perature reaction, which was then heated to 70 °C with the evolution of gas. Once gas evolution ceased, the reaction was cooled with a room-temperature water bath. A suspension of (methyl-d_3)triphenylphosphonium iodide (27 g, 0.066 mol) in dry DMSO-d_6 was added dropwise with rapid stirring to form the ylide. Freshly distilled methacrolein (5.04 mL, 0.061 mol) was added dropwise to the reaction mixture. After the reaction was stirred at room temperature for 1 h, evacuation of the system to 1 Torr allowed 4.4 mL (70% yield) of the isoprene product to be collected in a previously flame-dried trap cooled with a liquid nitrogen bath. Comparison of the H NMR spectra obtained to that of protioisoprene[20] indicated less than 2% hydrogen at the 4-position: NMR (300 MHz, $CDCl_3$) δ 6.45 (s, 1 H), 4.93 (s, 2 H), 1.85 (s, 3 H).

Preparation of Stock Solutions of d_0/d_2 and d_0/d_4 Isoprene. Stock solutions of isoprene were composed of equivalent amount of protio- and either dideuterio- or tetradeuterioisoprene (>97% *d*).[21] Equivalent amounts (by syringe) of freshly distilled isoprene and either dideuterio- or tetradeuterioisoprene were placed into a flame-dried flask under dry nitrogen. Dry benzene (2 equiv, distilled and stored over Na) was added as solvent. The stock solution was transferred by syringe to flame-dried Pyrex tubes (180 mm × 7 mm, flame sealed at one end) and sealed under vacuum. Each tube held aproximately 450 μL of solution.

General Procedure for the Diels–Alder Reactions. Pyrex tubes (180 mm × 7 mm), which were flame sealed at one end and could be sealed under vacuum, were used as reaction vessels. When a reaction was to be run, a tube of diene stock solution was frozen in liquid nitrogen and opened. Immediately after opening the tube, it was placed under dry N_2 until the solution thawed. Two reactions were set up using the stock solution. The first reaction had a large excess (70–100-fold) of diene. The second reaction had a large excess of dienophile. Once the reactants were combined, the reaction tube was degassed twice and sealed under vacuum. The reactions were run at the temperatures specified in the table. After the reaction was complete, the tube was frozen in liquid nitrogen and opened. The contents were transferred to a 5-mL pear-shaped flask by use of dry benzene. The solvent was then removed in vacuo until the desired concentration was reached. A GC/MS analysis or a capillary GC of the products from these reactions provided the kinetic isotope effects. The reaction product were confirmed by NMR analysis.

Acknowledgment. We thank the National Science Foundation for support, and we thank Professor Ronald A. Hites and Dr. William Simonsick for respectively providing the GC/MS-CI instrument and help in its use.

Registry No. Acrylonitrile, 107-13-1; fumaronitrile, 764-42-1; vinylidene cyanide, 922-64-5; dimethyl fumarate, 624-49-7; dimethyl maleate, 624-48-6; methyl *trans*-β-cyanoacrylate, 925-56-4; isoprene, 78-79-5; deuterium, 7782-39-0; 1,1,3,3-tetracyanopropane, 3695-98-5; malononitrile, 109-77-3; formaldehyde, 50-00-0; trichloroethylene, 79-01-6; paraformaldehyde, 30525-89-4; methyl α-chloroacrylate, 80-63-7; (methyl-d_3)triphenylphosphonium iodide, 1560-56-1; 4,4-dideuterio-2-methyl-1,3-butadiene, 64750-98-7; triphenylphosphine, 603-35-0; iodomethane-d_3, 865-50-9; methacrolein, 78-85-3.

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[20] Sadtler Research Laboratories Inc., Nuclear Magnetic Resonance ref no. 3434.

[21] Tanaka, Y.; Takeuchi, Y.; Kobayashi, M.; Tadokoro, H. *J. Pol. Sci. A-2* **1971**, *9*, 43.

Radical Anions of Esters of Carboxylic Acids. Effects of Structure and Solvent on Unimolecular Fragmentations

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Abstract: Pulse radiolysis of alkyl benzoates produces the ester radical anions, which have optical absorptions near 310 nm (~35 000 M^{-1} cm^{-1}) and 450 nm (~9500 M^{-1} cm^{-1}). The radical anions undergo unimolecular fragmentation to form alkyl radicals and carboxylate anions with rates that depend upon the presence of radical stabilizing groups on the alkyl fragment, the nature of the ester group, and the solvent. This cleavage occurs competitively with other processes, such as acyl carbon–oxygen (Bouveault–Blanc) cleavage and electron transfer. The decay rates in ethanol solvent correlate empirically with the bond dissociation energies BDE_{R-H} of the alkyl fragments. Cleavage to form methyl, primary, or secondary alkyl radicals occurs sufficiently slowly that the other mechanisms of decay are found to predominate.

Radical anions are intermediates in many kinds of processes, including dissolving-metal reductions,[1] cathodic reduction,[2,3] excited-state quenching reactions,[4] homogeneous redox reactions,[5] $S_{RN}2$ reactions,[6,7] and nucleophilic substitutions.[8] The radical anions generally form by single-electron transfer from suitable reducing agents (eq 1). Fragmentation of the radical anions to

$$R\text{–}X + e^- \rightleftarrows R\text{–}X^{\bullet -} \qquad (1)$$

$$R\text{–}X^{\bullet -} \rightarrow R^{\bullet} + X^- \qquad (2)$$

produce an anion and a radical (eq 2) is commonly observed.[2-4,6-11] The rate of this fragmentation determines, in part, the efficiencies

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[1] McOmie, J. F. W. *Protective Groups in Organic Chemistry*; Plenum Press: New York, 1973. Greene, T. W. *Protective Groups in Organic Synthesis*; Wiley: New York, 1981. Muth, H.; Sauerbier, M. In *Houben-Weyl Methoden der Organische Chemie*; Georg Thieme: Stuttgart, 1980; Part 4/1c, Reduktion, Vol 1.

[2] Andrieux, C. P.; Saveant, J.-M.; Su, K. B. *J. Phys. Chem.* **1986**, *90*, 3815.

[3] Saveant, J. M. *Acc. Chem. Res.* **1980**, *13*, 323.

[4] Julliard, M.; Chanon, M. *Chem. Rev.* **1983**, *83*, 425.

[5] Rorabacher, D. B., Endicott, J. F., Eds. *Mechanistic Aspects of Inorganic Reactions*; ACS Symposium Series 198; American Chemical Society: Washington, DC, 1982.

[6] Wade, P. A.; Morrison, H. A.; Kornblum, N. *J. Org. Chem.* **1987**, *52*, 3102.

[7] Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413.

[8] Bordwell, F. G.; Harrelson, J. A., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 8112.

[9] (a) Prasad, D. R.; Hoffman, M. Z.; Mulazzani, Q. G.; Rodgers, M. A. J. *J. Am. Chem. Soc.* **1986**, *108*, 5132. (b) Maslak, P.; Guthrie, R. D. *J. Am. Chem. Soc.* **1986**, *108*, 2628. (c) Lan, J. Y.; Schuster, G. B. *Ibid.* **1985**, *107*, 6710.

[10] Neta, P.; Behar, D. *J. Am. Chem. Soc.* **1981**, *103*, 103.

[11] Hamill, W. H. *Radical Ions*; Kaiser, E. T., Kevan, L., Eds.; Interscience: New York, 1968; Chapter 9, pp 408–412. Ward, J. A.; Hamill, W. H. *J. Am. Chem. Soc.* **1965**, *87*, 1853.

0002-7863/89/1511-9081$01.50/0

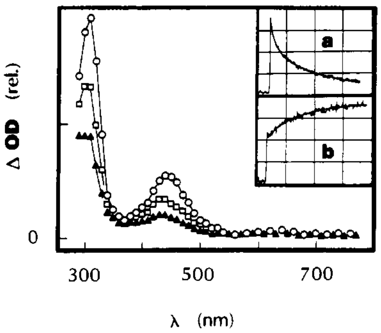

Figure 1. Difference transient absorption spectra of ethyl benzoate in alcohol determined 1 (○), 37 (□), and 135 (▲) μs after a 100-ns pulse of electrons. Insets show time dependence of absorption at 450 nm (a) in the absence of added base (110 μs/division) and (b) in the presence of 0.1 M KOH (260 μs/division), together with exponential fits (solid traces).

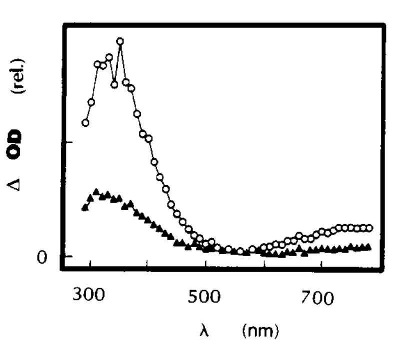

Figure 2. Difference transient absorption spectra of diethyl phthalate in alcohol determined 5 (circles) and 672 μs (triangles) after a 100-ns pulse of electrons.

