Experimental and computational thermochemistry of the dihydroxypyridine isomers

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Abstract

The standard ($p° = 0.1$ MPa) molar enthalpy of formation for crystalline 2,3-dihydroxypyridine was measured, at $T = 298.15$ K, by static bomb calorimetry and the standard molar enthalpy of sublimation, at $T = 298.15$ K, was obtained using Calvet microcalorimetry. These values were used to derive the standard molar enthalpy of formation of 2,3-dihydroxypyridine in gaseous phase, at $T = 298.15$ K, $-(263.9 \pm 4.6)$ kJ · mol^{-1}.

Additionally, high-level density functional theory calculations using the B3LYP hybrid exchange-correlation energy functional with extended basis sets have been performed for all dihydroxypyridine isomers to determine the thermochemical order of stability of these systems. The agreement between experiment and theory for the 2,3-dihydroxypyridine isomer gives confidence to the estimates of the enthalpies of formation concerning the other five isomers. It is found that the enthalpic increment for the dihydroxy substitution of pyridine is equal to the sum of the respective enthalpic increment of the monosubstituted pyridines.
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1. Introduction

Recently, we have reported experimental and theoretical studies on hydroxyquinoxalines [1], hydroxypyridines and hydroxypyridines *N*-oxide [2]. In this work, we continue with the study of dihydroxypyridines with the purpose of extending the thermochemical database still too scarce for nitrogen heterocycles and for a better understanding of the effect of the hydroxyl group on the energetics of pyridine.

This paper reports the standard energy of combustion for 2,3-dihydroxypyridine (2,3-pyridinediol) in oxygen, at $T = 298.15$ K, measured by static bomb calorimetry, the standard molar enthalpy of sublimation and the derived value for the standard molar enthalpy of formation in the gas phase. Although the hydroxypyridines exist in the keto form in the crystalline phase, the tautomeric equilibrium favours the hydroxy form (enol form) in the gaseous phase [3,4]. In addition to the experimental work, we have performed theoretical calculations for the six dihydroxypyridine isomers using density functional theory with the B3LYP functional and the 6-31G*, 6-311G** and cc-pVTZ extended basis sets.

2. Experimental

The crystalline 2,3-dihydroxypyridine obtained from Aldrich Chemical Co., with the minimum mass fraction of 0.98, was purified by repeated vacuum sublimation

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until the combustion results were consistent and the carbon dioxide recovery ratios were satisfactory. The average ratio of the mass of carbon dioxide recovered after combustion to that calculated from the mass of sample was: (0.9999 ± 0.0002), where the uncertainty is the standard deviation of the mean. The density 1.13 $g \cdot cm^{-3}$ was determined from the mass and dimensions of the pellets. The 2,3-dihydroxypyridine could not be studied by differential scanning calorimetry as it decomposes in the fusion process.

The combustion experiments were performed with a static bomb calorimeter, with a twin valve bomb, type 1108, Parr Instrument Company. The calorimeter, subsidiary apparatus and technique have been described [5,6]. Benzoic acid (Bureau of Analysed Samples, Thermochemical Standard, BCS-CRM-190 r) was used for calibration of the bomb. Its massic energy of combustion is $-(26432.3 \pm 3.8)$ $J \cdot g^{-1}$, under certificate conditions. The calibration results were corrected to give the energy equivalent $\varepsilon(calor)$ corresponding to the average mass of water added to the calorimeter: 3119.6 g. From six calibration experiments, $\varepsilon(calor) = (16007.3 \pm 0.7)$ $J \cdot K^{-1}$, where the uncertainty quoted is the standard deviation of the mean. Combustion experiments were performed in oxygen at $p = 3.04$ MPa, with 1.00 cm^3 of water added to the bomb. For all experiments, ignition was made at $T = (298.150 \pm 0.001)$ K. The electrical energy for ignition was determined from the change in potential difference across a capacitor when discharged through the platinum ignition wire. For the cotton-thread fuse, empirical formula $CH_{1.686}O_{0.843}$, $\Delta_c u^\circ = -16250$ $J \cdot g^{-1}$ [7]: this value was confirmed in our laboratory. The corrections for nitric acid formation were based on -59.7 $kJ \cdot mol^{-1}$ [8], for the molar energy of formation of 0.1 $mol \cdot dm^{-3}$ $HNO_3(aq)$ from N_2, O_2, and $H_2O(l)$. The amount of substance used in each experiment was determined from the total mass of carbon dioxide produced after allowance was made for that formed from the cotton thread fuse. An estimated pressure coefficient of massic energy: $(\partial u / \partial p)_T = -0.2$ $J \cdot g^{-1} \cdot MPa^{-1}$ at $T = 298.15$ K, a typical value for most organic compounds [9], was assumed. The massic energy of combustion $\Delta_c u^\circ$ was calculated by the procedure given by Hubbard *et al.* [9].

