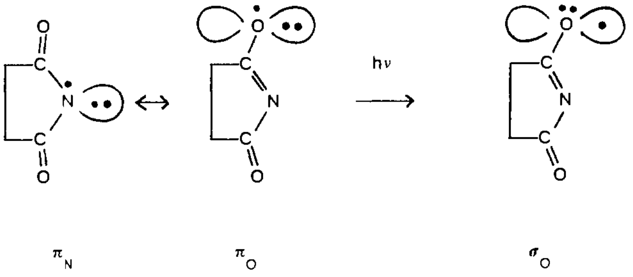
positive shift in g_y are those involving the nitrogen lone pair electrons and/or those of oxygen lone pair electrons. We note in Table I that the g_y shift is inversely related to the unpaired electron density in the N p_π orbital. Decreasing unpaired electron density in the N p_π orbital indicates increasing importance of the resonance structure π_O in an imidyl radical of the π ground state (see below). It must be that the oxygen lone pair electrons are mostly responsible for the observed g_y shift; the spin–orbit coupling constant of oxygen is $\sim$0.01 eV and is three times larger than that of nitrogen.[33]



The facility with which an imidyl radical undergoes the ring-opening process also appears to be inversely related to the unpaired electron density in the N p_π orbital. Possible importance of the (excited) σ_O state in the β scission of succinimidyl radical to form β-(isocyanatocarbonyl)ethyl radical had been pointed out by Koenig and Wielesek,[4] and also by Dewar and Olivella.[7] We suggest that the thermal and/or photo-induced ring-opening of succinimidyl and phthalimidyl radicals observed in the present study involves the $\pi \rightarrow \sigma_O$ transition, and its transition probability increases with increasing contribution of the resonance structure π_O in the π ground state. Succinimidyl radicals detected by Lund, et al.[15] in a single crystal of succinimide irradiated by X-ray at 26 K and maintained at that temperature must have been stabilized by the crystal environment. The radicals in the crystal decayed at $\sim$65 K. More significantly, the radicals were generated only in crystals grown from water and not in crystals grown from ketone. Hydrogen bonding involving the carbonyl oxygen, for example, could impede the ring-opening process involving the σ_O state.

---

[33] Moore, C. E. *Natl. Stand. Ref. Data Ser.* (*U.S. Natl. Bur. Stand.*) **1971**, 35.

Heats of Formation of Organic Molecules. 2. The Basis for Calculations Using Either ab Initio or Molecular Mechanics Methods. Alcohols and Ethers

Norman L. Allinger,[*,†] Lawrence R. Schmitz,[‡] Ioan Motoc,[§] Charles Bender,[⊥] and Jan K. Labanowski[⊥]

Contribution from the School of Chemical Sciences, Department of Chemistry, University of Georgia, Athens, Georgia 30602, Department of Chemistry, Marshall University, Huntington, West Virginia 25755, Bristol-Myers Squibb Corporation, Pharmaceutical Research Institute, Core Chemistry Resources, Princeton, New Jersey 08543-4000, and Ohio Supercomputer Center, 1224 Kinnear Road, Columbus, Ohio 43212-1163. *Received April 15, 1991*

Abstract: Heats of formation may be calculated by many different schemes, and a scheme that may be used with the ab initio method is herein outlined in detail. The method is essentially the same as that which is used with MM2 and MM3, although the numerical quantities that go into the calculation are somewhat different. The method can be applied in either of two ways. Either a bond energy scheme in the usual sense is employed, with the vibrational energies being absorbed in the bond energy increments, or one may explicitly consider these quantities. The first method is applied to 6-31G* Hartree–Fock calculations on alcohols and ethers, and it fits the experimental data on 28 compounds to a root-mean-square error of 0.52 kcal/mol, while the fit to a group of anomeric compounds is poorer.

Introduction

The heats of formation of organic compounds are important physical properties. Because the number of experimental values being determined in recent years has become quite small, the practical importance of being able to use calculational methods to obtain these data has been increasing. A previous publication[1] has shown that by utilizing ab initio calculations at the 6-31G* level, and a bond energy scheme based on the concept of homodesmic equations, one can calculate heats of formation for saturated hydrocarbons and for a wide variety of aliphatic amines with probable errors of less than 1 kcal/mol. In the present work we have extended these calculations to cover simple oxygen compounds, alcohols, and ethers, so as to ascertain the presence or absence of any adverse effect on the calculations resulting from the additional lone pairs of electrons in these molecules. Future papers will deal with compounds containing heavier atoms, conjugated systems, and special problems.

