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Supplementary Material Available: ^{1}H and/or ^{13}C NMR spectra of **24**, **26sf**, **30sf**, **31st**, and **33sf** (16 pages). Ordering information is given on any current masthead page.

Relative Homolytic Strengths of C–H Bonds in Meldrum's Acid and Dimethyl Malonate

M. J. Bausch,* C. Guadalupe-Fasano, R. Gostowski, D. Selmarten, and A. Vaughn

Department of Chemistry and Biochemistry, Southern Illinois University at Carbondale,
Carbondale, Illinois 62901-4409

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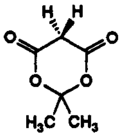
With the aid of a thermochemical cycle comprised of acidity and redox data in dimethyl sulfoxide and aqueous solution, relative homolytic bond dissociation energies (ΔBDE values) have been determined for 2,2-dimethyl-1,3-dioxane-4,6-dione (Meldrum's acid), dimethyl malonate, 5,5-dimethylcyclohexane-1,3-dione (dimedone), 2,4-pentanedione, acetone, 3-pentanone, and cyclopentanone. The ΔBDE data suggest that (a) secondary C–H bonds present in 3-pentanone are ca. 4 kcal/mol weaker (in a homolytic sense) than analogous primary C–H bonds in acetone; (b) C–H bonds located on carbon atoms adjacent to the carbonyl carbons in 3-pentanone and cyclopentanone are of equal homolytic strength, thus indicating a negligible effect due to cyclization; (c) homolytic BDEs for dimedone and 2,4-pentanedione are nearly equal, also indicative of no bond weakening due to cyclization; and (d) the C–H BDE for Meldrum's acid is ca. 3 kcal/mol less than that of the analogous C–H bond present in dimethyl malonate, indicative of a small cyclization effect on homolytic bond strengths. The Meldrum's acid/dimethyl malonate ΔBDE data are therefore in sharp contrast to published dimethyl sulfoxide solution pK_a's for Meldrum's acid and dimethyl malonate (7.3 and 15.9, respectively: Arnett et al. *J. Am. Chem. Soc.* 1987, *109*, 809–812). The difference in the pK_a's for Meldrum's acid and dimethyl malonate is thought to provide additional experimental support for the effects of rotational barriers on neutral closed-shell ester stabilities. The ΔBDE data in this article suggest that rotational barriers have substantial effects on the relative stabilities of the radicals derived from Meldrum's acid and dimethyl malonate as well.

In dimethyl sulfoxide (DMSO) solution, at 25 °C, 2,2-dimethyl-1,3-dioxane-4,6-dione, (Meldrum's acid, 1, pK_a = 7.3) is 11.8 kcal/mol more acidic than dimethyl malonate (2, pK_a = 15.9).[1] Under identical conditions, dimedone (3, pK_a = 11.2) is only 2.9 kcal/mol more acidic than 2,4-pentanedione (4, pK_a = 13.3).[1] The facile dimethyl sulfoxide solution ionization of Meldrum's acid has been attributed to two factors: (a) a 6–8 kcal/mol destabilization of Meldrum's acid (relative to dimethyl malonate) that results from its enforced *E* configuration and (b) a 3 kcal/mol stabilization of the conjugate based derived from Meldrum's acid (relative to the conjugate base derived from dimethyl malonate) that results from the enforced planarity of the cyclic enolate anion.[1] These data and the resulting interpretations are unique in that they enable analyses of structural and electronic factors that affect the relative stbilities of both partners in the respective acid–base equilibrium. In this article, we report our investigations of the cyclic voltammetric (CV) and, in some cases, second harmonic alternating current voltammetric (SHACV) oxidative reactions of the enolate anions derived from seven different organic acids. Redox data obtained in this fashion, when combined with the aforementioned acidity constants, enable comparisons of the free energy changes associated with the removal of hydrogen atoms from a given set of substrates. The resulting ΔBDE values



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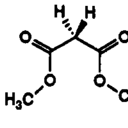

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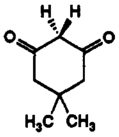

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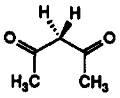