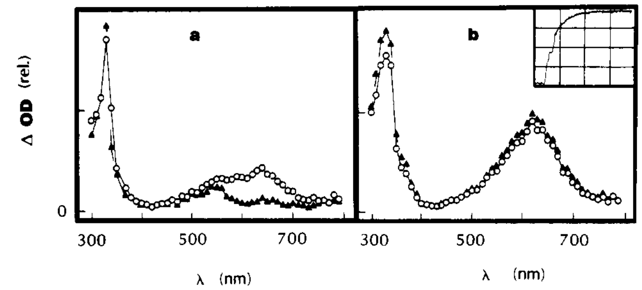

Figure 3. Difference transient absorption spectra of benzophenone determined 0.5 (circles) and 67 μs (triangles) after a 100-ns pulse of electrons (a) in alcohol and (b) in alcohol containing 0.1 M KOH. Inset shows time dependence (1.9 μs/division) of absorption of 640 nm together with first-order fit (solid trace) in the presence of KOH.

of processes in which the electron transfer of eq 1 occurs reversibly.[3-4,6-10] The reaction mechanism and products also may be affected by the rate of cleavage. For example, stable radical anions may form reactive dianions by a second electron transfer[12] or by dimerization,[13] and radical anions of unsaturated compounds may undergo acid–base reactions to form radicals.[14]

Esters of carboxylic acids are electrophiles that can serve as oxidants in certain reactions. Single-electron transfer to benzoate esters (eq 3) occurs under a variety of conditions.[15-21] The ester

$$\mathrm{ROCOC_6H_5} + \mathrm{e^-} \xrightarrow{k_e} \mathrm{ROCOC_6H_5}^{\bullet-} \qquad (3)$$

radical anions formed in eq 3 have been reported to undergo reduction,[15] condensation,[16] protonation,[17,18] alkylation,[19] or fragmentation,[20,21] depending upon the conditions and the manner in which the electron transfer occurs.

Our interest in the structural and environmental factors responsible for reactions that are driven by dissociative electron transfer[22-24] led us to examine carboxylic esters and related derivatives as electron acceptors. Because the reduction of esters by electron transfer has been reported to afford such a variety of products,[15-21,25,26] we have initiated our investigation with an examination of the fundamental reaction pathways of ester radical anions. This information is valuable for theoretical[27] as well as practical reasons, as reduction of esters is important in synthetic methodology.[20,25] Esters of benzoic acid proved to be well suited for this study. Because of conjugation involving the benzoate group, benzoates are readily reduced and benzoate finds use as a protecting group that can be removed by reduction. Furthermore, the conjugated system in the radical anions of benzoate esters presents an excellent chromophore for optical detection. Herein we report the results of a pulse radiolysis study concerning the reactivities of benzoate ester radical anions. Our findings also serve to explain the various reactivities obtained for esters under conditions of dissolving-metal reductions and photochemical electron-transfer processes.

Results

Pulse radiolysis of a deaerated solution of 2% 2-propanol in ethanol produces a broad absorption with maximum near 700 nm due to solvated electrons.[28] The 700-nm absorption decays with a half-time of ~1.5 μs, corresponding to reaction of the electrons with solvent (or with impurities contained or formed in the solvent).[29] Residual absorptions with maxima at <300 nm are observed on a longer time scale. Evidence for formation of 1-hydroxyalkyl radicals, which may be responsible for the absorptions at short wavelength, is obtained from product studies (vide infra).

Ethyl benzoate quenches the absorptions of the solvated electrons with rate constant $k_e = (5 \pm 1) \times 10^9$ M^{-1}.[30] Two transient

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[12] Aihara, J. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 3404. Gerson, F.; Hackendorn, R.; Cowan, D. O.; Kini, A. M.; Maxfield, M. *J. Am. Chem. Soc.* **1983**, *105*, 7017.

[13] Staples, T. L.; Jagur-Grodzinski, J.; Szwarc, M. *J. Am. Chem. Soc.* **1969**, *91*, 3721. Hirota, N.; Weissman, S. I. *Ibid.* **1964**, *86*, 2538.

[14] Garst, J. F. *Free Radicals*; Kochi, J. K., Ed.; Wiley-Interscience: New York, 1973; Chapter 9, pp 503–546.

[15] Bouveault, L.; Blanc, G. *C. R. Hebd. Seances Acad. Sci.* **1903**, *137*, 60.

[16] Bloomfield, J. J.; Owsley, D. C.; Nelke, J. M. *Org. React.* **1976**, *23*, 259. Finley, K. T. *Chem. Rev.* **1964**, *64*, 573.

[17] Hayon, E.; Simic, M. *Acc. Chem. Res.* **1974**, *7*, 114.

[18] Saito, I.; Ikehira, H.; Kasatani, R.; Watanabe, M.; Matsuura, T. *J. Am. Chem. Soc.* **1986**, *108*, 3115.

[19] Kharasch, M. S.; Sternfeld, E.; Mayo, F. R. *J. Org. Chem.* **1940**, *5*, 362.

[20] Ghosh, S.; Pardo, S. N.; Salomon, R. G. *J. Org. Chem.* **1982**, *47*, 4692. Barrett, A. G. M.; Godfrey, C. R. A.; Hollinshead, D. M.; Prokopiou, P. A.; Barton, D. H. R.; Boar, R. B.; Joukhadar, L.; McGhie, J. F.; Misra, S. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1501.

[21] Lin, C.-I.; Singh, P.; Ullman, E. F. *J. Am. Chem. Soc.* **1976**, *98*, 7848.

[22] Masnovi, J.; Koholic, D. J.; Berki, R. J.; Binkley, R. W. *J. Am. Chem. Soc.* **1987**, *109*, 2851.

[23] Masnovi, J. M.; Kochi, J. K.; Hilinski, E. F.; Rentzepis, P. M. *J. Am. Chem. Soc.* **1986**, *108*, 1126. Masnovi, J. M.; Kochi, J. K. *J. Am. Chem. Soc.* **1985**, *107*, 6781.

[24] For a preliminary communication, see: Masnovi, J.; Maticic, J. *J. Am. Chem. Soc.* **1988**, *110*, 5189.

[25] Barrett, A. G. M.; Godfrey, C. R. A.; Hollinshead, D. M.; Prokopiou, P. A.; Barton, D. H. R.; Boar, R. B.; Joukhader, L.; McGhie, J. F.; Misra, S. C. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1501.

[26] (a) Wu, T.-C.; Rieke, R. D. *J. Org. Chem.* **1988**, *53*, 2381. Luh, T.-Y.; Lee, K. S.; Tam, S. W. *J. Organomet. Chem.* **1983**, *248*, 221. (b) Kirrstetter, R. G. H. *Chem. Ber.* **1979**, *112*, 2804.

[27] Buncel, E.; Shaik, S. S.; Um, I.-H.; Wolfe, S. *J. Am. Chem. Soc.* **1988**, *110*, 1275.

[28] Taub, I. A.; Harter, D. A.; Sauer, Jr., M. C.; Dorfman, L. M. *J. Chem. Phys.* **1964**, *41*, 979.

[29] Swallow, A. T. In *Radiation Chemistry*; Farhataziz, Rodgers, M. A. J., Eds.; VCH: New York, 1987; pp 351–375.

[30] The observed rate constant is slightly lower than the rate of diffusion of electrons in ethanol (~2 × 10^{10} M^{-1} s^{-1})[31] or the rate of electron capture by benzoic acid (1.6 × 10^{10} M^{-1} s^{-1}),[32] but it is more than 2 orders of magnitude higher than the rate of reaction of electrons with benzene (1.4 × 10^7 M^{-1} s^{-1}).[33]

[31] Adams, G. E.; Michael, B. D.; Wilson, R. L. *Adv. Chem.* **1968**, *81*, 289.

Table I. Rates of Decomposition of Ester Radical Anions

substrate	k,[a] s^{-1} alcohol (λ_{MON})[c]	k,[a] s^{-1} hexane (λ_{MON})[c]	BDE(R–H),[b] kcal/mol
$CH_3OCOC_6H_5$	$5 \pm 2 \times 10^3$[d] (310, 445)	$4 \pm 2 \times 10^4$[d] (305, 440)	105
$CH_3CH_2OCOC_6H_5$	$5 \pm 2 \times 10^3$[d] (310, 445)	$4 \pm 2 \times 10^4$[d] (305, 440)	98
$(CH_3)_3CCH_2OCOC_6H_5$	$5 \pm 2 \times 10^3$[d] (310, 450)	$8 \pm 3 \times 10^4$[d] (305, 440)	99
$(CH_3)_2CHOCOC_6H_5$	$4 \pm 2 \times 10^3$[d] (310, 450)	4.0×10^4 (305, 440)	95
$(CH_3)_3COCOC_6H_5$	1.9×10^4 (310, 450)	2.3×10^5 (305, 440)	92, 93.2
$HC{\equiv}CC(CH_3)_2OCOC_6H_5$	3.0×10^4 (310, 450)	1.1×10^5 (310, 440)	
$C_6H_5CH_2OCOC_6H_5$	4.8×10^4 (310, 445)	2.2×10^5 (440)	85, 88.0
p-$CH_3OC_6H_4CH_2OCOC_6H_5$	3.2×10^4 (310, 450)	$5 \pm 2 \times 10^5$ (310, 440)	
$C_6H_5CH(CH_3)OCOC_6H_5$	1.5×10^5 (310, 450)	1.4×10^6 (310, 440)	
$(C_6H_5)_2CHOCOC_6H_5$	4.6×10^5 (330,[e] 450)	$\geq 5 \times 10^6$[f] (330,[e] 440)	76.7–78.3
C_6H_4-*o*-$(COOCH_2CH_3)_2$	$\leq \sim 1 \times 10^3$[d] (340, 780)	$\sim 4 \times 10^4$[d] (330)	
$C_6H_5COOCOC_6H_5$	*g*	3.2×10^5 (300, 450)	86.9
$C_6H_5CH_2OCOCH_3$	1.4×10^6 (310[e])	$\geq 2 \times 10^6$[f]	85, 88.0
$(C_6H_5)_2CHOCOCH_3$	$>2 \times 10^6$[f] (330[e])	$\geq 5 \times 10^6$[f]	76.7–78.3

[a] Decays of radical anions of benzoates (R–$OCOC_6H_5$) and related substrates at 22 ± 1 °C. Standard deviations of ±20% unless otherwise noted. [b] Dissociation energies for R–H bonds from ref 61. [c] Monitoring wavelength(s) in nm. [d] Higher rate of double-exponential fit. [e] Growth of radical $R^\bullet$ monitored (k or k'). [f] Rates greater than experimental resolution. [g] Not determined.

absorption bands, appearing at 310 nm ($\epsilon \sim 35\,000$ M^{-1} cm^{-1}) and 445 nm ($\epsilon \sim 9500$ M^{-1} cm^{-1}), form simultaneously with the bleach of the 700-nm absorptions (Figure 1). We assign these two absorption bands to the radical anions of the benzoate esters, on the basis of the following evidence.

