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Organic Reducing Agents: Some Radical Chain Reactions of Ketyl and 1,3-Dioxolanyl Radicals with Activated Bromides[1a]

Francesca Fontana,[1b] Ralph J. Kolt, Youqin Huang, and Danial D. M. Wayner*

Steacie Institute for Molecular Sciences, National Research Council of Canada, Ottawa, Ontario K1A 0R6, Canada

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The radical chain reduction of primary and secondary α-bromo esters by 2-propanol and 2-methyldioxolane has been shown to be a kinetically viable process with average chain lengths of >10 at temperatures between 30 and 60 °C. For electron-deficient bromides, these simple organic reagents may effectively replace the more commonly used (and more expensive) organosilicon or tin hydides. Some mechanistic insights have been obtained from a combination of kinetic and thermodynamic measurements. The rate constants for the reaction of the 2-hydroxy-2-propyl and the 2-methyl-1,3-dioxolan-2-yl radicals with a primary bromo ester have been estimated to be 8×10^3 M^{-1} s^{-1} and 6×10^3 M^{-1} s^{-1}, respectively, at 30 °C in acetonitrile. The electrochemical oxidation potentials of a number of electron-rich radicals derived from hydrogen atom abstraction from alcohols and dioxolanes, determined using photomodulation voltammetry, provide an assessment of the thermochemisty of the putative outer sphere electron-transfer reaction between the radical and the α-bromo ester (the value for 1,3-dioxolane has been redetermined and corrects an erroneous value previously published). From these data, it is shown that the order of reactivity of the organic reducing agents follows the same trend as the oxidation potentials of the corresponding radicals. Rate constants for the outer sphere electron-transfer reduction of the bromo esters by electrochemically generated radical anions were used to establish a Marcus-type relationship between the rate constants and the standard potential of the reducing agent. Comparison of these rate constants with those for the reactions of the electron-rich radicals suggest that the reactions of the methanol- and ethanol-derived radicals do not proceed via outer sphere electron transfer as had been previously suggested but have significant bonding (i.e., atom transfer) character at the transition state. Electron transfer in the reactions of the 2-propanol- and 2-methyl-1,3-dioxolane-derived radicals cannot be ruled out. Nevertheless, the order of reactivity of the organic reducing agents follows the same trend as the oxidation potentials of the corresponding radicals suggesting that these potentials can be used as a predictive tool for the design of new reagents.

The radical chain reduction of alkyl and aryl halides by metal hydrides (eqs 1−5) based on tin[2] and silicon[3] is well established as a synthetic method. Complex molecules can be constructed by incorporating inter- and intramolecular reactions of the free radical intermediates into the overall scheme (eq 3). Although tributyltin hydride is the most commonly used reagent, its toxicity has stimulated a search for alternatives. One possibility is tris(trimethylsilyl)silane[3] which appears to be less toxic than the tin hydrides yet incorporates the essential features that make these reagents useful chemically; a weak M−H bond[4] and a reasonably strong M−X bond[5] (where X is a halide).

$$\text{initiator} \rightarrow L_3M^\bullet \quad (M = Si, Sn) \tag{1}$$

$$RX + L_3M^\bullet \rightarrow R^\bullet + L_3MX \tag{2}$$

$$R^\bullet \rightarrow R'^\bullet \tag{3}$$

$$R'^\bullet + L_3MH \rightarrow R'H + L_3M^\bullet \tag{4a}$$

$$R^\bullet + L_3MH \rightarrow RH + L_3M^\bullet \tag{4b}$$

$$\text{radical} + \text{radical} \rightarrow \text{nonradical products (termination)} \tag{5}$$

The kinetic criteria for the design of new reagents are straightforward.[6] The pseudo-first-order rates of reactions 2 and 4 should be >200 s^{-1} in order to ensure that the chain length is >10. In addition, reaction 3 must be fast enough so that the reaction 4b does not compete effectively. In most cases there are sufficient kinetic data in the literature to allow one to calculate the relative concentrations of reagents required to give the optimum yield. The problem encountered in the design of new reagents is that strucural changes which increase the rate of one of the chain-propagating reactions will often decrease the rate of the other; i.e., if the M−H bond is weakened in order to increase k_4, a concurrent weakening of the M−X bond is expected and hence k_2 will decrease. For this reason, a simple reagent such as triethylsilane is not an effective chain carrier (k_2 is fast but k_4 is generally too slow). Similarly, replacement of metal hydrides with simple hydrocarbons has generally not been effective since, in these cases, k_2 is too slow.

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(1) (a) Issued as NRCC publication no. 37258. (b) Dipartimento di Chimica del Politecnico, piazza Leonardo de Vinci 32, 20133, Milano.

(2) Curran, D. P. *Synthesis* **1988**, 417−439 and references cited therein.

(3) Chatgilialoglu, C. *Acc. Chem. Res.* **1992**, *25*, 188−195 and references cited therein.

(4) Kanabus-Kaminska, J. A.; Al Hawari, J.; Griller, D.; Chatgilialoglu, C. *J. Am. Chem. Soc.* **1987**, *109*, 5267−5268.