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Table I. DMSO Solution pK_a's (25 °C) and Relative Acidity Constants (ΔpK_a) for Substrates 1–7, Oxidation Potentials ($E_{ox(n-H^+)}$) and Relative Oxidation Potentials (ΔE_{ox}) for the Conjugate Bases Derived from Substrates 1–7, and Relative Homolytic Bond Dissociation Energies (ΔBDE) for 1–7

substrate (n)	pK_a[4]	ΔpK_a[5] (kcal/mol)	$E_{ox(n-H^+)}$[6,7] (V)	ΔE_{ox}[8] (kcal/mol)	ΔBDE[9] (kcal/mol)
Meldrum's acid (1)	7.3[1]	(0.0)	1.16	(0.0)	(0.0)
dimethyl malonate (2)	15.9[1]	11.8	0.77	−9.0	+3
dimedone (3)	11.2	5.3	0.93 (0.88)	−5.3	0
2,4-pentanedione (4)	13.3	8.2	0.78 (0.73)	−8.8	−1
acetone (5)	26.5	26.3	0.10 (0.08)	−24.4	+2
3-pentanone (6)	27.1	27.1	−0.11	−29.3	−2
cyclopentanone (7)	25.8	25.3	−0.03	−27.4	−2

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[1] Arnett, E. M.; Maroldo, S. G.; Schilling, S. L.; Harrelson, J. A., Jr. *J. Am. Chem. Soc.* **1984**, *106*, 6759–6767. Arnett, E. M.; Harrelson, J. A., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 809–812.

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Table II. Aqueous Solution pK_a's (25 °C) and Relative Acidity Constants (ΔpK_a) for Meldrum's Acid (1), Dimedone (3), and 2,4-Pentanedione (4); Oxidation Potentials ($E_{ox(n-H^+)}$) and Relative Oxidation Potentials (ΔE_{ox}) for the Conjugate Bases Derived from Substrates 1, 3, and 4; and Relative Homolytic Bond Dissociation Energies (ΔBDE) for 1, 3, and 4

substrate (n)	pK_a[4]	ΔpK_a[5] (kcal/mol)	$E_{ox(n-H^+)}$[10] (V)	ΔE_{ox}[8] (kcal/mol)	ΔBDE[9] (kcal/mol)
Meldrum's acid (1)	4.8	(0.0)	1.33	(0.0)	(0.0)
dimedone (3)	5.2[11]	0.5	1.22	−2.5	−2
2,4-pentanedione (4)	8.9	5.6	1.07	−6.0	0

suggest that the *homolytic* strengths of the indicated C–H bonds in Meldrum's acid (1) and dimethyl malonate (2) are within 3 kcal/mol of each other, a difference in sharp contrast to the 11.8 kcal/mol difference in the pK_a's of 1 and 2. In an attempt to better understand these data, we have investigated the effects of cyclization on the homolytic strengths of chemical bonds present in various organic molecules.

Results and Discussion

Table I contains acidity and redox data for seven organic acids (1–7) and their conjugate bases, collected in DMSO solution. Table II contains analogous aqueous-phase data for three of these species (i.e., Meldrum's acid, 5,5-dimethylcyclohexane-1,3-dione (dimedone), and 2,4-pentanedione).

The ΔBDE data (in kcal/mol) listed in Tables I and II are determined by inserting ΔpK_a and ΔE_{ox} (in volts) data for a given acid and its respective conjugate base into eq 1. Equation 1 has been shown to yield relative homolytic

$$\Delta\text{BDE(H–A)} = \Delta\text{p}K_a\text{(H–A)} + \Delta E_{ox}(\text{A}^-) \qquad (1)$$

BDE data that allow *comparisons* of the homolytic strengths of several varieties of chemical bonds.[2] Inspection of the data in Table I reveals that the secondary C–H bonds present in 3-pentanone are ca. 4 kcal/mol weaker than the analogous primary C–H bonds present in acetone. Bond-weakening methyl effects of this magnitude agree nicely with published BDE and ΔBDE values that point to similar effects of adjacent methyl groups on the strengths of various C–H bonds, in DMSO solution[2a] as well as the gas phase.[3]