The difficulties in trying to calculate heats of formation by ab initio methods directly are well-known.[2] Much of the difficulty can be circumvented using the ideas described in the paragraph above (first suggested by Wiberg[3] and by Ibrahim and Schleyer[4]), and the necessary theory here has been developed in detail.[5] The

---

[†] University of Georgia.
[‡] Marshall University.
[§] Pharmaceutical Research Institute.
[⊥] Ohio Supercomputer Center.

[1] Allinger, N. L.; Schmitz, L. R.; Motoc, I.; Bender, C.; Labanowski, J. K. *J. Phys. Org. Chem.* **1990**, *3*, 732.

[2] Hehre, W.; Radom, L.; Schleyer, P. von R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.

[3] Wiberg, K. *J. Comput. Chem.* **1984**, *5*, 197. Wiberg, K. *J. Org. Chem.* **1985**, *50*, 5285.

[4] Ibrahim, M. R.; Schleyer, P. v. R. *J. Comput. Chem.* **1985**, *6*, 157.

[5] The general theory is outlined for the molecular mechanics case by Burkert and Allinger: Burkert, U.; Allinger, N. L. *Molecular Mechanics*; American Chemical Society, Washington, DC, 1982. Also see the users manuals for the MM2(87) and MM3(89) programs.

0002-7863/92/1514-2880$03.00/0

Table I. Heat of Formation Input Data for Alcohols and Ethers

wt	H^a_f	HFE	POP	TOR	T/R	compound
1	30.124 55	−115.035 42	0.000 00	−0.000 67	0.003 82	methanol
1	69.150 49	−154.075 74	0.000 24	0.000 00	0.003 82	ethanol
1	108.176 43	−193.110 50	0.000 69	0.000 67	0.003 82	1-propanol
1	108.178 85	−193.115 41	0.000 14	0.000 00	0.003 82	2-propanol
1	147.200 91	−232.145 88	0.000 89	0.000 67	0.003 82	2-methylpropanol
1	147.202 36	−232.145 07	0.001 24	0.001 34	0.003 82	1-butanol
1	147.204 78	−232.150 09	0.000 40	0.000 67	0.003 82	2-butanol
1	147.203 33	−232.153 47	0.000 00	0.000 00	0.003 82	1,1-dimethylethanol
1	186.228 30	−271.179 84	0.001 80	0.002 01	0.003 82	1-pentanol
1	186.230 72	−271.184 71	0.000 96	0.001 34	0.003 82	2-pentanol
1	186.229 26	−271.186 06	0.000 14	0.000 67	0.003 82	2-methyl-2-butanol
1	225.254 23	−310.214 53	0.002 36	0.002 68	0.003 82	1-hexanol
1	224.114 91	−309.060 23	0.000 41	0.000 00	0.003 82	cyclohexanol
1	59.107 36	−228.925 70	0.000 64	0.000 67	0.003 82	ethylene glycol
1	99.135 72	−267.965 94	0.000 64	0.000 67	0.003 82	1,2-propanediol
0	98.133 29	−267.961 19	0.000 32	0.001 34	0.003 82	1,3-propanediol
1	60.249 11	−154.064 74	0.000 00	0.000 00	0.003 82	dimethyl ether
1	99.275 04	−193.104 87	0.000 25	0.000 67	0.003 82	methyl ethyl ether
1	138.300 98	−232.144 80	0.000 48	0.001 34	0.003 82	diethyl ether
1	138.300 98	−232.139 54	0.000 62	0.001 34	0.003 82	methyl propyl ether
1	138.303 40	−232.141 59	0.000 06	0.000 67	0.003 82	methyl isopropyl ether
1	177.327 88	−271.175 63	0.000 00	0.000 67	0.003 82	methyl *tert*-butyl ether
1	177.326 91	−271.179 54	0.000 94	0.002 01	0.003 82	1-ethoxypropane
1	216.357 70	−310.218 85	0.000 00	0.001 34	0.003 82	diisopropyl ether
0	255.382 18	−349.251 81	0.000 00	0.001 34	0.003 82	isopropyl *tert*-butyl ether
1	294.406 66	−388.277 39	0.000 00	0.001 34	0.003 82	di-*tert*-butyl ether
1	98.133 29	−191.909 38	0.000 00	0.000 67	0.003 82	oxetane
1	137.159 23	−230.976 45	0.000 00	0.000 67	0.003 82	tetrahydrofuran
1	176.185 16	−270.017 89	0.000 00	0.000 00	0.003 82	tetrahydropyran
1	118.214 71	−305.825 31	0.000 00	0.000 00	0.003 82	1,4-dioxane