(5) Griller, D.; Kanabus-Kaminska, J. M.; Maccoll, A. *THEOCHEM* **1988**, *163*, 125−131.

(6) Giese, B. *Organic Synthesis: Formation of Carbon−Carbon Bonds*; Permagon Press: Oxford, 1986.

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Recently, we have shown that electron-deficient bromides such as ethyl bromoacetate (EBA) can be reduced by simple alcohols (e.g., 2-propanol) in a kinetically viable radical chain reaction (eqs 6–8).[7,8] The facility with

$$\text{initiator} \rightarrow \mathrm{Me_2\dot{C}OH} \tag{6}$$

$$\mathrm{Me_2\dot{C}OH + EtOC(O)CH_2Br} \rightarrow \mathrm{Me_2C{=}O + HBr + EtOC(O)CH_2^{\bullet}} \tag{7}$$

$$\mathrm{EtOC(O)CH_2^{\bullet} + Me_2CHOH} \rightarrow \mathrm{EtOC(O)CH_3 + Me_2\dot{C}OH} \tag{8}$$

which α-carboalkoxyalkyl radicals can be generated in these reactions makes the use of electron-rich alkyl radicals as reducing agents an attractive possibility since they are inexpensive and nontoxic and the byproducts are easy to remove from a reaction mixture. These radicals have been shown to undergo intramolecular cyclization reactions to form lactones and spirolactones.[8] In addition, the α-carbalkoxyalkyl radicals exhibit high stereoselectivity in their reactions with hydrogen atom donors or with unsaturated hydrocarbons.[9–12] In this paper, the reactivity of a number of alcohol- and 1,3-dioxolane-derived radicals toward these electron-deficient bromides is reported. In addition, electochemical measurements have been used to assess the overall thermochemistry of the putative electron-transfer reactions. Kinetics of some of the fundamental steps are estimated, and mechanistic implications of the kinetic and thermodynamic results are discussed.

Experimental Section

All solvents were of spectroscopic quality (Aldrich) and were used without further purification. Ethyl bromoacetate was obtained from Aldrich and used without further purification. Di-*tert*-butyl hyponitrite was prepared as outlined by Mendenhall.[13] The 2-phenylethyl bromo esters were prepared by the reactions of 2-phenylethanol with the appropriate acid bromide (i.e., bromoacetyl bromide, 2-bromopropionyl bromide, or 2-bromoisobutyryl bromide). In a typical preparation, a solution of 2-phenylethanol (1.63 mL, 13.6 mmol) in 4 mL of benzene was added dropwise with stirring over 10 min to an ice-cooled solution of the acid bromide (15 mmol) in 6.5 mL of benzene. The resulting mixture was stirred for 3 h at room temperature, washed successively with water, saturated sodium bicarbonate, and water, dried over anhydrous $MgSO_4$, and filtered. After evaporation of the solvent, the crude reaction mixture was purified by vacuum distillation. The products were characterized by ^1H NMR spectroscopy (Brüker AM-200) and by GC/MS which agreed with data from the literature. The (2-phenylethyl)-2-bromoisobutryl bromide was not reported in the literature and gave the following spectroscopic characteristics: ^1H NMR (200 MHz, $CDCl_3$) δ 1.88 (s, 6H), 2.98 (t, J = 8 Hz, 2H), 4.38 (t, J = 8 Hz, 2H), 7.23 (m, 5H); ^{13}C NMR (200 MHz, $CDCl_3$) δ 30.7, 34.8, 55.7, 66.3, 126.6, 128.3, 137.4, 171.5; IR ($CHCl_3$) $\nu_{max} = 1725\ cm^{-1}$. Anal. Calcd for $C_{12}H_{15}O_2Br$: C, 53.15; H, 5.58; Br, 29.47. Found: C, 53.45; H, 5.56; Br, 29.61.

All reductions were carried out in 0.2 M argon saturated solutions which contained either 2 or 6 mol % of the initiator and 1 equiv of 2,6-lutidine (which removes HBr that is generated in reaction 7). With one exception, the initiator was added from a freshly prepared stock solution in *n*-decane. The *n*-decane served as an internal standard for gas chromatography (HP Model 5890 equiped with an HP Model 7673A automatic injector). For reactions carried out in acetonitrile, biphenyl was used as an internal standard and the initiator and internal reference were added from separately prepared stock solutions. With di-*tert*-butyl hyponitrite as initiator, the reactions were initiated thermally at 60 °C for 5 h (ca. 5 half-lives). With benzophenone as the initiator, the reactions were initiated by irradiation in a Rayonet photochemical reactor (350 nm) at 30 °C for between 10 min and 5 h. In both cases, aliquots were removed periodically for GC analysis.

