Geminal Substituent Effects, 16[◇]

Do Alkoxycarbonyl Substituents Stabilize Small Cycloalkane Rings?

Sergey P. Verevkin[b], Martin Kümmerlin[a], Hans-Dieter Beckhaus[a], Carlo Galli[c] and Christoph Rüchardt*[a]

Institut für Organische Chemie und Biochemie der Universität Freiburg[a],
Albertstraße 21, D-79104 Freiburg i.Br., Germany
E-mail: ruechardt@oca.chemie.uni-freiburg.de

Institut für Physikalische Chemie, Universität Rostock[b],
Hermannstraße 14, D-18051 Rostock, Germany

Dipartimento di Chimica, Università 'La Sapienza'[c],
I-00185 Roma, Italy

Received December 8, 1997

Keywords: Enthalpy of formation / Enthalpy of vaporization / Enthalpy of combustion / Cycloalkanes

The standard enthalpies of formation $\Delta H_f°(g)$ of mono- and *gem*-di(alkoxycarbonyl)-substituted cyclopropanes **1**, cyclobutanes **2** and cyclopentanes **3** have been calculated from the standard enthalpies of combustion $\Delta H_c°$, which were measured calorimetrically, in combination with the standard enthalpies of vaporization $\Delta H_{vap}°$. The latter were obtained for **1a−c**, **2b−c** and **3b−c** from the temperature dependence of the vapor pressures, which were measured in a flow system. Contrary to suggestions in the literature, only weak stabilization ($\leq$ 8 kJ $\cdot$ mol^{-1}) of small rings by *gem*-alkoxycarbonyl substituents was observed. In this context, we give a revised value for the enthalpy of combustion of methyl cyclobutanecarboxylate. It is concluded that the known high rates of ring closure to *gem*-dialkoxycarbonyl cyclopropanes are not attributable to a 'stabilizing effect' resulting from conjugation between the alkoxycarbonyl substituents and the cyclopropane ring, as has been suggested in the literature. The operation of a Thorpe-Ingold- or *gem*-dimethyl-type effect would seem to offer a more satisfactory interpretation.

Introduction

The introduction of substituents into hydrocarbon structures has either a stabilizing or a destabilizing effect. A quantitative measure of this effect is given by the change of the thermochemical increment of the carbon atom at which the substituent is bound, i.e. the comparison of e.g. $CH_2[2C]$ and $CH_2[XC]$, remembering the definition that $CH_3[C] = CH_3[X]$.[2] If the increment, which expresses the contribution of that particular substituent X to the enthalpy of formation of the structure, becomes more negative, X exerts a stabilizing effect; if the increment becomes more positive, the effect is a destabilizing one.[1]

When *two substituents* are attached to the same carbon atom, then their stabilizing or destabilizing effect may, in addition, be dependent on geminal substituent interactions, these being either additive or synergistic (e.g. the anomeric effect).[1][3] The magnitude of these effects changes somewhat with the hydrocarbon structure, e.g. it may vary depending on whether substituents are bound to primary, secondary or tertiary carbon centers.

In this context, it is an interesting question whether cyclic hydrocarbon structures respond to the introduction of substituents similarly to, or differently from, open-chain structures. We have recently found[4] that cyclopropanes, and even bicyclic and tricyclic hydrocarbon structures, respond to the introduction of *electron-donating* substituents, i.e. one methoxy group or two *gem*-methoxy groups, in the same way as open-chain structures. The anomeric effect seems to be only slightly dependent on the carbon structure and even the exceptional electronic structure found in cyclopropanes[5][6] does not change this phenomenon substantially.

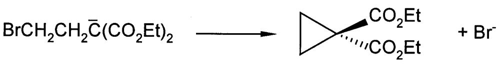
It is an open question, however, as to whether *electron-accepting* substituents attached to small cycloalkane rings deviate from this apparently "normal" behavior.[7][8] The capacity of the strongly distorted σ-bonds of cyclopropane to interact with the π-orbitals of an electron-withdrawing substituent is well-documented.[6][7][8] This conjugative interaction has several consequences: (i) it changes the bond lengths,[9] (ii) it lowers the ionization potential,[10][11] and (iii) it affects the spectroscopic behavior of the three-membered ring.[7][8] We became interested in elucidating whether there is a strong conjugative interaction between alkoxycarbonyl substituents and the strained small-ring cycloalkanes. It has been claimed[12] that such a conjugative interaction can relieve the strain of some cyclopropyl derivates, and therefore make easier their formation from suitable open-chain precursors.[13][14] The most remarkable manifestation of this puzzling behavior is the high rate of formation of 1,1-bis(ethoxycarbonyl)cyclopropane from 1,1-bis(ethoxy-

---

[◇] Part 15: Ref.[1].