The standard molar enthalpy of sublimation of 2,3-dihydroxypyridine was measured by the "vacuum sublimation" drop microcalorimetric method [10]. Samples about 3 to 5 mg at room temperature were dropped into the hot reaction vessel in the Calvet High Temperature Microcalorimeter (SETARAM HT 1000), held at $T = 422$ K, and then removed from the hot zone by vacuum sublimation. From the observed enthalpy of sublimation, the standard molar enthalpy of sublimation at $T = 298.15$ K was calculated using $\Delta_{298.15 \text{ K}}^{422 \text{ K}} H_m^\circ(g)$ estimated by a group method based on the values of Stull *et al.* [11]. For these measurements, the microcalorimeter

was calibrated in situ using the reported standard molar enthalpy of sublimation of naphthalene, (72.600 ± 0.600) $kJ \cdot mol^{-1}$ [12].

The relative atomic masses used throughout this paper were those recommended by the IUPAC Commission [13].

3. Experimental results

The results of combustion experiments for 2,3-dihydroxypyridine are given in table 1 and correspond to the following reaction:

$$C_5H_5NO_2(cr) + 21/4O_2(g) \rightarrow$$
$$5CO_2(g) + 5/2H_2O(l) + 1/2N_2(g) \qquad (1)$$
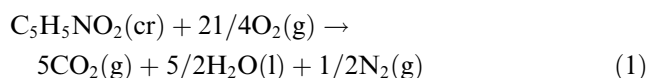
The symbols in this table have the same meaning as in reference [9]. As samples were ignited at $T = 298.15$ K

$$\Delta U(IBP) = -\{\varepsilon(calor) + c_p(H_2O, l)\Delta m(H_2O) + \varepsilon_f\} \times$$
$$\Delta T_{ad} + \Delta U(ign), \qquad (2)$$

where $\Delta U(IBP)$ is the energy associated to the isothermal bomb process, $\Delta m(H_2O)$ is the deviation of the mass of water added to the calorimeter from 3119.6 g, $c_p(H_2O, l)$ is the specific heat capacity of liquid water, ε_f is the energy of the bomb contents after ignition, ΔT_{ad} is the adiabatic temperature raise and ΔU_{ign} is the energy of ignition. The mean value of the standard massic energy of combustion is $\langle\Delta_c u^\circ\rangle = -(20789.7 \pm 5.6)$ $J \cdot g^{-1}$, at $T = 298.15$ K, the derived standard molar energy and enthalpy of combustion and the standard molar enthalpy of formation for the compound, in the crystalline phase, are respectively, $\Delta_c U_m^\circ(cr) = -(2309.7 \pm 1.3)$ $kJ \cdot mol^{-1}$, $\Delta_c H_m^\circ(cr) = -(2309.1 \pm 1.3)$ $kJ \cdot mol^{-1}$, and $\Delta_f H_m^\circ(cr) = -(373.0 \pm 1.5)$ $kJ \cdot mol^{-1}$. In accordance with normal thermochemical practice [14], the uncertainties assigned to the standard molar enthalpies of combustion and formation are twice the overall standard deviation of the mean and include the uncertainties in calibration and in the auxiliary quantities used. To derive $\Delta_f H_m^\circ(cr)$ from $\Delta_c H_m^\circ$ the standard molar enthalpy of formation for $CO_2(g)$: $-(393.51 \pm 0.13)$ $kJ \cdot mol^{-1}$ and for $H_2O(l)$: $-(285.83 \pm 0.04)$ $kJ \cdot mol^{-1}$, were used [15].

