state is involved in the reaction mechanism. For example, in the case of photodimerization of 2-cyclopentenone and 2-cyclohexenone,[31a−c] the ratio HH/HT varies depending on the solute concentration. Two differing interpretations for this result have been given: (i) "the concentration effect is no more than a solvent effect" and only one triplet state is involved;[31a, c] (ii) "the very sensitive stereospecific dependence upon concentration suggests that more than one intermediate is involved in the dimerization". The triplet dimerization is involved at low concentrations of 2-cyclopentenone, but the singlet dimerization may be important at high concentrations.[31b]

In the case of coumarin (a "rigid" solute bearing an α-enone moiety), it was pointed out that "the state of aggregation is solvent-dependent and that it exerts a direct influence on the course of photodimerization" [31e] which "involves both singlet and triplet excited states".[31f]

The first detailed study[2b] of photodimerization of isophorone in many solvents suggested an enone reaction in one or two steps involving singlet or triplet states, the triplet state being more probable owing to the short lifetime of the singlet state. Mechanistic complexities are suggested by the following observations of Chapman et al.[3] Quenching dimerization studies lead to the conclusion that all photodimers are derived from the isophorone triplet. But the benzophenone photosensitization results cannot be accounted for by one isophorone triplet: the ratio of the rate constants k_{sens}/k_0 for head-to-head photodimerization is 3.43, while it is 2.40 for head to tail photodimerization (k_{sens} correspond to sensibilization by benzophenone and k_0 to direct irradiation). Therefore, Chapman et al.[3] proposed two alternative hypotheses: (i) One is the possibility of benzophenone triplet energy transfer to not only isophorone (I) but also a ground-state complex of isophorone (I_2). If $(I_2)^3$ gives predominently or exclusively HH_a photodimer, this could provide an explanation of the unexpected sensitization result. (ii) The other is the direct irradiation of isophorone and triplet energy transfer from benzophenone to isophorone to produce two triplet species ("structural or geometric isomers"), which in turn give rise to the observed photodimers.

We suggest that the presence of supramolecular structures, even at low dilutions, detected by FTIR, can explain the above sensitization results of Chapman et al.[3] The energy transfer can take place to monomolecular or aggregated isophorone states; Since the dimers A, B, C, and D appear as precursors of corresponding photodimers, their geometry can be linked to the initial excited-state structure. One may remember that the calculated dipolar moment of the isophorone dimers A and B are close to those of photodimers HH_a and HT_a. We can observe that for aggregate A leading to the HH photodimer the two triplet states will be identical, whereas for aggregates B, C, and D, which lead to HT photodimers, the two triplet states will be different.

Consequently the sensitization of photodimerization can be explained by a preorganization that favors the triplet excited states, leading to HH at the cost of HT. The latter (HT) arise either from singlet excited states or from excited triplet states of isophorone that are geometrically different from those that lead to the HH photodimer.

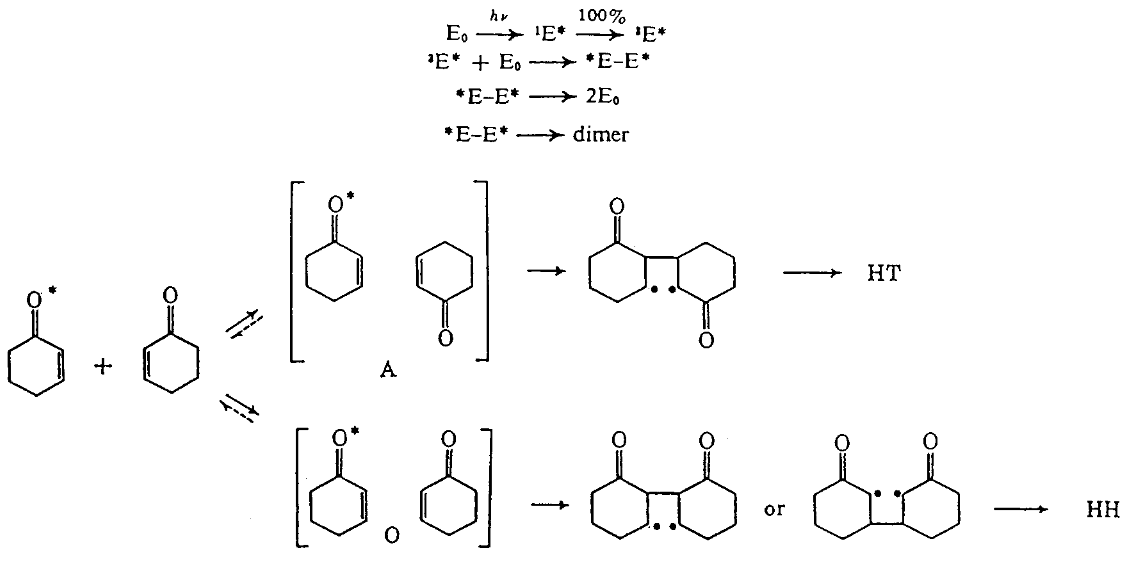
For aromatic molecules, a parallel arrangement of the two planes is preferred for singlet excited states. For triplet excited states, the two planar molecules can form a wide angle (110°), the optimum geometry being when the two molecules are at an angle of 70°, resembling the optimum arrangement of a van der Waals dimer in the gas phase.[32] The parameters determined by molecular mechanics correspond to aggregates in an isolated state, i.e., similar to that occurring in the gaseous state. The angle of the conjugated double bond planes in aggregates A, B, C, D (Table 2), and P (Table 4) is close to that of the optimum geometry for triplet states in HH aggregates (60°), while for HT aggregates (27−31°) the energy barrier is the determining factor.

