

The tube was sealed with a tight-fitting plastic cap, and then placed in water at 20 °C in a Dewar flask having an unsilvered slit. After 5 min (for temperature equilibration), the aluminum foil was removed and the mixture photolyzed with a 300-W tungsten lamp placed 10 cm away. The progress of the reaction was monitored by proton NMR; the tube was rewrapped with aluminum foil during transfers between the NMR probe and the photolysis apparatus. The reaction was usually complete within 10 min as judged by the disappearance of the <sup>1</sup>H NMR signal of the methylene protons of the starting material. The tube was then opened, attached to a high-vacuum line, and the volatiles vacuum-transferred to a trap cooled in liquid nitrogen. The trapped material was analyzed by GC/MS and <sup>1</sup>H NMR spectroscopy.

Sufficient amounts of dienes **20a** and **20b** for spectroscopic identification were prepared from **10** (0.49 g, 1.8 mmol) and excess selenophenol (2.7 g, 17 mmol) in THF under similar photolysis conditions. The dienes were separated by preparative GLC (5 ft × 1/4 in. column of 25% XE-60 on Chromosorb G; injector temperature 130 °C; detector, 150 °C).<sup>25</sup> Diene **20a** is a colorless liquid: <sup>1</sup>H NMR δ 6.05 (t, *J* = 2.4 Hz, 1 H), 5.89 (t, *J* = 2.4 Hz, 1 H), 5.76 (sym m, 1 H), 3.09 (m, 1 H), 2.96 (m,

1 H), 2.93 (m, 1 H), 2.78 (m, 1 H), 1.60 ppm (sym m, 3 H); <sup>13</sup>C NMR δ 146.2 (quaternary), 136.4, 135.8, 127.3 (CH, olefinic), 40.8, 40.2, 39.6, 34.0 (CH, aliphatic), 15.8 ppm (CH<sub>3</sub>). Diene **20b** is also a colorless liquid: <sup>1</sup>H NMR δ 6.43 (t, *J* = 2.5 Hz, 1 H), 6.35 (t, *J* = 2.5 Hz, 1 H), 4.69 (m, 1 H), 4.66 (m, 1 H), 3.47 (m, 1 H), 3.41 (m, 1 H), 3.33 (m, 1 H), 2.78–2.72 (m, 2 H), 2.46 ppm (dm, *J* = 17 Hz, 1 H); <sup>13</sup>C NMR δ 150.8 (quaternary), 140.4, 137.1, 106.1 (CH<sub>2</sub>, exocyclic olefinic), 45.3, 45.0, 44.1 (CH, aliphatic), 33.9 (CH<sub>2</sub>, methylene), 27.2 ppm (CH).

The selenophenol experiments were quantitated by using methylene chloride (ca. 0.5 equiv) as an internal standard, itself calibrated by careful integration against the methylene proton signals of the accurately weighed starting ester. Selenophenol was added, the mixture was photolyzed for 10 min, and then the <sup>1</sup>H NMR spectrum was taken. The yields of methylcubane and of dienes **20a** and **20b** were determined by integration of the appropriate proton NMR signals against that of methylene chloride.

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**Registry No.** **1**, 135191-71-8; **2**, 53578-15-7; **4**, 134078-23-2; **5**, 135191-72-9; **6**, 135191-73-0; **7**, 135191-74-1; **8**, 60462-27-3; **9**, 135191-75-2; **10**, 135191-76-3; **11**, 23096-16-4; **12**, 452-61-9; **18a**, 135356-15-9; **18b**, 135191-77-4; **19**, 135191-79-6; **20a**, 135191-80-9; **20b**, 135191-78-5; 1,4-bis(carbomethoxy)cubane, 29412-62-2; 4-iodo-1-methylcubane, 125762-85-8.

(25) (a) Decomposition of **20a** to methylcyclooctatetraene<sup>26</sup> and **20b** to an unidentified olefin was observed when the injection temperature was set to 190 °C and the detector temperature to 210 °C. (b) Methylcubane and diene **20a** collect in the same fraction. As only a small amount of methylcubane is formed and its spectroscopic properties are known, this does not interfere with the assignments to diene **20a**.

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## Lactones. 2. Enthalpies of Hydrolysis, Reduction, and Formation of the C<sub>4</sub>–C<sub>13</sub> Monocyclic Lactones. Strain Energies and Conformations

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**Abstract:** The enthalpies of hydrolysis of the monocyclic lactones from  $\gamma$ -butyrolactone to tridecanolactone were determined calorimetrically, and the acyclic ethyl esters having the same number of atoms were studied in the same fashion. The enthalpies of reduction of the lactones to the corresponding  $\alpha,\omega$ -alkanediols with lithium triethylborohydride also were determined. The enthalpies of formation of the lactones and the ethyl esters were derived from these data. They were converted to values for the gas phase by measuring the enthalpies of vaporization of ethyl esters and of lactones. In the cases of  $\gamma$ -butyrolactone and  $\delta$ -valerolactone, the enthalpies of formation were in good accord with the previously reported values determined via combustion calorimetry. The strain energies of the lactones were obtained via isodesmic reactions. Valerolactone had a strain energy of 11 kcal/mol, and the largest strain energy was found with octanolactone (13 kcal/mol). The conformations of  $\gamma$ -butyrolactone and  $\delta$ -valerolactone were studied via MP2/6-31G\* geometry optimizations, and the conformations of the other lactones were studied with use of the molecular mechanics program MM3. The energies of the lactones estimated via molecular mechanics were compared with the experimental results.

### 1. Introduction

We have initiated a study of the conformations and energies of monocyclic lactones in order to gain more information on the role of the *E* and *Z* conformations on their properties and to have data that would allow more satisfactory modeling of this important functional group via molecular mechanics. The results of a study of the conformations of nonanolactone and of tridecanolactone have been presented.<sup>1</sup> We have now studied the enthalpies of formation and the strain energies of all the monocyclic lactones with 5–14-membered rings. Lactones with relatively small rings are forced to adopt an *E* ester conformation,<sup>2</sup> and in the case of

methyl acetate, this conformation is 8.5 kcal/mol higher in energy than the *Z* form.<sup>3</sup> This is due to the lack of the dipole–dipole stabilization that is present in the *Z* form and both methyl–methyl and lone pair–lone pair steric repulsion in the *E* form.<sup>4</sup> How will these interactions affect the strain energies of the five- and six-membered ring lactones? In order to try to answer this question, we have carried out experimental studies aimed at giving additional thermochemical data, as well as theoretical calculations that will give information on the conformations and electronic interactions.

The enthalpy of formation of  $\gamma$ -butyrolactone has been determined from the enthalpy of combustion, and it is  $-100.56 \pm 0.20$  kcal/mol.<sup>5,6</sup>  $\delta$ -Valerolactone also has been studied, and it

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**Table I.** Enthalpies of Hydrolysis and Formation of Ethyl Esters<sup>a</sup>

ester	n <sup>b</sup>	$\Delta H_f$ , ester (l)( $\Delta H_1$ )	n	$\Delta H_f$ , acid (l) ( $\Delta H_2$ )	$\Delta H_f^c$ , hydrol	$\Delta H_f$ , acid, l	$\Delta H_f^e$ , ester, l	$\Delta H_f$ , ester	$\Delta H_f$ , ester, g
ethyl acetate	5	-10326 ± 22	5	-11434 ± 25	923 ± 33	-115.75 ± 0.07	-114.69 ± 0.11	8.40 ± 0.05	-106.3 ± 0.1
ethyl propionate	5	-9786 ± 36	5	-10716 ± 27	745 ± 45	-122.07 ± 0.8	-120.84 ± 0.12	9.35 ± 0.02	-111.5 ± 0.1
ethyl butyrate	4	-9571 ± 15	5	-10439 ± 61	683 ± 63	-127.59 ± 0.16	-126.29 ± 0.19	10.44 ± 0.3	-115.9 ± 0.3
ethyl valerate	5	-9120 ± 26	5	-10013 ± 21	708 ± 34	-133.71 ± 0.18	-132.44 ± 0.20	11.3 ± 0.3	-121.2 ± 0.4
ethyl hexanoate	5	-8820 ± 27	5	-9676 ± 16	671 ± 32	-139.73 ± 0.25	-138.42 ± 0.26	12.32 ± 0.3	-126.1 ± 0.4
ethyl heptanoate	5	-8611 ± 26	5	-9315 ± 64	519 ± 69	-145.76 ± 0.35	-144.30 ± 0.37	13.3 ± 0.3	-131.0 ± 0.5
ethyl octanoate	5	-8360 ± 25	6	-9059 ± 77	514 ± 75	-151.93 ± 0.25	-150.46 ± 0.27	14.22 ± 0.3	-136.2 ± 0.4
ethyl nonanoate	5	-8173 ± 44	4	-8934 ± 13	576 ± 46	-157.68 ± 0.48	-156.28 ± 0.49	15.2 ± 0.3	-141.1 ± 0.6
ethyl decanoate	5	-8041 ± 49	5	-2043 ± 17 <sup>d</sup>	439 ± 61	-163.97 ± 0.24 <sup>d</sup>	-162.43 ± 0.26	16.11 ± 0.3	-146.3 ± 0.4
ethyl undecanoate	5	-7716 ± 42	5	-2591 ± 33 <sup>d</sup>	494 ± 76	-170.09 ± 0.27 <sup>d</sup>	-168.60 ± 0.29	17.1 ± 0.3	-151.5 ± 0.4

<sup>a</sup> Enthalpies of reaction are given in calories/mole, and enthalpies of vaporization and formation are given in kilocalories/mole. <sup>b</sup> Number of runs. <sup>c</sup> Enthalpies of hydrolysis of the esters in the liquid phase. The enthalpies of solution were water,  $-200 \pm 2$  cal/mol ( $\Delta H_3$ ), and ethanol,  $-15 \pm 0.02$  cal/mol ( $\Delta H_4$ ). The data for decanoic acid and undecanoic acid include the enthalpies of fusion of these solid acids. <sup>d</sup> The enthalpies of reaction of these acids are for the crystalline state. The  $\Delta H_f(l)$  values for these acids are based on the reported values for the crystalline state (ref 8) and our measurements of the enthalpy of melting via DSC: decanoic acid,  $6.62 \pm 0.03$  kcal/mol and undecanoic acid,  $5.80 \pm 0.05$  kcal/mol. <sup>e</sup> Other  $\Delta H_f$  values used: ethanol,  $-66.34 \pm 0.09$  kcal/mol and water,  $-68.32 \pm 0.01$  kcal/mol.

