Coordination Chemistry Reviews, *125* (1993) 261–268

Photochemistry of cyclodextrin host-guest complexes

P. Bortolus[a], G. Grabner[b], G. Köhler[b], S. Monti[a]

[a] Istituto di Fotochimica e Radiazioni d'Alta Energia CNR, Via de' Castagnoli 1, 40126 Bologna, Italy

[b] Institut für Theoretische Chemie und Strahlenchemie , University of Vienna, Währinger Strasse 38, A-1090 Vienna, Austria

Abstract

Cyclodextrins, when used as molecular receptors, can induce significant modifications of the photophysical and photochemical deactivation pathways of aromatic molecules. On the basis of examples, taken from the authors' work, the factors determining the behaviour of a photoexcited guest molecule in a cyclodextrin cavity are discussed with particular attention to the role of cyclodextrin as constraint to molecular degrees of freedom and as tool for controlling the evolution of reaction intermediates to final photoproducts.

1. INTRODUCTION

An interesting development in the field of supramolecular chemistry is the study of host-guest molecular complexes. Large permanent macrocyclic compounds are employed for trapping smaller molecules in cavities of appropriate size. With respect to the separate units, these systems, characterized by non covalent bonds, exhibit new peculiar properties [1].

Cyclodextrins (CDx) are largely used as hosts for organic molecules. They possess cavities with hydrophobic properties, due to a cyclic arrangement of six (α-CDx), seven (β-CDx) or eight (γ-CDx) D(+)glucopyranose units, linked by an α(1,4) glycosidic linkage. The macrocycle is best described as a truncated cone, the narrow rim bearing primary -OH groups and the wide rim secondary -OH groups [2,3]. The characteristics of the different CDx's are resumed in figure 1. The association of the guest molecule normally occurs by partial or full fitting of the cavity. The stabilization of the complex is provided by several factors, like Van der Waals and hydrophobic forces, H-bonds, release of high energy water molecules from the cavity, decrease of strain energy of the macrocycle. The inclusion allows to modify the guest reactivity and this opens the way to applications in pharmacology, food science, analytical chemistry, chemical synthesis and catalysis [2].

0010-8545/93/$24.00

CDx	N° units	Diameter (Å)
α	6	8.8 - 5.6
β	7	10.8 - 6.8
γ	8	12.0 - 8.0

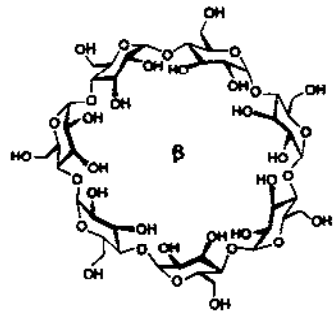

Figure 1. Schematic representation of cyclodextrins and cavity diameters.

The study of the photochemical behaviour of molecules included in CDx cavities has received in the last years increasing attention. Recent reviews [4-7] report changes in fluorescence and phosphorescence properties, in excimer and exciplexes formation and decay, in quenching processes and protolytic equilibria in the excited state.

Modifications in the features of electron transfer processes, in intra- and inter-molecular photoreactions of carbonyl compounds, in photoisomerization about the ethylenic double bond, in photodimerization and photocycloaddition reactions have been observed in presence of CDx [4-8].

The interpretation of the experimental results is difficult since the geometry of the complex is seldom available. Often, the overall effect of CDx on the photoprocess is reported, but the details of the mechanism are not investigated. In spite of these limitations, it is accepted that the factors which determine the behaviour of a molecule included in a CDx cavity are mainly the micropolarity of the cavity, its ability to shield the guest from the homogeneous medium, to impose steric constraints and to control the chemical evolution of the intermediates [4-7].

This paper illustrates some examples in which the mechanism of the CDx effect has been investigated by photochemical stationary and time resolved techniques.

2. CDx AS PHYSICAL CONSTRAINT TO MOLECULAR MOTIONS.

Molecular degrees of freedom provide assisting modes for radiationless transitions between electronic states. Important changes in the emission properties and in the photochemistry of the guest can be expected if molecular mobility is limited.

Phenols interact favourably with α- and β-CDx in aqueous solutions.