1434−193X/98/0404−0579 $ 17.50+.50/0

carbonyl)-3-bromopropane and EtO$^-$ as the base, by an intramolecular S_N2 process (eq. 1).[12][15]



(1)

It was suggested[12][16] that this high rate of ring-closure can be attributed to a reduction of the formal strain (see below) in the cyclopropane product due to a *stabilizing* interaction with the adjacent π-systems of the alkoxycarbonyl groups. This explanation, which is based on enthalpic considerations, was extended to other electron-attracting substituents.[12][17][18] On the other hand, other authors have shown[14][19][20] that the often invoked[21] entropic advantage of the proximity between the reactive end-groups of a short bifunctional chain can account only to a limited extent for the high rates of formation of some substituted small-ring structures.

Only few thermochemical data are available in the literature concerning the conjugative interaction of substituents with cycloalkane structures in general.[22][23][24][25][26][27] A quantitative thermochemical measure of such an interaction is given by the *formal* change of the strain enthalpy H_s of a cycloalkane structure by the introduction of a substituent. H_s of a (substituted) cycloalkane is defined as the difference between the experimental enthalpy of formation $\Delta H_f°$ (g, exptal.) and the value of $\Delta H_f°$ (g, calcd.) calculated from thermochemical group increments of the Benson-type, which represent strain-free homologues. In Table 1, a representative selection of enthalpic data from the literature on cyclopropane, cyclobutane and cyclopentane and some mono-substituted derivatives is presented.

For alkyl-, amino- and cyano-substituted cyclopropanes, only small substituent effects ($\Delta H_s \leq 3$ kJ·mol^{-1}) on the formal strain enthalpy are found, while for phenyl cyclopropane ($\Delta H_s = -7.4$ kJ·mol^{-1}) and acetyl cyclopropane ($\Delta H_s = -8.5$ kJ·mol^{-1}) a stabilizing interaction between the substituent and the ring is indicated. It is surprising that amino- ($\Delta H_s = -8.2$ kJ·mol^{-1}) and cyano substituents ($\Delta H_s = -11.0$ kJ·mol^{-1}) exert somewhat larger stabilizing effects in the cyclobutane series than in the cyclopropane series.[27b] The exceptionally large stabilizing effect of the methoxycarbonyl substituent on cyclobutane ($\Delta H_s = -28.6$ kJ·mol^{-1}) demands independent confirmation. In the cyclopentane series, methyl and amino substituents have only a weak effect on ΔH_s, the -4.7 kJ·mol^{-1} stabilization by the cyano substituent[27] being exceptional.

In order to get some appraisal of the possible thermochemical basis of the conjugative interaction between small rings and electron-accepting substituents, and in view of some inconsistency in the available thermochemical data collected in Table 1, we have carried out a systematic investigation of the formal strain energies of mono- and *gem*-

Table 1. Enthalpies of formation $\Delta H°_f$(g) of substituted small rings available from the literature and their corresponding calculated[a] strain enthalpies H_s in kJ·mol^{-1}

	cyclo-C_3H_4XY $\Delta H_f°$(g, exp.)	H_s	ΔH_s	*cyclo*-C_4H_6XY $\Delta H_f°$(g, exp.)	H_s	ΔH_s	*cyclo*-C_5H_8XY $\Delta H_f°$(g, exp.)	H_s	ΔH_s
X = Y = H	53.3 ± 0.6[24]	117.7	–	28.4 ± 0.6[24]	114.2	–	−76.4 ± 0.8[24]	30.9	–
X = H, Y = CH_3	25.9[26b]	119.9	+2.2	–	–	–	−106.2 ± 0.8[24]	30.7	−0.2
X = Y = CH_3	−8.2 ± 1.4[24]	120.1	+2.4	–	–	–	−138.2 ± 1.1[24]	33.0	+2.1
X = H, Y = C_6H_5	150.5[26a]	110.3	−7.4	–	–	–	–	–	–
X = H, Y = NH_2	77.0 ± 0.7[24]	120.4	+2.7	41.2 ± 0.8[24]	106.0	−8.2	−54.9 ± 0.9[24]	31.4	+0.5
X = H, Y = CN	182.7 ± 0.7[27]	118.2	+0.5	147.3 ± 1.1[27]	104.2	−11.0	48.8 ± 2.8[27]	27.4	−4.7
X = H, Y = CH_3CO	−115.3[26a]	109.3	−8.5	–	–	–	–	–	–
X = H, Y = CO_2CH_3	–	–	–	−355.3 ± 1.4[24][25]	85.6	−28.6	–	–	–

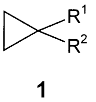
[a] Strain enthalpy is defined as the difference of the experimental standard enthalpy of formation $\Delta H°_f$(g, exptal.) and $\Delta H°_f$(g, calcd.), the value calculated from strain-free group increments.[1] The strain enthalpies of the unsubstituted three-, four- and five-membered rings define $H_{s(ring)}$. The strain enthalpies of substituted rings are termed $H_{s(compound)}$. The difference $\Delta H_s = H_{s(compound)} - H_{s(ring)}$ indicates a stabilization or destabilization of a compound relative to the unsubstituted ring.

