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Supramolecular Photochemistry in β -Cyclodextrin Hosts: A TREPR, NMR, and CIDNP Investigation

Olesya A. Krumkacheva,[†] Vitaly R. Gorelik,[†] Elena G. Bagryanskaya,^{*,†} Natalia V. Lebedeva,[‡] and Malcolm D. E. Forbes^{*,‡}

[†]International Tomography Center, Institutskaya 3a, Novosibirsk 630090, Russia, and [‡]Caudill Laboratories, Department of Chemistry, CB #3290, University of North Carolina, Chapel Hill, North Carolina 27599-3290

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A systematic investigation of the photochemistry and ensuing radical chemistry of three guest ketones encapsulated in randomly methylated β -cyclodextrin (β -CD) hosts is reported. Dibenzyl ketone (DBK), deoxybenzoin (DOB), and benzophenone (BP) triplet states are rapidly formed after photolysis at 308 nm. Time-resolved electron paramagnetic resonance (TREPR) spectroscopy, steady-state NMR spectroscopy, and time-resolved chemically induced nuclear polarization (TR-CIDNP) experiments were performed on the ketone/CD complexes and on the ketones in free solution for comparison. The major reactivity pathways available from these excited states are either Norrish I α -cleavage or H-atom abstraction from the interior of the CD capsule or the solvent. The DOB triplet state undergoes both reactions, whereas the DBK triplet shows exclusively α -cleavage and the BP triplet shows exclusively H-atom abstraction. Radical pairs are observed in β -CDs by TREPR, consisting of either DOB or BP ketyl radicals with sugar radicals from the CD interior. The TREPR spectra acquired in CDs are substantially broadened due to strong spin exchange. The electron spin polarization mechanism is mostly due to S-T₀ radical pair mechanism (RPM) in solution but changes to S-T_ RPM in the CDs due to the large exchange interaction. The TR-CIDNP results confirm the reactivity patterns of all three ketones, and DOB shows strong nuclear spin polarization from a novel rearrangement product resulting from the α -cleavage reaction.

Introduction

The structure, reactivity, and dynamics of free radicals in confined environments are a topic of substantial interest to the biochemical, photochemical, and nanotechnological communities.¹ For molecular recognition investigations,² synthesis and chemical modification of nanoassemblies,³ and control of product yields and/or stereochemistry in small molecule reactions,⁴ several different types of encapsulation strategies have been employed. Examples of such nanoreactors include micelles, reverse micelles, vesicles, zeolites, nanocapsules, nanotubes, and calixarenes.⁵ In photochemical reactions, encapsulation can substantially alter the nature of the excited states involved⁶ and the structures of the ensuing reactive intermediates, which are often free radicals.⁷ Encapsulation can cause product partitioning of these intermediates to deviate from those observed in free solution,⁸ and in some cases previously unobserved products are

detected due to confinement.⁹ Supramolecular host–guest complexes sometimes show significant reactivity between host and guest,¹⁰ which can complicate potential applications such as drug delivery or nanoencapsulation of dyes for imaging and printing processes.

The β -cyclodextrin (β -CD) molecule (Chart 1) has been a popular choice for encapsulation studies because of its general compatibility with biological solutions and tissues, its widespread availability, and its low cost.¹¹ It consists of an intramolecularly linked cycle of seven β -glucose rings with acetal bonds between the individual sugar units, and its macromolecular shape is that of a tapered cylinder. In aqueous solution, host molecules are incorporated into the interior of the cylinder due to the hydrophobic effect. The solubility of these complexes in aqueous solution can be improved by partial methylation of the CD hydroxyl groups, and several researchers have taken advantage of this strategy using singly or multiply methylated CD structures.¹² The origin of this increased solubility is thought to be due to the fact that methylation increases the hydrophobicity of the interior of the CD much more than the exterior. Because most guests are relatively nonpolar organic molecules, an increase in the hydrophobicity of the interior pushes the equilibrium association constant of the complex to higher values.

The photochemistry of small molecules encapsulated in CDs and the free radical chemistry resulting from photochemical excitation in the interior have been studied by several research groups with a variety of different physical methods. For example, Singh et al. examined the photochemistry of several substituted α -phenyl ketones and found that the product ratios from Norrish I

^{*}To whom correspondence should be addressed. E-mail: elena@tomo.nsc. ru (E.G.B.); mdef@unc.edu (M.D.E.F.).

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(α -cleavage) and Norrish II (intramolecular H-atom abstraction) reactions were only moderately altered by inclusion in β -CDs.¹³ It is somewhat surprising that inclusion in the CD would have only a minor effect on the outcome of *intramolecular* reactions. Reactions involving the photoexcited triplet state of naphthoquinone in CDs have been reported by Takamori et al.¹⁴ They observed carbon-centered radicals from intermolecular H-atom abstraction reactions as an exclusive reaction pathway. A report by Lehmann and Bakker examined alkyl ketone photoreactivity in β - and γ -CDs.¹⁵ Again, only H-atom abstraction site.