**Table II.** Enthalpies of Hydrolysis of Lactones (Calories/Mole)

lactone	medium <sup>a</sup>	n	$\Delta H_f$ , lactone, l	n	$\Delta H_f$ , acid, l	$\Delta H_m^c$ , acid	$\Delta H_f$ , hydrol, l	$\Delta H_f$ , ester, l	$\Delta \Delta H_f$ , l
butyrolactone	A	5	-12329 ± 11	5	-7461 ± 48	3991 ± 9	-1077 ± 50	923 ± 33	2000 ± 60
	B	5	-14261 ± 30	5	-9662 ± 118	3991 ± 9	-976 ± 122	923 ± 33	1899 ± 126
valerolactone	A	5	-14031 ± 15	5					
	B	5	-15815 ± 44	5					
caprolactone	B	6	-16044 ± 60	5	-6639 ± 27	6058 ± 26	-3714 ± 71	683 ± 63	4397 ± 95
heptanolactone	B	4	-18885 ± 35	4	-5619 ± 21	6417 ± 8	-7216 ± 42	708 ± 34	7924 ± 54
octanolactone	A	4	-18197 ± 73	5	-2722 ± 103	8309 ± 37	-7366 ± 132	671 ± 32	8037 ± 135
nonanolactone	A	5	-8589 ± 277 <sup>b</sup>	5	-2862 ± 27	7129 ± 13	-4555 ± 279	519 ± 69	5074 ± 287
decanolactone	A	5	-12665 ± 132	5	-634 ± 81	9346 ± 21	-2885 ± 156	514 ± 75	3399 ± 173
undecanolactone	A	5	-12217 ± 148	5	-306 ± 34	9978 ± 22	-2133 ± 154	576 ± 46	2709 ± 161
dodecanolactone	A	6	-11924 ± 85	4	1668 ± 32	11638 ± 21	-2154 ± 93	437 ± 61	2591 ± 111
tridecanolactone	A	4	-8242 ± 82 <sup>b</sup>	4	1413 ± 34	11832 ± 13	253 ± 90	490 ± 76	237 ± 118

<sup>a</sup> A is 60% ethanol/water and B is 50% DMSO/water. <sup>b</sup> Crystalline state; the enthalpies of fusion were nonanolactone,  $5757 \pm 21$  cal/mol and tridecanolactone,  $1724 \pm 23$  cal/mol (25 °C mesophase).<sup>1</sup> <sup>c</sup> Enthalpies of fusion of the hydroxy acids.

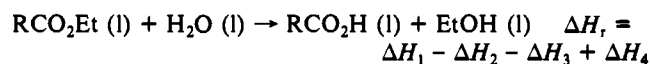
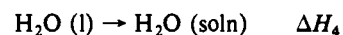
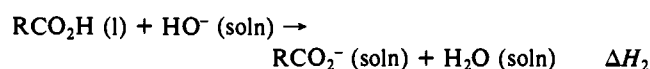
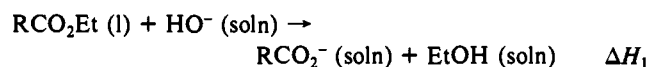
gave  $\Delta H_f = -104.60 \pm 0.20$  kcal/mol.<sup>5</sup> This type of calorimetry is a very difficult technique, and in some cases leads to errors larger than the uncertainty interval because of systematic errors that are difficult to detect.<sup>7</sup> Therefore, it appeared desirable to obtain additional experimental information via reaction calorimetry, which is not as demanding in terms of precision. Since the enthalpies of formation of the larger ring lactones have not been determined, agreement between the enthalpies of formation derived by combustion and by reaction calorimetry also would validate the latter procedure for the study of these lactones.

## 2. Enthalpies of Hydrolysis of Esters

One of our primary interests is the determination of the strain energies of the lactones. The most convenient group of unstrained reference compounds would be the series of ethyl esters of the *n*-alkanoic acids. The use of ethyl esters (rather than methyl) minimizes the difficulty that might be associated with differences in substitution patterns at the carboxylate groups. However, data for only a few ethyl esters are available. The enthalpies of formation of the *n*-alkanoic acids have been determined,<sup>8</sup> and a measurement of the enthalpy of hydrolysis of the ethyl esters would allow the calculation of the enthalpies of formation for the esters.<sup>9</sup>

The enthalpies of hydrolysis were determined by first measuring the enthalpies of reaction of the esters with 0.8 M sodium hydroxide in 60% aqueous ethanol. In all cases, the reactions proceeded rapidly and to completion. The enthalpy of reaction of the corresponding acids with the same reaction medium was

determined. These data, along with the enthalpies of solution of water and ethanol in the reaction medium, allowed the calculation of the enthalpies of hydrolysis in the pure liquid state:



The data are summarized in Table I. Since the enthalpies of formation of all of the compounds in the equation are known, except those of the esters, the enthalpies of reaction lead directly to  $\Delta H_f$  for the esters. In the cases of ethyl acetate, ethyl propionate, and ethyl valerate, there have been previous determinations of the enthalpies of formation,<sup>10</sup> and our data are in good agreement with these results.

Ideally, strain energies should be referenced to the gas phase, and therefore, we wished to have the enthalpies of vaporization of the esters. They were determined for several of the esters via measurement of the vapor pressure as a function of temperature. The  $\Delta H_v$  obtained at the average temperature of the measurements must be corrected to 25 °C. The approximations made in this correction lead us to assign an uncertainty of  $\pm 0.3$  kcal/mol to the values. The  $\Delta H_f$  for the remaining esters were estimated by interpolation. The enthalpies of vaporization and of formation for the esters in the gas phase also are given in Table I.

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(10) The literature values for the liquid phase are as follows: ethyl acetate,  $-114.44 \pm 0.17$ ; ethyl propionate,  $-120.15 \pm 0.18$ ; and ethyl valerate,  $-132.2 \pm 0.6$  kcal/mol (ref 8).

Table III. Estimates of Enthalpies of Reduction from Enthalpies of Hydrolysis

ester	$\Delta H_f^a$ ester, l	$\Delta H_f^b$ <i>n</i> -alcohol, l	$\Delta H$ , redn ester <sup>c</sup>	$\Delta\Delta H^d$ ester - lactone	$\Delta H$ , redn lactone <sup>e</sup>
ethyl acetate	-114.69 ± 0.11	-66.34 ± 0.09	-17.99 ± 0.17	2.00 ± 0.06	-20.0 ± 0.2
ethyl butyrate	-126.29 ± 0.19	-78.24 ± 0.11	-18.29 ± 0.24	4.40 ± 0.10	-22.7 ± 0.3
ethyl valerate	-132.44 ± 0.20	-84.04 ± 0.10	-17.94 ± 0.24	7.92 ± 0.05	-25.9 ± 0.3
ethyl hexanoate	-138.42 ± 0.26	-90.22 ± 0.13	-18.14 ± 0.30	8.04 ± 0.14	-26.2 ± 0.3
ethyl heptanoate	-144.30 ± 0.37	-96.39 ± 0.17	-18.43 ± 0.42	5.07 ± 0.29	-23.5 ± 0.5
ethyl octanoate	-150.46 ± 0.27	-102.30 ± 0.26	-18.18 ± 0.39	3.40 ± 0.13	-21.6 ± 0.4
ethyl nonanoate	-156.28 ± 0.49	-108.36 ± 0.21	-18.42 ± 0.54	2.71 ± 0.16	-21.1 ± 0.6
ethyl decanoate	-162.43 ± 0.26	-114.28 ± 0.28	-18.19 ± 0.39	2.59 ± 0.11	-20.8 ± 0.4
ethyl undecanoate	-168.60 ± 0.29	-120.66 ± 0.22	-18.40 ± 0.22	0.24 ± 0.19	-18.6 ± 0.3

<sup>a</sup>Table I, column 8. <sup>b</sup>Reference 8. <sup>c</sup>Calculated from columns 2 and 3. <sup>d</sup>Difference in experimental enthalpies of hydrolysis of esters and lactones with the same number of carbons. <sup>e</sup>Estimated values for lactones having the same number of carbons, assuming that the difference in enthalpies of hydrolysis and reduction between lactones and esters will be the same. The standard deviations are based on the assumption that the  $\Delta\Delta H$  values found for ester and lactone hydrolysis also apply to reduction.