(i) Both bands are quenched by oxygen with rate constant, k_O on the order of 2×10^{10} M^{-1} s^{-1}. Organic radical anions usually react with oxygen by electron transfer (eq 4) at near-diffusion-limited rates.[33]

$$ROCOC_6H_5^{\bullet-} + O_2 \xrightarrow{k_O} ROCOC_6H_5 + O_2^{\bullet-} \tag{4}$$

(ii) The other alkyl benzoates examined in Table I behave similarly. Identical spectra are observed for all of the benzoate esters, and values of k_e are uniformly (4–7) × 10^9 M^{-1} s^{-1}.[30] The 310- and 450-nm absorptions derived from each ester always are formed together and decay with identical rates.

(iii) The radical anion of acetophenone, acetophenone ketyl anion, produced under identical conditions, also exhibits absorption bands near 310 and 450 nm.[34]

(iv) Substituted benzoates, such as diethyl phthalate (Figure 2), afford transient absorption spectra that are quite different from those derived from benzoates.

(v) The radical anion of methyl benzoate generated in neutral aqueous solution by pulse radiolysis has been reported to have an absorption at 310 nm ($\epsilon \sim 27\,000$ M^{-1} cm^{-1}) and a weak absorption at 440 nm.[32]

Additional experiments were performed to definitively rule out the possibility of protonation of the radical anion by solvent or acid produced in the medium. Pulse radiolysis of benzophenone produced three transient absorption bands (Figure 3a). The absorption band near 640 nm is due to the radical anion of benzophenone.[35] The absorption band near 550 nm is due to the protonated radical anion, the benzophenone ketyl radical.[35] The time dependence of the more intense band appearing near 320 nm suggests that this peak is due to a superposition of absorptions of the radical anion and the ketyl radical. The absorption spectrum is affected by the addition of base. The transient absorptions observed in 0.1 M alcoholic KOH are shown in Figure 3b. Only absorptions of benzophenone radical anion are evident in the presence of base.[36]

The transient absorption spectra ascribed to the radical anions of the benzoate esters are unaffected by the presence of KOH.[36] However, addition of high (0.1 M) concentrations of hydroxide results in complicated kinetic behavior of the ketyl anion: a growth of the absorptions of the ester radical anions is observed (Figure 1, insets). Under the same conditions, a growth in the absorptions of the benzophenone radical anion also is observed at early times (Figure 3b, inset). This behavior is attributed to formation of radical anions of solute via a base-dependent pathway,[31,37] eq 5–7,

$$CH_3CH_2OH \rightarrow CH_3CH_2OH^{\bullet+} + e^- \tag{5}$$

$$CH_3CH_2OH^{\bullet+} + OH^- \rightarrow CH_3CH^{\bullet}OH + H_2O \tag{6}$$

$$CH_3CH^{\bullet}OH + OH^- \rightarrow CH_3CH{=}O^{\bullet-} + H_2O \tag{7}$$

$$CH_3CH{=}O^{\bullet-} + R'COC_6H_5 \xrightarrow{k_{et}} CH_3CH{=}O + R'COC_6H_5^{\bullet-} \tag{8}$$

followed by electron transfer (eq 8) to the carbonyl (R′ = C_6H_5) or carboxyl (R′ = O–R) species. The rate constants k_{et} for eq 8 obtained experimentally under the pseudo-first-order conditions of Figure 3b were determined to be 5.4×10^8 M^{-1} s^{-1} at 630 nm for benzophenone, 1.7×10^6 M^{-1} s^{-1} at 450 nm for *tert*-butyl benzoate, and 2.3×10^6 M^{-1} s^{-1} at 450 nm for isopropyl benzoate. A faster rate of electron transfer to benzophenone than to benzoate esters is consistent with benzophenone ($E_{1/2} = -1.88$ V vs SCE[39]) being a better electron acceptor than the benzoate esters ($E_{1/2} = -2.11$ V vs SCE for methyl benzoate[42]).

The absorptions of the benzoate radical anions were determined to decay by first-order processes. The radical anions of benzoates derived from tertiary or benzylic alcohols were found to decay monoexponentially. However, decays of the radical anions of methyl benzoate, ethyl benzoate, and isopropyl benzoate appeared to be double exponential (see Experimental Section). The rates observed for the decays are collected in Table I and depend on the ester and on the solvent.

Analysis of alcohol solutions of benzyl benzoate subject to pulse or γ radiolysis indicated that the major volatile products were benzoic acid, together with toluene, bibenzyl, and 1-phenyl-2-propanol. The relative yields of benzoic acid, bibenzyl, and 1-phenyl-2-propanol, which were formed in very low conversion (~0.5%), were about 1:0.4:0.4. The reaction products are consistent with the formation of benzyl radicals as intermediates.

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(32) Simic, M.; Hoffman, M. Z. *J. Phys. Chem.* **1972**, *76*, 1398.

(33) Hart, E. J.; Anbar, M. *The Hydrated Electron*; Wiley-Interscience: New York, 1970.

(34) Shida, T.; Iwata, S.; Imamura, M. *J. Phys. Chem.* **1974**, *78*, 741.

(35) Manring, L. E.; Peters, K. S. *J. Am. Chem. Soc.* **1985**, *107*, 6452.

(36) Benzophenone ketyl radical has a pK_a of 9.2, and the pK_a of the protonated anion radical of ethyl benzoate has been determined to be 5.5.[17]

(37) Radiolysis of primary alcohols in aqueous alkaline solutions produces aldehyde radical anions.[38]

(38) Neta, P.; Hoffman, M. Z.; Simic, M. *J. Phys. Chem.* **1972**, *76*, 847.

(39) Determined by using the value of $E_{1/2} = -1.84$ V vs Ag/AgCl,[40] the potential of which is −0.045 V relative to SCE.[41] Similarly, for acetophenone $E_{1/2} = -2.16$ V.[40]

(40) Loutfy, R. O.; Loutfy, R. O. *Can. J. Chem.* **1972**, *50*, 4052.

(41) Skoog, D. A.; West, D. M. *Fundamentals of Analytical Chemistry*, 2nd ed.; Holt, Rinehart and Winston: New York, 1969.

(42) Zuman, P. *Substituent Effects in Polarography*; Plenum: New York, 1967, p 61. Nakaya, J.; Kinoshita, H.; Ono, S. *Nippon Kagaku Zasshi* **1957**, *78*, 935; *Chem. Abstr.* **1959**, *53*, 21276.

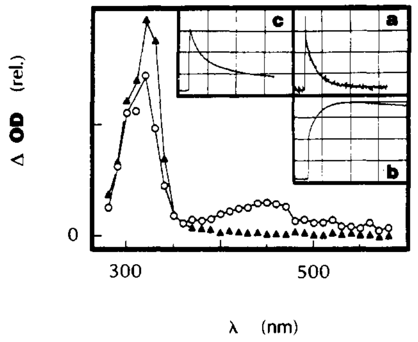

Figure 4. Difference transient absorption spectra of benzhydryl benzoate in alcohol determined 0.4 (circles) and 13.5 μs (triangles) after a 100-ns pulse of electrons. Insets show time dependence of (a) 450-nm absorption (6 μs/division) together with first-order fit (solid trace), (b) 320-nm absorption (5 μs/division) together with first-order fit (solid trace), and (c) 320-nm absorption (300 μs/division) together with second-order fit (solid trace).

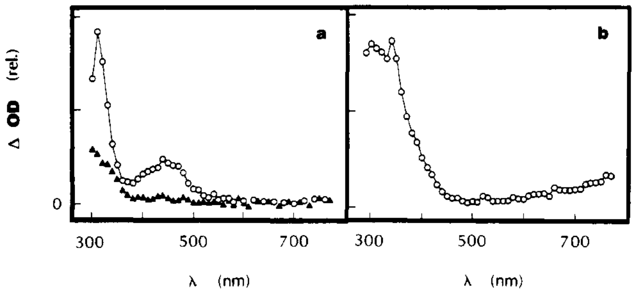

Figure 5. Difference transient absorption spectra of (a) ethyl benzoate determined 0.2 (circles) and 26.9 μs (triangles) after a 250-ns pulse of electrons and (b) diethyl phthalate 3.7 μs after a 500-ns pulse in hexane.

Bibenzyl and the phenylpropanol are the result of coupling of benzyl radicals with one another (eq 9) and with radicals derived from solvent (eq 10 and 11).

$$2C_6H_5CH_2^\bullet \rightarrow C_6H_5CH_2CH_2C_6H_5 \quad (9)$$

$$C_6H_5CH_2^\bullet + CH_3CH_2OH \rightarrow C_6H_5CH_3 + CH_3CH^\bullet(OH) \quad (10)$$

$$C_6H_5CH_2^\bullet + CH_3CH^\bullet OH \rightarrow C_6H_5CH_2CH(OH)CH_3 \quad (11)$$

Benzylic radicals may be observed directly. Benzyl radicals have an absorption band near 320 nm and a weaker band near 460 nm.[43] The time-resolved spectra indicate that the transient absorptions of the radical anions of benzylic benzoates evolve into those of the benzyl radicals. The decay of the absorptions due to benzyl radical is observed to be second order (5×10^9 M^{-1} s^{-1})[44,45] and occurs on a longer time scale than the decay of the radical anions. Results for benzhydryl benzoate are presented in Figure 4. Benzhydryl benzoate initially affords the spectrum predominantly of the radical anion (Figure 4, circles). At longer times, the absorptions of the radical anion are replaced by those of the diphenylmethyl radical, which has an intense maximum at 330 nm ($\epsilon \sim 4 \times 10^4$ M^{-1} cm^{-1}).[46] The formation of the radical (monitored at 330 nm) and the decay of the radical anion (monitored at 450 nm) occur with the same first-order rate constant (Figure 4, insets a and b). The diphenylmethyl radical subsequently decays with second-order rate constant, 3×10^9 M^{-1} s^{-1} (Figure 4, inset c).[47,48]

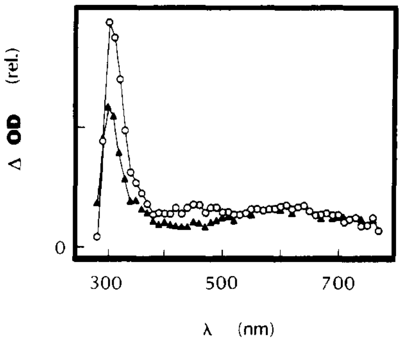

Figure 6. Difference transient absorption spectra of benzoic anhydride in hexane determined 0.4 (circles) and 2.7 μs (triangles) after a 250-ns pulse of electrons.