Association constants (K) for 1:1 complexes between β-CDx and para-substituted derivatives are relatively large (10^2 - 10^3 M^{-1}). Entropic terms contribute significantly to the stabilization of these complexes, which are characterized by a loose binding of the guest molecule in the large β-CDx cavity [9]. Fluorescence spectrum, emission intensity and lifetime of phenol and p-cresol are scarcely affected by complexation, in agreement with a small perturbation of the molecular mobility and of the -OH group environment. On the contrary, enhanced fluorescence quantum yields and longer lifetimes are observed in 2,4,6-trimethylphenol complexed with β-CDx (Table 1). In this case the non radiative deactivation rate parameter of S_1 strongly decreases upon complexation. Both the internal conversion and the intersystem crossing rates are affected. Comparison with phenol shows that an almost complete "freezing" of the degrees of freedom associated to the methyl groups occurs in the complex, in agreement with a tight interaction of the bulky molecule with the cavity walls [10].

Table 1
Fluorescence quantum yields and lifetimes of phenol and methylated derivatives and of their inclusion complexes with β-CDx at 295 K.

	no CDx				
	Φ	τ(ns)	$k_r(10^7 s^{-1})$	$k_{nr}(10^9 s^{-1})$	
phenol	0.13	3.2	4.05	0.27	
p-cresol	0.14	3.1	4.5	0.28	
2,4,6-TMP	0.025	0.6	4.1	1.6	
	β-CDx				
	Φ	τ(ns)	$k_r(10^7 s^{-1})$	$k_{nr}(10^9 s^{-1})$	K (M^{-1})
phenol	0.15	3.7			94[a]
p-cresol	0.17	3.8			250[a]
2,4,6-TMP	0.12	3.65	3.3	0.24	56[b]

(a) from Bertrand et al. 1989 [9].
(b) from fluorescence intensity measurements, uncertainty ± 15%.

Large molecular distortions are involved in double bond isomerisations. In the presence of α- and β-CDx a marked decrease of trans → cis photoconversion efficiency has been observed for stilbene [11]. Correspondently, there is a decrease of the S_1 fluorescence decay rate, which is determined by the rotation of the -C=C- bond to the twisted geometry [12].

Similar effects are observed in the trans → cis photoisomerization of azobenzene [13]. The main feature of this photoreaction in homogeneous solutions is a marked wavelength effect on the quantum yields as observed by

excitation in the S_1 (n,π^*) or S_2 (π,π^*) band [14]. For this molecule two different isomerization coordinates exist, one involving the twisting around the -N=N- bond and the other the in plane inversion at one of the two nitrogen atoms. The inversion mechanism operates in S_1, while the rotational coordinate plays an important role in the deactivation of S_2 [15-17]. In fact, the wavelength effect is absent if the rotational motion is hindered [16-17]. Encapsulation of trans-azobenzene in α- or β-CDx eliminates the wavelength effect, in agreement with severe restrictions imposed to the twisting of the molecule, like in stilbene (Table 2). Isomerization by inversion is only partially perturbed because it requires less room to be fulfilled.

Table 2
Photoisomerization quantum yields[a] for trans-azobenzene irradiated in the π,π^* and in the n,π^* absorption bands.

	Φ (trans → cis)	
	313 nm	436 nm
H_2O / CH_3OH (80/20 v/v)	0.20_5	0.31_5
tetrahydrofuran	0.08_5	0.19
α-CDx (10^{-2} M)	0.11	0.15
β-CDx (10^{-2} M)	0.13_2	0.13_8

(a) accuracy ± 7%, Bortolus and Monti, 1987 [13].

3. CDx AS CONTROLLING AGENT FOR THE EVOLUTION OF INTERMEDIATES.

Modification of photochemical reactivity by CDx complexation can be obtained through the control of thermal steps following the primary photochemical act. A "cage effect" has been invoked to explain the remarkable changes observed in the photoproduct distribution of the Norrish I reaction of alkyl-dibenzyl-ketones [18]. Product selectivity in unimolecular photo-Fries and photo-Claisen rearrangements has been attributed to the ability of CDx to regulate the reorganization of molecular fragments formed upon the photon absorption [19].

Control of rates of secondary reactions by CDx's has been observed in the photoreduction of benzophenone [20] and its heterocyclic homologues 3- and 4-benzoylpyridine [21]. In figure 2-4 the influence of the addition of α- and β-CDx on the photolysis products of 3-benzoylpyridine is reported. Strong changes are induced and there is a role of the cavity size. The formation of inclusion

complexes in the ground state has been studied by induced circular dichroism and absorption spectroscopy. Association constants for the 1:1 complexes range in the interval 10^2-10^3 M^{-1}.