The observed enthalpy, $\Delta_{cr,298.15 \text{ K}}^{g,T} H_m^\circ$, at $T = 422$ K, was corrected to $T = 298.15$ K using $\Delta_{298.15 \text{ K}}^{422 \text{ K}} H_m^\circ(g) = 17.8$ $kJ \cdot mol^{-1}$, estimated by a group method with the values of Stull *et al.* [11]. The standard molar enthalpy of sublimation at $T = 298.15$ K, $\Delta_{cr}^g H_m^\circ(298.15 \text{ K}) = (109.1 \pm 4.3)$ $kJ \cdot mol^{-1}$ (uncertainty of twice the standard deviation of the mean) was determined from six experiments, thus enabling the calculation of the standard molar enthalpy of formation in the gaseous phase $\Delta_f H_m^\circ(g) = -(263.9 \pm 4.6)$ $kJ \cdot mol^{-1}$.

Scheme 1 shows the enthalpic increments for the hydroxy substitution in the ortho and meta positions of the

TABLE 1
Results of the combustion experiments of 2,3-dihydroxypyridine, at $T = 298.15$ K ($p° = 0.1$ MPa)

$m(CO_2$, total)/g	1.45277	1.73344	1.67143	1.77637	1.79435	1.87216
m(compound)/g	0.73119	0.87280	0.84148	0.89444	0.90384	0.94305
m(fuse)/g	0.00281	0.00293	0.00295	0.00297	0.00258	0.00267
ΔT_{ad}/K	0.95455	1.13991	1.09789	1.16867	1.17884	1.23041
ε_f/(J·K^{-1})	15.64	15.95	15.83	15.89	15.94	16.01
$\Delta m(H_2O)$/g	−0.1	0.0	−0.1	0.0	−0.1	0.1
$-\Delta U$(IBP)/J	15293.10	18263.86	17589.97	18725.17	18887.14	19715.15
$-\Delta U(HNO_3)$/J	39.04	39.70	43.88	49.91	47.19	48.55
$-\Delta U$(carbon)/J	0.00	0.00	0.00	0.00	0.00	0.00
ΔU(ignition)/J	1.20	1.20	1.20	0.65	1.20	0.61
$-\Delta U_\Sigma$/J	13.59	16.51	15.80	16.86	17.08	17.89
$-\Delta U$(fuse)/J	45.63	47.58	47.91	48.23	41.90	43.36
$-\Delta_c u°$/(J·g^{-1})	20780.97	20806.68	20775.75	20806.50	20779.09	20789.30

$$\langle \Delta_c u° \rangle = -(20789.7 \pm 5.6) \text{ J} \cdot \text{g}^{-1}$$

$m(CO_2$, total) is the total mass of CO_2 formed in the experiment; m(compound) is the mass of compound burnt in the experiment; m(fuse) is the mass of fuse (cotton) used in the experiment; ΔT_{ad} is the corrected temperature rise; ε_f is the energy equivalent of contents in the final state; $\Delta m(H_2O)$ is the deviation of the mass of water added to the calorimeter from 3119.6 g; ΔU(IBP) is the energy change for the isothermal combustion reaction under actual bomb conditions; ΔU(IBP) includes ΔU(ignition); $\Delta U(HNO_3)$ is the energy correction for the nitric acid formation; ΔU(carbon) is the energy correction for carbon formation; ΔU(ignition) is the energy of combustion of the fuse; ΔU_Σ is the energy correction to the standard state; ΔU(fuse) is the energy of combustion of the fuse (cotton); $\Delta_c u°$ is the standard massic energy of combustion.
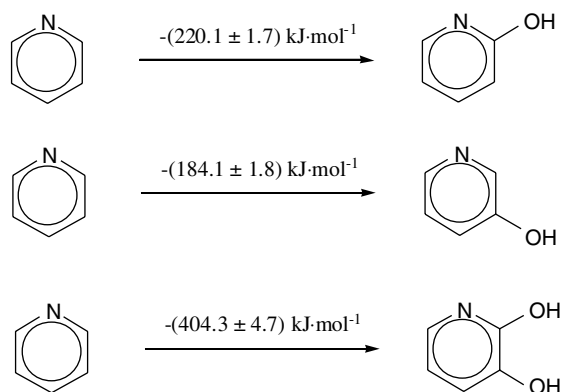
SCHEME 1. Enthalpic increments for hydroxyl substitution into pyridine.

pyridinic ring. It is found that the enthalpic increment for the 2,3-dihydroxy substitution of pyridine, $-(404.3 \pm 4.7)$ kJ·mol^{-1}, is equal to the sum of the enthalpic increment of the ortho and meta monohydroxy substitution in the pyridinic ring $-(220.1 \pm 1.7) + -(184.1 \pm 1.8) = -(404.2 \pm 2.5)$ kJ·mol^{-1}.