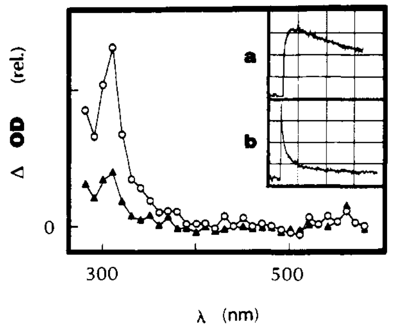

Figure 7. Difference transient absorption spectra of benzyl acetate in alcohol determined 8 (circles) and 269 μs (triangles) after a 250-ns pulse of electrons. Insets shows time dependence of absorption at 310 nm with time scales (a) 6 μs/division together with combined first-order (growth) and second-order (decay) fit (solid trace) and (b) 260 μs/division together with second-order fit.

Pulse radiolysis of benzoate esters in hexane (Figure 5) produces absorptions that are shifted hypsochromically by 5–10 nm compared to those observed in alcohol solution (Figures 1 and 2). The change in solvent only slightly affects the absorptions of the benzoate radical anions. Nevertheless, the rates of decay are higher by ~1 order of magnitude in hexane than in alcohol (Table I).

Pulse radiolysis of benzoic anhydride in hexane produced three absorption bands, appearing near 300, 450, and 650 nm in the transient spectrum (Figure 6). The kinetics behavior of these bands indicate that the 450-nm absorbing species decays to produce the 650-nm absorbing species,[49] and the absorptions near 300 nm result from a superposition of absorptions due to both species. The absorptions of the initially decaying species resemble those of the benzoate ester radical anions, and we assign the faster decaying absorptions near 300 and 450 nm to the radical anion of benzoic anhydride, $C_6H_5COOCOC_6H_5^{\bullet -}$. The absorption band near 650 nm, as well as residual absorptions near 300 nm, remain after the 450-nm absorptions have decayed (Figure 6, triangles). A broad absorption near 650 nm is characteristic of the benzoyl radical,[51] which then would be a product of the anhydride radical anion.[49]

The behavior of acetate esters also was examined because products and yields of reductions purportedly proceeding by electron transfer have been reported to depend on the nature of the ester group.[18,21] Acetates quench the absorptions of the

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(43) Christensen, H. C.; Sehested, K.; Hart, E. J. *J. Phys. Chem.* **1973**, *77*, 983.

(44) Determined by using the observed decay (2.0×10^6 A^{-1} s^{-1} with l = 2 cm) and the value $\epsilon \sim 5000$ M^{-1} cm^{-1} at λ_{max} = 317 nm[38] (see Experimental Section).

(45) Literature value 4×10^9 M^{-1} s^{-1}: Burkhart, R. D. *J. Am. Chem. Soc.* **1968**, *90*, 273.

(46) Bromberg, A.; Schmidt, K. H.; Meisel, D. *J. Am. Chem. Soc.* **1984**, *106*, 3056.

(47) Determined from the observed decay, 4×10^4 A^{-1} s^{-1} at 330 nm with l = 2 cm.

(48) Literature value ~2.4×10^9 M^{-1} s^{-1}: Weiner, S. A.; Hammond, G. S. *J. Am. Chem. Soc.* **1969**, *91*, 986.

(49) (a) On the time scale of Figure 6, the 650-nm absorption exists approximately in steady state. (b) Similar absorptions can be observed following pulse radiolysis of benzoyl chloride. The radical anion of benzoyl chloride produced under these conditions fragments to form benzoyl radical and chloride ion.[26,50]

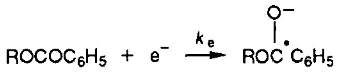
(50) Guirado, A.; Barba, F.; Manzanera, C.; Velasco, M. D. *J. Org. Chem.* **1982**, *47*, 142.

(51) Ito, O.; Sakaguchi, T.; Matsuda, M. *J. Chem. Soc., Faraday Trans. 1* **1978**, *74*, 1188.

solvated electrons with rate constants $k_e' = (2 \pm 0.5) \times 10^9$ M^{-1} s^{-1} in alcohol. No transients absorbing at wavelengths longer than 300 nm are observed initially in the radiolysis of alkyl acetates, and the radical anions have absorption maxima of <300 nm. Pulse radiolysis of benzyl acetate affords benzyl radical[43] as the only transient detected optically above 300 nm (Figure 7). The growth of the benzyl radical absorption (Figure 7, inset a, which also shows the early decay profile) is slower than quenching of the solvated electrons (it is independent of acetate concentrations of >3 mM) and is taken to represent k', the rate of generation of benzyl radical from benzyl acetate radical anion (Table I). The absorptions of the benzyl radical decay with second-order rate constant on a longer time scale (Figure 7, inset b). Acetic acid and benzyl radicals are formed equally in radiolysis experiments.[11]

Discussion

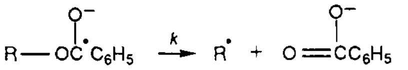
Pulse radiolysis of benzoate esters produces the ester radical anions (eq 12), which have absorptions near 310 and 450 nm (Figure 1). The resemblance of the absorptions of ester radical



$$\mathrm{ROCOC_6H_5} + e^- \xrightarrow{k_e} \mathrm{RO\overset{O^-}{\overset{|}{C}}{}^{\bullet}C_6H_5} \qquad (12)$$

anions in Figure 1 to those of acetophenone radical anion[34] and benzoic anhydride radical anion (Figure 6) suggests that delocalization of spin and charge density is similar in all of these species, which appear essentially as substituted benzylic radicals, $\rangle C^{\bullet}C_6H_5$.[32,52] However, the absorptions derived from substituted benzoates, such as diethyl phthalate (Figure 2), differ significantly. This is consistent with delocalization of spin and charge density involving the benzene rings (and substituents) of the radical anions.

The decays of the benzoate radical anions, $ROCOC_6H_5^{\bullet-}$, depend upon the alkyl group, R (Table I). The rate constants generally increase in the same order as stabilization of an alkyl radical center ($R^{\bullet}$). Simple alkyl benzoates decay slowest (rate constants $k \sim 5 \times 10^3$ s^{-1}). Tertiary and benzylic benzoates decay faster ($k > 10^4$ s^{-1}), and benzhydryl benzoate decays fastest ($k \sim 5 \times 10^5$ s^{-1}). These trends are consistent with fragmentation of the benzoate radical anions to afford benzoate and an alkyl radical (eq 13).[54] Formation of the alkyl radicals formed by decay



$$\mathrm{R{-}O\overset{O^-}{\overset{|}{C}}{}^{\bullet}C_6H_5} \xrightarrow{k} \mathrm{R^{\bullet}} + \mathrm{O{=}\overset{O^-}{\overset{|}{C}}C_6H_5} \qquad (13)$$

of the ester radical anions can be observed directly in those cases in which the radical possesses a suitable chromophore, such as benzylic radicals (Figure 4). The major products in these cases were identified as resulting from radical coupling reactions (eq 9–11).

Reaction 13 formally involves homolysis of a C—OC(=O) bond. Stabilization of the radical site is expected to weaken this bond and facilitate cleavage.[56] Similar effects have been found to operate in the decays of radical anions of other benzylic derivatives, such as benzyl halides[6,10] and benzyl acetate.[11] Pulse radiolysis of benzyl acetate affords a transient absorption near 310 nm. The radical anions of acetate esters, which lack a conjugated chromophore, have absorption maxima at <300 nm. Formation of benzylic radicals from benzylic acetates can be observed clearly (Figure 7). The acetate radical anions are more reactive than the analogous benzoate radical anions (Table I). Thus, the rate (k') of fragmentation of benzyl acetate anion (eq 14) is 30 times faster than that of benzyl benzoate anion.

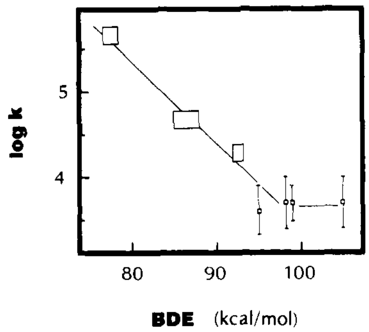


Figure 8. Correlation of the rates of fragmentation of benzoate radical anions $R{-}OCOC_6H_5^{\bullet-}$ (log k) with bond dissociation energies (BDE) of corresponding R–H bonds.

$$C_6H_5CH_2OCOCH_3^{\bullet-} \xrightarrow{k'} C_6H_5CH_2^{\bullet} + {}^{-}OCOCH_3 \quad (14)$$

Noteworthy is a 2 kcal/mol difference in bond dissociation energies of the O–C single bonds in benzyl benzoate and benzyl acetate.[57] Other considerations, including solvation, spin and charge delocalization (which will be less stabilizing for acetates than for benzoates), and steric effects,[58] also are expected to affect the rates of cleavage.