Table 2. Experimental thermochemical results for esters **1**–**3** at 298.15 K in kJ·mol^{-1}

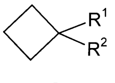
	$\Delta H_c°$ (l)[a]	$\Delta H_f°$ (l)	$\Delta H°_{vap}$ [b]	$\Delta H_f°$(g)
1a	−2758.32 ± 0.52	−352.34 ± 0.54	42.59 ± 0.39	−309.75 ± 0.67
1b	−3404.21 ± 0.39	−385.94 ± 0.39	43.97 ± 0.48	−341.97 ± 0.62
1c	−4766.7 ± 1.0	−775.8 ± 1.0	63.87 ± 0.45	−711.9 ± 1.1
2a	−3418.3 ± 1.2	−371.9 ± 1.2	44.23 ± 0.21	−327.7 ± 1.3
2b	−4056.1 ± 1.1	−413.5 ± 1.1	44.93 ± 0.37	−368.6 ± 1.2
2c	−5414.98 ± 0.66	−806.75 ± 0.66	65.77 ± 0.38	−740.98 ± 0.76
3b	−4640.33 ± 0.56	−508.56 ± 0.56	51.22 ± 0.57	−457.34 ± 0.80
3c	−5990.1 ± 2.5	−911.0 ± 2.5	66.79 ± 0.40	−844.2 ± 2.5

[a] Taken from the specific enthalpies of combustion in Table 7. – [b] From the measurements of vapor pressures at different temperatures given in Table 8, using the Clausius-Clapeyron equation.

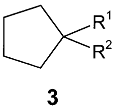
di(alkoxycarbonyl)-substituted three- (**1**), four- (**2**) and five-membered (**3**) cycloalkanes.



1



2



3

a $R^1 = H$ $R^2 = CO_2CH_3$
b $R^1 = H$ $R^2 = CO_2CH_2CH_3$
c $R^1 = R^2$ $= CO_2CH_2CH_3$

Results and Discussion

The standard enthalpies of combustion $\Delta H_c°$ were measured calorimetrically.[28][29] The enthalpies of vaporization $\Delta H_{vap}°$ of **1a−c**, **2a−c** and **3b−c** were obtained from the temperature dependence of the vapor pressures measured in a flow system.[30][31] The mean value of $\Delta H_{vap}°$ for **2a** is almost identical to that derived from *calorimetric measurements* at 298 K (44.72 ± 0.9 kJ·mol^{-1})[27] and is somewhat higher than that obtained from *vapor pressure measurements* at 320 to 380 K (39.7 ± 0.4 kJ·mol^{-1}).[24][25] A summary of the experimental results, and the standard enthalpies of formation $\Delta H_f°(g)$ calculated from them, is given in Table 2.

These thermochemical data constitute the experimental basis for the quantitative estimation of the formal strain enthalpies H_s of **1−3**. They are derived as the differences between the experimental $\Delta H_f°(g)$ and the sum of strain-free increments.[1][32][33] A summary of the strain-free increments used in this work is presented in Table 3.

The strain energies H_s of cyclopropane [$\Delta H_f°(g) = 53.3 \pm 0.6$ kJ·mol^{-1}, $H_s = 117.7$ kJ·mol^{-1}][24], cyclobutane [$\Delta H_f°(g) = 28.4 \pm 0.6$ kJ·mol^{-1}, $H_s = 114.2$ kJ·mol^{-1}] and cyclopentane [$\Delta H_f°(g) = -76.4 \pm 0.8$ kJ·mol^{-1}, $H_s = 30.9$ kJ·mol^{-1}][24] were taken as the basis for estimating the effect of the interaction between the substituent and the ring. The values of the formal strain energies of the alkoxycarbonyl-substituted small rings are listed in Table 4.

From the small ΔH_s values (less than −8 kJ·mol^{-1}), it is concluded that only weak stabilizing interactions exist for mono- and dialkoxycarbonyl-substituted cyclopropanes, cyclobutanes and cyclopentanes (ΔH_s in Table 4). The revised enthalpy of combustion determined for **2a** (Table 2) is in excellent agreement with the results for the ethyl ester **2b**. The data in the literature,[25] which lead to the $\Delta H_s = -28.68$ kJ·mol^{-1} quoted in Table 1, appear to be erroneous. The amended result for **2a** given in Table 4 falls in line with the others (ΔH_s is even only −1.0 kJ·mol^{-1}), and rules out strong conjugation between the cyclobutane ring and the methoxycarbonyl substituent. We note that **2a** is quite hygroscopic; it is possible that this fact was overlooked in the earlier work.[25]

The small enthalpic contribution of the interaction between the alkoxycarbonyl group and a cyclopropane ring, listed in Table 4, contradicts the suggestion[12][16] that this interaction could explain the high rates of three-membered ring formation (see eq. 1).[15] Since the strain energy of **1c** is not lower than that of the parent cyclopropane, there must be an alternative explanation for the high efficiency of ring closure. Tentatively, operation of the Thorpe-Ingold effect[14][19][37] by the geminal substitution pattern might be considered, even though this effect was originally reported for *gem*-dimethyl substitution only. Generally speaking, in the cyclization of a linear oligomethylene chain there is a significant increase in the non-bonded *gauche* interactions at the transition state. Whenever the chain is *gem*-disubsti-