Heavy atom effect can be used to show the formation of singlet states.[32a,b] Argon, for example, inhibits the photodimerization via the singlet state.[32c] We bubbled argon in a dilute aqueous solution: the result (Table 1) is unquestioned. The HH_a dimer formation is carried out only via the triplet state. The photodimerization is complete, and argon favors the formation of the HH_a photodimer ($HH_a/HT_a = 99/1$). Nevertheless, the interface packing in micellar solutions prevents isophorone, which is at the interface, from adopting a geometry promoting the triplet state. Thus, when the micellar medium is bubbled with argon, the photodimerization reaction is inhibited in part and the formation of the HH_a photodimer decreases by 35%. This result indicates that the formation of the HH_a photodimer in such micellar media goes through a singlet or triplet state.[32d]

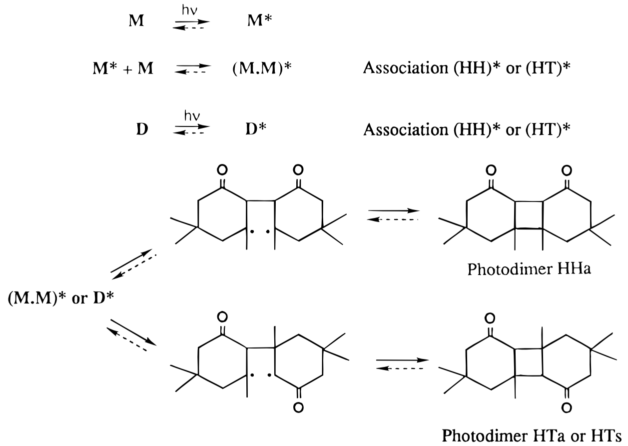
The mechanism proposed by Wagner et al.[31d] for the photodimerizations of 2-cyclopentenone and of 2-cyclohexenone involved the lowest energy triplet ($^3E^*$). Dimerization occurs via metastable dimeric species ($^*E{-}E^*$) decaying to two ground-state ketone (E_0) molecules as well as proceeding on to a stable ground state photodimer. Scheme 7 incorporates the various intermediates that can lead to photodimers. A and O are probably π complexes but may be simply collision complexes.

If we apply the mechanism proposed by Wagner et al.[31d] to isophorone, the metastable intermediates from which the 1,4-

SCHEME 7



SCHEME 8



biradicals HH and HT are formed can have several origins: monomeric (in a lipophilic environment) or from species with varying degrees of aggregation. For the initial excitation, we propose two mechanisms involving singlet or triplet states. Starting either from monomers (M) in essentially lipophilic media ("dynamic excimers")[33a] or from aggregates (D) ("static excimers")[33b,34] (Scheme 8), the spin multiplicity will be dependent on the medium and will take a value that "changes as required" depending on the geometry of the ground or excited states. The lifetimes of the initial excited species and the metastable intermediate states will determine whether 1,4-biradicals occur. The metastable intermediates should lead to 1,4-biradicals HH and HT and then to photodimers by "direct" cyclization in the singlet state or after spin inversion in the triplet state. We only considered the possibility of a biradical HH with a 2−2′ junction since it is always favored with respect to 3−3′ in a preorganization (the 3−3′ distance, most probably owing to the methyl substitution in the 3 position, is about 1.2 Å longer than that of 2−2′).

Conclusion

The investigation of isophorone solvation and photodimerization in cyclohexane, butanol, and water shows the occurrence of supramolecular structures that are central to explaining the molecular reactivity behavior. FTIR spectroscopy, combined with molecular mechanics, favored the occurrence of stable supramolecular assemblies. These assemblies are flexible structures, and their geometries are determined by the interactions of isophorone with the medium. For the conditions employed in the present study, we obtained mainly cis-anti-cis photodimers. Van der Waals dimers or structures with a molecule of water bridging two isophorone molecules lead to the topochemical control of photodimerization and stereospecificity of the product. On the basis of the present results and those reported in the literature, we propose an enone geometry-dependent mechanism of photodimerization reaction which is critically influenced by the solvation and aggregation state of the substrate.

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