Table IV. Enthalpies of Reduction of Lactones<sup>a</sup>

lactone	<i>n</i>	$\Delta H_f$ , lactone, l	<i>n</i>	$\Delta H_f$ , diol <sup>b</sup>	$\Delta H_m$ diol, c	$\Delta H_f$ , redn., l	$\Delta H_f$ , diol, l	$\Delta H_f$ , lactone,	$\Delta H_f$ ,	$\Delta H_f$ , lactone,
								l	lactone	g
butyrolactone	5	-36944 ± 211	4	-16873 ± 145		-20071 ± 256	-120.3 ± 0.5	-100.2 ± 0.6	13.2 ± 0.3	-87.0 ± 0.8
valerolactone	4	-38020 ± 71	4	-15301 ± 51		-22719 ± 88	-127.0 ± 0.7	-104.3 ± 0.7	14.4 ± 0.3	-89.9 ± 0.8
caprolactone	4	-38838 ± 69	4	-10318 ± 83	5824 ± 56	-22696 ± 122	-132.2 ± 0.5	-109.5 ± 0.5	14.8 ± 0.3	-94.7 ± 0.6
heptanolactone	4	-43376 ± 116	4	-16521 ± 52		-26855 ± 127	-138.0 ± 0.5	-111.1 ± 0.5	12.8 ± 0.3	-98.3 ± 0.6
octanolactone	5	-44985 ± 111	4	-9153 ± 258	8447 ± 42	-27385 ± 284	-143.8 ± 0.5	-116.4 ± 0.6	12.6 ± 0.3	-103.8 ± 0.6
nonanolactone	4	-33809 ± 111	4	-7693 ± 64	8752 ± 6	-23121 ± 128	-149.6 ± 0.5	-126.5 ± 0.5	14.1 ± 0.3	-112.4 ± 0.6
decanolactone	4	-39629 ± 193	4	-7124 ± 65	10757 ± 113	-21748 ± 204	-155.4 ± 0.5	-133.7 ± 0.5	15.1 ± 0.3	-118.6 ± 0.6
undecanolactone	4	-38397 ± 143	4	-5905 ± 64	10745 ± 10	-21747 ± 156	-161.1 ± 0.5	-139.4 ± 0.5	15.8 ± 0.3	-123.6 ± 0.6
dodecanolactone	4	-38757 ± 159	4	-5403 ± 156	12489 ± 36	-20865 ± 226	-166.9 ± 0.5	-146.0 ± 0.6	16.9 ± 0.3	-129.1 ± 0.6
tridecanolactone	4	-34199 ± 173	4	-3933 ± 87	13269 ± 21	-18721 ± 196	-172.7 ± 0.5	-154.0 ± 0.5	17.4 ± 0.3	-136.0 ± 0.6

<sup>a</sup>Enthalpies of reaction and fusion are given in calories/mole; enthalpies of vaporization and formation are given in kilocalories/mole. The number of runs is given as *n*. <sup>b</sup>The diols were liquids when no enthalpy of fusion ( $\Delta H_m$ ) is given and solids when this datum appears in the adjacent column.

### 3. Enthalpies of Hydrolysis of Lactones

The enthalpies of hydrolysis of the lactones were determined with use of 0.8 M sodium hydroxide in 60% aqueous ethanol or 0.8 M sodium hydroxide in 50% DMSO/water, depending on their solubility. In each case, the enthalpy of hydrolysis of the lactone was determined, followed by a measurement of the enthalpy of solution of the corresponding hydroxy acid (Table II). Although  $\delta$ -hydroxybutyric acid is quite reactive toward lactonization, it was possible to obtain it in pure form, and its enthalpy of solution in the hydrolysis solvent could be determined. However,  $\gamma$ -hydroxyvaleric acid was too unstable to allow its isolation in sufficiently pure form. The remainder of the  $\omega$ -hydroxy acids were readily obtained in high purity as determined by titration. The enthalpies of reaction, along with the enthalpies of fusion of the hydroxy acids ( $\Delta H_m$ ) and the enthalpy of solution of water in the solvents, allowed the calculation of the enthalpies of hydrolysis in the pure liquid state.

One way in which to examine the strain energies is to compare the enthalpies of hydrolysis of the lactones with the enthalpies of hydrolysis of the ethyl esters with the same number of carbons (Table II). It can be seen that the  $\Delta\Delta H$  values cover a range from 0.2 to 8.0 kcal/mol, indicating a substantial range of strain energies in the lactones. Strain energies should be referred to the gas phase, and in order to do this it would be necessary to correct for the differences in enthalpies of vaporization of all of the components. These data are not available for the hydroxy acids nor does it appear practical to measure them.

Therefore, we have used a different procedure. From the known enthalpies of formation of the *n*-alcohols<sup>8</sup> and of the ethyl esters it is possible to calculate the enthalpies of reduction of the esters. The enthalpies of reduction of the lactones could then be estimated, assuming that the  $\Delta\Delta H$  values for hydrolysis would also apply to reduction. The values thus obtained are summarized in Table III. As we will show in the following section, it is possible to convert these enthalpies of reduction to enthalpies of formation for the lactones and then calculate strain energies for the gas-phase molecules.

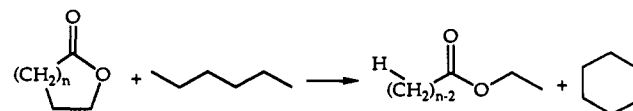
### 4. Enthalpies of Reduction of Lactones

The measurement of the enthalpies of hydrolysis provides estimates of the enthalpies of reduction in an indirect fashion,

requiring an assumption that the differences between lactones and the corresponding esters would be the same for hydrolysis and reduction. We have recently shown that the enthalpies of reduction of carbonyl compounds may be determined by their reaction with lithium triethylborohydride in triglyme solution.<sup>11</sup> Therefore, in a second study, we have experimentally determined the enthalpies for reduction of the lactones to the corresponding  $\alpha,\omega$ -alkanediols. Here, the enthalpy of reaction of the lactone is measured, followed by a determination of the enthalpy of reaction of the diol with the hydride. The difference between the two enthalpies of reaction gives the enthalpy of reduction. This procedure reproduces the literature value for the enthalpy of reduction of ethyl acetate determined from the literature values of the enthalpies of formation of the ester and of ethanol.<sup>11</sup>

The results of the application of this procedure to the lactones are summarized in Table IV. The enthalpies of reduction estimated from the enthalpies of hydrolysis were in good accord with the directly measured enthalpies of reduction, indicating that the assumption of equal lactone/ester energy differences for the two reactions is satisfactory. If the enthalpies of formation of all of the product diols were known, the enthalpies of formation of the lactones could be easily derived. Data are available for some diols, and assuming a linear relationship between the enthalpies of formation and the number of carbons as is usually found to be the case, the  $\Delta H_f$  values for all of the diols were estimated (cf. Experimental Section). These data and the enthalpies of reduction allowed the  $\Delta H_f$  values of the lactones to be calculated. The enthalpies of vaporization were also determined and allowed  $\Delta H_f$  values to be obtained for the gas phase. These data also are included in Table IV.

It is now possible to calculate the strain energies of the lactones from the isodesmic reaction:



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**Table V.** Strain Energies for the Lactones (Kilocalories/Mole)<sup>a</sup>

compound	hydrolysis <sup>b</sup>	reduction <sup>c</sup>
butyrolactone	8.7 ± 0.8	8.8 ± 0.9
valerolactone		11.2 ± 0.9
caprolactone	10.7 ± 0.8	10.7 ± 0.7
heptanolactone	11.4 ± 0.8	12.4 ± 0.8
octanolactone	10.8 ± 0.8	11.6 ± 0.8
nonanolactone	8.6 ± 0.8	8.2 ± 0.8
decanolactone	7.1 ± 0.8	7.3 ± 0.7
undecanolactone	6.5 ± 0.8	7.1 ± 0.9
dodecanolactone	6.7 ± 0.8	6.7 ± 0.8
tridecanolactone	4.9 ± 0.8	4.5 ± 0.8

<sup>a</sup>The strain energies were calculated from the isodesmic reaction in the text and the following enthalpies of formation: cyclohexane, -29.49 kcal/mol and *n*-hexane, -14.89 kcal/mol. The major component of the stated uncertainties arises from the enthalpies of vaporization. <sup>b</sup>Based on the enthalpies of formation of the lactones derived from their enthalpies of hydrolysis (Table III and the enthalpies of formation of the diols). <sup>c</sup>Based on the enthalpies of formation of the lactones derived from their enthalpies of reduction (Table IV).

Here, all of the compounds except the lactone are normally considered to be strain-free. The energy change for the reaction may then be equated to the strain energy of the lactones. The results of this analysis are summarized in Table V. The strain energies derived from the enthalpies of hydrolysis and of reduction are generally in good agreement. The latter values are preferred because they are directly obtained from the experimental results without making any assumptions.