Determination of Chain Lengths. The chain lengths were determined by product studies using capillary gas chromatography. Plots of the concentrations of product as a function of time were used to estimate the rates of propagation, R_p, by two methods. The first method used linear interpolation between data points to estimate the derivative at the midpoint (i.e., $d[P]/dt$ at $t + \Delta t/2$ is $[[P]_t + [P]_{t+\Delta t}]/\Delta t$). The second method simply fit the experimental points to an exponential function from which the derivative at any time could be obtained analytically. Both methods gave the same results within a factor of 2. The concentration of RX used for chain length determinations (see eqs 9–11 in next section) also were measured by GC and show that $d[P]/dt = -d[RX]/dt$ (as expected). The same approach was used to estimate the rates of initiation, R_i, using benzophenone and photochemical initiation. For di-*tert*-butyl hyponitrite, it was possible to determine the rate of initiation from literature data.[14]

Electrochemistry. Cyclic voltammetry measurements were carried out using a standard three electrode cell with a glassy carbon working electrode, a platinum coil counter electrode, and an aqueous silver/silver chloride reference electrode. The solvent for all measurements was acetonitrile which contained 0.1 M tetrabutylammonium perchlorate (TBAP) as the supporting electrolyte. Measurements were conducted using a PAR Model 273A potentiostat/galvanostat which was interfaced to a personal computer via the PAR M270 electrochemical analysis software package. The standard potential for ferrocene in acetonitrile/0.1 M TBAP at 25 °C using our system was found to be 0.531 V vs Ag/AgCl.

The photomodulation voltammetry technique has been described in detail elsewhere.[15] In this experiment, radicals were generated by photolysis of di-*tert*-butyl peroxide with the light intensity varying sinusoidally in time in the presence of the saturated precursor of the radical to be studied (i.e., the alcohol or dioxolane). The initially generated *tert*-butoxyl radicals reacted with the subtrate by hydrogen atom transfer to generate the electron-deficient radicals. Oxidation of these product radicals produced a small alternating current that was demodulated with a lock-in amplifier. All of the radicals are easily oxidized with half-wave potentials well below 0.0 V vs Ag/AgCl.

Results and Discussion

Oxidation Potentials of the Radicals. The oxidation potentials of the α-hydroxyalkyl and dioxolanyl radicals were measured using photomodulation voltammetry (Table 1). Our data for the alcohol-derived radicals correspond reasonably well with data in aqueous solution reported by Henglein.[16] Most of the data are easily

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[7] Kolt, R. J.; Wayner, D. D. M.; Griller, D. *J. Org. Chem.* **1989**, *54*, 4259–4260.

[8] Kolt, R. J.; Griller, D.; Wayner, D. D. M. *Tetrahedron Lett.* **1990**, *31*, 7539–7540.

[9] Durkin, K.; Liotta, D.; Rancourt, J.; Lavallée, J.-F.; Boisvert, L.; Guindon, Y. *J. Am. Chem. Soc.* **1992**, *114*, 4912–4914.

[10] Guidon, Y.; Lavallée, J.-F.; Llinas-Brunet, M.; Horner, G.; Rancourt, J. *J. Am. Chem. Soc.* **1991**, *113*, 9701–9702.

[11] Guindon, Y.; Lavallée, J.-F.; Boisvert, L.; Chabot, C.; Delorme, D.; Yoakim, C.; Hall, D.; Lemieux, R.; Simoneau, B. *Tetrahedron Lett.* **1991**, *32*, 27–30.

[12] Guindon, Y.; Yoakim, C.; Lemieux, R.; Boisvert, L.; Delorme, D.; Lavallée, J.-F. *Tetrahedron Lett.* **1990**, *31*, 2845–2848.

[13] Mendenhall, G. D. *Tetrahedron Lett.* **1985**, *24*, 451–2.

[14] Kiefer, H.; Traylor, T. G. *Tetrahedron Lett.* **1966**, 6163–6167.

[15] Wayner, D. D. M.; McPhee, D. J.; Griller, D. *J. Am. Chem. Soc.* **1988**, *110*, 132–137.

[16] Lilie, J.; Beck, G.; Henglein, A. *Ber. Bunsenges. Phys. Chem.* **1971**, *75*, 458.

Table 1. Oxidation Potentials of Some Electron-Rich Radicals Derived from Alcohols and 1,3-Dioxolanes[a]

reducing agent	$E_{1/2}^{ox}(R^\bullet)$ V vs Ag/AgCl[b]
2-methyl-1,3-dioxolane	−1.15
2-propanol	−1.11
ethanol	−0.95
1,3-dioxolane[c]	−0.90
2-phenyl-1,3-dioxolane	−0.84
methanol	−0.80

[a] Measured by photomodulation voltammetry at a gold minigrid electrode in acetonitrile/0.1 M TBAP at 25 °C. [b] A standard potential of 0.531 V was obtained for ferrocene. [c] This value has been redetermined and corrects an erroneous value that was reported in ref 14.

rationalized.[17] For example, as the degree of alkylation of the alcohol derived radical is increased, the oxidation potential decreases in accord with the expected relative carbocation stabilities. Surprisingly, 2-phenyl-1,3-dioxolan-2-yl appears to be more difficult to oxidize than the 2-methyl derivative even though the benzylic cation should be more stabilized by delocalization into the aryl ring. AM1 calculations suggest that the ionization potential of the 2-phenyl-substituted radical is 0.4 eV less than that of the 2-methyl derivative in the gas phase. However, in solution the redox potentials also are influenced by the solvation energies of the oxidized and reduced forms. In a similar system, we have estimated the solvation energies of benyzl, α-methoxybenzyl, and methoxymethyl cations to be ca. −40, −48, and −56 kcal mol^{-1}, respectively,[18] suggesting that the solvation energy increased as the charge on the carbocation became more localized. By analogy, it is reasonable to suggest that the solvation energy of 2-methyl-1,3-dioxolanyl cation is more exergonic than that of the 2-phenyl-substituted cation, thus accounting for the relative oxidation potentials.