Rao and co-workers reported that the photochemistry of alkyldibenzyl ketones included in CDs is dramatically different in solution compared to the solid state.¹⁶ In the 1990s, Lehmann et al. used steady-state electron paramagnetic resonance (EPR) spectroscopy to examine the thermal and photochemical reactions of several peroxides included in β -CD.¹⁷ They found significant reactivity between the alkoxy radicals produced on heating and the sugar ring interior and exterior of the CD, depending on sample preparation conditions. Other steady-state EPR work on stable radicals in CDs has demonstrated a different reactivity. For example, Beckett et al. studied the tetracyanonaphthoguinone radical anion and found that it reacts with the CD interior to create a diamagnetic product.¹⁸ Also, Lucarini and Pedulli found that the ³¹P hyperfine interactions of phosphoruscontaining hydrazyl radicals were dramatically lowered when the radicals were included in β -CD.¹⁹

Clearly, previous EPR studies on CD radical chemistry have lacked systematic structural variation. In many of these previous investigations, the steady-state spectroscopic and kinetic methods employed do not always account for the primary mechanistic events due to secondary reactions or rearrangements. An additional problem is that transient optical absorption spectra often exhibit broad lines that can be difficult to assign. Rearrangements of reactive intermediates and secondary photolysis processes can obfuscate the interpretation of results and lead to incorrect assignments of intermediates and mechanisms. This problem is compounded by the lack of structural resolution of optical spectra in the condensed phase. Magnetic resonance (EPR and NMR) spectroscopy offers high structural resolution and high sensitivity, and one can often make unambiguous assignments of free radical intermediates and final products. Additionally, time-resolved methods such as chemically induced nuclear spin polarization (CIDNP)²⁰ and time-resolved EPR (TREPR)²¹ spectroscopy, with time resolution on the order of 100 ns, are ideal experimental techniques for observation of the primary photochemical events in host-guest chemistry. Indeed, TREPR and CIDNP have been applied routinely to study radical reactions in other nanoreactors such as micelles and reverse micelles.²² To the best of our knowledge, there exist only two previous reports of TREPR investigations of photochemical reactions in CDs,^{14,15} and only one involving the use of the powerful CIDNP experiment in either steady-state or time-resolved mode.²

Background

Given the limitations of the previous studies described above, we were motivated to carry out a more systematic study of photoexcited triplet states in β -CDs, in particular those that could react by either α -cleavage *or* intramolecular H-atom abstraction reactions. It is also possible to design experiments involving triplet states that could undergo both reactions competitively. In this regard, we report here a combined NMR, TREPR, and TR-CIDNP study of the radical chemistry that takes place after UV laser flash photolysis of the three ketones shown in Chart 2 when they are encapsulated in β -CDs in aqueous solution at room temperature: deoxybenzoin (DOB), dibenzyl ketone (DBK), and benzophenone (BP). All three molecules were selected for their structural simplicity and for their known rapid formation of a reactive excited triplet state upon UV excitation.

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Scheme 1 outlines the photochemistry and possible radicals formed in free solution and in the interior of CDs for the triplet states of the ketones shown in Chart 1. Upon laser excitation, these molecules have both (n,π^*) and (π,π^*) excited states available to them. In DOB, the carbonyl group simultaneously carries aryl and benzyl character, and the two lowest energy triplet states may be close in energy for this ketone. This is important because triplet (n,π^*) states tend to undergo Norrish I α -cleavage reactions, while triplet (π,π^*) states are more likely to abstract H atoms from the solvent or other surrounding media.²⁴ If these two states are strongly mixed, as they are, for example, in acetophenone,²⁵ both types of reactivity can be observed. For such ketones, the partitioning of the two reaction pathways may be very sensitive to the local environment.

Intersystem crossing from the excited singlet state to the molecular triplet state is expected to be fast,²⁶ and all three triplet states should be completely formed shortly after the laser flash, well before the detection of radicals by TREPR or reaction products by TR-CIDNP. For this reason, it is assumed that all radical pairs (RPs) produced in our photochemical reactions will be triplet-borne. For DOB, the Norrish I α -cleavage reaction will produce benzoyl and benzyl radicals, and H-atom abstraction from a suitable hydrogen donor will lead to a ketyl radical and a donor radical. As indicated in Scheme 1, we will abbreviate the two radical pairs as RP1 for the pair created from Norrish I α -cleavage and RP2 for the pair created from H-atom abstraction. For CD-encapsulated DOB (DOB/CD), the hydrogen donor is the CD host, in particular the interior facing H's at the 3 and 5 positions of the sugar rings (Chart 3).

Hyperfine interactions and g-factor differences between the members of each geminate RP will induce mixing between the initial RP triplet state and its corresponding RP singlet state, from which geminate recombination can occur to give a nuclear spin polarized product. In free solution, triplet RPs will also escape into the bulk and form random or out-of-cage products (Scheme 2): for DOB, this includes benzyl, diphenylethane, and the starting material. Interestingly, the rearranged product paramethylbenzophenone (PMB) also appears in this photochemistry. The PMB molecule is created via recombination of RP1 where the benzoyl radical attacks the 4-position of the benzyl radical, followed by intramolecular H-atom transfer. Because the latter reaction is slow on the time scale of TR-CIDNP, it is the vinvl protons of the initially formed intermediate compound (Scheme 2, bottom left) that appear in the CIDNP spectrum. Such a rearrangement has been observed previously in steady-state photolysis experiments involving DBK.27

The bulk of this description of the photochemistry in Schemes 1 and 2 has been focused rather intentionally on the DOB triplet state, as it exhibits the widest range of chemical reacitvity. It should be noted that the DBK molecule follows exclusively the α -cleavage reaction pathway and BP undergoes only H-atom abstraction. Radical structures from the triplet states of these ketones are also depicted in Scheme 2. All of the products (or radicals) in Scheme 2 have been observed in our TR-CIDNP (or TREPR) experiments. Their role in the mechanistic photochemistry in Scheme 1, with regard to inclusion in CDs versus free solution, will be discussed in detail below.