4. Theoretical calculations and discussion

The most stable conformations of the six dihydroxy-pyridine isomers were obtained from density functional theory (DFT) calculations based on the Becke 3-parameter hybrid exchange [16] and Lee–Yang–Parr [17] correlation density functional (B3LYP) and the Pople's split valence 6-31G* [18] and 6-311G** [19] extended basis sets. Harmonic vibrational frequencies were then calculated at the optimum B3LYP/6-31G* conformations.

These harmonic vibrational frequencies, after scaling by the factor 0.9614 [20] were used to obtain estimates of the thermal factors at $T = 298.15$ K properly corrected for the anharmocity. More accurate energies were also obtained from single-point calculations at the most stable B3LYP/6-311G** geometries, using the triple-zeta correlation consistent basis set, cc-pVTZ [21].

The obtained electronic energies for all isomers are given in table 2. All calculations were performed using the UK version of GAMESS [22,23].

The hydroxyl group is found to be coplanar with the aromatic pyridinic ring in the most stable conformations of all dihydroxypyridine systems, as found for the monosubstituted hydroxypyridine isomers [2]. This fact is a clear indication of the existence of electronic delocalisation from the π electron donor hydroxyl groups to the π electron deficient pyridinic ring and consequent energetic stabilization. The importance of the extended electronic delocalisation from the hydroxyl groups at the ortho and meta positions to the pyridinic ring is evident from the predicted C–O bond lengths, 0.135 to 0.136 nm, which are smaller than the one found when the hydroxyl group is at the meta position 0.137 nm. This last value is equal to the one in the phenol molecule. We can also observe that for the ortho and meta substituted isomers the hydrogen atom of the hydroxyl group is found to be oriented cis relative to the nitrogen atom of the ring, a fact which possibly facilitates the occurrence of further stabilizing interactions by intramolecular hydrogen bonds of the type O-H···N. It is also observed that for the dihydroxypyridines where the hydroxyl groups are adjacent to each other (2,3- and 3,4-) the hydrogen atom of the second hydroxyl group is oriented cis relative to the first hydroxyl group (O-H···O). As can be seen from the electronic energies in table 2 the most

TABLE 2
Calculated total energies (Hartree) at the optimum B3LYP/6-311G** geometries and thermal corrections to $T = 298.15$ K

Compound	B3LYP/6-311G**	B3LYP/cc-pVTZ	ZP(B3LYP/6-31G*)	Total(B3LYP/6-31G*)[a]
Py	−248.349880	−248.377418	224.72	236.30
2,3-DOHPy	−398.853824	−398.898533	246.73	264.01
2,4-DOHPy	−398.857033	−398.902189	247.15	264.21
2,5-DOHPy	−398.849222	−398.894309	245.99	264.44
2,6-DOHPy	−398.867408	−398.912092	247.80	264.66
3,4-DOHPy	−398.840858	−398.885980	245.68	263.53
3,5-DOHPy	−398.837036	−398.882761	244.99	262.68
Benzene	−232.311523	−232.337553	254.22	266.14
Phenol	−307.555586	−307.590749	264.45	279.44
Methane	−40.534250	−40.538814	114.11	121.65
Methanol	−115.758691	−115.773731	129.89	138.62

[a] $E_{total}(T = 298.15 \text{ K}) = E_{trans} + E_{rot} + E_{ZP} + \Delta_{0 \text{ K}}^{298.15 \text{ K}} E_{vib}$.

stable dihydroxypyridine isomer is 2,6- and the least stable is 3,5-.