The bond dissociation energies BDE_{R-H} for the hydrocarbons R–H (eq 15)[59] will provide an indication of relative radical stabilities.[56] An energetic dependence of the rate of cleavage of the

$$R{-}H \rightarrow R^{\bullet} + H^{\bullet} \quad (15)$$

ester radical anions on available values of BDE_{R-H} (Table I) is illustrated in Figure 8. The empirical linear free energy relationship of Figure 8 indicates that the rates of radical anion cleavage are proportional to the bond dissociation energies. The relatively small[60] proportionality constant (determined from the slope in Figure 8 to be ~0.15) is probably due to several factors. Carbon–oxygen bonds are weaker than carbon–hydrogen bonds (BDEs for R–H and $R{-}OCOC_6H_5$ for R = $C_6H_5CH_2$ are 85–88[61a,b] and 69 kcal/mol,[61b] respectively).[61] Therefore, a hydrocarbon model overestimates the bond strengths by ~25%. Furthermore, the R–O bond is likely to be weaker in a radical anion than in a neutral molecule. It also is possible for the

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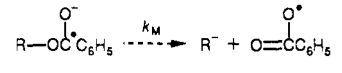
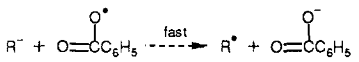
[52] Benzyl radical has absorption maxima at 317 nm and a weak absorption band near 460 nm.[38,53]

[53] Claridge, R. F. C.; Fischer, H. *J. Phys. Chem.* **1983**, *87*, 1960.

[54] The faster cleavage of tertiary benzoates than of primary benzoates is inconsistent with a mechanism involving radical anion decay to afford alkyl anions and benzoyloxy radicals as intermediates (eq i). Absorptions indicative



$$\mathrm{R{-}O\overset{O^-}{\overset{|}{C}}{}^{\bullet}C_6H_5} \xrightarrow{k_M} \mathrm{R^-} + \mathrm{O{=}\overset{O^{\bullet}}{\overset{|}{C}}C_6H_5} \qquad (i)$$



$$\mathrm{R^-} + \mathrm{O{=}\overset{O^{\bullet}}{\overset{|}{C}}C_6H_5} \xrightarrow{\text{fast}} \mathrm{R^{\bullet}} + \mathrm{O{=}\overset{O^-}{\overset{|}{C}}C_6H_5} \qquad (ii)$$

of benzoyloxy ($\lambda_{max} > 700$ nm[55]) are not observed. This result requires that k_M be rate limiting and the following electron-transfer step to produce benzoate and alkyl radicals (eq ii) be fast. However, tertiary alkyl anions should be much more difficult to form than benzylic, or even primary, alkyl anions, and the relative rate data in Table I suggest that k is not related to k_M.

[55] Chateaneuf, J.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1988**, *110*, 2886.

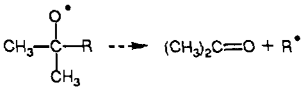
[56] Benson, S. W. *Thermochemical Kinetics*; Wiley: New York, 1976.

[57] Weast, R. C., Ed. *CRC Handbook of Chemistry and Physics*, 65th ed.; CRC Press: Boca Raton, FL, 1984; pp 182–188.

[58] For a discussion of these effects and an application to cyclopropylcarbinyl radicals, see: Masnovi, J.; Samsel, E. G.; Bullock, R. M. *J. Chem. Soc., Chem. Commun.* **1989**, 1044.

[59] The bond dissociation energies of the oxygen–alkyl carbon bonds of esters of carboxylic acids have been reported for only a few cases.[57]

[60] Note the high sensitivity of rates of cleavage of alkoxy radicals (eq iii) to the radical $R^{\bullet}$ that is formed: Walling, C. McGuinness, J. A. *J. Am.*



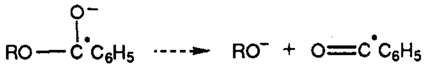
$$\mathrm{CH_3{-}\overset{O^{\bullet}}{\overset{|}{\underset{\underset{CH_3}{|}}{C}}}{-}R} \dashrightarrow \mathrm{(CH_3)_2C{=}O} + \mathrm{R^{\bullet}} \qquad (iii)$$

Chem. Soc. **1969**, *91*, 2053. Walling, C.; Padwa, A. *Ibid.* **1963**, *85*, 1593.

[61] (a) McMillan, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493. (b) Weast, R. C., Ed. *CRC Handbook of Chemistry and Physics*, 65th ed.; CRC Press: Boca Raton, FL, 1984; pp F182–F188. (c) Heicklen, J. *Int. J. Chem. Kinet.* **1981**, *13*, 651. (d) Juan, B.; Schwarz, J.; Breslow, R. *J. Am. Chem. Soc.* **1980**, *102*, 5741. (e) McKean, D. C.; Duncan, J. L.; Batt, L. *Spectrochim. Acta* **1973**, *29A*, 1037.

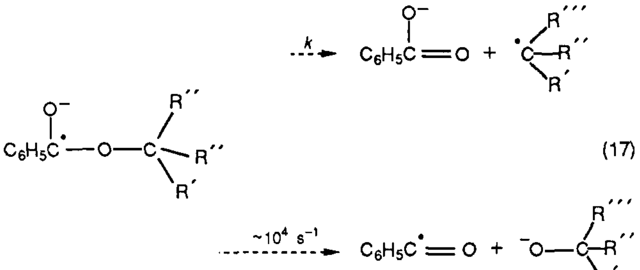
transition state to be "early", in that the O–R bond has only partially cleaved. Finally, the radical anions are charged species, and the strong solvation of ester radical anions (estimated 70–90 kcal/mol in water[27]) also affects the rates of the fragmentations (vide infra).

The radical anion of methyl benzoate apparently fails to follow the correlation of Figure 8. The leveling of the rates of decay observed for benzoates of methyl, primary, and secondary alcohols, which have relatively high values of BDE_{R-H}, suggests the incursion of a different process when cleavage of the oxygen–alkyl carbon bond (eq 13) is slow. This new process also exhibits a first-order dependence on the radical anion concentration, and it is relatively insensitive to the nature of R[60] and to the presence of 1 mM base. A competing reaction in which the acyl carbon–oxygen bond is cleaved to generate alkoxide and a benzoyl radical (eq 16) would



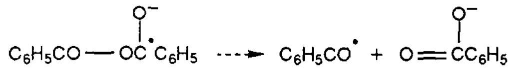
$$RO{-}\overset{O^-}{\dot{C}}C_6H_5 \dashrightarrow RO^- + O{=}\dot{C}C_6H_5 \quad (16)$$

account for these observations.[62] A process such as eq 16 should not be sensitive to the nature of the alkyl group R, since in the product alkoxide, substituents would not be conjugated with the charge (eq 17).



(17)

Benzoyl radicals are formed in the pulse radiolysis of benzoic anhydride (eq 18). The benzoyl radical has a broad absorption near 650 nm, which may be observed independently of the absorptions due to the radical anions (Figure 6). The rate of cleavage of the anhydride radical anion in hexane is similar to that for the radical anion of benzyl benzoate, and it is significantly faster than the rates of cleavage of alkyl benzoates. This result indicates that acyl radical is about as good a leaving group as are benzyl radicals under these conditions, consistent with bond dissociation energy considerations (Table I). Benzoyl radicals should be observable if they were produced in eq 16 from fast-decaying radical anions, and their absence signifies that benzoyl is not a significant product in these cases. However, benzoyl radicals would not be observed if they were formed from slowly decaying radical anions, such as methyl benzoate radical anion, because the rate of decay of the benzoyl radicals ($>10^5$ s^{-1}) would exceed that of their formation ($k \sim 10^4$ s^{-1}).



$$C_6H_5CO{-}O\overset{O^-}{\dot{C}}C_6H_5 \dashrightarrow C_6H_5C\dot{O} + O{=}\overset{O^-}{C}C_6H_5 \quad (18)$$

Product Studies. Products of benzyl radical intermediates can be observed by analysis of solutions of benzyl benzoate that have been subjected to pulse radiolysis (vide infra). However, experimental difficulties were encountered in the quantification of the products derived from radiolysis experiments (see Experimental Section). Consequently, attempts were undertaken to examine products of radical anions prepared by two alternative techniques:[63] (1) dissolving-metal reduction and (2) photochemical electron transfer.

(1) Reductions of esters by sodium in ethanol (the Bouveault–Blanc reaction) have been reported to proceed by formation of ester radical anion intermediates.[25,26] The radical anions were proposed to fragment by mechanisms that depend on the solvent. Reduction of esters in nonnucleophilic solvents purportedly leads to formation of carboxylates and alkanes, whereas reduction in nucleophilic solvents affords two alcohols as products.[25]

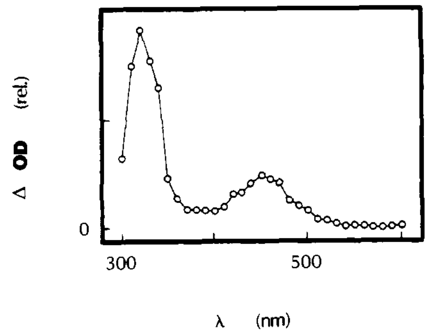
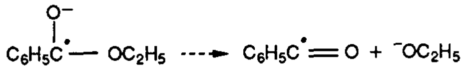


Figure 9. Difference transient absorption spectrum observed 60 ns following 266-nm excitation of ethyl benzoate in ethanol containing 0.1 M triethylamine.