Table 3. Strain-free increments for the calculation of $\Delta H_f°(g)$ of alkanes, ester, amines, nitriles and ketones[a]

Alkanes[32]		Esters[3]		Amines[34]		Nitriles[35]		Ketones[36]	
$CH_3[C]$	−42.05	$CH_3[CO_2]$	−42.05	$CH_3[N]$	−42.05	$CH_3[CN]$	−42.05	$CH_3[CO]$	−42.05
$CH_2[2C]$	−21.46	$CH_2[CO_2,C]$	−17.40	$CH_2[N,C]$	−25.02	$CH_2[CN,C]$	−18.37	$CH_2[CO,C]$	−21.76
$CH[3C]$	−9.04	$CH[CO_2,2C]$	−7.40	$CH[N,2C]$	−18.66	$CH[CN,2C]$	−7.66	$CH[CO,2C]$	−10.00
$C[4C]$	−1.26	$C[CO_2,3C]$	4.51	$C[N,3C]$	−13.43	$C[CN,3C]$	6.86	$C[CO,3C]$	2.59

[a] All values in kJ·mol^{-1}; neighboring atoms in square brackets. – [b] Additional increments[3][34][35][36] $CO_2[2C] = -327.1$, $C[(2CO_2),2C] = 19.58$, $CH_2[O,C] = -33.76$, $NH_2[C] = 18.20$, $[CN] = 116.10$, $[CO] = -130.54$ kJ·mol^{-1}.

Table 4. Experimental enthalpies of formation $\Delta H_f°(g)$ of *gem*-dialkoxycarbonyl-substituted small rings, and their derived strain enthalpies H_s in kJ·mol^{-1} [a]

	cyclo-C_3H_4XY			*cyclo*-C_4H_6XY			*cyclo*-C_5H_8XY		
	$\Delta H_f°(g)$	H_s	ΔH_s	$\Delta H_f°(g)$	H_s	ΔH_s	$\Delta H_f°(g)$	H_s	ΔH_s
X = Y = H	53.3[24]	117.7	–	28.4[24]	114.2	–	−76.4[24]	30.9	–
X = H, Y = CO_2CH_3	−309.75	109.7	−8.1	−327.7	113.2	−1.0	–	–	–
X = H, Y = $CO_2CH_2CH_3$	−341.97	111.2	−6.5	−368.6	106.1	−8.1	−457.3	38.9	+8.0
X = Y = $CO_2CH_2CH_3$	−711.9	117.3	−0.4	−740.98	109.6	−4.6	−844.2	27.8	−3.1

[a] For a definition of strain enthalpy H_s, see the footnote to Table 1 [$\Delta H_s = H_{s(compound)} - H_{s(ring)}$]

Table 5. Densities $d_{(293\ K)}$, specific heat capacities $c_{p(298\ K)}$ and expansion coefficients of the investigated compounds and auxiliary materials

	$d_{(293\,K)}$[a]/ g·cm^{-3}	$c_{p(298K)}$[b]/ J·K^{-1}·g^{-1}	$10^{-6}\cdot(\delta V_m/\delta T)_p$[c]/ dm^{-3}·K^{-1}
1a	0.985	2.26	1.0
1b	0.958	2.34	1.0
1c	1.057	1.51	1.0
2a	1.033	1.80	1.0
2b	0.928	2.01	1.0
2c	1.045	1.70	1.0
3b	0.989	1.86	1.0
3c	1.049	1.46	1.0
polyethylene[d]	0.920	2.53	0.1
cotton[e]	1.500	1.67	0.1
mylar[f]	1.380	1.32	0.1

[a] Measured with a pycnometer for the liquids **1**−**3**. − [b] From DSC measurements; the mean values from two experiments are quoted. − [c] Estimated. − [d] $CH_{1.930}$, $\Delta u_c{}^0{}_{(polyethylene)} = -46361.0 \pm 3.1$ J·g^{-1}. − [e] $CH_{1.774}$, $O_{0.887}$, $\Delta u_c{}^0{}_{(cotton)} = -16945.2 \pm 4.2$ J·g^{-1}. − [f] $C_{10}H_8O_4$, $\Delta u_c{}^0{}_{(mylar)} = -22856.1 \pm 4.8$ J · g^{-1}, $m_{(mylar)} = m_{(mylar,moist)}\ [1 - 4.64 \times 10^{-5}$ (relative moisture of air in%)].

tuted, *gauche* interactions are already present and, therefore, the formation of the transition state of ring-closure becomes *less disfavored* for enthalpic reasons. Likewise, the internal rotational freedom of a chain is reduced in a cyclization event. Upon geminal substitution of one methylene group, the rotational entropy of the chain is reduced. Consequently, the entropy loss of the ring-closure process becomes *less severe.* In conclusion, *gem*-substitution makes formation of the small rings easier both for enthalpic and entropic reasons.[19] This could explain the high efficiency of three-membered ring formation[13][14] without invoking "stabilization" of the ring by electron-accepting substituents,[12] the supposed favorable interaction which does not emerge from the present thermochemical investigation.