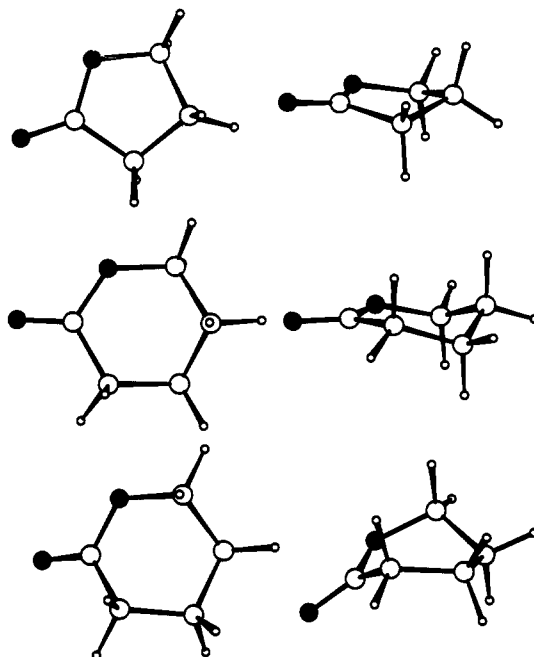
Aliphatic compounds with six-membered rings usually have relatively low strain energies. However, the strain energy of valerolactone is relatively large (11 kcal/mol). Much of the strain energy must be associated with the *E* ester conformation, which in the case of methyl acetate leads to a 8.5 kcal/mol destabilization. In addition, the introduction of a trigonal center into a cyclohexane ring leads to an increase in strain.<sup>12</sup> Therefore, the relatively large strain energy does not seem unreasonable.

The lactones with an *E* ester conformation all have relatively large strain energies, and it decreases considerably on going to the larger ring lactones with a *Z* ester conformation. Part of the strain on these compounds is associated with the hydrocarbon chains, and therefore it is necessary to examine the overall conformations of these molecules.

### 5. Conformational Studies

It is not easy to obtain experimental structural data for  $\gamma$ -butyrolactone and  $\delta$ -valerolactone, since they are liquids and not suitable for X-ray analysis and are too large and unsymmetrical to be good candidates for either detailed microwave or electron-diffraction studies. Both lactones have been studied via microwave spectroscopy,<sup>13,14</sup> but only the moments of inertia of the parent molecules have been determined. Therefore, we have investigated their structures via ab initio molecular orbital calculations. Electron correlation has a significant effect on the carbonyl bond length, and therefore the geometries were studied both at the HF/6-31G\* and MP2/6-31G\* theoretical levels. It is known that MP2/6-31G\* calculations usually reproduce experimental structures remarkably well. The structures obtained by geometry optimization are shown in Figure 1, and the structural parameters and energies are given in Table VI.

Although detailed experimental structural information is not available for these compounds, it is possible to compare the inertial constants of the calculated structures with the observed inertial constants (Table VII). It can be seen that the constants derived



**Figure 1.** Conformers of butyrolactone and valerolactone. The top and side views are given next to each other. The middle structure is that of the lower energy conformer of valerolactone.

from the HF/6-31G\* geometries are uniformly too large, corresponding to the general underestimation of bond lengths at this level of theory.<sup>15</sup> The constants derived from the MP2/6-31G\* geometries are in quite good agreement with the experimental values.

We have been interested in using data for esters and lactones as a test of current molecular mechanics force fields. Therefore, the structures of butyrolactone and valerolactone were derived by using MM3 with the preliminary (not optimized) parameters for esters and lactones. Butyrolactone had only one conformer, but valerolactone had two (Figure 1). The inertial constants were calculated for butyrolactone and the lower energy conformer of valerolactone and are given in Table VII. They also are in good agreement with the experimental values. The structural data obtained via MM3 are compared with the ab initio structures and with the average structures of butyrolactones and valerolactones derived from the data in the Cambridge-Crystallographic Database<sup>16</sup> in Table VI.

One feature of the ab initio structure for butyrolactone is that the C—C=O angle is larger than the O=C—O angle by 6.3°. This is in good agreement with the X-ray crystallographic data for  $\gamma$ -lactones examined by Schweizer and Dunitz, who found an average difference of 6.9°. This is not so well-reproduced by MM3, which makes the angle ~2°. Burgi et al. have shown that MM2 consistently underestimates the C—C=O/O=C—O angle difference in lactones.<sup>17</sup> Valerolactone provides another example in which the MP2/6-31G\* bond angles are in good agreement with the average found for  $\delta$ -lactones. The MM3 angles are quite different, and here the C—O—C angle is calculated to be 128.4°, much larger than either the calculated or average experimental value.<sup>18</sup> The ab initio calculations suggest that the O=C—O—C torsional angle should be -165°, whereas MM3 predicts ~180°. It would be interesting to have some detailed gas-phase structural data for this lactone.

(12) An isodesmic reaction involving cyclohexanone reacting with *n*-pentane to give 3-pentanone and cyclohexane suggests the cyclohexanone has a strain energy of 1 kcal/mol.

(13) Butyrolactone: (a) Lopez, J.; Alonso, J.; Cervellati, R.; Degli Esposti, A.; Lister, D.; Palmieri, P. *J. Chem. Soc., Faraday Trans.* **1990**, *86*, 453. (b) Degli Esposti, A.; Alonso, J.; Cervellati, R.; Lister, D.; Lopez, J.; Palmieri, P. *J. Chem. Soc., Faraday Trans.* **1990**, *86*, 459. (c) Legon, A. *Chem. Commun.* **1970**, 838.

(14) Valerolactone: Philip, T.; Cook, R. L.; Malloy, T. B., Jr.; Allinger, N. L.; Chang, S.; Yuh, Y. *J. Am. Chem. Soc.* **1981**, *103*, 2151.

(15) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986; p 224. Wiberg, K. B. *J. Org. Chem.* **1985**, *50*, 5285.

(16) Schweizer, W.; Dunitz, J. *Helv. Chim. Acta* **1982**, *65*, 1547.

(17) Nørskov-Lauritsen, L.; Bürgi, H.-B.; Hofmann, P.; Schmidt, H. *Helv. Chim. Acta* **1985**, *68*, 76.

(18) This geometry was obtained by either starting with the ab initio geometry or the MM2 geometry derived from Chem-3D (Cambridge Scientific Computing, Cambridge, MA).

Table VI. Calculated Structures and Energies for Butyrolactone and Valerolactone

parameter	butyrolactone				valerolactone			
	HF 6-31G*	MP2 6-31G*	MM3 <sup>a</sup>	CCDB <sup>b</sup>	HF 6-31G*	MP2 6-31G*	MM3 <sup>a</sup>	CCDB <sup>b</sup>
energy, hartree	-304.705 19	-305.590 92			-343.736 65	-344.758 48		
r(C=O)	1.180	1.120	1.207	1.198 (7)	1.184	1.215	1.201	1.204 (7)
r(C-O)	1.335	1.371	1.351	1.350 (9)	1.336	1.364	1.342	1.337 (8)
r(O-C)	1.419	1.444	1.429	1.462 (8)	1.420	1.445	1.419	1.462 (13)
∠C-O-C	112.1	109.9	111.3	110.2 (14)	123.4	121.3	128.4	122.9 (29)
∠O=C-O	123.0	122.4	124.7	121.7 (9)	119.7	118.8	120.2	118.5 (10)
∠C-C=O	127.8	128.7	126.5	128.6 (8)	122.0	122.4	122.4	123.0 (13)
∠O=C-O-C	-177.2	-177.8	-178.1		-162.7	-165.0	-179.6	
∠C-C-O-C	2.4	1.9	2.6		21.6	20.5	1.2	

<sup>a</sup>MM3 1989 force field (ref 38). <sup>b</sup>Data from the Cambridge Crystallographic Data Base (ref 16).

Table VII. Calculated and Observed Initial Constants (Megahertz) and Dipole Moments (Debye)

constant	butyrolactone					valerolactone			
	HF	MP2	obsd <sup>13a</sup>	obsd <sup>13b</sup>	MM3	HF	MP2	obsd <sup>14</sup>	MM3
A	7412.5	7299.5	7279.8	7279.6	7327.3	4722.6	4675.9	4661.2	4655.2
B	3651.4	3571.9	3585.4	3585.3	3575.8	2597.7	2551.9	2558.6	2556.0
C	2602.9	2564.2	2562.6	2562.6	2564.5	1794.4	1769.4	1771.2	1770.9
μ <sub>x</sub>	4.709				3.807	4.950		4.53	3.646
μ <sub>y</sub>	1.668				1.008	1.281		1.30	0.608
μ <sub>z</sub>	0.437				0.380	0.066		~0.1	0.011
μ	5.015				3.956	5.113		~4.71	3.696

In order to see how well the ab initio calculations reproduce the energies of the compounds, we have calculated the energy changes corresponding to the reaction given above. Here, it was necessary to have the calculated energies of ethyl acetate, ethyl propionate, *n*-hexane, and cyclohexane, and they were found to be (HF/6-31G\*) -305.876 63, -344.912 39, -235.367 79, and -234.208 02, respectively. The calculated strain energies derived from these data are 7.3 kcal/mol for butyrolactone and 10.0 kcal/mol for valerolactone. They are slightly smaller than the experimental values but in quite reasonable agreement.<sup>19</sup>