Experimental Section

Materials. DOB (Aldrich) was purified by sublimation. Randomly methylated β -CD (Fluka) was used as received. To prepare the complex, DOB (8 mM) was added to an aqueous solution of β -CD (2 mM). The solution was sonicated for 30 min, stirred for 6 h, and then filtered immediately prior to experiments. The concentration of DOB in the complex was 1 mM, as measured by UV and NMR spectroscopy. Deuterated solvents for the NMR and CIDNP spectra, CD₃CN 99% and D₂O 98%, were purchased from ISOTOPE and used as received. High purity solvents 2-propanol, acetonitrile, cyclohexane, and distilled water were used in the TREPR experiments.

TREPR Experiments. The TREPR signals²⁸ were obtained using a double-gated integrator (Stanford Research Systems) in direct detection mode over 2-4 min. Low temperature TREPR experiments were carried out on a JEOL JES RE-1X spectrometer equipped with a liquid nitrogen variable temperature quartz dewar. The temperature was maintained at 100 K. Samples were prepared in single tubes that underwent five freeze-pump-thaw cycles. The EPR signal was passed from the preamplifier of the microwave bridge to the two boxcar gates as the magnetic field was swept. Traces were collected at each field point and then subtracted from the off-resonance signal. For solution TREPR experiments, the sample was flowed through the microwave resonator to prevent heating and sample depletion, while nitrogen gas was bubbled continuously through a reservoir of typical volume 20 mL. A more complete description of the apparatus can be found in ref 28.

NMR and CIDNP Studies. ¹H NMR experiments were performed on an Avance 200 MHz Bruker DRX spectrometer. A standard $\pi/2$ pulse sequence was used with 64 scans. NMR spectra were measured at room temperature. The DOB concentration

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Chart 3

Type II: H⁵ abstraction site Type I: H³ abstraction site Н н н HO ·H3 HO H⁵ OR RC $= H. CH_{2}$ $R = H, CH_3$ Scheme 2 S-T conversion $R_1 \rightarrow R_2$ escape into bulk **DOB**: $R_1 = Ph-, R_2 = PhCH_{2}-$ DOB only **DBK**: $R_1 = PhCH_2-$, $R_2 = PhCH_2-$ **BP**: $R_1 = Ph-$, $R_2 = Ph-$

was 1 mM in the complex and 3 mM in the CD₃CN solution. The concentration of randomly methylated β -CD was 2 mM in the aqueous solution. In TR-CIDNP experiments,²⁹ the sample was purged with argon and sealed in a standard NMR Pyrex tube and then irradiated by an excimer laser (308 nm, 30 mJ) inside the NMR probe. CIDNP experiments were carried out with the usual pulse sequence: presaturation-laser pulse-evolution timedetection pulse-free induction decay. A complete description of the technical details for this experiment can be found in ref 29. Because the background signals in CIDNP spectra are suppressed by the presaturation pulses, only signals of the polarized products appear in the CIDNP spectra. The number of scans was 32.

Results and Discussion

PMB

NMR Analysis of the Ground State DOB/CD Complex. In order to understand the photochemistry of the DOB/CD complex and how DOB behaves differently in CDs than in free solution, the structure of the complex itself was investigated in the absence of light using ¹H NMR spectroscopy. As mentioned above, random methylation means that C^2 , C^3 , and C^6 can each have substitutents that are either -OH or -OCH₃ (Chart 1). This can affect the chemical shifts of neighboring protons, some of which may be involved in the photochemical H-atom abstraction reaction. Therefore, care should be taken to identify these signals if they can be resolved in the NMR spectrum. Figure 1a shows NMR data acquired at 400 MHz for randomly methylated β -CD, while Figure 1c shows the NMR spectrum of pure DOB in free

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Figure 1. (a) NMR spectrum of randomly methylated β -CD aqueous solution; (b) NMR spectra of the encapsulated DOB and CD (solid line) in H₂O, and the (uncomplexed) materials are presented for comparison (dashed line); (c) NMR spectrum of DOB in CD₃CN solution: β -CD (I), DOB (II) = Ph^A-CO-CH₂^C-Ph^B. The asterisk marks a transition due to the residual solvent.

solution. To facilitate comparison, expanded chemical shift regions for the two DOB phenyl group protons and the aliphatic CD protons are shown in Figure 1b, which is the NMR spectrum of the host/guest complex. There are two different chemical shifts observed for the (exterior) H¹ protons (5.28 and 5.05 ppm) of the CD. As mentioned above, these arise due to the possible presence of different substituents at the neighboring C² position (-OH vs $-OCH_3$). The unresolved signals between 3.3 and 4.02 ppm are also due to protons in the CD, but a more detailed analysis of this region is difficult because of the overlap of signals from the two structural types.