[a] Contribution to the heat of formation from the hydrocarbon portion of the molecule for which parameters are already established (ref 1).

accuracy of the approximations required for these calculations in the ab initio case is not known, however, except for the previously cited[1-5] quite limited studies. The present work shows that one can extend these calculations to alcohols and ethers and obtain heats of formation for these compounds of a similar quality to those obtained earlier, and with an accuracy competitive with experiment.

Theory

The derivation of an equation which gives the heat of formation of an arbitrary molecule has been carried out from quantum mechanical principles employing statistical mechanical methods. Although lengthy and somewhat complicated, the derivation is quite straightforward and yields eq 3 (among other formulations). The terms in eq 3 have the

$$H_f^\circ = \sum_i \mathrm{BE} + \sum_i \mathrm{GE} + \mathrm{HFE} + \mathrm{POP} + \mathrm{TOR} + 2.4\ (\mathrm{kcal/mol,\ gas,\ 25\ ^\circ C}) \qquad (3)$$

following meanings. BE and GE are bond energy and group energy increments. HFE is the (6-31G*) Hartree–Fock energy. POP and TOR are energy increments that arise if there are higher energy conformations mixed in with the ground-state conformation and the contribution from low-frequency torsional modes, respectively. The 2.4 kcal/mol is from translation and rotation ($^6/_2$ RT for a nonlinear molecule) plus RT to convert energy to enthalpy. The full derivation is given in Supplementary Material.

Computational Methods. The calculations described in the present work utilized the 6-31G* basis set.[6] The calculations were carried out using the programs CADPAC[7] and HONDO8.[8]

The computer time required for the ab initio geometry optimization depends on the quality of the starting geometry. We have found that we can calculate good 6-31G* geometries for many kinds of molecules using MM3, but substituting a parameter set designed to fit these geometries (approximately r_e) instead of r_g geometries. When the root-mean-square net force on the atoms is calculated for our MM3 (r_e) structure with the 6-31G* basis set, it is usually found to be about 0.01 hartree/bohr, which

Table II. Heat of Formation Output Data for Alcohols and Ethers (au)

Best Values[a]
C–O = 46.871048 au (29412.521 kcal)
O–H = 37.961033 au (23821.308 kcal)
O–ME = −0.000246 au (−0.154 kcal)
O–SE = −0.003472 au (−2.179 kcal)
O–TE = −0.006569 au (−4.122 kcal)
OCCO = 0.001114 au (0.699 kcal)