Product studies on alkyl benzoates in ethanol performed by dissolving-metal reduction are complicated by formation of ethoxide anion. Addition of sodium to dilute ethanol solutions of benzyl benzoate under Bouveault–Blanc conditions leads to extensive evolution of hydrogen gas and concomitant formation of ethyl benzoate and benzyl alcohol (eq 19). Ethyl benzoate was the principle product even at low temperature (−40 °C) and high initial concentration of ester. Subsequent reaction of the ethyl benzoate led to formation of benzaldehyde and benzyl alcohol as major products[64] (eq 20). These results support the mechanism of Barton[25] for the Bouveault-Blanc reduction, which in nucleophilic solvent leads to transacylation. Here, nucleophilic substitution by ethoxide affords ethyl benzoate. Subsequent formation of benzaldehyde and benzyl alcohol from the ethyl benzoate is consistent with radical anion cleavage at least in part to form ethoxide and benzoyl radical (eq 21), which is reduced further under the reaction conditions (eq 22).

$$C_6H_5CO_2CH_2C_6H_5 + Na/C_2H_5OH \rightarrow C_6H_5CO_2C_2H_5 + C_6H_5CH_2OH \quad (19)$$

$$C_6H_5CO_2C_2H_5 + Na/C_2H_5OH \rightarrow C_6H_5CHO + C_6H_5CH_2OH \quad (20)$$



$$C_6H_5\overset{O^-}{\dot{C}}{-}OC_2H_5 \dashrightarrow C_6H_5\dot{C}{=}O + {}^-OC_2H_5 \quad (21)$$

$$C_6H_5C^{\bullet}{=}O \rightarrow C_6H_5CHO \rightarrow C_6H_5CH_2OH \quad (22)$$

(2) Photochemical reductions of benzoate esters also have been proposed to involve the formation of ester radical anions.[18,21] This technique proved expeditious for examination of radical anions in the absence of ethoxide. Photolysis of benzyl benzoate in the presence of an amine (DABCO) as electron donor resulted in formation of four products of benzyl radical (toluene, bibenzyl, 1-phenyl-2-propanol, and a benzylammonium salt, eq 23) in combined yield of 90%. Other benzylic benzoates and *tert*-butyl benzoate behaved similarly and afforded related products. On the other hand, methyl benzoate, ethyl benzoate, and isopropyl benzoate all failed to react under these conditions.

$$C_6H_5CO_2CH_2C_6H_5 + R'_3N\colon \xrightarrow{h\nu} C_6H_5CH_3\ (3\%) + C_6H_5CH_2CH_2C_6H_5\ (16\%) + C_6H_5CH_2CH(OH)CH_3\ (1\%) + C_6H_5CH_2N^+R'_3\ C_6H_5CO_2^-\ (70\%) \quad (23)$$

Flash photolysis experiments (Figure 9) confirmed that radical anions of the benzoate esters were formed together with the radical cations of the amines (eq 24). The properties of the ester radical

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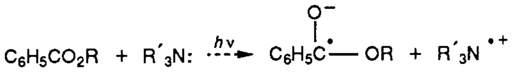
[62] Radical anions of sulfonate esters have been observed to produce alkoxide in a similar manner.[22]

[63] Electron transfer to esters has been reported to occur under a variety of conditions. The formation of alkyl radicals by dissolving-metal,[25,26] electrochemical,[50] and photochemical[18,21] reductions of esters is useful synthetically.[25,26]

[64] (a) Note that the reaction of ethyl benzoate with ethoxide would amount to an identity exchange. (b) Benzoin also is a product at high ester concentrations and may arise by acyloin condensation.[26b]



$$C_6H_5CO_2R + R'_3N: \xrightarrow{h\nu} C_6H_5\overset{O^-}{\overset{|}{\dot{C}}}—OR + R'_3N^{\bullet +} \tag{24}$$

anions produced in this way had properties identical with those produced by pulse radiolysis, with three exceptions: the decays of the radical anions of methyl benzoate, ethyl benzoate, and isopropyl benzoate all were predominantly second order.

The results admit to the following interpretation. Benzoate radical anions and amine radical cations initially are formed by photochemical electron transfer. The radical anions of benzylic benzoates and *tert*-butyl benzoate fragment to form benzoate anion and alkyl radicals. The alkyl radicals then react, either by hydrogen atom abstraction from solvent (eq 25) or by coupling

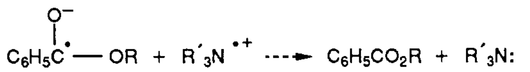
$$R^{\bullet} + CH_3CH_2OH \rightarrow R\text{-}H + CH_3CH^{\bullet}OH \tag{25}$$

$$R^{\bullet} + CH_3CH^{\bullet}OH \rightarrow R\text{-}CH(OH)CH_3 \tag{26}$$

$$R^{\bullet} + R^{\bullet} \rightarrow R\text{-}R \tag{27}$$

$$R^{\bullet} + R'_3N^{\bullet +} \rightarrow R\text{-}N^{+}R'_3 \tag{28}$$

reactions with solvent radicals (eq 26), with one another to form a dimer (eq 27), or with amine radical cation to form an ammonium salt (eq 28). In the cases of R = methyl, ethyl, or isopropyl, however, cleavage of the radical anion is sufficiently slow to allow the reverse electron transfer process (eq 29) to



$$C_6H_5\overset{O^-}{\overset{|}{\dot{C}}}—OR + R'_3N^{\bullet +} \dashrightarrow C_6H_5CO_2R + R'_3N: \tag{29}$$

proceed. In a polar solvent, the ions largely will be unpaired and recombination would exhibit second-order kinetics.[65] A competition between fragmentation and reverse electron transfer would explain the reports that benzoate esters of tertiary alcohols may be reduced selectively in the presence of esters of primary alcohols.[18,20,66]

Solvent effects were determined to be important in the rates of reactions of the radical anions. The higher rates of radical anion fragmentation in hexane may reflect better stabilization of the radical anion by solvation in alcohol.[67] The charge appears to be more localized (on a single oxygen) in the anion radical than in either of the transition states for eq 17, in both of which the charge is delocalized on two oxygens. Therefore, a polar protic solvent will result in a decrease in reaction rates compared to a nonpolar aprotic solvent. On the other hand, nonpolar solvents disfavor the charge separation in eq 24, and the efficiency of photochemical reaction is decreased despite the enhancement in fragmentation rates.[67,68]

Conclusion

Radical anions of benzoate esters in ethanol undergo unimolecular fragmentation by two processes involving cleavage of the oxygen–alkyl carbon [PhC(=O)O—C] bond or of the acyl carbon–oxygen PhC(=O)—OC) bond. Product distributions obtained from electron-transfer reductions of benzoate esters may be explained in terms of these two competitive cleavages.

Formation of relatively high energy alkyl radicals such as methyl or ethyl is a relatively unfavorable process. For cases such as methyl benzoate or ethyl benzoate, the radical anions react preferentially by cleavage of the acyl carbon–oxygen bond. Under Bouveault–Blanc conditions, for example, ethyl benzoate is formed from benzoate esters (with the release of an alcohol). Subsequent reduction of the ethyl benzoate affords benzyl alcohol. Thus, the Bouveault–Blanc reduction is characterized by the formation of two alcohols.

On the other hand, radicals such as benzyl are sufficiently stabilized that cleavage to form alkyl radicals and benzoate anion becomes favorable. The microscopic rate constants for oxygen–alkyl bond cleavage depend on the stabilization afforded the radical by substituents. Under conditions that limit transacylation, products of oxygen–alkyl bond cleavage obtain when the rate constants for this cleavage exceed $\sim 10^4\ s^{-1}$. When the initial electron transfer is reversible, the efficiency of reaction depends on the relative rates of cleavage and reverse electron transfer. This explains the low reactivity of primary benzoates, compared to tertiary benzoates and benzylic benzoates, in photochemical reductions.

The dependence of the rates of fragmentation of radical anions upon the stability of the radical products also serves to explain, in part, the selectivities and efficiencies observed for these reactions. For example, it has been demonstrated that esters of tertiary alcohols may be reduced selectively in the presence of esters of primary alcohols.[18,20] This result is anticipated on the basis of the slower rates of cleavage for radical anions of primary esters, in the face of reversible electron transfer processes.

Experimental Section

Instrumentation. Proton NMR spectra were recorded on a Varian FT-80 (80-MHz) spectrometer. UV/Vis spectra were recorded on Hewlett-Packard HP 8452A or HP 8450A diode-array spectrophotometers. GC/MS data were obtained on a Finnigan TSQ GC/MS/MS/DS system by EI and routine GC data were obtained on a Hewlett-Packard HP 5890A/5895A GC/workstation.

Reagents. Methyl benzoate (Fisher), ethyl benzoate (Aldrich), and benzyl benzoate (Eastman) were distilled before use. Benzoic anhydride (Aldrich) and diethyl phthalate (MCB) were used as received. Newly opened pyridine (Fisher) was used as received. The other benzoate esters were prepared from the alcohols and benzoyl chloride (Aldrich, Gold Label, used as received) according to literature methods.[69] Benzyl acetate was prepared from benzyl alcohol (Fisher) and acetic anhydride (Sargent-Welch). Benzophenone (MCB) was recrystallized from ethanol, and acetophenone (MCB) was distilled before use. Newly opened hexane (Aldrich, Gold Label), 3-methylpentane (Aldrich), and isooctane (Aldrich) were used as received. Ethanol (AAPER) and 2-propanol (Mallinckrodt) were distilled before use. Pellets of 85% potassium hydroxide (Fisher) were used to prepare basic solutions, and concentrated hydrochloric acid (Fisher) was used to prepare acidic solutions. 1,4-Diazabicyclo[2.2.2]octane (DABCO, Aldrich) was sublimed before use, and triethylamine (Fisher) was distilled from KOH.

Pulse Radiolysis. The pulse radiolysis system has been described previously.[70] The probe assembly consisted of a 150-W Xenon lamp, SPEX minimate monochromator, Hamamatsu R928 NM photomultiplier, and a Biomation 8100 wave-form recorder or a Tektronix R7912 digitizer. Digitized signals were averaged and analyzed on a PDP 11/70 computer.

Procedure. Generally, a 50-mL solution containing substrate was deaerated by nitrogen purge for at least 30 min. The ester concentration routinely was made 2 mM so that reaction of the electrons occurred mostly within the pulse. The decays did not depend upon concentration of ester. Experiments to test the quenching of solvated electrons under pseudo-first-order conditions also were performed on alcoholic solutions of ethyl benzoate and benzyl benzoate at concentrations of 0.05, 0.1, and 0.2 mM and of benzyl acetate at concentrations of 0.1, 0.2, and 0.3 mM. The alcohol solvent system used consisted of ethanol containing 2% 2-propanol as a hydrogen atom scavenger; alkanes (hexane, 3-methylpentane, and isooctane) used were pure solvents. The deaerated solution was transferred by glass syringe,[71] which then was connected by a glass tube[71] to a 1 cm × 1 cm or a 1 cm × 2 cm quartz flow cell. A variable

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[65] Masnovi, J. M.; Kochi, J. K. *J. Am. Chem. Soc.* **1985**, *107*, 7880.