The ¹H NMR spectrum of DOB in CD₃CN (Figure 1c) consists of five signals in the aromatic region (7.4–8.1 ppm) and one signal due to the CH₂ group (4.34 ppm). The two aromatic rings of DOB have different chemical shifts. The first aromatic ring is proximal to the CH₂ group (multiplets centered at 7.23, 7.34, and 7.56 ppm). The second ring is distal to the CH₂ group (multiplets centered at 7.74 and 7.9 ppm). The chemical shifts of the protons in both CD and DOB are changed after complexation due to modification of the local environment of the protons. The change in the chemical shift of the first and second aromatic rings upon complexation is evidence of significant interaction between the CD cavity and both aromatic rings. Analyses by NMR for DBK and BP ground states in β -CDs were also carried out and showed similar features (spectra not shown).

CIDNP of DOB in Free Solution. After laser flash photolysis of DOB in acetonitrile, CIDNP signals are observed, as shown in Figure 2. The nuclear polarization is formed exclusively from the benzyl and benzoyl radicals formed after α -cleavage. In acetonitrile solution, the contribution from RP2 (radical pairs from H-atom abstraction) is negligible due to the very slow rate of this process in acetonitrile. For ³DOB* photolysis, the expected



Figure 2. (a) Dark NMR spectrum of a 10 mM solution of DOB in CD₃CN, (* = H₂O, ** = CD₂HCN). (b) CIDNP spectrum obtained after photolysis of DOB in CD₃CN. In this and all subsequent CIDNP spectra, the time delay between the laser pulse and the rfpulse is 1 μ s. Assignment of the CIDNP signals is as follows (superscript letters indicate polarized NMR transitions): starting material DOB (I) = Ph^A-CO-CH₂^B-Ph^C, diphenylethane (IV) = (PhCH₂^A)₂, rearrangement product PMB (III) = Ph-CO-C₆H₅-CH₂^A.

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in-cage products are the starting material DOB and the rearrangement product PMB, while the major escape product is diphenylethane. The CH₂ group of the benzyl radical has the largest hyperfine coupling constant (2 $A_{\rm H}$ (CH₂) = -16.28 G); therefore, the most intense CIDNP signals are observed for these protons (4.34 ppm) of DOB. The phase of this CIDNP signal (emissive) is in agreement with Kaptein's rules.^{20a} Taking into account the *g*-factors for the benzoyl radical (*g* = 2.0006) and benzyl radical (*g* = 2.0026) ($\Delta g > 0$) as well as the negative sign of the HFI constants for the CH₂ group,³⁰ the sign of the observed CIDNP is calculated to be $\Gamma_n = \mu \epsilon \Delta g A_{\rm H} < 0$ (μ is the spin multiplicity of the precursor, which is +1 for a triplet, ϵ represents the in-cage or the escape product, and is +1 for the in-cage product). Thus, the phase is predicted to be emissive, which is exactly what is observed experimentally for these protons.

Another fairly intense peak (2.91 ppm) assigned to the CH_2 groups of the escape product diphenylethane formed by the recombination of two benzyl radicals. The absorptive phase of this CIDNP signal is also predicted by Kaptein's rules ($\mu = 1, \varepsilon =$ -1, $\Delta g > 0$, $A_{\rm H} < 0$). We have also observed CIDNP for the meta and para protons of the phenyl groups ($A_{\rm H} < 0$) (7.23 ppm) of the starting material DOB and diphenylethane. The structure of the CIDNP spectrum is complicated due to overlapping of signals of these two carriers, which contribute polarizations of opposite phase. An emissive CIDNP signal from the CH₂ group of PMB was observed at 4.98 ppm. In summary, these CIDNP results show unambiguously that, in free solution, the dominant reaction pathway for ³DOB* is Norrish I α -cleavage. The structures of the products formed and their nuclear polarization phases are those expected from the in-cage versus escape reactions shown in Scheme 2.

CIDNP of Ketone/CD Complexes. The solubility of DOB in D_2O is very low, with a maximum of 0.5 mM. For this reason, we did not observe CIDNP during the photolysis of pure DOB in D_2O solution. We therefore assume that all CIDNP signals observed in our experiments with host/guest complexes arises from photochemistry involving CD-included DOB molecules. The TR-CIDNP signals from the products formed after laser flash photolysis of DOB/CD complexes are shown in Figure 3. Emissive polarization is observed for the CH₂ (4.33 ppm) and

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Figure 3. (a) Dark NMR spectrum of DOB in CD in D₂O. (b) CIDNP spectrum obtained after photolysis of DOB with CD in aqueous solution. CIDNP assignments are made for the following products: starting material DOB (I) = $Ph^{A}-CO-CH_{2}^{B}-Ph^{C}$, β -CD (II), PMB (III) = $Ph-CO-Cf_{2}^{A}$, diphenylethane (IV) = $(PhCH_{2}^{A})_{2}$.

phenyl (7.26 and 7.3 ppm) protons of DOB and for the CH_2 protons (5.1 ppm) of the rearrangement product PMB. Observation of the rearrangement product PMB in CDs suggests that, after α -cleavage, there is substantial mobility of at least one member of the radical pair. Unfortunately, it is not possible to tell from this experiment if the mobility is translational or rotational. Positive CIDNP is observed for the CH_2 protons of DPE. In addition, polarized signals were observed for the protons of the CD molecule at 3.2 ppm. From this observation, we can conclude that the CD host participates in this photochemistry, most likely via the H-atom abstraction reaction outlined in Scheme 1.