DMSO-phase pK_a and redox data necessary for the ΔBDE determination for cyclopentanone are also listed in Table I. Comparison of ΔBDE data for cyclopentanone and 3-pentanone reveals that cyclization has essentially no effect on the homolytic strengths of the analogous C–H bonds present in these species. Published gas-phase bond strengths for allylic C–H bonds in 1-butene and cyclopentene (82 kcal/mol each) also indicate that hydrocarbon cyclization has little effect on homolytic C–H bond strengths.[3] These data serve to foreshadow BDE comparisons for Meldrum's acid (1) and dimethyl malonate (2), as well as for dimedone (3) and 2,4-pentanedione (4).

Homolytic ΔBDE data for dimedone (3) and 2,4-pentanedione (4), in both DMSO (Table I) and aqueous (Table II) solution, indicate that cyclization has little effect on the stabilities of $3 - \text{H}^\bullet$ and $4 - \text{H}^\bullet$, relative to 3 and 4, respectively. Data for the homolytic cleavages therefore contrast with the heterolytic data, since, in DMSO and aqueous solution, 3 is 2.6 and 5.1 kcal/mol more acidic than 4, its acyclic cognate.

Homolytic ΔBDE data for Meldrum's acid (1) and dimethyl malonate (2) listed in Table I suggest that cyclization weakens the indicated sp^{3}C–H bond in 2 by 3 kcal/mol, again in DMSO solution. This value is somewhat larger than the experimental error in solution-phase ΔBDE values determined via eq 1, in light of previously published results that utilized similar cycles.[2,12,13] The homolytic ΔBDE data for Meldrum's acid (1) and dimethyl malonate (2) are striking when compared to the ΔpK_a data for the same species. Evidently, the cis ester dipole contribution present in 1, a conformationally dependent inductive effect that destabilizes 1 and acts to facilitate C–H heterolysis,[1,14] acts in a rather minimal fashion to facilitate C–H homolysis. We rationalize these observations by postulating that the cis ester dipole contribution that destabilizes 1 also has a similar (but slightly smaller) destabilizing effect on the stability of $1 - \text{H}^\bullet$, the radical derived from 1. It has long been known that esters constrained to be in an *E* conformation are more reactive than esters free to rotate into the energetically preferred *Z* conformation.[15] Deslongchamps has invoked arguments based on the overlap of unpaired electrons on the ether oxygen with the σ* orbital of the carbonyl carbon as a likely explanation for the observed conformationally dependent reactivity effects.[16] Arnett has suggested that

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(2) (a) Bordwell, F. G.; Bausch, M. J. *J. Am. Chem. Soc.* 1986, *108*, 1979–1985. (b) Bausch, M. J.; Gostowski, R.; Jirka, G.; Selmarten, D.; Winter, G. *J. Org. Chem.* 1990, *55*, 5805–5806. (c) Bordwell, F. G.; Cheng, J.-P.; Harrelson, J. A., Jr. *J. Org. Chem.* 1989, *54*, 3101–3105.

(3) McMillen, D. F.; Golden, D. M. *Ann. Rev. Phys. Chem.* 1982, *33*, 493–532.

(4) All acidity data in Tables I and II (except where noted): Bordwell, F. G. *Acc. Chem. Res.* 1988, *21*, 456–463. Acidity constants determined in this way are believed to be accurate to ±0.1 pK_a unit (ca. 0.1 kcal/mol).

(5) At 25 °C, 1 pK_a unit is equal to 1.37 kcal/mol. Therefore, in Table I, for a given substrate n, ΔpK_a (kcal/mol) = 1.37 (p$K_{a(n)}$ − 7.3); while in Table II, ΔpK_a = 1.37 (p$K_{a(n)}$ − 4.8), where 7.3 and 4.8 are the pK_a's for Meldrum's acid in DMSO and aqueous solution, respectively. Positive ΔpK_a values signify that the molecule in question is a weaker acid than Meldrum's acid.

(6) DMSO-phase electrochemistry conditions: see Experimental Section. Values in parentheses are those published in refs 2c (3 and 4) and 12 (5).