[66] It is likely that, for radical anions of benzoates derived from secondary alcohols, both types of cleavage may occur with similar rate constants, and product distributions may be sensitive to conditions that affect the ratio of the rates of the competitive cleavages.

[67] Involvement of excited states in hexane, suggested by a reviewer, is ruled out by flash photolysis experiments. Reaction of the radical anions by protonation has not been ruled out, but is unlikely because protonation on the time scale of the pulse experiments should exhibit second-order kinetics.

[68] Masnovi, J.; Glaser, P. M., manuscript in preparation.

[69] Bender, M. L. *J. Am. Chem. Soc.* **1951**, *73*, 1626. Magnani, A.; McElvain, S. M. *Ibid.* **1938**, *60*, 813. Baker, *J. Org. Chem.* **1952**, *17*, 77. Harvey, G. J.; Stimson, V. R. *J. Chem. Soc.* **1956**, 3629. Baker, B. R.; Schaub, R. E.; Querry, M. V.; Williams, J. H. *J. Org. Chem.* **1952**, *17*, 77. Kuo, M.-Y.; Liu, K.-T. *J. Org. Chem.* **1987**, *52*, 2927.

[70] (a) Atherton, S. J. *J. Phys. Chem.* **1984**, *88*, 2840. (b) Foyt, D. C. *Comput. Chem.* **1981**, *5*, 49. (c) Rodgers, M. A. J.; Foyt, D. C.; Zimek, Z. A. *Radiat. Res.* **1978**, *75*, 296.

[71] Phthalate esters are used as plasticizers (di-2-ethylhexyl phthalate in Tygon tubing is readily extracted from tubing by organic solvents); therefore, the apparatus was assembled entirely from glass.

pulse width was employed to test kinetic order. Pulse widths of ≥100 ns in alcohol and ≥250 ns in alkane solvents were found necessary to produce sufficient signal for analysis. The decays were found to be independent of pulse widths ranging between 100 and 500 ns. A pulse width of 250 ns in water corresponded to a dose of ~2 krad as determined by thiocyanate dosimetry.[72] Each run consisted of 4–10 pulses. Runs were performed in triplicate at each pulse width. Decays were analyzed for >4 half-lives or for the maximum possible time resolution (1 ms) allowed by the stability of the flash lamp.

Decays in the presence of oxygen were measured for the slower decaying radical anions, with concentration of radical anion in excess over that of oxygen. A small bubble of air was admitted to the deaerated solution before pulsing so that the decay induced by the presence of air amounted to consumption of 20–30% of the transient absorption due to the radical anion, and the rate constant was estimated from the initial decay by assuming pseudo-first-order conditions for the radical anion.

Rates were determined for radical anion decays by monitoring both the 310- and the 450-nm bands. For benzylic esters, the growth and decay of the absorptions of benzylic radicals near 320–330 nm also were measured. The rate constants for decay of the 450-nm absorptions were judged to be most reliable because this band usually was isolated from absorptions due to other species (such as benzyl radical products or species derived from solvent[29]). The decays monitored at 310 nm were more complex than were those at 450 nm. Other, persistent absorbing species (reaction products and solvent-derived species) also have absorptions in the 300-nm region, and the decays monitored at 310 nm do not approach base line. Kinetics at 310 nm, determined by the method of initial rates and accounting for residual absorption, agreed with those determined at 450 nm within experimental error (±30%). Decays at 450 nm had standard deviations of ≤20% (100-ns pulse). Identical rate constants were obtained in hexane, in 3-methylpentane, and in isooctane solvents.

Pulse radiolysis of aliphatic alkyl acetates produced transients that absorbed near 265 nm, but these absorptions also overlapped those of other species. Therefore, only rate constants are reported in Table I for growths of the absorptions at $\lambda > 300$ nm, due to the formation of benzyl radical products from benzylic acetates.

The absorptions of the benzoate radical anions were determined to decay by first-order kinetics, as the rates were essentially invariant of dose. The radical anions of benzylic benzoates followed single-exponential decay kinetics. However, residuals analysis indicated the decays of the radical anions of methyl benzoate, ethyl benzoate, neopentyl benzoate, isopropyl benzoate, and diethyl phthalate appeared to be nonexponential. Concentration studies indicated that second-order processes were not important, and the decays could be satisfactorily reproduced by double-exponential fits. The higher rate constant in each case was always determined to be in the range $(3-8) \times 10^3$ in alcohol, and it is these faster decay rates that are reported in Table I. A higher error is associated with these measurements since only the initial decay could be followed (flash lamp stability was ~1 ms), and the smaller rate constant could not be determined accurately by the curve-fitting procedure.

Extinction coefficients ϵ of the radical anions were estimated by comparison of the signal intensities observed for benzyl radical products[43,46] (assuming stoichiometric conversion for eq 13) and agreed (±20%) with those calculated by dosimetry.[72] The benzyl radicals do not interfere with kinetic measurements of the radical anions because the radicals decay on a much longer time scale and absorb only weakly at 450 nm, compared to the radical anions. The second-order decays of the benzyl radicals (units of $M^{-1}\ s^{-1}$) were calculated as $\epsilon l k_{obs}$ where the observed rate constant, k_{obs}, has units $A^{-1}\ s^{-1}$ and the path length l was 1 or 2 cm.

Effects of pH. The absorptions and decays of the radical anions were essentially unaffected by the presence of small amounts (1< mM) of KOH. In the presence of 0.1 M concentrations of base, however, the absorptions of the radical anion were stronger, and they continued to grow in for some time following the pulse of electrons. With 2 mM concentrations of esters, the pseudo-first-order rate constants for growth of the radical anion absorptions were 4.6×10^3, 3.4×10^3, and 1.1×10^6 s^{-1} for isopropyl benzoate, *tert*-butyl benzoate, and benzophenone, respectively. In order to avoid reaction of solutes with alcohol solvent, ethyl benzoate was examined only in ethanol solution containing HCl, and benzoic anhydride was examined in hexane only. Hydrolysis or transesterification was not observed for any of the reactants under the conditions reported. Experiments performed on ethyl benzoate in the presence of 0.1 mM alcoholic hydrogen chloride produced transients with absorptions at <300 nm, which overlapped those of starting materials. This is consistent with protonation of the radical anions at low pH[36] to form the ketyl radicals, which do not absorb strongly above 300 nm.[32] However, the competition of protons for electrons produced by the pulse may lead to side reactions (such as formation of H atoms) under these conditions.

Benzophenone afforded transients due to both the radical anion and the ketyl radical within the spur of the pulse. Kinetic analysis indicated that at longer times the radical anions decayed, at least in part, to form the ketyl radical, which exhibited a growth coincident with radical anion decay.

Flash Photolysis. The flash photolysis system has been described previously.[73] Three lasers and detection systems were employed: 266-nm (fourth harmonic) pulses from a Quantel YG481 Nd:YAG laser (11-ns pulse, Q switched), a Quantel YG581 laser (11-ns pulse, Q switched) or a mode-locked Quantel YG402 laser (200 ps), together with probe assemblies consisting of a 150-W Xenon lamp, SPEX minimate monochromator, Hamamatsu R928 M photomultiplier, and a Biomation 8100 wave-form recorder or a Tektronix R7912 digitizer. Digitized signals were averaged and analyzed on a PDP 11/70 computer. Identical results were obtained on all three systems. Light intensity was attenuated with wire mesh filters (4–100% transmission) in order to moderate the concentrations of transients and test kinetic order.

Generally, solutions of benzoates in alcohol were diluted until the optical densities at the excitation wavelength of 266 nm were ~0.6 (no effect of concentration was observed). The solutions were deaerated by gentle nitrogen purge for at least 20 min preceding and then during photolysis. Photolysis performed in the absence of added amines indicated no absorptions due to the benzoate radical anions. Photolysis in the presence of an amine resulted in the formation of intense transients due to the benzoate radical anions. Amine concentrations in the range 0.06–0.2 M had the same effect. Use of DABCO resulted in absorptions near 460 nm due to the radical cation of DABCO, which interfered with observation of the kinetic behavior of the benzoate radical anions. Therefore, the kinetics for radical anion decay were determined in the presence of triethylamine (absorptions of $Et_3N^{\bullet+}$ above 300 nm are weak).

Product Analysis. Pulse Radiolysis. Analysis of solutions that were subjected to pulse radiolysis indicated very low conversions of starting materials. Extensive radiolysis (75 shots using a 1-μs pulse for each 0.5 mL of solution) afforded conversions of only ~0.5%. Analysis (GC and GC/MS) of a 2 mM alcoholic solution of benzyl benzoate radiolyzed in this fashion indicated formation of benzoic acid (100%), bibenzyl (50%), 1-phenyl-2-propanol (30%), and toluene (not quantified), identified by comparison with authentic samples (yields are relative and are based upon total volatile products observed).