For analysis of CIDNP signal phases, *g*-factors and hyperfine coupling constants for the intermediate radicals are required. Such parameters for the DOB ketyl radical are not available from the literature. However, we can use parameters for radicals of similar structures, one of which is shown in Table 1.³⁰ From the TREPR data (see below), we have determined that the *g*-factor for the ketyl radical is 2.0030, which matches well with the literature data for the model radical. Other parameters used in the analysis are also listed in Table 1, including those from the two sugar radical structures used as models for the CD radicals.^{31,32}

H-atom abstraction can take place from two accessible sites in the CD interior, leading to two different radical structures that are illustrated in Chart 3. The abstraction sites are the H^3 or H^5 protons of the sugar rings, of which there are a total of seven of each type in a given CD structure. The expected magnetic parameters for these radicals should be consistent with literature parameters for sugar radicals. The CD radical on the left side of Chart 3 is formed if H³ is abstracted from the β -CD. Sugar radicals of this type have the following parameters: g = 2.0031and two different hyperfine coupling constants, $A_{\rm H} = 29.5$ G and $A_{\rm H} = 27.4$ G. The CD radical on the right side of Chart 3 is formed when H⁵ is the abstraction site. Sugar radicals of this type have g = 2.0031 and three different coupling constants: $A_{\rm H} =$ 33.3 \overline{G} , $A_{\rm H} = 9.9 \, \text{G}$, and $A_{\rm H} = 7.1 \, \text{G}$. From comparison to the values of the chemical shifts in the dark NMR spectrum of randomly methylated β -CDs, the observed CIDNP signal is assigned to the H^2 proton, that is, from the radical created by H-atom abstraction at H^3 (Chart 3, left side).

The phase of the CIDNP polarization for the CD protons (3.38 ppm) should be positive according to Kaptein's rules for this geminate radical pair ($\varepsilon = 1, \mu = 1, \Delta g < 0, A_{\rm H} > 0$). However, in the experiment, we observed a negative sign of polarization for these protons. It should be noted that Kaptein's rules were developed to predict the phase of $S-T_0$ radical pair mechanism polarization. When the sign of the nuclear polarization does not follow the sign of the hyperfine coupling constant in the intermediate radicals, a possible explanation is that the polarization is formed via the $S-T_{-}$ mechanism²⁰ or due to a mutual effect of magnetic nuclei.³³ The necessary condition for Kaptein's rules to violated is the following: $\Delta g B_0 \leq |A_1|, |A_2|$, where A_1 and A_2 are the hyperfine constants of radical 1 and radical 2, and B_0 is the magnetic field of the NMR spectrometer. In our case, this condition is not met and we should not expect a violation of Kaptein's rules for our system.

Compared to free solution, the intensity of the CIDNP signal for the escape product diphenylethane (2.9 ppm) is decreased in CDs. There are two reasons for this observation. First, the concentration of benzyl radicals is lower because H-atom abstraction has become an alternative reaction pathway. The product yield of diphenylethane from α -cleavage is expected to decrease. Second, even if α -cleavage takes place, radicals must escape from the CD into the bulk solution in order to form this product. The long residence time of the radicals in the CD means that nuclear spin relaxation will take place before recombination, leading to a decrease in the CIDNP intensity. This is in good agreement with the conclusions of Petrova et al.²³ in a CIDNP study of DBK photolysis in unmodified β -CDs. To confirm this for our system, we ran a similar CIDNP experiment, that is, DBK irradiated in randomly methylated β -CDs. The results are shown in Figure 4. No nuclear spin polarization is observed for the CD protons (compare the chemical shift region from 3.0 to 3.5 ppm in Figure 3b vs that in Figure 4b). The CIDNP results in Figure 4 strongly suggest that Norrish I α -cleavage is by far the dominant reaction pathway for DBK included in CDs.

To make further sense of these reactivity pathways, CIDNP results were also obtained for BP included in CDs, and these results are shown in Figure 5. The BP triplet state does not undergo the α -cleavage reaction, and so for this ketone the H-atom abstraction reaction becomes the dominant pathway. The intense nuclear polarization observed for the CD protons in Figure 5b strongly supports this statement. It should be noted that the phase of the polarization is also emissive, indicating that S-T_ mixing is also taking place in this system. The observed CIDNP signals for the CD protons are also broader than those in the case of photolysis of DOB in CD (Figure 3b), and the signals seem to arise from several different protons rather than just one site. This indicates that BP is much more reactive toward the interior of the CD and will abstract protons from the H³ as well as the H⁵ position, and possible even the $-OCH_3$ protons.

Figure 6 shows two dark NMR spectra of BP/CD solutions, one acquired before photolysis and one immediately after 10 min of photolysis. These spectra show the disappearance of the BP phenyl ring signals and the growth of a recombination product via the reaction of CD and BP ketyl radicals. These signals were used to assist in the assignment of Figure 5b above. Positive but weak CIDNP polarization was observed in the recombination product. The mechanism of formation of this polarization is not clear and will be the subject of future investigations.