It was not practical to study the larger ring systems via ab initio calculations both because of their size and because of the number of low-energy conformers that are present. Saunders and Jimenez-Vazquez<sup>20</sup> have studied the conformers of the monocyclic lactones by using the stochastic kick method that Saunders has developed,<sup>21</sup> and they have graciously supplied us with the coordinates of the lower energy conformers of these compounds. The geometries have been reoptimized by MM3. The number of conformers that were considered and had energies close to that of the lowest energy conformer is given as *n* in Table VIII, and the structures of the lowest energy conformers are shown in Figure 2.<sup>22</sup> With caprolactone, the four conformers previously studied by Allinger<sup>23</sup> were found and had a 3.5 kcal/mol range of energies. The other lactones had many more conformers, and those within 1.5–2.0 kcal/mol were examined in obtaining the estimated energies. All of the lower energy conformers of octanolactone and the larger ring lactones had the *Z* conformation, whereas with heptanolactone, both *E* and *Z* conformers were found. This is in good accord with the dipole moment measurements of Huisgen and Ott.<sup>2</sup>

## 6. Comparison with MM3 Predictions

Although the MM3 parameters have not as yet been optimized for esters, we were interested in seeing how well the preliminary parameters would reproduce the experimental data. Semiempirical

Table VIII. Comparison with MM3 Predictions (Kilocalories/Mole)

compound	MM3 <sup>a</sup>				
	ΔH <sub>f</sub> <sup>b</sup>	<i>n</i>	ΔH <sub>f</sub> <sup>c</sup>	ΔH <sub>f</sub> , exptl	ΔΔH <sub>f</sub>
butyrolactone	-100.1	1	-100.1	-87.0 ± 0.8	13.1
valerolactone	-103.1	2	-103.0	-89.9 ± 0.8	13.1
caprolactone	-104.9	4	-104.9	-94.7 ± 0.6	10.2
heptanolactone	-105.7	7	-105.4	-98.3 ± 0.6	7.1
octanolactone	-110.4	10	-110.0	-103.8 ± 0.6	6.2
nonanolactone	-118.5	5	-118.2	-112.4 ± 0.6	5.8
decanolactone	-124.3	9	-124.0	-118.6 ± 0.5	5.4
undecanolactone	-131.5	10	-130.9	-123.6 ± 0.6	7.3
dodecanolactone	-137.4	9	-136.9	-129.1 ± 0.6	7.8
tridecanolactone	-144.9	10	-144.6	-136.6 ± 0.6	8.0
( <i>Z</i> )-methyl formate		1	-91.0	-85.0 ± 0.2	6.0
( <i>E</i> )-methyl formate		1	-87.8	-80.6 ± 0.5	7.2
( <i>Z</i> )-methyl acetate		1	-102.6	-98.5 ± 0.4	4.1
( <i>E</i> )-methyl acetate		1	-99.5	-90.0 ± 1.1	9.5
( <i>Z</i> )-ethyl acetate		1	-111.0	-106.1 ± 0.2	4.8
( <i>Z</i> )-ethyl propionate		1	-116.4	-110.8 ± 0.2	5.6

<sup>a</sup>Based on the preliminary (not optimized) parameters in MM3 for the ester group. <sup>b</sup>ΔH<sub>f</sub> of the lowest energy conformer. <sup>c</sup>The ΔH<sub>f</sub> of the lactones are corrected for the populations and energies of the *n* lower energy conformers assuming negligible differences in entropy.

procedures of this type require the use of experimental data for the evaluation of the potential energy functions for stretching, bending, torsional, and other interactions, but the needed data have not previously been available for a sufficiently large number of esters and lactones. A comparison between the current predictions and the new experimental data would provide information on how the parameters should be modified.

The energies of the lactones calculated via MM3 are shown in Table VIII. Here, the energy of the lowest energy conformer is given first, followed by the number of somewhat higher energy conformers that were examined, and then the final estimated ΔH<sub>f</sub> corrected for the energies and populations of the higher energy conformers. The estimates are compared with the experimental enthalpies of formation, and the deviation between the two is given in the last column. It can be seen that the deviations are fairly large. In order to determine the origin of the deviations, corresponding calculations were carried out for the *E* and *Z* conformers of methyl formate and methyl acetate and for the *Z* conformers of ethyl acetate and ethyl propionate. The deviation for the *Z* conformers averaged 5 kcal/mol, similar to the deviation found for the lactones having the *Z* conformation. Thus, part of the difference between the estimated and experimental values is due

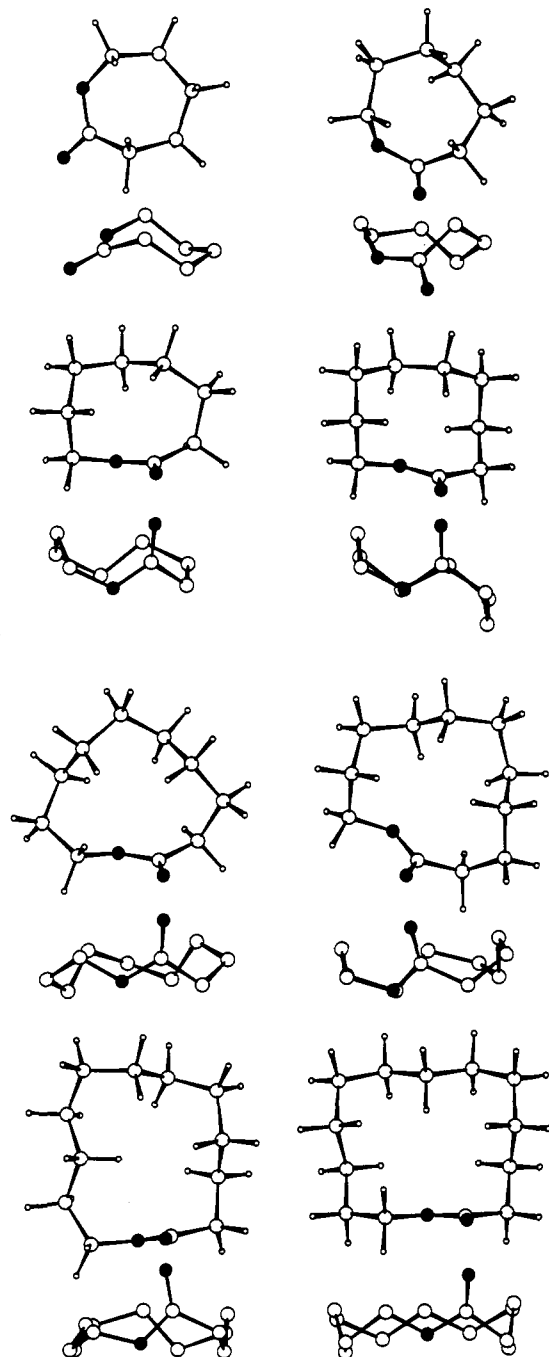
(19) The calculated energies should be corrected for the differences in zero-point energies and for the difference in  $H - H^0$  on going from 0 K to 298 K. However, these quantities are not known and would be expected to approximately cancel for reactions of the type shown.

(20) Saunders, M.; Jimenez-Vazquez, H. To be published.

(21) Saunders, M. *J. Am. Chem. Soc.* **1987**, *109*, 3150. Saunders, M.; Krause, N. *J. Am. Chem. Soc.* **1990**, *112*, 1791. Saunders, M. *J. Comput. Chem.* **1989**, *10*, 203.

(22) The structures of the other conformers may be found: Waldron, R. F. Ph.D. Thesis, Yale, University, New Haven, CT, 1991.

(23) Allinger, N. L. *Pure Appl. Chem.* **1982**, *54*, 2515.



**Figure 2.** Minimum-energy conformers as calculated via MM3. In the cases of nonanolactone and tridecanolactone, the conformations agree with the X-ray crystal structures.<sup>1</sup>

to an error in the energy increment assigned to an ester group. The estimate for (*E*)-methyl formate has a similar error, but it becomes much larger for (*E*)-methyl acetate. Thus, the esters and lactones having an *E* arrangement (except for methyl formate) have a larger deviation than the other esters and lactones. This appears to be due to an underestimation of the repulsive interaction between the groups attached to the carboxyl group in an *E* conformer. A probable cause is too weak of a C–O–C bending potential, as can be seen in the very large angle calculated by MM3 for valerolactone. This results in a smaller bond bending strain and a smaller repulsion energy for the groups attached to the carboxyl group. It might be noted that MM2 gave more satisfactory estimates of the energies of acyclic esters,<sup>24</sup> but also failed to reproduce the *E/Z* energy difference for methyl acetate.

(24) Allinger, N. L.; Chang, H. *Tetrahedron* 1977, 33, 1561.