Debromination of α-Bromo Esters. Chain reactions are often characterized by the kinetic chain length which is defined by eqs 9–11 where R_i is the rate of initiation, f is the efficiency of chain initiation by the intiator, In (ca. 0.8 for di-*tert*-butyl hyponitrite[19]), k_d is the rate constant for decomposition of the initiator, $[\mathrm{In}]_0$ is the inital concentration of the initiator, R_p is the rate of propagation, k_P is the propagation rate constant, and RX is either the reducing agent or the bromide, depending on whether reaction 7 or 8 is rate limiting. In this case, the chain lengths were determined from plots of [P] versus time and [In] versus time (see Experimental Section).

$$R_i = \frac{d[\mathrm{In}]}{dt} f = fk_d[\mathrm{In}] \qquad (9)$$

$$R_p = \frac{d[P]}{dt} = \frac{k_p[\mathrm{RX}]R_i^{1/2}}{(2k_t^{1/2})} \qquad (10)$$

$$\text{chain length} = \frac{R_p}{R_i} = \frac{k_p[\mathrm{RX}]}{(2R_ik_t)^{1/2}} = \frac{k_p[\mathrm{RX}]\, e^{k_dt/2}}{(2fk_tk_d[\mathrm{In}]_0)^{1/2}} \qquad (11)$$

The average chain lengths for the debromination of a number of 2-phenylethyl bromoacetate (2-PhEBA) in neat alcohols (radical chain initiation either by thermal decomposition of di-*tert*-butyl hyponitrite or photochemical initiation by benzophenone photolysis at 350 nm) decreased in the order 2-propanol > ethanol > methanol (Table 2). This order of reactivity is consistent with the changes in the oxidation potentials of the α-hydroxy alkyl radicals (Table 1) and, hence, with our previous suggestion that reaction 7 procedes via an outer sphere electron-transfer process.[7,8] We also carried out reactions with a secondary and a tertiary α-bromo ester using 2-propanol as the reducing agent (Table 2). In this case it was found that the chain length decreased with increased substitution at the incipient radical center. For the two dioxolanes used, the decrease in the average chain length in the order 2-methyl-1,3-dioxolane > 1,3-dioxolane in the reaction with ethyl bromoacetate also was consistent with the change in the oxidation potentials. The 2-phenyl-1,3-dioxolanyl radical was unreactive.

Similar trends in reactivity were observed for the dioxolanes when the reactions were carried out in acetonitrile although the chain lengths were much shorter. In isooctane, the alcohols were completely unreactive. However, the reactivities of the two dioxolanes studied were similar in both polar and nonpolar solvents. The lack of reactivity of the alcohols in hydrocarbon solvent is expected for an outer sphere electron-transfer reaction. However, the significant oligomerization of the alcohols in these solvents also may contribute to the decreased reactivity.[20] The facility with which the reductions using the dioxolanes proceed in a hydrocarbon solvent raises some questions concerning the suggestion that reaction 7 is, indeed, an electron-transfer reaction for this reagent.

Closer examination of the kinetics of these reactions in the neat alcohols can give further mechanistic insights. A plot of chain length verus time (Figure 1) reveals a very interesting trend. For 2-propanol and ethanol the chain length decreases with time while for methanol and deuterated 2-propanol it increases with time. The explanation for this qualitative observation is straightforward. For 2-propanol and ethanol, reaction 7 is rate limiting and so the RX in eqs 10 and 11 is the bromide. Since the bromide concentration decreases as the reaction proceeds, the chain length also decreases. For the other two solvents reaction 8 is rate limiting so RX in eqs 10 and 11 is the alcohol. The chain length is now independent of the concentration of bromide and since the concentration of the solvent is constant, k_p[RX] in eq 11 is constant. However, the initiator is consumed in the reaction, so R_i must decrease with time, and hence, the chain length increases. It is interesting to note that deuteration of 2-propanol results in a change in the rate-determining step. In this case the rates of the two propagation steps must be of the same order of magnitude so that a moderate decrease in the hydrogen atom abstraction rate (from a primary isotope effect) has a striking effect on the overall kinetics.

It is possible to fit the data in Figure 1 to the kinetic expression (eq 11) to obtain estimates of the rate constants for the rate-limiting step (Table 3). It should be pointed out that this method of obtaining absolute kinetics is not precise, and hence, the rate constants have very large errors (i.e., ± a factor of 4 or 5). At best this approach is useful for estimating the order of magnitude

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(17) A previous publication (ref 15) incorrectly reported the oxidation potential of the dioxolanyl radical.