(7) The technique of second harmonic alternating current voltammetry (SHACV) was also used to collect oxidation potentials for the anions derived from 1–4. The SHACV crossing potentials for these species are each ca. 50 mV cathodic of the irreversible CV peak potentials listed in Table I. We were not able to collect meaningful SHACV data for the oxidations of the enolate anions derived from 5–7.

(8) At 25 °C, 1 V is equal to 23.06 kcal/mol. In Table I, for the anion derived from a given substrate n, ΔE_{ox} (kcal/mol) = 23.06($E_{ox(n-H^+)}$ − 1.16]; while in Table II, ΔE_{ox} (kcal/mol) − 23.06($E_{ox(n-H^+)}$ − 1.33), where 1.16 and 1.33 are the E_{ox} values for the anion derived from Meldrum's acid in DMSO and aqueous solution, respectively.

(9) The ΔBDE values in Tables I and II have been determined with the aid of eq 1. Positive ΔBDE values signify that the bond in question is stronger than the analogous bond in Meldrum's acid. The ΔBDE data are believed to be accurate to ±1 kcal/mol.

(10) Aqueous-phase electrochemistry conditions: see Experimental Section.

(11) Davidson, D.; Bernhard, S. A. *J. Am. Chem. Soc.* 1948, *70*, 3426–3428.

(12) Bordwell, F. G.; Cheng, J.-P.; Harrelson, J. A., Jr. *J. Am. Chem. Soc.* 1988, *110*, 1229–1231.

(13) We estimate the uncertainty in the ΔBDE values in Table I and II to be <1 kcal/mol: the pK_a and E_{ox} data are believed to be accurate to ±0.1 pK unit (0.1 kcal/mol) and 25 mV (0.5 cal/mol), respectively.

(14) (a) The anomalously high acidity of Meldrum's acid has also been examined from a theoretical perspective.[14b,c] Results from these studies point to destabilizing dipole–dipole interactions between the ether oxygen and the carbonyl group in the *E* conformation of methyl acetate, compared to the *Z* conformation for the same species. The magnitude of the destabilization of the *E* conformer, relative to the *Z* conformer, is greatly reduced in the corresponding ester enolates. (b) Wang, X.; Houk, K. N. *J. Am. Chem. Soc.* 1988, *110*, 1870–1872. (c) Wiberg, K. B.; Laidig, K. E. *J. Am. Chem. Soc.* 1988, *110*, 1872–1874.

(15) Huisgen, R. *Angew. Chem.* 1957, *59*, 341–359. Huisgen, R.; Ott, H. *Tetrahedron* 1959, *6*, 253–267.

it is mainly an "initial state" destabilization of the E diester that results in the anomalously high acidity of Meldrum's acid (1) relative to dimethyl malonate (ΔpK_a = 11.6 kcal/mol).[1] Results presented in this article imply that the stereoelectronic factors (i.e., restricted rotation) that are thought to result in the destabilization (6–8 kcal/mol) of Meldrum's acid (1; relative to dimethyl malonate (2))[1] may also result in a similar but somewhat smaller destabilization (3–5 kcal/mol) of the radical derived from Meldrum's acid (i.e., $1 - H^\bullet$) relative to $2 - H^\bullet$. We are not aware of any published quantitative estimates of the effects of restricted rotation on the stabilities of solution-phase radicals.

Also interesting are comparisons of the ΔpK_a and ΔBDE values for 1–7. While acetone (5), 3-pentanone (6), and cyclopentanone (7) are all about 25 kcal/mol less acidic than Meldrum's acid, their homolytic C–H BDEs differ from that of Meldrum's acid by no more than 2 kcal/mol. These data serve as further evidence that substituent and structural effects on radical stabilities are very different from analogous effects on anion stabilities. It is also of interest to compare the effects of solvent on the data listed in Tables I and II. Bordwell, for BDEs in DMSO solution,[12] and Friedrich,[17] for BDEs in aqueous solution, have shown that eq 1 can yield absolute solution-phase BDEs that are in remarkable agreement with gas-phase BDEs when constants of ca. 56 and 57 kcal/mol, respectively, are added to the right side of eq 1. Treatment of the pK_a and redox data listed in Tables I and II in this fashion yields results indicating that the effect of solvent on homolytic BDEs (i.e., changing solvent from DMSO to water) is minimal: DMSO and aqueous phase BDEs for 1, 3, and 4 obtained using the Bordwell and Friedrich approximations[18] differ by less than 2 kcal/mol. We have obtained similar results for several other organic molecules,[19] and Griller has presented evidence suggesting that homolytic BDEs for relatively large organic molecules will be the same in both gas and condensed phases.[20]

Experimental Section

None of the pK_a values in Tables I and II were determined in our laboratories; references for these values are listed in Tables I and II.

