Identification by time-resolved EPR spectroscopy of cyclodextrin radicals produced by photochemical hydrogen abstraction

Marc N. Lehmann and Martin G. Bakker *

Department of Chemistry, The University of Alabama, Tuscaloosa, AL 35487-0336, USA

2 PERKIN COMMUNICATION

Laser flash photolysis/time-resolved EPR spectroscopy of acetone, methyl ethyl ketone, pyruvic acid, and levulinic acid included in α-, β- and γ-cyclodextrins has identified a number of cyclodextrin radicals, and shows that the relative radical yields differ for different cyclodextrin–ketone pairs.

Cyclodextrins (CDs) are water soluble cyclic polysaccharides that contain a hydrophobic interior and so can form inclusion complexes.[1,2] There has been considerable interest in using these molecules as photo- and thermal-stabilizers,[3,4] 'micro-reactors'[5–7] and to stabilize reactive species.[8–14] Cyclodextrins are also one of the most popular hosts for studies of inclusion and molecular recognition phenomena.[15] Recently it has become apparent that for reactions involving free radicals, CDs cannot be treated as inert hosts,[16–21] and that in many systems there exists the potential for a number of different cyclodextrin radicals to be formed. We report here the use of time-resolved EPR (TREPR) to give the first identification of radicals from α-, β- and γ-cyclodextrins (α-CD, β-CD and γ-CD, respectively). TREPR is particularly sensitive to the dynamics of radical recombination[22,23] and is therefore expected to give an insight into the inclusion behavior of the radicals.

Fig. 1 shows the TREPR spectra obtained from laser photolysis of aqueous solutions of acetone and the three CDs, accompanied by fitted simulations of the experimental spectra. The peaks marked with (X) result from the 2-hydroxy-2-propyl counter-radical which has a coupling constant of 1.936 mT from six hydrogens and a *g*-value of 2.0032. The peaks labeled 2–5 and 2′–5′ in Fig. 1(*a*) comprise a doublet of doublet of doublets and can readily be assigned to the α-CD C5 carbon-centered radical based on the coupling constants of 3.12 (1 H), 0.85 (1 H) and 0.70 mT (1 H). This assignment closely matches splitting constants for the C5 glucose and dextrin radicals obtained by Gilbert *et al.*[24,25] The *g*-value of 2.0030 for this radical is also consistent with the radical center being located on C5 and rules out the carbonyl radicals commonly seen from glucopyranose radical rearrangements. The peaks labeled 1, 6, 1′ and 6′ in Fig. 1(*a*) comprise a doublet of doublets with hyperfine splittings of 3.23 and 2.78 mT and a *g*-value of 2.0031. These couplings are indicative of β-couplings, and their magnitude and the *g*-value are consistent with the radical center being located on C3.[25,26] Both the C3 and C5 radicals as well as the 2-hydroxy-2-propyl radical were found to be heavily spin polarized by the Triplet Mechanism (TM). This is in contrast to the results of our TREPR study of acetone with glucose,[27] where the polarization generated is almost entirely due to the radical pair mechanism (RPM).

Fig. 1(*c*) shows the experimental and Fig. 1(*d*) the simulated spectra obtained from β-CD. The experimental spectrum shows some similarities to those obtained from α-CD. Peaks 3, 4, 6′, 4′ and 3′ are simulated with splitting constants of 3.350 (1 H), 0.783 (1 H) and 0.696 mT (1 H), and a *g*-value of 2.0032 in agreement with the C5 radical.[24,25] Peaks 2, 8′ and 2′ are fitted with splitting constants of 3.30 and 2.70 mT, and the *g*-value of 2.0031 is in agreement with the C3 radical.[25,28] Peaks 5 and 5′