**Table IX.** Ethyl *n*-Alkanoates

ester	purity (%)	bp (°C)
ethyl acetate	99.9	76.5–77.5
ethyl propionate	99.8	99
ethyl butyrate	99.8	120
ethyl valerate	99.6	144–145
ethyl hexanoate	99.9	168
ethyl heptanoate	99.9	188–189
ethyl octanoate	99.9	206
ethyl nonanoate	99.6	225
ethyl decanoate	99.8	242
ethyl undecanoate	99.5	261 (105 at 4 mm)

**Table X.** Alkanolic Acids

acid	purity (%)	bp (°C)
acetic	99.9	117.5
propionic	99.9	141
butyric	99.5	163
valeric	99.9	185
hexanoic	99.8	202–203
heptanoic	99.8	223
octanoic	99.9	237
nonanoic	99.9	127–128 at 0.8 mm
decanoic	99.8	268–270
undecanoic	99.6	112 at 0.25 mm

The deviations between the preliminary MM3 predictions and the experimental data are of types that should readily be corrected. Allinger is currently working on the adjustment of the parameters.<sup>25</sup>

## 7. Conclusions

The smaller ring lactones have relatively large strain energies, which result from a combination of the higher energy associated with an *E* ester conformation and the repulsive interaction between the groups attached to the carboxyl group. The strain energies decrease considerably on going to the larger ring lactones having a *Z* ester conformation. Since one of the objectives of this study was to provide data that would be of use in refining the parameters used in molecular mechanics procedures, comparisons were made with the predictions of MM3 using the preliminary ester parameters. It gives fairly good estimates of structures for butyrolactone, nonanolactone, and tridecanolactone,<sup>1</sup> except for a small difference in bond angles at the carboxyl group. With valerolactone, the predicted geometry was less satisfactory, and the predicted energies of the lactones were not satisfactory. Part of the deviation from the experimental data is due to a systematic error associated with the energy terms for a carboxyl group, and part is due to an underestimation of the repulsion between the groups attached to the carboxyl group. It should be readily possible to modify the parameters in the program so as to give much better estimates of the energies and structures of esters and lactones. With the better studied systems, such as alkanes, alkenes, and alcohols, the MM3 predictions have been quite good.<sup>26</sup>

## 8. Experimental Section

**Materials. a. Ethyl Alkanoates.** All of the ethyl esters were available from Aldrich in relatively high purity. Ethyl acetate was purified via distillation from calcium hydride. The remaining ethyl esters were first dried over anhydrous CuSO<sub>4</sub> and then purified by fractional distillation through a glass helices filled column. In each case a substantial fore-fraction was taken, and a middle fraction was taken for reaction calorimetry. The purity as determined via GC and the observed boiling points (atmospheric pressure) are given in Table IX.

**b. Alkanolic Acids.** The acids were commercial samples. As recommended by Perrin,<sup>27</sup> acetic and propionic acids were heated to reflux with 1 g of CrO<sub>3</sub> per 100 mL of acid prior to fractional distillation through

(25) Allinger, N. L. Private communication.

(26) Allinger, N. L.; Yuh, Y. H.; Lii, J.-H. *J. Am. Chem. Soc.* 1989, 111, 8551. Allinger, N. L.; Rahman, M.; Lii, J.-H. *J. Am. Chem. Soc.* 1990, 112, 8293.

(27) Perrin, D.; Armarego, W.; Perrin, D. *Purification of Laboratory Chemicals*; Pergamon Press: New York, 1966.

Table XI. Lactones

lactone	bp °C (pressure)	purity (%)
γ-butyrolactone	205 (atm)	99.5
δ-valerolactone	218–220 (atm), 48.0 (0.3 mm)	100.0
ε-caprolactone	238 (atm), 74–75 (0.5 mm)	99.9
ζ-heptanolactone	202 (atm), 55 (1.2 mm)	100.0
η-octanolactone	198 (atm), 72–73 (11 mm)	99.7
θ-nonanolactone	218 (atm), 73 (3 mm)	100.0
ι-decanolactone	236 (atm), 58 (1 mm)	100.0
κ-undecanolactone	248 (atm), 97 (0.6 mm)	100.0
λ-dodecanolactone	272 (atm), 78 (0.4 mm)	99.9
μ-tridecanolactone	285 (atm), 89.5 (0.5 mm)	99.6

Table XII. Lactone Synthesis

lactone	cycloalkanone (g)	t (h)	yield
ζ-heptanolactone	5.0 (39 mmol)	3.5	4.0 g (70%)
η-octanolactone	22.0 (155 mmol)	3.5	19.5 g (77%)
θ-nonanolactone	9.0 (64 mmol)	10.0	8.8 g (88%)
ι-decanolactone	10.0 (64 mmol)	12.0	9.2 g (84%)
κ-undecanolactone	12.0 (71 mmol)	16.0	12.0 g (91%)
λ-dodecanolactone	15.0 (82 mmol)	3 days	11.5 g (71%) <sup>a</sup>
μ-tridecanolactone	5.0 (26 mmol)	20	3.6 g (65%)

<sup>a</sup> *m*-Chloroperbenzoic acid was used in this case.

a 20-cm wire wool packed column. For acetic acid, a small amount of acetic anhydride was added before distillation. The higher acids were heated to reflux with several crystals of  $\text{KMnO}_4$  prior to distillation through a 20-cm Vigreux column. A large forefraction was collected in each case, and the middle fraction was collected as the calorimetry sample. The purity was determined by titration with 0.1 N NaOH using phenolphthalein as the indicator and is given in Table X.

c. **Lactones.** γ-Butyrolactone, δ-valerolactone, and ε-caprolactone were Aldrich gold label samples with a stated purity of 99+%. They were dried over anhydrous  $\text{CaSO}_4$  overnight and then purified by fractional distillation under reduced pressure through a 20-cm glass helices filled vacuum-jacketed column. A substantial forefraction was taken, and the purity was determined by GC (Table XI).

The remaining lactones were prepared from the corresponding cycloalkanones via Baeyer–Villiger oxidation with trifluoroperoxyacetic acid in the presence of powdered anhydrous  $\text{NaHPO}_4$  in methylene chloride.<sup>28</sup> The yields are given in Table XII. The NMR spectral data are as follows ( $^{13}\text{C}$  at 62.9 MHz in  $\text{CD}_2\text{Cl}_2$ ,  $^1\text{H}$  at 250 MHz in  $\text{CD}_2\text{Cl}_2$ ). Data for nonanolactone and tridecanolactone were reported previously.<sup>1</sup> ζ-Heptanolactone:  $^1\text{H}$  NMR δ 4.23 (t, 2 H), 2.43 (t, 2 H), 1.70 and 1.50 (m, 8 H);  $^{13}\text{C}$  NMR δ 176.2, 67.8, 31.4, 30.8, 28.5, 25.9, 24.0. η-Octanolactone:  $^1\text{H}$  NMR δ 4.21 (t, 2 H), 2.21 (t, 2 H), 1.64 and 1.40 (m, 10 H);  $^{13}\text{C}$  NMR δ 175.3, 64.5, 35.8, 29.8, 28.1, 25.4, 24.5, 23.3. ι-Decanolactone:  $^1\text{H}$  NMR δ 4.12 (t, 2 H), 2.28 (t, 2 H), 1.67 and 1.32 (m, 14 H);  $^{13}\text{C}$  NMR δ 173.8, 64.8, 35.5, 26.7, 25.9, 25.9, 25.2, 24.5, 22.9, 21.8. κ-Undecanolactone:  $^1\text{H}$  NMR δ 4.14 (t, 2 H), 2.31 (t, 2 H), 1.64 and 1.34 (m, 16 H);  $^{13}\text{C}$  NMR δ 173.7, 64.6, 30.9, 26.3, 25.1, 25.0, 24.7, 24.2, 24.0, 23.7, 23.5. λ-Dodecanolactone:  $^1\text{H}$  NMR δ 4.12 (t, 2 H), 2.33 (t, 2 H), 1.35 (m, 18 H);  $^{13}\text{C}$  NMR δ 173.9, 64.7, 37.0, 27.9, 27.1, 26.9 (2), 25.9 (2), 25.5, 25.0, 24.7.

**Ketones.** Most of the ketones needed for the preparation of the lactones were commercially available. Cyclononane and cyclodecane were obtained via a two-carbon ring expansion of cycloheptanone and cyclooctanone, respectively. Here, the ketones were converted to the pyrrolidine enamines and were treated with methyl propiolate to give the 2 + 2 cycloadduct. Thermolysis of the cyclobutene ring followed by hydrogenation, hydrolysis with methanolic sodium hydroxide, and acidification gave the ketones.<sup>29</sup> Cycloundecanone was prepared by a Favorski ring contraction of α,α'-dibromocyclodecanone ( $\text{NaOMe}$  in benzene) followed by hydrolysis and a Schmidt reaction on the unsaturated acid thus formed.<sup>30</sup> Cyclotridecanone was formed by a Tiffaneau–Demjanov ring expansion of cyclododecanone.<sup>31</sup>

**ω-Hydroxy Acids.** With the exception of 5-hydroxyvaleric acid, which could not be isolated and purified, all of the ω-hydroxy acids have been reported in the literature. They were prepared by hydrolysis of the

Table XIII. Hydroxy Alkanoic Acids from Hydrolysis of Lactones

<i>n</i> <sup>a</sup>	lactone (g)	yield <sup>b</sup>	mp (°C)	purity (%)
4	10.0 (116 mmol)	4.4 g (35%)	34	99.8
6	4.0 (35 mmol)	3.2 g (69%)	40	99.5
7	2.0 (16 mmol)	0.8 g (39%)	46.2	99.8
8	2.0 (14 mmol)	1.5 g (67%)	61.7	99.8
9	1.0 (6 mmol)	1.1 g (99%)	51.2	99.9
10	1.0 (6 mmol)	1.1 g (99%)	74	99.9
11	2.0 (11 mmol)	2.0 g (90%)	68	99.5
12	3.9 (19 mmol)	2.7 g (63%)	79	99.9
13	1.1 (5 mmol)	0.95 g (79%)	77	99.8

<sup>a</sup> Number of carbons in the lactone. <sup>b</sup> The yields were largely determined by the efficiency of the ion-exchange column.

corresponding lactones with NaOH. Subsequently, the solution of the sodium salts of the hydroxy acids was passed through an activated column of Dowex 50W-X8 ion exchange resin. The eluted solutions were concentrated and the acids were isolated by extraction with ether. Removal of the ether was followed by recrystallization from diethyl ether or petroleum ether. Purity was determined by titration with 0.1 N NaOH (Table XIII).