(18) Wayner, D. D. M.; Sim, B. A.; Dannenberg, J. J. *J. Org. Chem.* **1991**, *56*, 4853–4858.

(19) Kiefer, H.; Traylor, T. G. *J. Am. Chem. Soc.* **1967**, *89*, 6667–6671.

(20) Griller, D.; Lui, M. T. H.; Scaiano, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 5549–5551.

Table 2. Average Chain Length Radical Chain Reduction of Some α-Bromo Esters by Alcohols and Dioxolanes[a]

reducing agent	RBr	solvent		
		neat[b]	acetonitrile[c]	isooctane[c]
methanol	$PhCH_2CH_2OC(O)CH_2Br$	4	0	0
ethanol	$PhCH_2CH_2OC(O)CH_2Br$	18	3	0
2-propanol	$PhCH_2CH_2OC(O)CH_2Br$	28	5	0
1,3-dioxolane	$PhCH_2CH_2OC(O)CH_2Br$	4	0	6
2-methyl-1,3-dioxolane	$PhCH_2CH_2OC(O)CH_2Br$	11	7	12
2-propanol	$PhCH_2CH_2OC(O)CHMeBr$	10		
2-propanol	$PhCH_2CH_2OC(O)CMe_2Br$	3		

[a] At 60 °C for 5 h in the indicated solvent using di-*tert*-butyl hyponitrite as initiator [RBr] = 0.1 M. [b] 2 mol % (based on the bromide) of initiator. [c] Solutions containing 10 equiv of the reducing agent and 6 mol % (based on the bromide) of initiator.

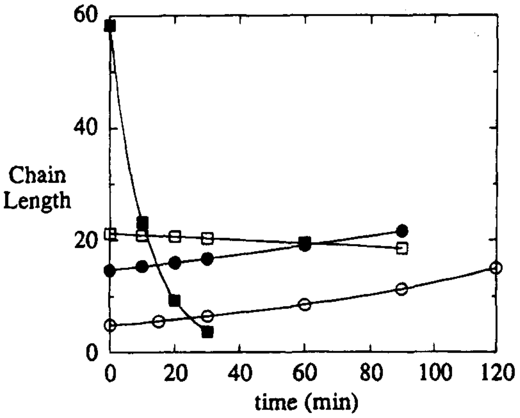

Figure 1. Plot of the chain length versus time for the radical chain reduction of ethyl bromoacetate by 2-propanol (■), 2-propanol-d_8 (●), ethanol (□) and methanol (○). The reactions were carried out in the neat alcohol. The reactions were initiated by the irradiation of benzophenone (355 nm) at 30° C.

Table 3. Estimated Rate Constants for the Rate-Limiting Step in the Reduction of 2-PhEBA[a]

reducing agent	rate-limiting reactn	$10^{-3}k$ (M^{-1} s^{-1})
methanol	8	0.016
ethanol	7	8 (3)[b]
2-propanol	7	20 (8)[b]
2-propanol-d_8	8	0.042
2-methyldioxolane	7	6[b]

[a] Using photochemical initiation with benzophenone at 30 °C using the reducing agent itself as solvent. [b] In acetonitrile as solvent using thermal initiation.

for a rate constant. Nevertheless, our data are consistent with other data reported in the literature for reactions of electron-rich radicals with electron-deficient halides which also have been described as electron-transfer processes.[21,22] For the hydrogen atom abstraction rates (reactions in methanol and 2-propanol-d_8), the estimated rate constants are in the same range as those reported previously for alkyl radical reactions.[21-23]

Mechanistic Considerations. The correlation of the average chain lengths with the oxidation potentials of the radicals is necessary but insufficient evidence that the mechanism of reaction 7 is electron transfer. In fact, there are at least two plausible mechanistic alternatives. The first is outer sphere electron transfer which generates, initially, a carbocation, a halide ion, and an alkyl radical. These intermediates ultimately lead to the formation of acetone and HBr. The second, and perhaps equally plausible mechanism, is simple atom abstraction (which can be thought of as an inner sphere electron-transfer process[24]) to form an intermediate bromohydrin which ultimately leads to the same products (Scheme 1). Factors which influence the rate of the electron transfer will have a similar effect (i.e., in the same direction) on the atom-transfer mechanism since the latter must procede via a polar transition state in which the carbon of the electron-rich radical has a partial positive charge and the carbon of the electron-deficient bromide has a partial negative charge.