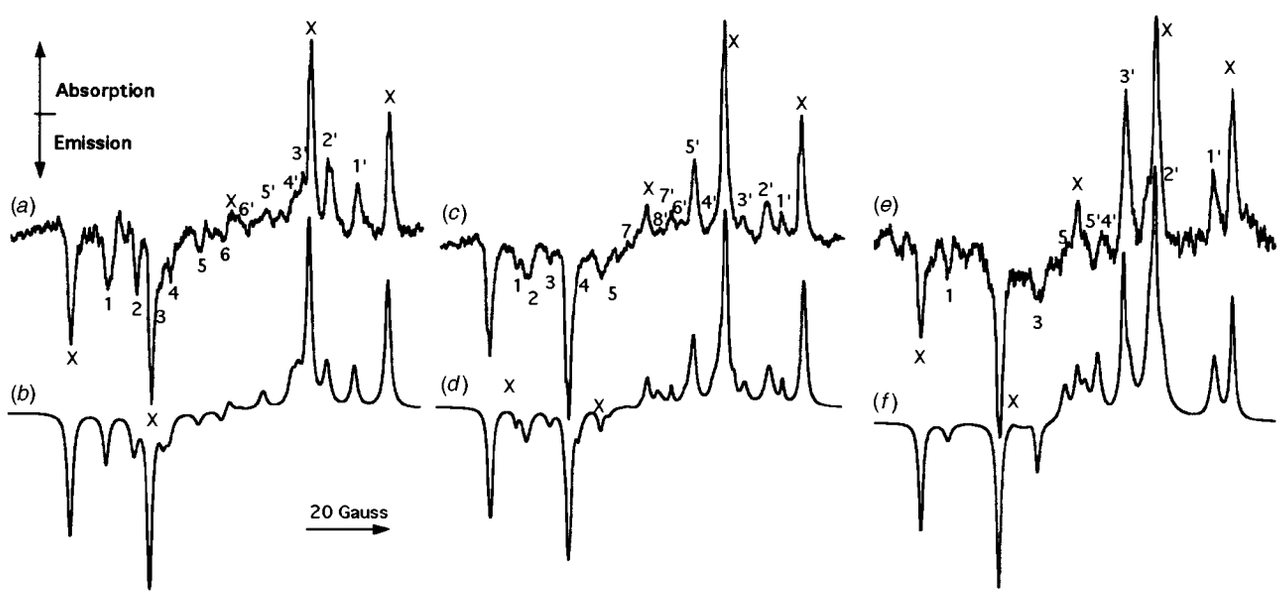
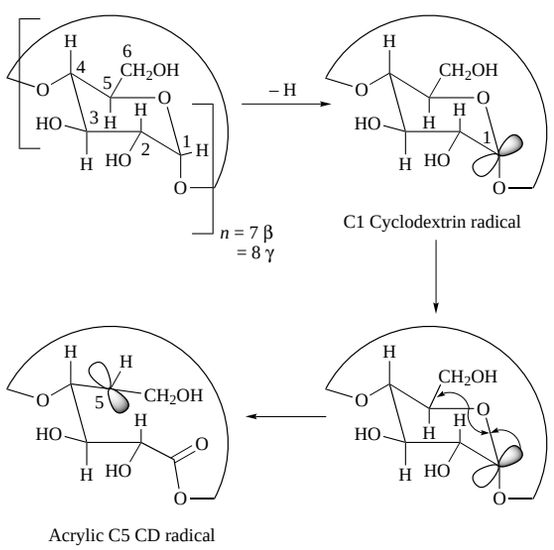


Fig. 1 TREPR spectra from cyclodextrin (10% w/v) in aqueous acetone (10% v/v) solutions. The spectra were recorded using a boxcar averager with a window from immediately after the laser pulse (308 nm, *ca.* 150 mJ, 15 ns pulse) to 500 ns after the pulse. Each point is the average of 10 laser pulses. Peaks marked (X) are from the 2-hydroxy-2-propyl radical. The simulated spectra were calculated using a substantially modified FORTRAN version of program MASTER obtained from Dr M. D. E. Forbes. Fitting was carried out using a Simplex Algorithm. (*a*) Experimental spectrum of α-CD; (*b*) simulated spectrum of α-CD; (*c*) experimental spectrum of β-CD; (*d*) simulated spectrum of β-CD; (*e*) experimental spectrum of γ-CD; (*f*) simulated spectrum of γ-CD.

form a doublet with a splitting of 2.30 mT and a *g*-value of 2.0031. This coupling could only arise from a C1 radical, as abstraction from any other site on the ring leads to multiple, large β-couplings. The absence of the small coupling normally observed for C1 glucopyranose radicals can be rationalized as due to changes in conformation of the glucopyranose radical caused by it being part of the CD ring. In the work of Korth and co-workers,[29,30] the size of the small C1 coupling constant was found to change substantially when the geometry was constrained, and we have observed that the small coupling constant in the C1 glucose radical also disappears in alkaline solution.[27]

The peaks marked 1, 7, 1′ and 7′ are due to a species with a *g*-value of 2.0029, and splitting constants of 2.30 (1 H), 1.55 (2 H) and 1.20 mT (1 H), similar to splitting constants that we have observed in glucose.[27] The splitting constants do not match any of the primary glucose radicals[25,28] and the *g*-value rules out the cyclic ketone dehydration products typically observed.[25] This spectrum is tentatively assigned to an acyclic C5 radical formed from the C1 radical by glucose ring opening according to the mechanism in Scheme 1.