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Table 1. Mag	netic parameters f	or Simulations in	Figures 7 and	d 9 and in CIDNP	' Analyses
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Radical	Hyperfine Coupling, mT	g-factor	Ref.
H 0	$2A_{\rm H} ({\rm CH_2}) = -1.628$		
m H	$2A_{\rm H}(o) = -0.515$		
p	$2A_{\rm H}(m) = 0.179$	2.0026	30
	$A_{\rm H}(p) = -0.617$		
o	$2A_{\rm H}(o) = 0.02$		
m J.	$2A_{\rm H}(m) = 0.118$		
p	$A_{\rm H}(p) = 0.007$	2.0006	30
OH ○			
m	$2A_{\rm H} ({\rm CH_2}) = 0.818$		
p	$A_{\rm H}(o) = 0.466$		
OH OH	$A_{\rm H}(o) = 0.497$		
for	$A_{\rm H}\left(p ight) = -0.587$	2.0030	30
	$2A_{\rm H}(m) = 0.16$		
	$A_{\rm H}$ (OH) = 0.075		
	$4A_{\rm H}(o) = -0.324$		
OH 0	$4A_{\rm H}(m) = 0.126$	2.0030	31
p · · · · · · · · · · · · · · · · · · ·	$A_{H}(p) = -0.239$		
Гион Л			
	$A_{\rm H}({\rm H}) = 2.95$		
Н	$A_{\rm H}$ (OH) = 2.745		
		2.0031	32
(Type I CD)			
Гңон			
	$A_{\rm H}$ (H) = 3.33		
H H	$A_{\rm H}$ (CH ₂) = 0.99		
но Н Н	$A_{\rm H}$ (CH ₂) = 0.71	2.0031	32
(Type II CD)			

The TR-CIDNP data presented above confirm that, in CDs, the photochemical reaction mechanism of ³DOB* is significantly altered compared to that observed in free solution. It moves away from the α -cleavage reaction observed for ³DBK* and toward the H-atom abstraction reaction observed for BP. The data reveal that abstraction of the H³ CD proton is taking place and that there is subsequent formation of a "tight" radical pair experiencing a large electron spin-spin exchange interaction. This leads to formation of CIDNP due to the S-T_ mechanism, vide infra.

Time-Resolved EPR in Free Solution. The TREPR experiment can be very informative when comparing reaction pathways in free solution versus confined media. In this regard, we have

carried out several experiments using X-band TREPR spectroscopy to detect directly the free radical intermediates involved in this photochemistry. When DOB is photoexcited in a solvent that is a good H-atom donor, such as 2-propanol, the TREPR spectrum in Figure 7 is obtained. Multiplet polarization (E/A) from the radical pair mechanism (RPM) of CIDEP is observed for both the ketyl radical and the solvent radical. Spectral simulation identifies the signal carriers as the familiar 2-propanol radical (seven-line spectrum with $A_{\rm H} = 19.48$ G) and the DOB ketyl radical (center). Clearly, H-atom abstraction is the major reaction pathway observed in free solution for DOB in 2-propanol.



Figure 4. (a) Dark NMR spectrum of DBK in CD in D₂O (* = residual H₂O or HDO). (b) CIDNP spectrum obtained after photolysis of DBK with CD in aqueous solution. Assignments are made as follows: starting material DBK (I) = Ph^A-CH₂^B-CO-CH₂^B-Ph^A, β -CD (II), PMB (III) = Ph-CH₂-CO-C₆H₅-CH₂^A, diphenylethane (IV) = (PhCH₂^A)₂.



Figure 5. (a) NMR spectra of BP in CD in D_2O (* = residual H₂O or HDO). (b) CIDNP spectrum obtained after photolysis of BP in CD in aqueous solution. (I) (Ph)₂^A-CO, (II) β -CD, (III) recombination product of β -CD and BP ketyl radicals.



Figure 6. Dashed line: Dark NMR spectrum of BP/CD in D₂O before photolysis in aqueous solution. Solid line: NMR spectrum of BP/CD in D₂O after 10 min of photolysis (* = residual H₂O or HDO). (I) = (Ph)₂^A-CO, (II) = β -CD, (III) = product of recombination of β -CD and BP ketyl radicals.

The phase of RPM CIDEP is defined by the sign of the exchange interaction (J < 0) and the spin multiplicity of the precursor $\mu = 1$. Multiplet polarization of phase E/A is predicted according to $\Gamma = -\mu J > 0$ and is indeed observed. As mentioned above, spectral parameters for the DOB ketyl radical were not found in the literature. We simulated its spectrum using the parameters for the structurally similar Ph–C•(OH)–CH₂–CH₃ radical (Table 1), which has been fully characterized.³⁰ The center



Figure 7. Time-resolved EPR spectra detected 300 ns after laser flash photolysis of DOB in 2-propanol solution. The black solid line corresponds to the experimental data, and the gray line to a simulated spectrum of the 2-propanol radical (outer lines; see text for parameters) and the DOB ketyl radical (unresolved lines in center).

of the TREPR spectrum in Figure 7 corresponds to a *g*-factor of 2.0030. From Figure 7, we can see that the values for the hyperfine coupling constant of the model radical $Ph-C\bullet(OH)-CH_2-CH_3$ provide a good fit of the ketyl radical spectrum in terms of overall spectral width and relative intensities.