In an effort to differentiate between these two possibilities, we have studied the reactions of some aromatic radical anions with ethyl bromoacetate, ethyl 2-bromopropionate and ethyl 2-bromo-2-methylpropionate. Since these reactions are believed to proceed by outer sphere electron transfer, the relationship between the driving force and the rate constants of these reactions provides a semiquantitative prediction of the kinetics expected for electron transfer from the electron-rich radical described above to the bromo esters. The rate constants were determined using an indirect electrochemical method, homogeneous redox catalysis. This method, which has been described in detail by Savéant and his co-workers,[25,26] takes advantage of the large overpotential associated with the direct electrochemical reduction of halides. Briefly, radical anions ($A^{\bullet -}$) are generated at an electrode (eq 12) at potentials more

$$A + e^{-} \rightleftharpoons A^{\bullet -} \tag{12}$$

$$A^{\bullet -} + RBr \rightarrow A + R^{\bullet} + Br^{-} \tag{13}$$

$$A^{\bullet -} + R^{\bullet} \rightleftharpoons A + R^{-} \tag{14}$$

positive than the onset of direct electrochemical reduction of the bromide. In the absence of the bromide, the reduction is a simple one-electron reversible process. However, in the presence of the bromide, the dissociative reduction of RBr by $A^{\bullet -}$ (eq 13) increases the concentration of A near the electrode, thus increasing the observed current. In this particular case, the product radical, $R^{\bullet}$, is further reduced to the carbanion, R^{-}, by a second radical anion (eq 14). As the increase in the current is a function of the concentration of the bromide and the rate constant for electron transfer, the rate constant can be

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(21) Timpe, H.-J.; Wagner, R.; Dusi, R.; Paleta, O.; Dadak, V. *Z. Chem.* **1986**, *26*, 256–257.

(22) Ayscough, P. B.; Lambert, G. *J. Chem. Soc., Faraday Trans. 1* **1978**, 2481–2489.

(23) Gilbert, B. C.; Norman, R. O. C.; Sealy, R. C. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1435–1441.

(24) Lexa, D.; Savéant, J. M.; Schäfer, H. J.; Su, K.; Vering, B.; Wang, D. L. *J. Am. Chem. Soc.* **1990**, *112*, 6162.

(25) Andrieux, C. P.; Dumas-Bouchait, J. M.; Savéant, J. M. *J. Electroanal. Chem.* **1980**, *113*, 19.

(26) Andrieux, C. P.; Gelis, L.; Savéant, J. M. *J. Am. Chem. Soc.* **1990**, *112*, 786.

Scheme 1

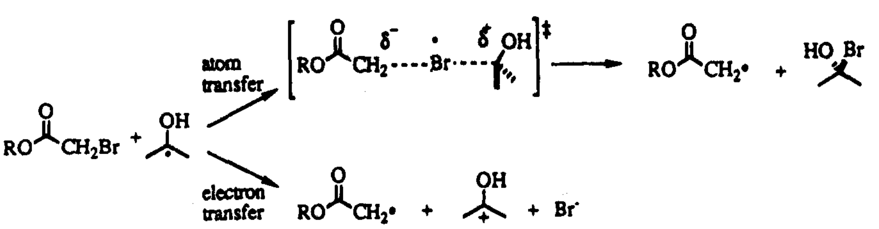

Table 4. Rate Constants for the Reaction of Some Radical Anions ($A^{\bullet -}$) with α-Bromo Esters

A	E° ($A/A^{\bullet -}$) V vs SCE	RX	E° ($RX/R^\bullet X^-$) V vs SCE	ΔG°_{ET} (kcal mol^{-1})	log(k_{13})
1-cyanophenanthrene	−1.815	EtOC(O)CMe$_2$Br	−0.74	−22.7	7.41
1,4-dicyanobenzene	−1.550	EtOC(O)CMe$_2$Br	−0.74	−16.5	6.43
	−1.550	EtOC(O)CHMeBr	−0.80	−15.2	6.39
	−1.550	EtOC(O)CH$_2$Br	−0.83	−14.5	6.32
azobenzene	−1.352	EtOC(O)CH$_2$Br	−0.83	−9.9	4.20
9-fluorenone	−1.270	EtOC(O)CH$_2$Br	−0.83	−8.0	4.11
1,4-dicyanonaphthalene	−1.175	EtOC(O)CMe$_2$Br	−0.74	−7.9	3.41
	−1.175	EtOC(O)CHMeBr	−0.80	−6.6	2.86
	−1.175	EtOC(O)CH$_2$Br	−0.83	−5.9	2.83
nitrobenzene	−1.075	EtOC(O)CH$_2$Br	−0.83	−3.4	2.58

[a] Determined by cyclic voltammetry (homogeneous redox catalysis) in acetonitrile/0.1 M TBAP at 25 °C.