In order to obtain estimates of the enthalpies of formation for the dihydroxypyridine isomers not studied experimentally, we have considered two different types of isodesmic reactions:

$$C_5H_5NO_2 + 2CH_4 \rightarrow C_5H_5N + 2CH_3OH \quad (3)$$

$$C_5H_5NO_2 + 2C_6H_6 \rightarrow C_5H_5N + 2C_6H_5OH \quad (4)$$

whose energy variations represent the stabilizing effect of the hydroxyl group on the pyridine, relative to its effect on the stability of methane and benzene, respectively. From the calculated reaction enthalpies, at $T = 298.15$ K (table 3), and the known experimental enthalpies of formation of pyridine (140.4 ± 0.7) kJ · mol^{-1}, methane $-(74.4 \pm 0.4)$ kJ · mol^{-1}, methanol $-(201.5 \pm 0.2)$ kJ · mol^{-1}, benzene (82.6 ± 0.7) kJ · mol^{-1}, and phenol $-(96.4 \pm 0.9)$ kJ · mol^{-1} (values taken from reference [24]) estimates of the enthalpies of formation for all dihydroxypyridine isomers were obtained. These are shown in table 4 under the headings reactions (3) and (4). The theoretical estimates obtained from these two types of reactions are in very good agreement with the experimental observed one, the largest

TABLE 4
Theoretical standard molar enthalpies of formation of the dihydroxy-pyridine isomers, at $T = 298.15$ K

	Reaction (3)		Reaction (4)	
	$\Delta_f H_m^\circ$		$\Delta_f H_m^\circ$	
	kJ · mol^{-1}		kJ · mol^{-1}	
	6-311G**	cc-pVTZ	6-311G**	cc-pVTZ
2-OHPy[a]	−79.7	−74.6	−78.6	−77.1
3-OHPy[a]	−40.2	−36.4	−37.5	−37.2
4-OHPy[a]	−49.4	−45.7	−46.6	−46.5
2,3-DOHPy	−264.6	−254.7	−258.0	−255.1
2,4-DOHPy	−272.8	−264.1	−266.2	−264.5
2,5-DOHPy	−253.1	−44.1	−246.5	−244.6
2,6-DOHPy	−299.6	−289.6	−293.0	−290.1
3,4-DOHPy	−231.0	−222.2	−224.4	−222.7
3,5-DOHPy	−221.9	−214.6	−215.3	−215.1

[a] From reference [2].

error obtained being of only about 9 kJ · mol^{-1}. We can see from the data presented in table 3 for the mono- and dihydroxypyridines that the theoretical DFT calculations also predict an additive scheme of enthalpic increments for the disubstitution of pyridine.

Acknowledgements

TABLE 3
Theoretical standard molar enthalpies of reaction, at $T = 298.15$ K

	Reaction (3)		Reaction (4)	
	$\Delta_r H_m^\circ(T = 298.15K)$		$\Delta_r H_m^\circ(T = 298.15K)$	
	kJ · mol^{-1}		kJ · mol^{-1}	
	6-311G**	cc-pVTZ	6-311G**	cc-pVTZ
2-OHPy[a]	94.9	89.9	39.7	38.2
3-OHPy[a]	53.7	49.9	−1.5	−1.7
4-OHPy[a]	63.0	59.3	7.8	7.7
2,3-DOHPy	150.8	140.9	40.4	37.5
2,4-DOHPy	159.0	150.3	48.6	46.9
2,5-DOHPy	139.3	130.3	28.9	27.0
2,6-DOHPy	185.8	175.8	75.4	72.5
3,4-DOHPy	117.2	108.4	6.8	5.1
3,5-DOHPy	108.1	100.8	−2.3	−2.5

[a] From reference [2].

References

[1] M.A.V. Ribeiro da Silva, V.M.F. Morais, M.A.R. Matos, C.M.A. Rio, M.S. Miranda, J. Phys. Chem. A 104 (2000) 6644–6648.
[2] M.D.M.C. Ribeiro da Silva, M.A.R. Matos, M.S. Miranda, V.M.F. Morais, W.E. Acree Jr., J. Chem. Thermodyn. 36 (2004) 107–113.
[3] J.E. Del Bene, J. Am. Chem. Soc. 101 (1979) 6184–6189.
[4] P. Beak, F.S. Fry Jr., J. Lee, F. Steele, J. Am. Chem. Soc. 98 (1976) 171–179;

M.J. Cook, S. El-Abbady, A.R. Katritzky, C. Guimon, G. Pfister-Guillouzo, J. Chem. Soc., Perkin Trans. II 13 (1977) 1652–1656.

[5] M.D.M.C. Ribeiro da Silva, M.A.V. Ribeiro da Silva, G. Pilcher, J. Chem. Thermodyn. 16 (1984) 1149–1155.