	H_f°		diff	
wt	calc	exp[15,16]	calc − exp	compound
1	−0.07589	−0.07660	0.00071	methanol
1	−0.08911	−0.08962	0.00051	ethanol
1	−0.09681	−0.09748	0.00067	1-propanol
1	−0.10399	−0.10377	−0.00022	2-propanol
1	−0.10751	−0.10810	0.00059	2-methylpropanol
1	−0.10423	−0.10484	0.00061	1-butanol
1	−0.11181	−0.11152	−0.00029	2-butanol
1	−0.12081	−0.11907	−0.00174	1,1-dimethylethanol
1	−0.11183	−0.11260	0.00077	1-pentanol
1	−0.11926	−0.11952	0.00026	2-pentanol
1	−0.12666	−0.12599	−0.00067	2-methyl-2-butanol
1	−0.11936	−0.12006	0.00070	1-hexanol
1	−0.11248	−0.11045	−0.00203	cyclohexanol
1	−0.14794	−0.14763	−0.00031	ethylene glycol
1	−0.16329	−0.16366	0.00037	1,2-propanediol
0	−0.15826	−0.14933	−0.00893	1,3-propanediol
1	−0.07021	−0.07010	−0.00011	dimethyl ether
1	−0.08324	−0.08242	−0.00082	methyl ethyl ether
1	−0.09608	−0.09603	−0.00005	diethyl ether
1	−0.09093	−0.09064	−0.00029	methyl propyl ether
1	−0.09526	−0.09600	0.00074	methyl isopropyl ether
1	−0.10798	−0.10785	−0.00013	methyl *tert*-butyl ether
1	−0.10376	−0.10368	−0.00008	1-ethoxypropane
1	−0.12084	−0.12143	0.00059	diisopropyl ether
0	−0.13242	−0.13625	0.00383	isopropyl *tert*-butyl ether
1	−0.13661	−0.13788	0.00127	di-*tert*-butyl ether
1	−0.02950	−0.03068	0.00118	oxetane
1	−0.07063	−0.07015	−0.00048	tetrahydrofuran
1	−0.08681	−0.08508	−0.00173	tetrahydropyran
1	−0.12036	−0.12033	−0.00003	1,4-dioxane

standard deviation = 0.00082 au (0.52 kcal)

[a] By least-squares fitting to the data given with weights as indicated.

---

(6) See ref 2, p 80.

(7) Amos, R. D.; Rice, J. E. CADPAC 4-Analytic Derivative Package, Issue 4, Cambridge, 1987.

(8) Dupuis, M.; Mougenot, P.; Watts, J. D.; Hurst, J. B.; Villar, H. O. In *Modern Techniques in Computational Chemistry*; Clementi, E., Ed.; ESCOM, Leiden, 1989; Chapter 7.

Table III. Heat of Formation Input Data for Anomeric Compounds

$H_f°$	HFE	POP	TOR	T/R	compound
−0.132 70	−267.954 43	0.000 00	0.001 34	0.003 82	dimethoxymethane
−0.148 62	−306.990 90	0.000 05	0.001 34	0.003 82	1,1-dimethoxyethane
−0.114 90	−266.792 56	0.000 00	0.000 67	0.003 82	1,3-dioxolane
−0.133 40	−305.834 50	0.000 00	0.000 00	0.003 82	1,3-dioxane
−0.152 19	−383.910 02	0.000 48	0.000 67	0.003 82	2-methoxytetrahydropyran
−0.132 01	−344.868 58	0.000 16	0.000 67	0.003 82	1,3-dioxacycloheptane
−0.162 78	−346.030 77	0.000 00	0.001 34	0.003 82	2,2-dimethoxypropane
−0.177 44	−341.656 14	0.000 00	0.000 00	0.003 82	1,3,5-trioxane

is 10–100 times less than what is found with the structure obtained from most model building programs.

The geometry optimizations were carried out until the largest component of the gradient was less than 5×10^{-4} hartree/bohr.

The MM2 force field was introduced in 1977,[9] and its usefulness was intended to be primarily in the calculation of structures and energies of molecules. Under the latter heading we also included heats of formation, because these give a standard basis to which comparisons can be made. The details of these calculations using molecular mechanics have been published in scattered places over the years and are summarized in several reviews.[5] The same general scheme has also been used with the ab initio method, but the rigorous derivation of the necessary equations has never really been published in any one place. We thought it would be best to outline in detail in one place the complete method, including all of the approximations and assumptions made, and have done so in this paper. The method is then applied to the specific example of alcohols and ethers.

All of the heat of formation data pertain to the gas phase at 25 °C, and energies are in hartrees unless otherwise specified.

Results and Discussion

The equation used here for the calculation of the heat of formation of a molecule is eq 3. The terms therein are all defined above.

Table I presents the data used in the calculations. Table II presents the values derived for the parameters and the results for the individual compounds. The root-mean-square error over the set of 28 compounds, mostly monofunctional, is 0.52 kcal/mol. This value is similar to the expected experimental error and shows that the calculational method employed here is competitive in accuracy with the heat of combustion methods usually used to determine heats of formation[15,16] for these compounds. We exclude from the discussion for the moment compounds that have two oxygens attached to the same carbon (anomeric compounds).