The tendency of 4-hydroxybutyric acid to lactonize required a modified procedure. After the hydrolysis solution was passed through the Dowex resin, the solution was immediately frozen and the water was removed over 36 h under vacuum. The remaining viscous liquid was extracted with a large amount of ether. The ether solution was cooled to  $-78^\circ\text{C}$ , water crystals were removed by filtration, and ether was removed under reduced pressure. The product was recrystallized from small amounts of ether at  $-48^\circ\text{C}$ .

**Reaction Media.** a. **0.8 M NaOH in 60% Ethanol.** An approximately 18.2 M NaOH solution was formed by dissolving 2000 g of NaOH (98.5%) in 2 L of deionized water, allowing the carbonates to settle, and filtering. Its concentration was determined by titration. To 647.1 g (440 mL) of 18.18 M NaOH (containing 320.0 g (8 mol) of NaOH and 327.1 g of  $\text{H}_2\text{O}$ ) was added 490.7 mL of ethanol to give a concentrate with the desired 3:2 ethanol/water (by volume) ratio. This was diluted with premixed 60% ethanol to just under 10 L. The solution was titrated against potassium hydrogen phthalate to determine its concentration and diluted to 0.8 M. Precautions were taken to minimize exposure to carbon dioxide or oxygen, and nitrogen was passed through the final solution for 15 min before it was stored in a large glass vessel fitted with a nitrogen inlet and a glass siphon. The solution had virtually no discoloration over a 6-month period, and the concentration was found to remain unchanged.

b. **0.8 M NaOH in 50% DMSO.** A solution was prepared from 647.3 g (440 mL) of the 18.18 M NaOH solution and 287.3 mL of DMSO and was diluted to just under 10 L with 1:1 DMSO/water (by volume). After titration, the solution was adjusted to 0.8 M by adding the appropriate amount of the solvent mixture. The solution was handled as described above.

**Enthalpies of Vaporization.** The rate of change of vapor pressure with temperature was determined by using two different methods. The compounds that were available in large quantity were studied with an ebulliometer in which the boiling point was determined at several fixed pressures. Mesitylene was used as a standard since its  $\Delta H_v$  has been determined at 298 K by two groups both reporting  $11.36 \pm 0.05$  kcal/mol. The temperature was measured with an HP digital thermometer, the pressure was measured with a Wallace and Tiernan absolute pressure gauge, and the pressure was controlled by two tandem pressure regulators. The slopes (A) and intercepts (B) of plots of  $\ln P$  vs  $1/T$  are given in Table XIV.

The measured enthalpies of vaporization at the midpoint of the temperature range were converted to 298 K by means of Watson's equation<sup>32</sup>

$$\Delta H_{v,T_1} = \Delta H_{v,T_2} \left( \frac{1 - T_{r1}}{1 - T_{r2}} \right)^{0.38}$$

where  $T_m = T_n/T_c$ , with  $T_c = 1.027T_b + 159$  and  $T_b$  is the boiling point at atmospheric pressure. The value for mesitylene thus obtained (11.55 kcal/mol) is in good agreement with the literature value ( $11.36 \pm 0.05$  kcal/mol).<sup>33</sup> The previously reported  $\Delta H_v$  for butyrolactone<sup>13</sup> and valerolactone<sup>14</sup> (13.0 and 13.86 kcal/mol, respectively) are in reasonable agreement with our data.

The lactones that were available in smaller quantity were studied by measuring the vapor pressures of a sample maintained at a set of constant

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Table XIV. Enthalpies of Vaporization via Ebulliometer

compound	<i>T</i> range (K)	A	B	<i>T</i> <sub>av</sub> (K)	$\Delta H_v(T)$ (kcal/mol)	$\Delta H_v(298\text{ K})$ (kcal/mol)
butyrolactone	378–406	–5908	19.246	392	11.82 ± 0.03	13.20 ± 0.30
valerolactone	393–428	–6303	19.327	410	12.53 ± 0.02	14.39 ± 0.30
caprolactone	395–436	–6499	19.459	415	12.91 ± 0.02	14.81 ± 0.30
ethyl butyrate	310–336	–5062	19.670	323	10.06 ± 0.01	10.44 ± 0.30
ethyl hexanoate	345–374	–5706	19.780	360	11.34 ± 0.07	12.32 ± 0.30
ethyl octanoate	382–412	–6318	19.940	397	12.55 ± 0.05	14.22 ± 0.30
ethyl decanoate	404–440	–7018	20.397	422	13.95 ± 0.03	16.11 ± 0.30
mesitylene	372–352	–5325	18.924	362	10.58 ± 0.01	11.55 ± 0.30

Table XV. Enthalpies of Vaporization via Vapor Pressure Measurement

lactone	<i>T</i> range (K)	A	B	<i>T</i> <sub>av</sub> (K)	$\Delta H_v(T)$ (kcal/mol)	$\Delta H_v(298\text{ K})$ (kcal/mol)
butyrolactone	345–370	–6233	19.774	358	12.39 ± 0.14	13.29 ± 0.33
heptanolactone	368–390	–5800	18.799	379	11.53 ± 0.07	12.75 ± 0.31
octanolactone	345–380	–5876	19.148	362	11.68 ± 0.05	12.63 ± 0.30
nonanolactone	352–381	–6554	20.232	366	13.02 ± 0.04	14.10 ± 0.30
decanolactone	365–387	–6945	20.485	376	13.80 ± 0.19	15.05 ± 0.36
undecanolactone	368–389	–7308	20.910	379	14.52 ± 0.12	15.83 ± 0.32
dodecanolactone	377–403	–7720	21.072	390	15.34 ± 0.27	16.85 ± 0.40
tridecanolactone	375–405	–8006	21.339	390	15.91 ± 0.26	17.42 ± 0.40
mesitylene	296–342	–5559	19.259	319	11.05 ± 0.33	11.35 ± 0.45

Table XVI. Enthalpies of Hydrolysis of Ethyl Acetate in 0.8 M NaOH in 60% Aqueous Ethanol

run	mmol	$\epsilon$ (cal/K)	$\Delta T$ (K)	<i>Q</i> (cal)	$\Delta H$ (cal/mol)
1	2.3879	95.23	0.2589	24.664	–10 329
2	2.8728	97.79	0.3022	29.551	–10 286
3	3.1999	95.77	0.3459	33.131	–10 353
4	3.4779	97.53	0.3683	35.916	–10 327
5	3.6602	92.29	0.4100	37.838	–10 338
				av	–10 327 ± 22

Table XVII. Enthalpies of Hydrolysis of Butyrolactone in 0.8 M NaOH in 50% Aqueous DMSO

run	mmol	$\epsilon$ (cal/K)	$\Delta T$ (K)	<i>Q</i> (cal)	$\Delta H$ (cal/mol)
1	1.9896	93.75	0.3017	28.279	–14 213
2	2.2778	91.38	0.3564	32.569	–14 299
3	2.3522	89.02	0.3613	33.595	–14 283
4	2.7780	95.60	0.4146	39.632	–14 267
5	3.3622	94.32	0.5078	47.895	–14 245
				av	–14 262 ± 30

temperatures. The vapor pressure was determined with a mercury manometer, and the distance between the mercury levels was measured to ±0.1 mm with a cathetometer. The data were analyzed in the same fashion as described above but gave somewhat larger experimental errors (Table XV). The values for butyrolactone and mesitylene were in good agreement with those obtained with the ebulliometer.