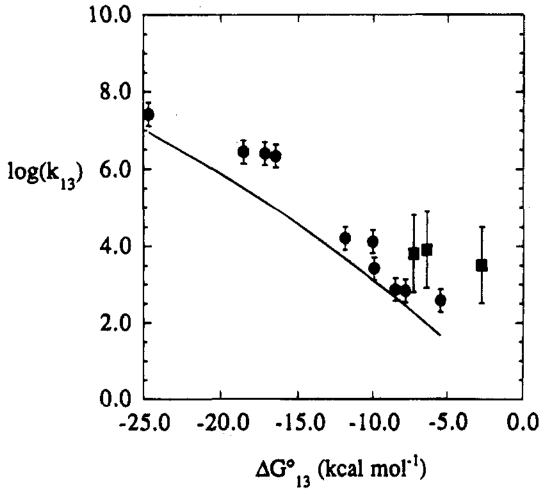

Figure 2. Marcus-type plot for the reactions of some radicals anions (●, data from Table 4) and the electron-rich radicals (■, data from Table 3) with α-bromo esters. The line drawn is the theoretical prediction using eqs 18 and 19 (see text).

obtained from an appropriate working curve obtained from digital simulation.[27]

In this analysis, it is assumed that the first electron transfer is rate limiting (eq 13). This is reasonable since the second electron transfer (eq 14) is exergonic by ca. 1 eV. In order to avoid the complication of competing self-protonation (i.e., the enolate will deprotonate the bromo ester[28]), all of the reactions were carried out in the presence of 2−4 equiv of 2,2,2-trifluoroethanol which does not protonate the radical anions used in this study but quickly protonates the enolate ions formed in reaction 14.[29] The rate constants obtained by this method are given in Table 4.

A Marcus-type plot of the logarithm of the rate constant versus the driving force is shown in Figure 2. The driving force is simply the difference between the standard potential of the redox catalyst and the standard potential for the dissociative reduction. The latter potentials were derived from the sum of the bond dissociation free energy for the R−Br bond and the standard reduction potential of Br• in acetonitrile (eqs 15−17). The

$$\mathrm{RBr} \rightleftharpoons \mathrm{R}^\bullet + \mathrm{Br}^\bullet \quad \Delta G^\circ_{\mathrm{BDE}} \tag{15}$$

$$\mathrm{Br}^\bullet + e^- \rightleftharpoons \mathrm{Br}^- \quad -FE^\circ(\mathrm{Br}^\bullet/\mathrm{Br}^-) \tag{16}$$

$$\mathrm{RBr} + e^- \rightleftharpoons \mathrm{R}^\bullet + \mathrm{Br}^- \quad -FE^\circ(\mathrm{RBr}/\mathrm{R}^\bullet,\mathrm{Br}^-) \tag{17}$$

bond dissocation enthalpies of ethyl bromoacetate, ethyl-2-bromopropionate, and ethyl 2-bromo-2-methylpropionate were estimated[30] to be 62, 61.3, and 60 kcal mol^{-1}, respectively, leading to an estimates of −0.83, −0.80, and −0.74 V vs SCE for the standard potential for the dissociative reductions (eq 17) after corrections for the entropies of the reactions.[31]

The line drawn in Figure 2 is the theoretical prediction using the model of dissociative electron transfer recently developed by Savéant and his co-workers (eq 18)[32−34] in

$$\Delta G^\ddagger = \Delta G_0^\ddagger\left(1 + \frac{\Delta G^\circ_{\mathrm{et}}}{4\Delta G_0^\ddagger}\right)^2 \tag{18}$$

$$\Delta G_0^\ddagger = \frac{\Delta G^\circ_{\mathrm{BDE}} + \lambda_0}{4} \tag{19}$$

which the activation free energy, $\Delta G^\ddagger$, is expressed as a

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(27) Feldberg, S. W. In *Electroanalytical Chemistry*; A. J. Bard, Ed.; Marcel Dekker: New York, 1969; Vol. 3; pp 199−296.

(28) Maran, F.; Celadon, D.; Severin, M. G.; Vianello, E. *J. Am. Chem. Soc.* **1991**, *113*, 9320−9329 and references cited therein.

(29) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456−463 and references cited therein.

(30) The C−Br bond of *tert*-butyl bromoacetate was determined to be 62 kcal mol^{-1} by photoacoustic calorimetry (for a description of this technique, see: Clark, K. B.; Wayner, D. D. M. *J. Am. Chem. Soc.* **1991**, *113*, 9363). We have assumed that the ΔBDE values for ethyl 2-bromopropionate and ethyl 2-bromo-2-methylpropionate were the same as those values for 2-bromopropane and 2-bromo-2-methylpropane, 0.7 and 2 kcal mol^{-1}, respectively (ref 5). The entropy changes were estimated from group additivities (ref 31).

(31) Benson, S. W. *Thermochemical Kinetics*; John Wiley and Sons: New York, 1976.

(32) Savéant, J. M. *J. Am. Chem. Soc.* **1992**, *114*, 10595−10602.

(33) Savéant, J. M. *J. Am. Chem. Soc.* **1987**, *109*, 6788−6795.