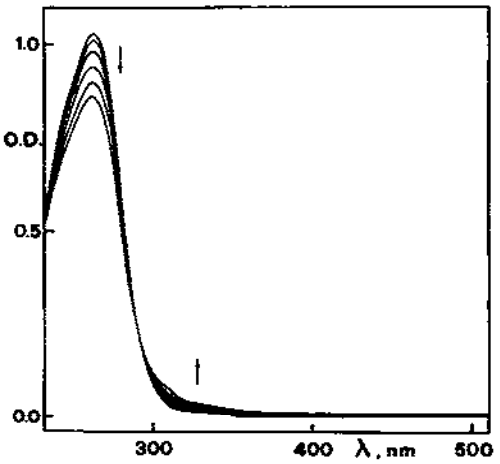

Figure 2. Spectral changes in 3-benzoylpyridine aqueous solutions after irradiation at 254 nm. Phosphate buffer 10^{-3} M, pH 7.

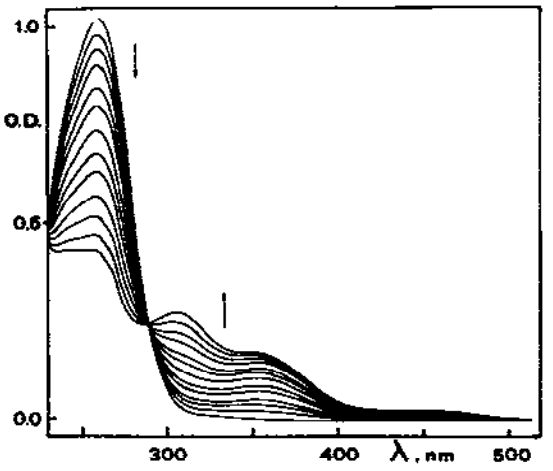

Figure 3. Spectral changes in 3-benzoylpyridine aqueous solutions after irradiation at 254 nm. Phosphate buffer 10^{-3} M, pH 7, α-CDx 10^{-2} M.

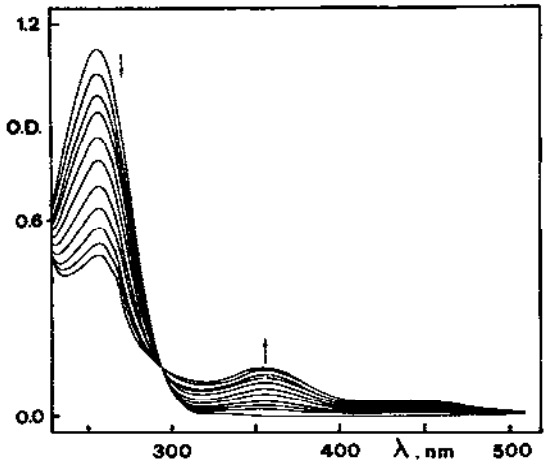

Figure 4. Spectral changes in 3-benzoylpyridine aqueous solutions after irradiation at 254 nm. Phosphate buffer 10^{-3} M, pH 7, β-CDx 10^{-2} M.

The interaction of the triplet state of the ketones with the CDx's has been studied by bimolecular quenching of the ketone phosphorescence, in conditions of negligible concentrations of ground state complexes. The rate constants measured are lower than diffusion but much higher than those obtained with model saccharides like glucose or saccharose, even taking into account for the number of glucose units in the molecules (table 3). These data support a very efficient inclusion of the ketone triplet in the cavity, where the quenching process takes place by a quantitative H-abstraction from a glucose unit. The triplet radical pair, formed by the aromatic ketyl radical and the CDx-radical, has been detected by nanosecond laser-flash-photolysis and characterized on the basis of its spectral and kinetic properties. It has been shown that its decay paths depend on the cavity size which influences directly the relative yields of intersystem crossing (ISC) and separation of the radical moieties. The β-CDx cavity favours triplet to singlet ISC followed by fast cage recombination reactions, while α- and γ-CDx tend to release the guest molecule leading to high yields of free radicals (Table 4). Higher selectivity is obtained in the reactions occurring in the cage and involving the geminate radical pair. This accounts for the dependence of the product distribution on the cavity size. No marked influence of the CDx's is found on the photoreduction products of benzophenone and 4-benzoylpyridine in spite of the large effects observed on the decay paths of the respective radical pair. A low

yield and/or a thermal instability of the recombination products can account for this behaviour.

Table 3
Quenching of phosphorescence of benzophenone and 3-benzoylpyridine by CDx's.

	$k_q(M^{-1}s^{-1})$		
	BP[a]	3-BPy[b]	4-BPy[b]
α-CDx	$5.0x10^7$	$1.1x10^8$	$1.5x10^8$
β-CDx	$8.3x10^8$	$7.1x10^8$	$4.0x10^8$
γ-CDx	$4.6x10^8$	$6.3x10^8$	$3.4x10^8$
Glucose	$1.4x10^6$	$2.7x10^6$	
Saccharose	$2.5x10^6$	$4.2x10^6$	

(a) water, Monti et al. 1988 [20].
(b) phosphate buffer 10^{-3} M, pH 7, Monti et al. 1991 [21].