Substrates 1–7 are all commercially available (Aldrich). Meldrum's acid and dimedone were crystallized according to literature melting points prior to use; 2,4-pentanedione and dimethyl malonate were distilled prior to use, while acetone (HPLC grade), 3-pentanone (spectral grade), and cyclopentanone (+99%) were used without further purification.

Dimethyl sulfoxide was purified, and potassium dimsylate was synthesized, as described by Matthews and Bordwell.[21] $Et_4N^+BF_4^-$ was recrystallized from acetone, and K^+Cl^- was recrystallized from water; both were allowed to dry at 110 °C under vacuum before dissolution in DMSO and water, respectively.

Dimethyl sulfoxide electrochemistry: 0.1 M $Et_4N^+BF_4^-$ electrolyte; Pt working and Ag/AgI reference electrodes (ferrocene/ferrocenium = +0.875 V as internal standard, values corrected to NHE_{aq} by subtracting 0.125 V). In the argonated electrochemical cell, the enolates were present in 1–2 mM concentrations. The E_{ox} values are the anodic peak potentials as reported by a BAS 100A electrochemical analyzer, are the averages of several runs for each compound, and are reproducible to ≤25 mV (ca. 0.5 kcal/mol). Cyclic voltammetry sweep rate: 0.1 V/s. Second harmonic alternating current voltammetry specifications: 20/110° ϕ shift, ac amplitude = 25 mV, and frequency = 50 Hz.

Aqueous-phase electrochemistry: 0.1 M K^+Cl^- electrolyte solution buffered to pH 10; glassy carbon working and Ag/AgCl reference electrodes (internal standard: $Fe(CN)_6^{3-}/Fe(CN)_6^{2-}$ = 0.458 V (vs NHE);[22] CV, 0.1 V/s sweep rate. In the nitrogenated electrochemical cell, the anions were generated by adding the neutral acid H–A to the buffered K^+Cl^- solution. The E_{ox} values are the anodic peak potentials as reported by a BAS 100A electrochemical analyzer, are the averages of several runs for each compound, and are reproducible to ≤25 mV.

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Registry No. 1, 2033-24-1; 1 (conjugate base), 12256-88-1; 2, 108-59-8; 2 (conjugate base), 33673-07-3; 3, 126-81-8; 3 (conjugate base), 12275-63-7; 4, 123-54-6; 4 (conjugate base), 17272-66-1; 5, 67-64-1; 5 (conjugate base), 24262-31-5; 6, 96-22-0; 6 (conjugate base), 29263-72-7; 7, 120-92-3; 7 (conjugate base), 55886-83-4.

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(17) Friedrich, L. E. *J. Org. Chem.* **1983**, *48*, 3851–3852.

(18) (a) That *absolute* solution-phase BDEs obtained in this manner are only estimates has been adequately demonstrated.[18b,18c] The fact remains that acid base and redox data for large organic molecules, when incorporated into the appropriate cycle as described in ref 12, yields solution-phase enthalpic BDEs generally within 3 kcal/mol of gas-phase values. (b) Sawyer, D. T. *J. Phys. Chem.* **1989**, *93*, 7977–7978. (c) Golden, D. M.; Bierbaum, V. M.; Howard, C. J. *J. Phys. Chem.* **1990**, *93*, 5413–5415.

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(20) Mulder, P.; Saastad, O. W.; Griller, D. *J. Am. Chem. Soc.* **1988**, *110*, 4090–4092. Kanabus-Kaminska, J. M.; Gilbert, B. C.; Griller, D. *J. Am. Chem. Soc.* **1989**, *111*, 3311–3314.

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