(34) Andrieux, C. P.; Legorande, A.; Savéant, J. M. *J. Am. Chem. Soc.* **1992**, *114*, 6892−6904.

function of the overall driving force, ΔG°_{13}, and an intrinsic barrier, $\Delta G^\ddagger_0$. In this model the intrinsic barrier (eq 19) depends on the bond energy, ΔG°_{BDE}, and the reorganization energy, λ_0. We have used a value of 11 kcal mol^{-1} for λ_0 as has been suggested recently by Lund.[35] The fit to the data is reasonably good considering the large change in the driving force (ca. 20 kcal mol^{-1}) and the fact that the line is derived from eq 18 with no fitted variables (in this case, $\Delta G^\ddagger_0 = 16.0$ kcal mol^{-1}). The rate of electron transfer to the bromides increases in the order primary < secondary < tertiary. This is in accord with the order of E° values for the dissociative electron transfer although the rate constant only changes by a factor of about of 4 rather than ca. 10 as predicted by the theory. It is noteworthy that for simple alkyl bromides the order of reactivity with a number of radical anions is tertiary < secondary < primary. This is not expected from the theory and has been interpreted in terms of increasing S_N2-like reactivity of the radical anions with the less substituted bromides.[34,35]

The kinetic and thermodynamic data obtained for the reactions of the electron-rich radicals with ethyl bromoacetate also are shown in Figure 2. Although the errors on these rate contants are large, it is clear that the point for the ethanol-derived radical is almost 4 orders of magnitude above the line for the radical anions. This reaction is much faster than is predicted on the basis of the data in Figure 2. There are a number of differences between the reactions of the electron-rich radicals and those of the radical anions that preclude a strict quantitative comparison. For example, the reactions of the electron-rich radicals result in the formation of two charged products (i.e., charge separation) while those of the radical ion have do not involve the formation or destruction of charge (i.e., charge shift). Electrostatic forces involved in charge separation lead to a different energy gap dependence; however, the differences are expected to be small (certainly less than 1 order of magnitude).[36] In addition, it was not possible to make the electrochemical measurements under conditions that were identical to the reactions of the electron-rich radicals. However, these variations also are expected to have only small effects on the rates of outer sphere electron transfer. Variations in solvation properties of the ions formed can result in small variations in polar solvents. For example, the oxidation potentials of the alcohol-derived radicals are ca. 200 mV more negative in water than in acetonitrile.[16] Nevertheless, we found that for the reactions of ethanol and 2-propanol, the rate contants in acetonitrile and in the neat reducing agents were within a factor of 3 (Table 3). We conclude, therefore, that the reaction of the ethanol-derived radical (and, therefore, the methanol-derived radical) with the bromo ester is not a simple outer sphere electron-transfer process but, in fact, an atom-transfer reaction.

For reasons outlined above, electron transfer cannot be unequivocally ruled out in the reactions of the other two radicals (those derived from 2-propanol and 2-methyl-1,3-dioxolane) since these rate constants are within 1 order of magnitude of those predicted using the reactions of radical anions. The observation that the reaction with 2-methyl-1,3-dioxolane proceeds in isooctane points to some bonding interactions at the transition state even for this somewhat more hindered species in this nonpolar solvent. However, one cannot rule out the possiblity of a mechanistic change upon changing the solvent from acetonitrile to isooctane. In fact, there have been recent reports of S_N2-like reactivity of delocalized radical anions with a number of halides.[37,38] In the former case,[37] a change of mechanism from outer sphere ET to an S_N2-like process was observed simply by changing the solvent from acetonitrile to *N,N*-dimethylformamide.

Conclusions

The radical chain reduction of α-bromo esters by 2-propanol and 2-methyldioxolane has been shown to be a kinetically viable process with average chain lengths of > 10 at temperatures between 30 and 60 °C for primary and secondary bromides. The reactions are less efficient when a tertiary bromide is used. The rate constants for the reaction of the methanol- and ethanol-derived radicals clearly indicate that these reactions proceed via an atom-transfer mechanism. Those for the 2-propanol- and the 2-methyl-1,3-dioxolane-derived radicals with a primary bromo ester at 30 °C are only 1 order of magnitude faster than was predicted for an outer sphere electron-transfer mechanism (as has been suggested previously). For these reactions, electron transfer cannot be unequivocally ruled out. Irrespective of the mechanism, the order of reactivity of the organic reducing agents follow the same trend as the oxidation potentials of the corresponding radicals suggesting that these potentials can be used as a predictive tool for the design of new reagents.

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Registry Nos. provided by the author: acetic acid, 2-phenylethyl ester, 103-45-7; propanoic acid, 2-phenylethyl ester, 122-70-3; 2-methylpropanoic acid, 2-phenylethyl ester, 103-48-0; bromoacetic acid, 2-phenylethyl ester, 3785-33-9; 2-bromo-2-methylpropanoic acid, 2-phenylethyl ester, 43216-34-8.

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[35] Larsen, H.; Pedersen, S. U.; Pedersen, J. A.; Lund, H. *J. Electroanal. Chem.* **1992**, *331*, 971–983.

[36] Kakitani, T.; Yoshimori, A.; Mataga, N. In *Electron Transfer in Inorganic, Organic and Biological Systems*; Bolton, J. R., Mataga, N., McLendon, G., Eds.; American Chemical Society: Washington, DC, 1991; pp 45–69.

[37] Huang, Y.; Wayner, D. D. M. *J. Am. Chem. Soc.* **1994**, *116*, 2157–2158.

[38] Hebert, E.; Mazaleyrat, J. P.; Nadjo, L.; Savéant, J.-M.; Welvart, Z. *Nouv. J. Chim.* **1985**, *9*, 75.