**Enthalpies of Hydrolysis of Ethyl Esters and Lactones.** The calorimeter used in this study is one based on the design by Wadsö,<sup>9</sup> and the calorimetric system was operated under computer control as previously described.<sup>34</sup> The temperature was measured to ±0.0001 °C with an HP quartz thermometer probe and a counting circuit that eliminated the usual ±1 quantization error. In a typical hydrolysis run, 100 mL of 0.8 N NaOH in either 60% ethanol or 50% DMSO was placed in the calorimetric vessel, and the sample was placed in an ampule that could be broken under computer control. For a typical reaction, data were obtained for a ~10-min foreperiod, a 25-min reaction period, and a 10-min afterperiod. With slower reactions, the reaction period was lengthened appropriately. The reaction was followed by cooling the cell to the original temperature and carrying out an electrical calibration. The data were worked up as described previously. An example of typical hydrolysis data for an ester is given in Table XVI, and typical data for the hydrolysis of a lactone are given in Table XVII. The standard deviations are given as 2 $\bar{s}$  where  $\bar{s}$  is the standard deviation of the mean.<sup>35</sup>

**Enthalpies of Reduction of Lactones.** A new calorimetric vessel developed by Crocker was used in order to keep the reaction solution from exposure to air.<sup>11</sup> A solution of 0.50 g of lithium triethylborohydride in 133 mL of freshly dried triglyme was prepared in the calorimetric vessel

Table XVIII. Enthalpies of Reduction of Valerolactone with 0.0355 M Lithium Triethylborohydride

run	mmol	$\epsilon$ (cal/K)	$\Delta T$ (K)	<i>Q</i> (cal)	$\Delta H$ (cal/mol)
1	1.1528	79.61	0.5500	43.790	–37 986
2	1.4683	78.08	0.7134	55.705	–37 039
3	1.5909	79.32	0.7641	60.604	–38 094
4	1.8004	82.37	0.8320	68.532	–38 063
				av	–38 020 ± 71

Table XIX. Enthalpies of Formation of  $\alpha,\omega$ -Alkanediols (Kilocalories/Mole)

$\alpha,\omega$ -alkanediol	$\Delta H_f$ (l) obsd <sup>a</sup>	$\Delta H_f$ (l) estim <sup>d</sup>
1,2-ethanediol	–108.7 ± 0.2	–109.0
1,3-propanediol	–114.9 ± 1.2	–114.7
1,4-butanediol	–120.3 ± 0.5	–120.6
1,5-pentanediol	–127.0 ± 0.7	–126.4
1,6-hexanediol	(–130.1 ± 1.2) <sup>b</sup>	–132.2
1,7-heptanediol		–138.0
1,8-octanediol		–143.8
1,9-nonanediol		–149.6
1,10-decanediol	–155.0 ± 0.6 <sup>c</sup>	–155.3
1,11-undecanediol		–161.1
1,12-dodecanediol		–166.9
1,13-tridecanediol		–172.7

<sup>a</sup>Reference 8. <sup>b</sup>The data for this compound does not fit the normal methylene increment and was not included in the correlation. <sup>c</sup>Enthalpy of fusion = 10.7 ± 0.1 kcal/mol. <sup>d</sup>Estimated assuming a constant methylene increment. The estimated uncertainty in the values is ±0.5 kcal/mol.

under argon, and the sample was placed in a sealed ampule. The reaction run was carried out essentially as described above. A set of typical data for the reduction of a lactone is given in Table XVIII.

**Enthalpies of Formation of *n*-Alcohols and Acids.** It is known that for a homologous series, the enthalpies of formation are generally linearly related to the number of carbons.<sup>36</sup> An examination of the data for the *n*-alcohols from C<sub>2</sub> to C<sub>11</sub> showed that most of them fit this description. The largest error for the selected values was found with *n*-octanol, where the deviation was 0.36 kcal/mol. The older value –102.30, gave an exact fit to the correlation line and was used in the present calculations.

**Enthalpies of Formation of the  $\alpha,\omega$ -Diols.** There have been two experimental studies of the enthalpies of formation of the diols. The earlier study used larger samples and gave smaller standard deviations. However, their data for 1,3-propanediol appears to be about 3 kcal/mol in error, and here the more recent value was used. The experimental data were found to be linearly related to the number of carbons, and the values for the compounds that had not been studied experimentally were estimated from the linear relationship (Table XIX). An uncertainty of ±0.5

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kcal/mol was assigned to the values thus derived. It is possible that these diols will give some deviation from a linear relationship because of internal hydrogen bonding. However, the available data do not suggest such deviations, and the data for 1,3-propanediol was not used in calculating the enthalpies of formation of the lactones.

**Calculations.** The ab initio calculations were carried out with Gaussian-90,<sup>37</sup> and the molecular mechanics calculations were carried out with MM3.<sup>38</sup>

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Energy Sciences, Department of Energy. We thank Prof. Saunders for providing his data on the conformations of lactones prior to publication.

**Registry No.** Ethyl acetate, 141-78-6; ethyl propionate, 105-37-3; ethyl butyrate, 105-54-4; ethyl valerate, 539-82-2; ethyl hexanoate, 123-66-0; ethyl heptanoate, 106-30-9; ethyl octanoate, 106-32-1; ethyl nonanoate, 123-29-5; ethyl decanoate, 110-38-3; ethyl undecanoate, 627-90-7; butyrolactone, 96-48-0; valerolactone, 542-28-9; caprolactone, 502-44-3; heptanolactone, 539-87-7; octanolactone, 5698-29-3; nonanolactone, 6008-27-1; decanolactone, 706-14-9; undecanolactone, 1725-03-7; dodecanolactone, 947-05-7; tridecanolactone, 1725-04-8; 4-hydroxybutyric acid, 591-81-1; 6-hydroxycaproic acid, 1191-25-9; 7-hydroxyheptanoic acid, 3710-42-7; 8-hydroxyoctanoic acid, 764-89-6; 9-hydroxynonanoic acid, 3788-56-5; 10-hydroxydecanoic acid, 1679-53-4; 11-hydroxyundecanoic acid, 3669-80-5; 12-hydroxydodecanoic acid, 505-95-3; 13-hydroxytridecanoic acid, 7735-38-8; 1,7-heptanediol, 629-30-1; 1,8-octanediol, 629-41-4; 1,9-nonanediol, 3937-56-2; 1,11-undecanediol, 765-04-8; 1,12-dodecanediol, 5675-51-4; 1,13-tridecanediol, 13362-52-2.

### Lactones. 3. A Comparison of the Basicities of Lactones and Esters

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**Abstract:** The basicity of lactones and esters toward triethyloxonium ion was studied via NMR spectroscopy. The equilibrium constants were measured, and the order of decreasing basicity was found to be  $\delta$ -valerolactone >  $\gamma$ -butyrolactone > diethyl carbonate > ethyl acetate > ethyl propionate. The rates of reaction were parallel to the equilibrium constants. The origin of the differences in basicity was explored via ab initio calculations of structures and energies of ions formed by adding  $H^+$  or  $CH_3^+$  to methyl acetate. The calculated proton affinity of the *Z* ester rotamer agreed with the experimental data and was found to be considerably smaller than that for the *E* rotamer. The relative energies of the four ions that could be formed by adding a proton to methyl acetate were related to the orientation of the dipole components at oxygen. The methyl cation affinities of the methyl acetate conformers were found to parallel the proton affinities and gave the same preferred direction of addition. The proton affinity of valerolactone was calculated to be greater than that for butyrolactone in good accord with the experimental results.

In their study of the reactions of triethyloxonium ion, Meerwein et al.<sup>1</sup> observed that the ion transfers an ethyl cation to  $\gamma$ -butyrolactone and to  $\delta$ -valerolactone. The reaction has been used for the conversion of lactones to the corresponding diethyl ortho esters.<sup>2</sup> However, most acyclic esters do not appear to react with this reagent to any great extent. In order to gain more quantitative information concerning the basicity of lactones and esters, we have studied the ethyl cation transfer reaction in methylene chloride solution via NMR.

The reaction of  $\delta$ -valerolactone with triethyloxonium tetrafluoroborate in stoichiometric amounts went to completion, indicating that the lactone is more basic than diethyl ether, the other product of the reaction. The reaction of  $\gamma$ -butyrolactone proceeded to 89% completion under these conditions. In order to gain information on the relative basicity of these two lactones, the salt was formed from butyrolactone and was treated with valerolactone in methylene chloride. The NMR spectrum showed the disappearance of the bands for the ethylated butyrolactone and the formation of the ethylated valerolactone. The reaction proceeded

Table I. Relative Basicities of Esters and Lactones

compound	concn (M)	% react	$K^a$	$\Delta\Delta G$
valerolactone	0.167	~100	14800	-5.7
butyrolactone	0.167	89	65.5	-2.5
diethyl carbonate	0.375	28	0.16	1.1
ethyl acetate	0.31	20	0.06	1.6
dodecanolactone	0.167	15	0.02	2.3
undecanolactone	0.25	3	0.001	4.1
ethyl propionate	0.25	0	<0.0005	>5
nonanolactone	0.167	0	<0.0005	>5

<sup>a</sup>  $K = [\text{salt}][\text{Et}_2\text{O}]/[\text{ester}][\text{Et}_3\text{O}^+]$ .

Table II. Rates of Reaction with Triethyloxonium Tetrafluoroborate

compound	$[A_0]$	$x_{\text{eq}}$	$K_{\text{eq}}$	$k_1$	$k_{-1}$
valerolactone	0.167	0.167	14800	$1.06 \times 10^{-3}$	$7.16 \times 10^{-8}$
butyrolactone	0.167	0.149	65.5	$2.68 \times 10^{-4}$	$4.09 \times 10^{-6}$
ethyl carbonate	0.375	0.105	0.16	$1.96 \times 10^{-5}$	$1.22 \times 10^{-4}$
ethyl acetate	0.312	0.062	0.06	$3.90 \times 10^{-6}$	$6.50 \times 10^{-5}$

essentially to completion (15:1 ratio of the two ions). When the reaction was carried out in the reverse fashion with an initial formation of the salt from valerolactone followed by the reaction with butyrolactone, a small amount of ethylated butyrolactone was seen, in essentially the same ratio as noted above. From these

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