Thanks are due to the *Deutsche Forschungsgemeinschaft* and the *Fonds der Chemischen Industrie* for financial support, and to *F. Schillinger* and *E. Hickl* for technical assistance. S. P. Verevkin thanks the *Alexander-von-Humboldt-Stiftung* for a research fellowship. We also thank Prof. *A. L. J. Beckwith* for stimulating discussions.

Experimental Section

The general methods used have been reported in ref.[1].

Materials: Compounds **1a**−**1c**, **2b**−**2c** and **3b**−**3c** were purchased from Aldrich, Acros or Fluka and carefully purified by distillation in a spinning band column. No impurities > 0.001% were detected in the samples by GC or by NMR analysis. **2a** was prepared by acid-catalyzed transesterification of **2b** in methanol and purified as described above.

Table 6. Results from typical combustion experiments

	1a	**1b**	**1c**	**2a**	**2b**	**2c**	**3b**	**3c**
$m_{(substance)}$/g[b]	0.344057	0.528193	0.579247	0.036493	0.512729	0.598496	0.385374	0.038787
$m'_{(cotton)}$/g[b]	0.000766	0.001114	0.001132	0.000625	0.000999	0.001126	0.001012	0.000475
$m''_{(polyethylene)}$/g[b]	0.529727	0.265755	0.258441	−	0.275096	0.286819	0.291685	−
$m'''_{(mylar)}$/g[b]	−	−	−	0.011170	−	−	−	0.010203
ΔT_c/K[c]	1.35649	1.11778	1.06818	0.84905	1.15372	1.17411	1.03923	0.94544
$\varepsilon_{calor}(-\Delta T_c)$/J[c]	−34033.7	−28070.4	−26824.7	−1356.9	−28973.0	−29485.0	−26097.7	−1324.7
$\varepsilon_{cont}(-\Delta T_c)$/J[c]	−19.92	−15.67	−14.95	−2.23	−16.10	−16.74	−14.11	−2.59
$\Delta E_{corr.}$/J[d]	13.96	12.05	12.82	0.74	11.95	13.75	10.00	0.75
$-m'\Delta u'_c$/J	12.97	18.87	19.18	10.60	16.92	19.08	17.14	8.08
$-m''\Delta u''_c$/J	24558.6	12320.7	11981.6	−	12753.7	13297.2	13522.8	−
$-m'''\Delta u'''_c$/J	−	−	−	255.29	−	−	−	233.01
$\Delta u_{c(sub)}$/J·g^{-1}	−27514.7	−29786.6	−25592.9	−29896.0	−31605.5	−27018.0	−32592.8	−27945.4

[a] For the definition of the symbols, see ref.[29] $T_h = 298.15$ K macrocalorimeter; $V_{bomb} = 0.2664$ l; $p^i{}_{gas} = 30.45$ bar; $m^i{}_{water} = 0.78$ g; $E_{ignition} = 1.5$ J, $m_{platin} = 12.18$ g; microcalorimeter; $V_{bomb} = 0.0460$ l; $p^i{}_{gas} = 30.45$ bar; $m^i{}_{water} = 0.23$ g; $E_{ignition} = 1.5$ J; $m_{platin} = 2.883$ g. − [b] Masses obtained from weight by calculating the buoyancy. − [c] $\Delta T_c = T^f - T^i + \Delta T_{corr.}$, $\varepsilon_{calor} = 25089.5 \pm 1.2$ J·K^{-1} (0.0048%) for **1a**; $\varepsilon_{calor} = 25112.6 \pm 1.9$ J·K^{-1} (0.0077%) for **1b**, **1c**, **2b**, **2c**, **3b**; $\varepsilon_{calor} = 1484.60 \pm 0.28$ J·K^{-1} (0.019%) for **2a**; $\varepsilon_{calor} = 1401.13 \pm 0.22$ J·K^{-1} (0.0159%) for **3b** from calibration with benzoic acid; $\varepsilon_{cont}(-\Delta T_c) = \varepsilon^i{}_{cont}\,(T^i - 298.15\ K) + \varepsilon^f{}_{cont}\,(298.15\ K - T^f + \Delta t_{corr.})$. − [d] $\Delta E_{corr.}$ is sum of items 81−85, 87−90, 93 and 94 in ref.[29].