It is noteworthy that the E/A pattern from RPM CIDEP is completely symmetrical in Figure 7. The central line of the 2-propanol radical is split into emissive and absorptive components from its -OH hyperfine splitting (0.7 G). This is a rather striking and unusual result for a triplet state reaction, which almost always shows some net polarization from the tripet mechanism (TM) of CIDEP. Based on this result, we can state with certainty that the TM is not operating in this system. Because the lifetime of the ³DOB* is quite long in this solution (\sim 170 ns), the electron spin state populations in the triplet manifold have completely relaxed to their Boltzmann levels, which are in general undetectable by TREPR. The same observation has been made for ³BP* in similar solvents. Similar results to those in Figure 7 were obtained during the photolysis of DOB in cyclohexane (spectrum not shown). This solvent was chosen to better mimic the hydrophobic interior of the CD moiety.

In Figure 7, there is no evidence for the presence of benzyl or benzoyl radicals from the α -cleavage reaction, which differs from the CIDNP results. However, the NMR experiments were carried out in acetonitrile, which is a relatively poor H-atom donor compared to 2-propanol. Therefore, the rate of H-atom abstraction is substantially increased in the TREPR experiment, and this reaction pathway dominates. In the absence of any TM contribution, RPM is the only available polarization mechanism. However, the hyperfine coupling constant differences for benzyl and benzoyl radicals are in general quite small, and this means that any RPM CIDEP generated by these radicals is likely to be weak.

TREPR of DOB/CD Complexes in Water. X-band TREPR spectra recorded at several delay times after 248 nm laser flash photolysis of DOB/CD complexes are shown in Figure 8. While it is possible that a different wavelength of excitation of a molecule can lead to a change in the mechanism of a photochemical reaction due to formation of higher energy states, we have confirmed that, for DOB, the radicals produced and the mechanism of CIDEP formation are both independent of the wavelength of photolysis (248 vs 308 nm). These spectra are tentatively assigned to one or more radicals from the H-atom abstraction reaction between ³DOB* and the randomly methylated CD. The spectra are about 22 G wide (FWHM), and their



Figure 8. TREPR spectra detected after laser flash photolysis of DOB with CD in aqueous solution using 300 ns sampling gates at the delay times indicated. Transitions below the baseline are in emission.

line shape does not depend on the delay time. The most reasonable explanation for the broad line shape is an increase in electron spin relaxation time T_2 due to a strong exchange interaction in RP2 consisting of the ketyl and CD radicals. It is also possible that hyperfine anisotropy is appearing in the spectra due to an increase in the rotational correlation time of the ketyl radical when it is confined to the CD. The time dependence of this TREPR signal can be described using a monoexponential decay with a characteristic decay constant $\tau = 3.1 \,\mu$ s.

To confirm this assignment, the experimental spectrum acquired at 300 ns delay (Figure 8) was compared with two calculated TREPR spectra for RP1 and RP2. Figure 9 shows the experimental spectrum from Figure 8 (300 ns delay time) with simulations for different radical pairs: (a) RP2, that is, the DOB ketyl radical and the type I CD radical (Chart 3, left), and (b) RP1, the benzoyl radical and the benzyl radical. The type I CD radical is used in the simulations to remain consistent with the CIDNP results above. Magnetic parameters used in the simulations were taken from Table 1 for all species. From Figure 9, we conclude that RP2 (DOB ketyl radical and type I CD radicals), with a line width of 5 G, gives the best fit to the experimental spectrum.

The net emissive polarization in the spectra shown in Figure 8 can be formed via two distinct mechanisms: the triplet mechanism (TM) or an S–T₋ contribution to the RPM. As previously discussed, in order to observe TM CIDEP from radical reactions involving DOB, the rates of the chemical reactions leading to the radicals (i.e., the inverse of the triplet lifetime) must compete with electronic spin relaxation in the triplet state (1–10 ns). It is known from the literature that the lifetime of ³BP* in CD aqueous solution (350 ns) does not change much from its lifetime in cyclohexane (300 ns).³⁴ The molecular structures of DOB and BP are similar, and we can assume that their rate constants for H-atom abstraction from β -CD should also be similar. The BP/CD CIDNP results above, coupled with our solution TREPR experiments presented here for DOB, support our assertion that TM polarization is unlikely to be generated in reactions of DOB in CDs.

As a rule, when the $S-T_{-}$ mechanism of CIDEP is operative, the observed spectra are asymmetric, because $S-T_{-}$ flip-flop transitions are allowed only for definite spin levels; thus, EPR lines corresponding to T_{-} levels with α_i projection of nuclear spins are the only ones that become polarized. However, the observed CIDEP spectrum in Figure 8 has a symmetrical line shape. It is possible that fast nuclear relaxation of the radical electronic spin levels is taking place, which can happen when there are numerous



Figure 9. (a) Stickplot EPR spectrum of the DOB ketyl radical, (b) TREPR spectrum of the experimentally observed TREPR spectrum detected after laser flash photolysis of DOB with CD in aqueous solution at a delay time of 300 ns (from Figure 8), and (c) stickplot EPR spectrum of the type I CD radical. Magnetic parameters for simulations are listed in Table 1. See text for discussion.



Figure 10. (a) Stickplot TREPR spectrum of the BP ketyl radical, (b) experimentally observed TREPR spectrum detected after laser flash photolysis of BP with CD in aqueous solution at a delay time of 600 ns, and (c) stickplot TREPR spectrum of the type I CD radical. Magnetic parameters for simulations are listed in Table 1.

nuclei coupled to both electrons. Figure 10b shows the TREPR spectrum obtained when BP/CD complexes are irradiated. The same broad emissive signal as observed in Figure 8 for DOB/CD is observed here.