We can also compare the results obtained here with those obtained by molecular mechanics.[17] In a few cases where molecular mechanics did not agree with experiment, it was not completely clear which method was in error. In the cases studied here, it is sometimes found (for example, in 1,3-propanediol) that the MM3 value[17] and the ab initio value for the heat of formation agree quite well, but the experimental value differs by several kilocalories. It seems most probable that the experimental value is in error in such a case, and the calculated values are correct. Similarly, we feel the experimental value for isopropyl *tert*-butyl ether is in error.[17]

Table IV. Heat of Formation Output Data for Anomeric Compounds (au)

Best Values
OCH_2 = 0.001048 au (0.658 kcal)
OCHRO = −0.002816 au (−1.767 kcal)
OCR_2O = −0.001171 au (−0.735 kcal)

$H_f°$			
calc	exp[15,16]	diff calc − exp	compound
−0.13504	−0.13270	−0.00234	dimethoxymethane
−0.14310	−0.14862	0.00552	1,1-dimethoxyethane
−0.11399	−0.11490	0.00091	1,3-dioxolane
−0.13178	−0.13340	0.00162	1,3-dioxane
−0.15210	−0.15219	0.00009	2-methoxytetrahydropyran
−0.13909	−0.13201	−0.00708	1,3-dioxacycloheptane
−0.16162	−0.16278	0.00116	2,2-dimethoxypropane
−0.18177	−0.17744	−0.00433	1,3,5-trioxane

The adjustable parameters that were used in this work are generally the same as those that were used in molecular mechanics. There are six such parameters required for alcohols and ethers, and three more are needed for the anomeric compounds. If we have only a single oxygen atom in each molecule, we need a CO bond and an OH bond energy term. Additionally, we need group increments for methyl, secondary, and tertiary centers attached to oxygen. (If the oxygen is attached to a primary center, that is taken to be our zero point, and no parameter is needed for that.) It is found that the oxygen attached to a methyl, primary, secondary, or tertiary center has an increasingly negative heat of formation, and this effect is reproduced by these parameters. The parameters previously evaluated for hydrocarbons[1] were also used here unchanged.

If there are two oxygens in the molecule, the situation is more complicated. If they are attached to the same CH_2 group (anomeric compounds), there is a small adverse effect, and the necessary parameter has a value +0.658 kcal/mol. If they are attached in a vicinal manner, the effect is still adverse, but small, 0.699 kcal/mol. It is assumed that attachment more distant than 1,2 leads to a negligible interaction effect beyond what is calculated as part of the Hartree–Fock energy. On the other hand, if we put one or two carbons on the central carbon atom (replacing one or two of the hydrogens) of an anomeric compound, they have a stabilizing effect, and negative values. Curiously, the parameter is more negative when there is one carbon attached than when two carbons are attached, contrary to what would be anticipated. The former parameter is established by only two compounds which agree poorly, and the latter parameter is established by only one compound, 2,2-dimethoxypropane. These values seem sufficiently odd as to call into question the experimental values for the heats of combustion for these compounds, but without further data we cannot be sure what the problem is. The numerical values for the parameters were established by a least-squares optimization of the calculated heats of formation of the compounds listed in

---

(9) (a) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127. (b) The MM2 force field for hydrocarbons was described in ref 9a. Extensions to functionalized molecules have been described in subsequent papers (summarized in ref 5). The original program (MM2(77)) is available from the Quantum Chemistry Program Exchange, University of Indiana, Bloomington, IN 47405, Program 395. The latest version of MM2, referred to as MM2(87), is available to academic users from QCPE and to commercial users from Molecular Design Limited, 2132 Farallon Dr., San Leandro, CA 94577. The MM3 program is available from the Technical Utilization Corp., Inc., 235 Glen Village Court, Powell, OH 43065, and from Molecular Design Limited. The input format for MM3 is identical with that of MM2 (with some minor exceptions), so that the same input files may be used for both (the MM3 program will edit the input and make the changes needed).

(10) This information is discussed in textbooks on the subject, for example: Hill, T. L. *Introduction to Statistical Thermodynamics*; Addison-Wesley: Reading, MA, 1960.

(11) Benson, S. W. *Thermodynamical Kinetics*; Wiley: New York, 1976.