Table 7. Specific energies of combustion ($\Delta u_c{}^o$) and the mean results from all combustion experiments

1a	**1b**	**1c**	**2a**	**2b**	**2c**	**3b**	**3c**
$-\Delta u_c{}^o$ /J·g^{-1}							
27514.7	29786.6	25570.6	29893.1	31605.5	27011.5	32588.6	27904.2
27524.8	29791.3	25573.6	29935.5	31614.0	27018.0	32581.1	27892.9
27520.9	29791.8	25576.1	29944.1	31623.7	27022.5	32593.1	27932.1
27541.7	29795.8	25592.9	29896.0	31583.9	27020.6	32592.8	27964.2
27537.2			29901.2				27933.7
							27945.4
mean values							
27527.9 ± 5.1	29791.4 ± 1.9	25578.3 ± 5.0	29914.0 ± 10.7	31606.8 ± 8.5	27018.2 ± 2.4	32588.9 ± 2.8	27928.8 ± 10.7

Table 8. Results of measurements of the vapor pressure p by the transpiration method

	$T^{[a]}$/K	$m^{[b]}$/mg	$V_{N2}{}^{[c]}$/dm^3	$p^{[d]}$/mbar	$\Delta H°_{vap}, T$ [e]/ kJ · mol^{-1}
1a	273.4	9.75 E+00	0.527	5.07 E+00	42.59 ± 0.39
	278.3	1.25 E+01	0.469	7.07 E+00	
	283.2	1.49 E+01	0.381	1.02 E+01	
	288.1	1.45 E+01	0.277	1.34 E+01	
	293.0	1.46 E+01	0.205	1.81 E+01	
	298.2	1.23 E+01	0.132	2.37 E+01	
	303.2	1.49 E+01	0.118	3.17 E+01	
	308.1	1.51 E+01	0.088	4.30 E+01	
	313.1	1.30 E+01	0.058	5.58 E+01	
1b	278.2	1.12 E+01	0.787	3.21 E+00	43.97 ± 0.48
	283.2	5.62 E+00	0.284	4.43 E+00	
	288.2	6.75 E+00	0.233	6.41 E+00	
	293.2	9.65 E+00	0.247	8.60 E+00	
	298.3	1.17 E+01	0.222	1.16 E+01	
	303.3	1.12 E+01	0.160	1.53 E+01	
	308.3	1.17 E+01	0.123	2.08 E+01	
1c	288.2	5.39 E−01	1,625	4.43 E−2	63.87 ± 0.45
	293.2	8.92 E−01	1.662	7.15 E−02	
	298.3	8.55 E−01	1.034	1.10 E−01	
	303.3	1.02 E+00	0.787	1.73 E−01	
	308.3	1.02 E+00	0.542	2.52 E−01	
	313.3	1.11 E+00	0.394	3.75 E−01	
	318.3	1.56 E+00	0.369	5.63 E−01	
2a	323.1	4.23 E+01	0.231	4.01 E+01	44.23 ± 0.21
	283.1	4.58 E+00	0.266	4.03 E+00	
	288.3	3.51 E+00	0.143	5.61 E+00	
	293.1	3.44 E+00	0.102	7.58 E+00	
	278.0	2.41 E+00[f]	0.184	2.84 E+00	
	272.8	3.67 E+00[f]	0.415	1.92 E+00	
	268.2	4.63 E+00[f]	0.746	1.35 E+00	
	298.1	4.13 E+00	0.091	1.01 E+01	
	303.1	8.01 E+00	0.131	1.36 E+01	
	308.3	5.58 E+00	0.068	1.80 E+01	
	313.4	5.09 E+00	0.046	2.45 E+01	
2b	273.7	4.97 E+00	1.150	9.08 E−01	44.93 ± 0.37
	278.4	5.31 E+00	0.882	1.24 E+00	
	283.3	5.90 E+00	0.690	1.73 E+00	
	288.1	5.97 E+00	0.498	2.39 E+00	
	293.0	7.09 E+00	0.422	3.32 E+00	
	298.2	8.17 E+00	0.345	4.65 E+00	
	303.2	8.49 E+00	0.268	6.20 E+00	
	308.3	7.93 E+00	0.192	8.06 E+00	
2c	288.3	2.66 E−01	1.197	2.78 E−02	65.77 ± 0.38
	293.3	3.30 E−01	0.925	4.43 E−02	
	298.3	2.76 E−01	0.497	6.88 E−02	
	303.3	3.77 E−01	0.440	1.06 E−01	
	308.3	7.84 E−01	0.576	1.69 E−01	
	313.3	9.84 E−01	0.497	2.45 E−01	
	318.3	1.21 E+00	0.406	3.69 E−01	
3b	274.5	1.94 E+00	1.280	2.79 E−01	51.22 ± 0.57
	278.4	2.36 E+00	1.080	3.96 E−01	
	283.4	2.48 E+00	0.781	5.70 E−01	
	288.3	3.06 E+00	0.632	8.60 E−01	
	293.5	3.40 E+00	0.484	1.24 E+00	
	298.3	3.74 E+00	0.372	1.77 E+00	
	303.4	4.41 E+00	0.316	2.45 E+00	
	308.5	4.17 E+00	0.223	3.27 E+00	
3c	293.2	7.11 E−01	3.411	2.42 E−02	66.79 ± 0.40
	298.3	5.38 E−01	1.606	3.88 E−02	
	303.3	4.11 E−01	0.816	5.83 E−02	
	308.3	7.03 E−01	0.890	9.13 E−02	
	313.3	1.02 E+00	0.841	1.40 E−01	
	318.3	8.98 E−01	0.494	2.10 E−01	
	323.4	1.13 E+00	0.420	3.11 E−01	

[a] Temperature of saturation, N_2 gas stream 0.95−1.88 l h^{-1}. − [b] Mass of the transferred sample cooled to the temperature of condensation $T_{cond.}$ = 243 K. − [c] Amount of nitrogen used to transfer the mass of the sample m. − [d] Vapor pressures at the temperatures T of the experiment, corrections were made for the residual vapor pressure by $T_{cond.}$. − [e] $\Delta H°_{vap}$ for the mean temperature of the series of experiments.