The CIDNP results in Figure 5 clearly indicate that H-atom abstraction from the CD cavity interior by ³BP* is indeed taking place during the photolysis of the BP/CD complex. This means that the CIDEP spectrum has contributions from the BP ketyl radical and at least type I CD radicals if not both. The FWHM of the observed signal (2.8 mT) in Figure 10b is less than the FWHM

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of the type I CD radical (5 mT), but is larger than the FWHM of the BP ketyl radical (1.1 mT). It should also be noted that the observed FWHM in Figure 10b is about two times less than the predicted spectral width of the type I CD radical. This indicates that the exchange interaction in this RP is substantially larger than the HFI constants of the type I CD radical. The $S-T_$ emissive phase of the observed CIDEP also points to the existence of a large exchange interaction in this system, comparable to the Zeeman interaction. We did not perform an accurate simulation of the TREPR spectra, as this needs to take into account, for each individual radical pair system, the value of the exchange interaction and its degree of modulation by radical motion inside the CD cavity. We know little about these parameters at the moment.

It is interesting to note that the asymmetry typical of $S-T_$ mixing is clearly present in the BP/CD (Figure 10b) spectrum, in contrast with the DOB/CD CIDEP (Figure 8) spectrum. This could be due to the difference in spin relaxation times. For the DOB ketyl radical, the spin relaxation time is expected to be less than that for BP ketyl radical, because of the former's larger HFI constants (see Table 1).

Another possible interaction that can affect the shape of EPR spectrum and create CIDEP is the electron dipole-dipole interaction. If the distance between the two radical centers in RP2 does not exceed several angstroms, then the value of the dipole-dipole interaction will be in the range of 1-10 mT. As shown by Shushin,³⁵ in the absence of an exchange interaction, the dipoledipole interaction itself can generate multiplet polarization with opposite phase to that contributed by $S-T_0$ RPM CIDEP. We did not observe any multiplet polarization in our spectrum, and we can conclude either that the contribution from this polarization is negligible or that it is canceled by $S-T_0$ RPM CIDEP. Of course, we expect a large exchange interaction to be present in RP2, which might lead to a different polarization pattern than that predicted by Shushin. Such a theoretical consideration is outside the scope of the present paper. It should be noted that, in previous reports of TREPR spectroscopy of flexible biradicals experiencing large exchange interactions and S-T₋ mixing, the same asymmetry appears in the spectra.

We have also studied CIDEP during the photolysis of ³DBK* in CDs using TREPR (spectra not shown). It is known that the lifetime of the triplet DBK molecule is very short in solution at room temperature³⁶ and that the only reaction pathway to radicals is α -cleavage. In cyclohexane solution, we observed a strong positive CIDEP polarization due to the TM, in agreement with literature data³⁷ and a small contribution from the RPM (E/A). We did not observe any CIDEP during the photolysis of aqueous solutions of DBK in CDs. The most reasonable explanation for this is the fast recombination of radicals formed after α -cleavage.

TREPR of DOB and DOB/CD Complexes in Frozen Solutions. The signal carrier in Figure 8 could be the partially averaged DOB molecular triplet state. To rule out this possibility, an X-band TREPR spectrum of the DOB/CD complex in frozen aqueous solution was obtained at 100 K. The spectrum we obtained at a delay time of 500 ns, using flash photolysis at 308 nm and 300 ns gates, is shown in Figure 11. A very strong half-



Figure 11. X-band TREPR spectrum acquired 500 ns after 308 nm laser flash photolysis of the DOB/CD complex in a frozen aqueous solution at 100 K. Note the half-field transition near $B_0 = 100 \text{ mT}$, which is the signature of a randomly oriented molecular triplet state.

field transition is observed at about 100 G, highly indicative of a randomly oriented powder pattern triplet state EPR spectrum.³⁸ From the approximate *D* value of 2000 G (based on the spectral width) and estimated rotational correlation time of β -CDs in water ($\tau_r \sim 3$ ns), we can conclude that the lifetime of the triplet molecule is substantially longer that its electron relaxation time. Thus, we can state conclusively that we are *not* observing molecular triplet states in our TREPR spectra of DOB/CD complexes in water.

Conclusions

We have examined in detail the photophysics and photochemistry of DOB, DBK, and BP in permethylated β -CD inclusion complexes and compared these reactions to free solution using time-resolved magnetic resonance (TREPR, TR-CIDNP) techniques. The results clearly show that, in confined conditions such as the interior of β -CDs, the reaction pathways for the DOB triplet state include both α -cleavage and H-atom abstraction. This correlates well with the behavior of DOB in free solution; however, the partitioning of the reaction pathways depends on the presence or absence of a H-atom donor. Many of the free radicals involved in this photochemistry have been characterized for the first time, as have their products. The rearrangement product of the radicals from α -cleavage (PMB) has been conclusively identified by NMR spectroscopy for the first time. The observation of this rearrangement implies that there is significant mobility of the radicals in the CD interior, but whether it is translational or rotational freedom remains unclear. The spin polarization mechanism observed in DOB/CD and BP/CD complexes is attributed to $S-T_{-}$ RPM CIDEP, with no contribution from the TM in the case of either DOB or BP. The exchange interaction between the members of RP1 must be large, quite possible comparable to the Zeeman interaction at X-band (~0.34 mT).

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