Table 4
Kinetic properties of triplet ketone–β-CDx radical pairs and yields of escape of aromatic ketyl radicals for the different CDx's.

	τ^{β}(ns)	$k^{\beta}_{ISC}(s^{-1})$	$k^{\beta}_{ESC}(s^{-1})$	Φ^{β}_{ESC}	Φ^{α}_{ESC}	Φ^{γ}_{ESC}
BP[a]	1600	$5.3x10^5$	$0.9x10^5$	0.14	0.70	0.62
3-BPy[b]	750	$1.1x10^6$	$2.5x10^5$	0.19	0.68	0.60
4-BPy[b]	650	$\sim 1.3x10^6$	$\leq 2x10^5$	≤0.1	≤0.3	≤0.4

(a) water, Monti et al. 1988 [20].
(b) phosphate buffer 10^{-3} M, pH 7, Monti et al. 1991 [21].

Cyclodextrins proved to be useful "reaction vessels" for controlling rates and induce selectivity in photochemical processes. Further studies in this field can extend the possibilities of synthetic and analytical applications. In addition, given the sensitivity of the excited state behaviour to micro-environmental factors, photochemical investigations on CDx inclusion complexes can contribute significantly to the basic understanding of the chemical consequences of the weak interactions, which are of fundamental importance in biological systems like enzymes, antibodies, genes.

4. REFERENCES

1 H. J. Schneider and H. Dürr (eds.), Frontiers in Supramolecular Chemistry and Photochemistry, VCH, Weinheim, 1991; V. Balzani and L. De Cola (eds.), Supramolecular Chemistry, Kluwer Academic Publishers, Dordrecht, 1992.
2 M.L. Bender and M. Komiyama, Cyclodextrin Chemistry, Springer Verlag, New York, 1978; Szejtli, Cyclodextrins and Their Inclusion Complexes, Akademiai Kiado, Budapest, 1982.
3 I. Tabushi, Acc. Chem. Res., 15 (1982) 66.
4 V. Ramamurthy, Tetrahedron, 42 (1987) 5753.
5 K. Kalyanasundaram, Photochemistry in Microheterogeneous Systems, Academic Press, Orlando, 1987, chapter 9.
6 V. Ramamurthy and D.F. Eaton, Acc. Chem. Res., 21 (1988) 300.
7 V. Balzani and F. Scandola, Supramolecular Photochemistry, Ellis Horwood, Chichester, 1991, chapter 10.
8 W.-S. Chung, N.J. Turro, J. Silver and W.J. Le Noble, J. Am. Chem. Soc., 112 (1990) 1202.
9 G.L. Bertrand, J.R. Faulkner Jr., S.M. Han and D.W. Armstrong, J. Phys. Chem., 93 (1989) 6863.
10 G. Grabner, G. Köhler and S. Monti, to be published.
11 M.S. Syamala, M. Devanathan and V. Ramamurthy, J. Photochem., 34 (1986) 219.
12 G.L. Duveneck, E.V. Sitzman, K.B. Eisenthal and N.J. Turro, J. Phys. Chem, 93 (1989) 7166.
13 P. Bortolus and S. Monti, J. Phys. Chem, 91 (1987) 50.
14 P. Bortolus and S. Monti, J. Phys. Chem., 83 (1979) 648.
15 S. Monti, G. Orlandi and P. Palmieri, Chem. Phys., 71 (1982) 87.
16 H. Rau and E. Lüddecke, J. Am. Chem. Soc., 104 (1982) 1616.
17 H. Rau, J. Photochem., 26 (1984) 221.
18 B. Nageshwer Rao, M.S. Syamala, N.J. Turro and V. Ramamurthy, J. Org. Chem., 52 (1987) 5517; B. Nageswara Rao, N. J. Turro and V. Ramamurthy, J. Org. Chem., 51 (1986) 460.
19 M.S. Syamala, B. Nageshwer Rao and V. Ramamurthy, Tetrahedron, 44 (1988) 7234; M.S. Syamala and V. Ramamurthy, Tetrahedron, 44 (1988) 7223.
20 S. Monti, L. Flamigni, A. Martelli and P. Bortolus, J. Phys. Chem., 92 (1988) 4447.
21 S. Monti, N. Camaioni and P. Bortolus, Photochem. Photobiol., 54 (1991) 577.