Scheme 1

The polarizations of the C1, C5, acyclic C5 and 2-hydroxy-2-propyl radicals were all found to have substantial TM contributions. The contributions of TM to C1 and acyclic C5 radicals are about equal and noticeably larger than for the cyclic C5 and 2-hydroxy-2-propyl radicals, consistent with the ring opening of the C1 radical to give the acyclic C5 radical.

Fig. 1(*e*) and (*f*) show the experimental and simulated spectra obtained from γ-CD. Peaks 3 and 3′ [2.13 mT (1 H), *g*-value 2.0028] are assigned to the C1 radical. Peaks 1, 5, 5′, 4′, 2′ and 1′ are assigned to an acyclic C5 radical [2.11 mT (1 H), 1.61 mT (2 H) and 1.30 mT (1 H), *g*-value 2.0029] resulting from ring opening of a C1 radical. Again there is a substantial TM contribution to the polarization.

When pyruvic acid was used instead of acetone, strong signals from the C3 radical and (cyclic) C5 radicals were observed from α-CD. With β-CD, pyruvic acid gave C3 radicals. With γ-CD, pyruvic acid gives the C6 radical [1.40 (1 H), 0.65 (1 H), 0.14 (1 H) and 0.07 mT (2 H), *g*-value 2.0032] and a spin-correlated radical pair similar to that observed in glucose[27,31] and maltose.[27] Methyl ethyl ketone (MEK) gives only a weak C3 radical spectrum from α-CD and no observed sugar radical spectra from β-CD and γ-CDs. Levulinic acid (4-oxovaleric acid) gives spectra from C3 and C1 radicals from α-CD, but no sugar radical spectra from β-CD or γ-CDs.

The hydrogens on C3 and C5 which are abstracted to give the C3 and C5 carbon-centered radicals are both on the inside of the CD cavity. The hydrogen on C1, however, is on the outside of the CD cavity. The lifetime of the triplet state of acetone in water is *ca.* 20 μs,[32] however the rate constant for quenching by propan-2-ol[33] is *ca.* 1×10^6 M^{-1} s^{-1}. At the concentrations used in our experiments, and allowing for the greater number of activated C–H bonds in cyclodextrin, gives an estimated lifetime of the triplet excited state of acetone of *ca.* 100 ns. This is sufficiently long for the triplet excited state to diffuse from outside of the cavity into the cyclodextrin cavity.

The observation of some radicals, but not others, suggests that hydrogen abstraction is selective, however care must be exercised in drawing such conclusions when the TREPR spectra are polarized by the radical pair mechanism. A number of factors, including relaxation times and the rates of re-encounter and recombination of radicals, determine the absolute intensity of the TREPR spectral lines. However, if only the relative spectral intensities of a group of structurally similar radicals is considered then comparison is simplified. Preliminary analysis of the decay kinetics indicates that the lifetimes of the cyclodextrin radicals are approximately the same. If the relaxation time is longer than the radical lifetime, which is likely to be the case for cyclodextrin radicals, then the relative intensities of the spectral lines are proportional to the relative concentrations of the radicals. That C1 but not C2 or C6 radicals are observed for β-CD and γ-CD with acetone does suggest that hydrogen abstraction is selective for C1 over C2 and C6. Likewise the changes in hydrogen abstraction patterns between α-CD, β-CD and γ-CD, and the changes when different ketones are used are likely to reflect changes in the position of the various ketones or their triplet excited states within the cyclodextrin cavity.