[6] M.A.V. Ribeiro da Silva, M.D.M.C. Ribeiro da Silva, G. Pilcher, Rev. Port. Quím. 26 (1984) 163–172.

[7] J. Coops, R.S. Jessup, K. Van Nes, in: F.D. Rossini (Ed.), Experimental Thermochemistry, vol. 1, Interscience, New York, 1956 (Chapter 3).

[8] D.D. Wagman, W.H. Evans, V.B. Parker, R.H. Schumm, I. Halow, S.M. Bailey, K.L. Churney, R.L. Nutall, J. Phys. Chem. Ref. Data 11 (Suppl. 2) (1982).

[9] W.N. Hubbard, D.W. Scott, G. Waddington, in: F.D. Rossini (Ed.), Experimental Thermochemistry, vol. 1, Interscience, New York, 1956 (Chapter 5).

[10] F.A. Adedeji, D.L.S. Brown, J.A. Connor, M. Leung, M.I. Paz-Andrade, H.A. Skinner, J. Organomet. Chem. 97 (1975) 221–228.

[11] D.R. Stull, E.F. Westrum Jr., G.C. Sinke, The Chemical Thermodynamics of Organic Compounds, Wiley, New York, 1969.

[12] J.S. Chickos, W.E. Acree Jr., J. Phys. Chem. Ref. Data 31 (2002) 537–698.

[13] T.B. Coplen, J. Phys. Chem. Ref. Data 30 (2001) 701–712.

[14] F.D. Rossini, in: F.D. Rossini (Ed.), Experimental Thermochemistry, vol. 1, Interscience, New York, 1956 (Chapter14).

[15] CODATA, J. Chem. Thermodyn. 10 (1978) 903-906.

[16] A.D. Becke, J. Chem. Phys. 98 (1993) 5648–5652.

[17] C.T. Lee, W.T. Yang, R.G. Parr, Phys. Rev. B 37 (1988) 785–789.

[18] P.C. Hariharan, J.A. Pople, Chem. Phys. Lett. 16 (1972) 217–219;
M.M. Francl, W.J. Pietro, W.J. Hehre, J.S. Binkley, M.S. Gordon, D.J. DeFrees, J.A. Pople, J. Chem. Phys. 77 (1982) 3654–3665.

[19] P.C. Hariharan, J.A. Pople, Theoret. Chim. Acta 28 (1973) 213–222;
M.J. Frisch, J.A. Pople, J.S. Binkley, J. Chem. Phys. 80 (1984) 3265–3269.

[20] A.P. Scott, L. Radom, J. Phys. Chem. 100 (1996) 16502–16513.

[21] T.H. Dunning Jr., J. Chem. Phys. 90 (1989) 1007–1023;
D.E. Woon, T.H. Dunning Jr., J. Chem. Phys. 98 (1993) 1358–1371;
D.E. Woon, T.H. Dunning Jr., J. Chem. Phys. 100 (1994) 2975–2988;
A.K. Wilson, D.E. Woon, K.A. Peterson, T.H. Dunning Jr., J. Chem. Phys. 110 (1999) 7667–7676.

[22] GAMESS-UK is a package of ab initio programs written by M.F. Guest, J.H. van Lenthe, J.Kendrick, K. Schoffel, and P. Sherwood, with contributions from R.D. Amos, R.J. Buenker, H.J.J. van Dam, M. Dupuis, N.C. Handy, I.H. Hillier, P.J. Knowles, V. Bonacic-Koutecky, W. von Niessen, R.J. Harrison, A.P. Rendell, V.R. Saunders, A.J. Stone, A.H. de Vries. The package is derived from the original GAMESS code due to M. Dupuis, D. Spangler and J. Wendoloski, NRCC Software Catalog, Vol. 1, Program No. QG01 (GAMESS), 1980.

[23] The initial DFT module within GAMESS-UK was developed by Dr. P. Young under the auspices of EPSRC's Collaborative Computacional Project No. 1 (CCP1) (1995–1997). Subsequent developments have been undertaken by staff at the Daresbury Laboratory.

[24] J.B. Pedley, Thermochemical Data and Structures of Organic Compounds, vol. I, Thermodynamics Research Center, College Station, TX, USA, 1994.

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