Enthalpies of Formation. − Combustion Calorimetry: The combustion experiments were performed in an isoperbolic macrocalorimeter[38] employing sealed polyethylene ampoules. Those of **2a** and **3b** were carried out in mylar bags in an aneroid microcalorimeter[28] equipped with a stirred water bath. The energy equivalent of the calorimeter was calibrated with a standard reference sample of benzoic acid (sample SRM 39i, National Bureau of Standards). Conventional procedures[29] were used for reduction of the data to standard conditions. The densities of the substances were determined in a calibrated 10 ml pycnometer. The specific heat capacities were measured by DSC (Table 5). It was found that after distillation, the samples of esters contained about 0.4−0.7% mass of water (by Karl Fischer titration). It was possible to remove this amount of water by the addition of activated molecular sieves. Each sample (ca. 0.5 g) was stored over molecular sieves (ca. 0.3−0.4 g) for about half an hour prior to the combustion experiment. This procedure proved to be crucial for obtaining consistently dry samples yielding reproducible results. Results of a typical combustion experiment for each compound are given in Table 6. The individual values of the specific enthalpies of combustion, and their averaged values, are listed in Table 7.

Enthalpies of Vaporization. − Transpiration Method: The enthalpies of vaporization $\Delta H°_{vap}$ of **1a**−**1c**, **2a**−**c** and **3b**−**3c** were determined by the method of transference in a saturated N_2 stream.[30][31] The substances were mixed with glass beads and placed in thermostatted U-tubes. At several temperatures, a slow stream of nitrogen was passed through the U-tube, and the transported material was cooled and condensed in a second U-tube. The amount of transported material was determined by GC analysis using an internal standard (n-hydrocarbon). The vapor pressure p at the saturation temperature was calculated from the amount of condensed material by adding the residual vapor pressure at the condensation temperature. The latter was calculated iteratively from the linear correlation between $\ln[m/V_{(N2)}]$ and T^{-1}. The enthalpies of vaporization were calculated using the Clausius-Clapeyron equation $\Delta H°_{vap} = -R \cdot (\ln[m/V_{(N2)}]/dT^{-1})$; (where R = ideal gas constant, m = mass of transported compound, $V_{(N2)}$ = volume of transporting gas, T = temperature). The results are given in Table 8.

Enthalpies of Formation in the Gas Phase. − Strain Enthalpies: A summary of experimental results, including the standard enthalpies of formation $\Delta H°_f(g)$ derived from our measurements, is given in Table 2. The standard deviations quoted take account of the uncertainties inherent in the calibration method as well as errors due to the combustion energies of the auxiliary materials. The $\Delta H°_f(g)$ data of **1**−**3**, together with similar data available from the literature[24][25][26][27] (Table 1), were utilized for calculation of the strain enthalpies of the substituted rings (H_s), as the difference between the experimental $\Delta H°_f(g)$ value of the molecule and the sum of the appropriate strain-free increments. The definition of the strain-free increments[32][33] and the procedure for calculating them in the case of esters (alkoxycarbonyl group),[3] amines,[34] nitriles,[35] and ketones[36] are the same as in previous work. A summary of the strain-free increments used is provided in Table 3.

[1] F. Schaffer, S. P. Verevkin, H.-J. Rieger, H.-D. Beckhaus, C. Rüchardt, *Liebigs Ann.* **1997**, 1333−1344.

[2] H.-D. Beckhaus, B. Dogan, S. P. Verevkin, J. Hädrich, C. Rüchardt, *Angew. Chem.* **1990**, *102*, 313−314; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 320−321.

[3] K. Rakus, S. P. Verevkin, H.-D. Beckhaus, M. Keller, C. Rüchardt, *Liebigs Ann.* **1995**, 1483−1493; K. Rakus, S. P. Verevkin, W.-H. Peng, H.-D. Beckhaus, C. Rüchardt, *Liebigs Ann.* **1995**, 2059−2067.

[4] W.-H. Peng, Dissertation, University of Freiburg, **1996**.

[5] A. Greenberg, J. F. Liebman, *Strained Organic Molecules*, Academic Press, **1978**, 29.

[6] A. de Meijere, *Angew. Chem.* **1979**, *91*, 867−884; *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 809−826.

[7] A. D. Walsh, *Trans. Faraday Soc.* **1949**, *45*, 179.

[8] R. Hoffmann, *Tetrahedron Lett.* **1970**, *33*, 2907−2909.

[9] R. Hoffmann, W.-D. Stohrer, *J. Am. Chem. Soc.* **1971**, *93*, 6941−6948.