(12) Allinger, N. L.; Hirsch, J. A.; Miller, M. A.; Tyminski, I. J.; van-Catledge, F. A. *J. Am. Chem. Soc.* **1968**, *90*, 1199.

(13) Even in the best MM3 calculations (ref 9), however, it does appear. These calculations use the harmonic approximation to calculate the excited vibrational frequencies, however.

(14) Pitzer, K. S.; Gwinn, W. D. *J. Chem. Phys.* **1942**, *10*, 428.

(15) Pedley, J. B.; Naylor, R. D.; Kirby, S. P. *Thermochemical Data of Organic Compounds*, 2nd ed.; Chapman and Hall: London, 1986.

(16) Cox, J. D.; Pilcher, G. *Thermochemistry of Organic and Organometallic Compounds*; Academic Press: New York, 1970.

(17) Allinger, N. L.; Imam, M. R.; Lii, J.-H. *J. Am. Chem. Soc.* **1990**, *112*, 8293.

Table III, and all of the input data are given there. The results of the optimization are given in Table IV.

It was found that the anomeric compounds were fit more poorly than the remainder of the compounds. Thus, without the anomeric compounds in the least-squares fitting of the compounds as in Table II, the root-mean-square error was 0.52 kcal/mol (28 compounds), but with them it was 0.78 kcal/mol (35 compounds of which 7 were anomeric). Consequently, we decided to first fit the non-anomeric compounds and establish the numerical values for the parameters needed for them. We then treated the anomeric compounds alone as a group, carrying over the parameters for simple ethers/alcohols and evaluating only the anomeric parameters. The root-mean-square error for the anomeric compounds alone was then 1.24 kcal/mol. The notably larger value here than with the simple molecules suggests that one of two situations obtains: either the experimental data are less good for the anomeric compounds or else the heat calculation method (the homodesmic equations and 6-31G* basis) is less good for these compounds. We are unable to choose between these alternatives at present. It is now known that anomeric compounds which have a hydrogen on the carbon between the oxygens are attacked fairly easily by atmospheric oxygen. The storage of such compounds over sodium in the presence of air can therefore lead to contamination of the sample with oxidized products, and this problem has not always been recognized.[18] The experimental data on these compounds may therefore be less correct than supposed. On the other hand, the 6-31G* basis set without electron correlation is an approximate calculational scheme, and it may simply be inadequate for compounds of the anomeric type. The question in principle can be resolved by additional careful experiments, and/or by larger ab initio calculations.

Having now investigated the calculation of the heats of formation of organic molecules, including saturated hydrocarbons, aliphatic amines, alcohols, and ethers, we can draw the following conclusions. The calculational scheme described is adequate for compounds of these classes for determining heats of formation to within better than 1 kcal/mol (approximately to within experimental error). In the case of anomeric compounds, the results are somewhat poorer, and it is not clear if this is due to a defect in the method or to experimental error.

It is intended to extend these calculations to compounds containing heavier atoms, conjugated systems, and other organic molecules of general interest. It is uncertain as to whether or not the 6-31G* basis will be sufficiently large to treat molecules in general, or whether it will have some definite limitations, the nature of which is not yet clear. It seems doubtful that one will be able to avoid explicit inclusion of electron correlation in conjugated molecules, but this remains to be established. For now, it would seem that one can calculate, reliably, the heats of formation of molecules belonging to the classes of compounds discussed above, except possibly for the anomeric compounds.

Acknowledgment. The authors are indebted to the National Institutes of Health (Grant No. 5, R24RR02165) and the National Science Foundation (Grant No. CHE 8614548) for financial support, to the Ohio Supercomputer Center for a grant of Cray-YMP time, and to Marshall University for a Faculty Summer Research Stipend and for release time for teaching. The authors are indebted to Drs. D. H. Wertz and M. A. Duncan for helpful discussion on the TOR parameter and to Mr. B. Bergner and Dr. G. Burnham of the Scientific Information Systems of the Institute for their support.

Supplementary Material Available: Details of the theory behind the research (17 pages). Ordering information is given on any current masthead page.

---

(18) Personal communication from M. Mansson.

(19) Allinger, N. L.; Yuh, Y.; Lii, J.-H. *J. Am. Chem. Soc.* **1989**, *111*, 8551, 8566, 8576.