γ Radiolysis. Analysis of an identical solution of benzyl benzoate subjected to γ radiolysis afforded a similarly low conversion; bibenzyl and 1-phenyl-2-propanol were formed in approximately equal amounts as the major volatile products. Products derived from γ radiolysis of benzyl acetate previously have been reported to be equally acetic acid and benzyl radical.[11]

Alkali Metal Reductions. Benzyl benzoate (5 mM) in ethanol was deaerated by passage of a slow stream of nitrogen through the solution for ~1 h prior to the addition of sodium. The solution was heated to reflux, and sodium metal (1.2 equiv) was added in small portions over a period of ~1 h with vigorous stirring. Nitrogen purge was continued throughout. Aliquots (50 mL) were removed at 10-min intervals. To each aliquot was added 50 mL of ether, and the organic layer was extracted three times with 50-mL portions of water. The ether was dried over sodium sulfate, and the progress of the reaction was monitored by GC. In this way the initial products were identified as benzyl alcohol (100%) and ethyl benzoate (95%). Similar results were obtained when the reaction was conducted at room temperature or with cooling to −40 °C; at −40 °C, the reaction with sodium was slower and benzyl alcohol and ethyl benzoate were formed in equal amounts. Small amounts of other products that appeared during the reaction were determined to arise from reduction of ethyl benzoate as follows.

Reaction of ethyl benzoate (10 mM) in ethanol at room temperature using 2.2 equiv of sodium was performed under nitrogen purge. After addition of the sodium, the mixture was stirred for 2 h. At this time, removal of an aliquot and workup as described above indicated ~1 equiv of sodium had been consumed. The major products were benzyl alcohol (5%) and benzaldehyde (5%) in addition to unreacted ethyl benzoate (80%). Repeating the reaction with cooling in a dry-ice–acetone bath to maintain the internal temperature at ~−40 °C and stirring an additional 3 h after the addition of the sodium afforded a similar result. Repeating the reaction at −40 °C using a 50 mM concentration of ethyl

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[72] (a) Farhataziz; Rodgers, M. A. J. *Radiation Chemistry*; VCH Publishers: New York, 1987. (b) Hart, E. J., Ed. *Adv. Chem. Ser.* **1968**, *No. 81*.

[73] Masnovi, J. M.; Sankararaman, S.; Kochi, J. K. *J. Am. Chem. Soc.* **1989**, *111*, 2263–2276.

J. Am. Chem. Soc. **1989**, *111*, 9089–9098

benzoate resulted in formation of benzyl alcohol (5%), benzaldehyde (5%), and benzoin (1%) in addition to unreacted ethyl benzoate (85%).

Photochemical Reductions. General procedure: A benzoate ester (20 mM) and DABCO (0.1 M) were dissolved in 60 mL of ethanol and the solution was deaerated by nitrogen purge for 15–25 min. The solution was irradiated with a 450-W medium-pressure mercury lamp in a water-cooled quartz immersion well for 10 min. A sample (~2 mL) of the crude solution was taken for immediate analysis by GC and GC/MS. No reactions was observed for any of the benzoate esters in the absence of added amine. Aryl alkanes, radical coupling products, and benzoic acid were identified by comparison with authentic samples. Evaporation of solvent under reduced pressure followed by trituration of the residue with benzene afforded insoluble amonium salts.

Irradiation of benzyl benzoate for 20 min followed by workup as described indicated consumption of ~35% benzyl benzoate. The major product was obtained as a fluffy white solid, which was insoluble in benzene, identified from its spectroscopic properties as an ammonium salt of benzoic acid, $N(CH_2CH_2)_3N^+CH_2Ph\ PhCO_2^-$: NMR ($CDCl_3$) δ 8.11 (dd, 2 H, $J = 3, 6.5$ Hz), 7.28–7.46 (m, 8 H), 4.86 (s, 2 H), 3.57 (br t, 6 H, $J = 7$ Hz), 3.01 (br t, 6 H, $J = 7.2$ Hz). This material was photochemically and thermally unstable, and it reacted in the injector port (250 °C) of a GC apparatus to afford a neutral adduct identified by GC/MS as $PhCH_2N(CH_2CH_2)_2NCH_2CH_2OCOPh$: MS (EI) m/z (RIC) 324 (2, M^+), 202 (80, $M^+ - PhCOOH$), 189 (55), 146 (30), 105 (50, $PhCO^+$), and 91 (100, $PhCH_2^+$). Because this salt was found to decompose photochemically under the reaction conditions, the product yields were determined after ~50% conversion of benzyl benzoate. The salt formed in 70% yield, together with toluene (3%), $PhCH_2CH(OH)CH_3$ (1%), benzoic acid (~10%), and bibenzyl (16%), as quantified by GC.

Reaction of *p*-methoxybenzyl benzoate, 1-phenylethyl benzoate, benzhydryl benzoate, and *tert*-butyl benzoate afforded analogous products. Isopropyl benzoate, ethyl benzoate, and methyl benzoate did not react under these conditions, and starting materials were obtained in 90–100% recovery. The product distributions depend upon the amine used as reductant and upon the reaction conditions, and the complete results will be reported elsewhere.[68]

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Registry No. $CH_3OCOC_6H_5^{\bullet-}$, 34533-12-5; $CH_3CH_2OCOC_6H_5^{\bullet-}$, 34533-19-2; $(CH_3)_3CCH_2OCOC_6H_5^{\bullet-}$, 123412-28-2; $(CH_3)_2CHOCOC_6H_5^{\bullet-}$, 34533-20-5; $(CH_3)_3COCOC_6H_5^{\bullet-}$, 92344-51-9; $HC{\equiv}CC(CH_3)_2OCOC_6H_5^{\bullet-}$, 123412-29-3; $C_6H_5CH_2OCOC_6H_5^{\bullet-}$, 115116-44-4; p-$CH_3OC_6H_4CH_2OCOC_6H_5^{\bullet-}$, 123412-30-6; $C_6H_5CH(CH_3)OCOC_6H_5^{\bullet-}$, 123484-47-9; $(C_6H_5)_2CHOCOC_6H_5^{\bullet-}$, 115077-09-3; $(C_6H_5)_2C(CH_3)OCOC_6H_5^{\bullet-}$, 123412-31-7; C_6H_7-o-$(COOCH_2CH_3)_2^{\bullet-}$, 34537-32-1; $C_6H_5COOCOC_6H_5^{\bullet-}$, 69209-67-2; $C_6H_5CH_2OCOCH_3^{\bullet-}$, 115116-45-5; $(C_6H_5)_2CHOCOCH_3^{\bullet-}$, 115077-10-6; $CH_3CHO^{\bullet-}$, 60427-04-5; $CH_3OCOC_6H_5$, 93-58-3; $(CH_3)_3CCH_2OCOC_6H_5$, 3581-70-2; $(CH_3)_2CHOCOC_6H_5$, 939-48-0; $(CH_3)_3COCOC_6H_5$, 774-65-2; $HC{\equiv}CC(CH_3)_2OCOC_6H_5$, 56438-73-4; $C_6H_5CH_2OCOC_6H_5$, 120-51-4; p-$CH_3OC_6H_4CH_2OCOC_6H_5$, 24318-41-0; $C_6H_5CH(CH_3)OCOC_6H_5$, 13358-49-1; $(C_6H_5)_2CHOCOC_6H_5$, 7515-28-8; $(C_6H_5)_2C(CH_3)OCOC_6H_5$, 24318-53-4; C_6H_4-o-$(COOCH_2CH_3)_2$, 84-66-2; $C_6H_5COOCOC_6H_5$, 93-97-0; $C_6H_5CH_2OCOCH_3$, 140-11-4; $(C_6H_5)_2CHOCOCH_3$, 954-67-6; $CH_3CH_2OCOC_6H_5$, 93-89-0; benzyl radical, 2154-56-5; diphenylmethyl radical, 4471-17-4; benzophenone, 119-61-9.

Bioactive Peptides: Solid-State and Solution Conformation of Cyclolinopeptide A

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Abstract: The solid-state and solution conformational analysis of cyclolinopeptide A, a cyclic nonapeptide isolated from linseed, is reported. The X-ray crystal structure determination of the orthorhombic form obtained from a 2-propanol–water mixture [$a = 32.98$ (3) Å, $b = 21.65$ (2) Å, $c = 9.83$ (1) Å, space group $P2_12_12_1$, $Z = 4$] shows the presence of five strong transannular intramolecular hydrogen bonds with the formation of one C_7, two C_{10} (one type I and one type III), one C_{13}, and one C_{17} ring structures. One peptide unit (linking residues Pro^1 and Pro^2) is cis ($\omega = 10°$); all others are trans. The results of the conformational study in solution by NMR spectroscopy indicate that, provided one choses the right environment, solid-state and solution conformations are essentially identical, even if this cyclic system tends to give rise to a complex mixture of quasi-isoenergetic conformations, favored by the flexibility of the ring enhanced by the isomerism of the Pro–Pro bond and by polar solvents.

Cyclolinopeptide A (henceforth called CLA) is a cyclic nonapeptide of the following sequence:

cyclo-(Pro-Pro-Phe-Phe-Leu-Ile-Ile-Leu-Val)

It has been isolated from linseed[1] and subsequently synthesized by Prox and Weigand[2] by classical solution methods. Soon after its synthesis it has been the object of intensive structural studies[3–5] mainly because it is one of the first isolated natural cyclic peptides and also because the presence of two Pro residues suggests that the accessible conformational space might be limited with respect to those of known medium-sized peptides.

Neither the CD[3] nor NMR[4] studies (in spite of the assignment of the resonances in DMSO-d_6 to residue types[4,6]) have given an

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(1) Kaufmann, H. P.; Tobschirbel, A. *Chem. Ber.* **1959**, *92*, 2805–2809.

(2) Prox, A.; Weygand, F. In *Peptides. Proceedings of the 8th European Peptide Symposium*; Beyerman, H. C.; van de Linde, A.; Maasen van den Brink, W., Eds.; Elvesier/North-Holland Biomedical Press: Amsterdam and New York, 1966; pp 158–172.

(3) Naider, F.; Benedetti, E.; Goodman, M. *Proc. Natl. Acad. Sci. U.S.A.* **1971**, *68*, 1195–1198.

(4) Brewster, A. I.; Bovey, F. A. *Proc. Natl. Acad. Sci. U.S.A.* **1971**, *68*, 1199–1202.

(5) Tonelli, A. E. *Proc. Natl. Acad. Sci. U.S.A.* **1971**, *68*, 1203–1207.

0002-7863/89/1511-9089$01.50/0