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References

1 W. Saenger, *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 344.
2 J. Szejtli, *Cyclodextrin Technology*, Kluwer Academic Publishers, Dordrecht, 1988.
3 Y. Matsui, H. Naruse, K. Mochida and Y. Date, *Bull. Chem. Soc. Jpn.*, 1970, **43**, 1909.
4 Y. Matsui, H. Naruse, K. Mochida and Y. Date, *Bull. Chem. Soc. Jpn.*, 1970, **43**, 1910.
5 V. Ramamurthy and D. F. Eaton, *Acc. Chem. Res.*, 1988, **21**, 300.
6 B. N. Rao, N. J. Turro and V. Ramamurthy, *J. Org. Chem.*, 1986, **51**, 460.
7 M. S. Syamala and V. Ramamurthy, *Tetrahedron*, 1988, **44**, 7223.
8 J. Bardsley, P. J. Baugh, J. I. Goodall and G. O. Phillips, *J. Chem. Soc., Chem. Commun.*, 1974, 890.
9 P. J. Baugh, O. Hinojosa and J. C. J. Arthur, *J. Phys. Chem.*, 1967, **71**, 1135.
10 V. P. Rao, M. B. Zimmt and N. J. Turro, *J. Photochem. Photobiol. A*, 1991, **60**, 335.
11 Y. Kubozono, M. Ata, M. Aoyagi and Y. Gondo, *Chem. Phys. Lett.*, 1987, **137**, 467.
12 M. Ata, Y. Suzuki, Y. Kubozono, M. Aoyagi and Y. Gondo, *Chem. Phys. Lett.*, 1989, **157**, 19.
13 M. Ata, M. Aoyagi, Y. Kubozono and Y. Gondo, *Chem. Lett.*, 1989, 341.
14 M. Lucarini and B. P. Roberts, *Chem. Commun.*, 1996, 1577.
15 R. J. Clarke, J. H. Coates and S. F. Lincoln, *Adv. Carbohydr. Chem. Biochem.*, 1988, **46**, 205.
16 A. M. Aquino, C. J. Abelt, K. L. Berger, C. M. Darragh, S. E. Kelley and M. V. Cossette, *J. Am. Chem. Soc.*, 1990, **112**, 5819.
17 A. Beeby and J. R. Sodeau, *J. Photochem. Photobiol. A: Chem.*, 1990, **53**, 335.
18 Y. L. Chow, J. Michon, P. Michon, C. Morat and A. Rassat, *Tetrahedron Lett.*, 1992, **33**, 3315.
19 M. Lehmann, M. G. Bakker, H. Patel, M. L. Parton and S. Dormady, *J. Inclusion Phenom., Mol. Recogn.*, 1995, **23**, 99.
20 K. I. Priyadarsini, H. Mohan, J. P. Mittal, D. M. Guldi and K.-D. Asmus, *J. Phys. Chem.*, 1994, **98**, 9565.

21 S. Monti, L. Flamigni, A. Martelli and P. Bortolus, *J. Phys. Chem.*, 1988, **92**, 4447.
22 K. A. McLauchlan, *Modern Pulse and Continuous-Wave Electron Spin Resonance*, ed. L. Kevan and M. K. Bowman, Wiley, New York, 1990.
23 M. D. E. Forbes, J. Peterson and C. S. Breivogel, *Rev. Sci. Instrum.*, 1991, **62**, 2662.
24 B. C. Gilbert, D. M. King and C. B. Thomas, *Carbohydr. Res.*, 1984, **125**, 217.
25 B. C. Gilbert, D. M. King and C. B. Thomas, *J. Chem. Soc.*, *Perkin Trans. 2*, 1981, 1186.
26 K. P. Madden and R. W. Fessenden, *J. Am. Chem. Soc.*, 1982, **104**, 2578.
27 M. N. Lehmann, Dissertation Thesis, University of Alabama, 1997.
28 K. P. Madden and W. A. Bernhard, *J. Chem. Phys.*, 1979, **70**, 2431.
29 H.-G. Korth, R. Sustmann, J. Dupuis and B. Giese, *J. Chem. Soc.*, *Perkin Trans. 2*, 1986, 1453.
30 R. Sustmann and H.-G. Korth, *J. Chem. Soc.*, *Faraday Trans. 1*, 1987, **83**, 95.
31 I. A. Shkrob, M. C. Depew and J. K. S. Wan, *Chem. Phys. Lett.*, 1993, **202**, 133.
32 G. Porter, R. W. Yip, J. M. Dunston, A. J. Cessna and S. E. Sugamori, *Faraday Trans.*, 1971, **67**, 2149.
33 G. Porter, S. K. Dogra, R. O. Loutfy, S. E. Sugamori and R. W. Yip, *J. Chem. Soc.*, *Faraday Trans. 1*, 1973, **69**, 1462.

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