[10] P. Asmus, M. Klessinger, *Angew. Chem.* **1976**, *88*; 343−344; *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 310−311.

[11] C. Cauletti, M. L. Di Vona, P. Gargano, F. Grandinetti, C. Galli, C. Lillocci, *J. Chem. Soc., Perkin Trans. II*, **1986**, *2*, 667−670.

[12] C. J. M.Stirling, *J. Chem. Educ.* **1973**, *50*, 844−845.

[13] B. Capon, *Quart. Rev.* **1964**, *18*, 45−111.

[14] G. Illuminati, L. Mandolini, *Acc. Chem. Res.* **1981**, *14*, 95−102.

[15] A. C. Knipe, C. J. M. Stirling, *J. Chem. Soc. B*, **1968**, 67−72.

[16] R. Bird, G. Griffiths, G. F. Griffith, C. J. M. Stirling, *J. Chem. Soc., Perkin Trans. II*, **1982**, 579−584.

[17] R. Bird, C. J. M. Stirling, *J. Chem. Soc., Perkin Trans. II*, **1973**, 1221−1226.

[18] A. Di Martino, C. Galli, P. Gargano, L. Mandolini, *J. Chem. Soc., Perkin Trans. II*, **1985**, 1345−1349.

[19] L. Mandolini, *Adv. Phys. Org. Chem.* **1986**, *22*, 1−111.

[20] L. Mandolini, *Bull. Soc. Chim. Fr.* **1988**, 173−176.

[21] F. G. Menger, *Acc. Chem. Res.* **1985**, *18*, 128−134.

[22] N. Cohen, S. W. Benson, in *Chemistry of Alkanes and Cycloalkanes* (Eds.: S. Patai, Z. Rappoport), John Wiley & Sons Ltd., **1992**, 215−288.

[23] R. Fuchs, J. Hallman, M. O. Perlman, *Can. J. Chem.* **1982**, *60*, 1832−1835.

[24] J. B. Pedley, R. D. Naylor, S. P. Kirby, *Thermochemical Data of Organic Compounds*, 2nd. ed., Chapman and Hall, London **1986**.

[25] K. H. Hall Jr., J. H. Baldt, *J. Am. Chem. Soc.* **1971**, *93*, 140−145.

[26] [26a] J. F. Liebman, A. Greenberg, *Chem. Rev.* **1989**, *89*, 1225−1246. − [26b] A. Greenberg, T. A. Stevenson, in *Molecular Structures and Energetics* (Eds.: J. F. Liebman, A. Greenberg), VCH Publishers Inc. **1986**, 193.

[27] [27a] R. Fuchs, J. Hallman, *Can. J. Chem.* **1983**, *61*, 503−505. − [27b] The heat of formation of the reference compound cyclobutane has been questioned, however, ref.[27a]. If this were, indeed, too positiv by about 8 kJ·mol^{-1}then ΔH_s cyclo-C_4H_6XY (X = H, Y = NH_2 and X = H, Y = CN) in Table 1 would be more positiv by about 8 kJ·mol^{-1}and hence in line with the cyclo-C_3H_4XY and cyclo-C_5H_8XY compounds.

[28] H.-D. Beckhaus, C. Rüchardt, M. Smisek, *Thermochim. Acta* **1984**, *79*, 149−159.

[29] W. N. Hubbard, D. W. Scott, G. Waddington, *Experimental Thermochemistry*, (Ed. F. D. Rossini), Interscience Publ., New York, **1956**, pp. 75−127.

[30] J. D. Cox, G. Pilcher, *Thermochemistry of Organic and Organometallic Compounds*, Academic Press, London, **1970**.

[31] W. Bernlöhr, H.-D. Beckhaus, C. Rüchardt, K. Peters, H. G. von Schnering, *Chem. Ber.* **1984**, *117*, 1013−1025.

[32] P. v. R. Schleyer, J. E. Williams, K. B. Blanchard, *J. Am. Chem. Soc.* **1970**, *92*, 2377−2386.

[33] S. W. Benson, *Thermochemical Kinetics*, Wiley, New York, **1976**, p. 274; N. Cohen, S. W. Benson, *Chem. Rev.* **1993**, *93*, 2419−2438.

[34] F. Welle, S. P. Verevkin, M. Keller, H.-D. Beckhaus, C. Rüchardt, *Chem. Ber.* **1994**, *127*, 697−710.

[35] K. Rakus, S. P. Verevkin, H.-D. Beckhaus, C. Rüchardt, *Chem. Ber.* **1994**, *127*, 2225−2234.

[36] M. Nölke, S. P. Verevkin, H.-D. Beckhaus, C. Rüchardt, *Liebigs Ann.* **1995**, 41−51.

[37] See E. L. Eliel, S. H. Wilen, *Stereochemistry of Organic Compounds*, Wiley-Interscience, New York, **1994**, p. 682.

[38] H.-D. Beckhaus, G. Kratt, K. Lay, J. Geiselmann, C. Rüchardt, B. Kitschke, H. J. Lindner, *Chem. Ber.* **1980**, *113*, 3441−3445.

[97380]