Available online at www.sciencedirect.com
SCIENCE DIRECT®
J. Chem. Thermodynamics 37 (2005) 1312–1317
JCT
www.elsevier.com/locate/jct

Thermochemical studies of 1-hydroxyisoquinoline, 5-hydroxyisoquinoline and 1,5-dihydroxyisoquinoline

Manuel A.V. Ribeiro da Silva *, Maria Agostinha R. Matos, Luísa M.P.F. Amaral

Centro de Investigação em Química, Department of Chemistry, Faculty of Science, University of Porto, Rua do Campo Alegre, 687, P-4169-007 Porto, Portugal

Received 3 March 2005; received in revised form 9 March 2005; accepted 9 March 2005
Available online 24 May 2005

Abstract

The standard (p° = 0.1 MPa) molar enthalpies of formation, $\Delta_f H^\circ_m$, for crystalline 1-hydroxyisoquinoline, 5-hydroxyisoquinoline and 1,5-diidroxyisoquinoline, were derived from the standard molar enthalpies of combustion, in oxygen, at the temperature 298.15 K, measured by static bomb-combustion calorimetry. The standard molar enthalpies of sublimation, $\Delta^g_{cr} H^\circ_m$, at T = 298.15 K, were determined by Calvet microcalorimetry. The results were as follows:

	$-\Delta_c H^\circ_m(cr)/kJ \cdot mol^{-1}$	$\Delta^g_{cr} H^\circ_m/kJ \cdot mol^{-1}$
1-Hydroxyisoquinoline	4395.1 ± 1.5	113.6 ± 2.2
5-Hydroxyisoquinoline	4455.2 ± 1.9	109.6 ± 2.1
1,5-Dihydroxyisoquinoline	4194.1 ± 2.2	123.6 ± 2.2

The derived standard molar enthalpies of formation, in the gaseous state, are analysed in terms of enthalpic increments and interpreted in terms of molecular structure.

Keywords: Standard molar enthalpy of formation; Standard molar enthalpy of sublimation; Combustion calorimetry; Hydroxyisoquinolines

1. Introduction

Nitrogen heterocycle compounds are important part of the chemical structures of many natural products with a large number and variety of applications and a wide range of properties from medical to toxic effects. Among them, quinoline and isoquinoline alkaloids are a heterogeneous group of alkaloids with known toxicity to humans and domestic animals. They are found in plants from a wide group of genera. Among the plants containing quinoline alkaloids, the most significant human toxins are to be found in the *Laburnum* tree and in the mescal bean which is the seed of a small tree from the *Sophora* species: cystisine, the alkaloid common to these plants, has nicotine like effects on the gastrointestinal (GI) tract and the central nervous system (CNS).

Isoquinoline alkaloids are found in varying quantities in the prickly poppy, bloodroot and celandine poppy. The isoquinoline alkaloids papaverine, sanguinarine, protoverine and chelidonine are GI tract irritants and CNS stimulants. Many of these alkaloid plants have varying degrees of neurological effects, ranging from relaxation and euphoria to seizures; they also cause vasodilatation. Many of these plants have been used in

* Corresponding author. Tel.: +351 22 6082821; fax: +351 22 6082822.
E-mail address: risilva@fc.up.pt (M.A.V. Ribeiro da Silva).

0021-9614/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jct.2005.03.009

herbal preparations: scotch broom is smoked for relaxation and has mild sedative–hypnotic effects; prickly poppy is smoked as a euphoriant; mescal bean is a hallucinogenic, which is used in Native American rituals and medicinally. *Sanguinaria* species (bloodroot) extract is used commercially as a dental plaque inhibitor. Papaverine, found in prickly poppy and bloodroot has been used medically as a smooth muscle relaxant. Prickly poppy extracts act as a capillary dilators and have been implicated in epidemic glaucoma in India. Celandine extracts are used as treatment of gastric and biliary disorders, but they may also cause dermatitis and have been implicated in cases of acute hepatitis. Ingestion of poppies may result in narcotic effects from opiate alkaloids and papaverine, as well as hypotension and cardiovascular collapse.

As a group, the isoquinolines have proven to be more poisonous to the domestic livestock than to humans. Interestingly, some domestic species tolerate ingestion of isoquinoline and other alkaloids, and humans can ingest toxic alkaloids from the milk of poisoned animal and manifest symptoms.

Examples of hydroxyisoquinoline alkaloids are codeine and morphine, both with medical application, and heroin most known as a drug.

We have already studied, in our laboratory, several substituted quinoline [1–4] and pyridines [5,6], in order to look for the possibility of establishing a similar estimation scheme to the one developed by Cox [7] for benzene derivatives. In order to see if the same scheme can be applied to isoquinolines, we extended our thermochemical studies to three hydroxyisoquinolines, namely 1-hydroxyisoquinoline [491-30-5], 5-hydroxyisoquinoline [2439-04-5] and 1,5-dihydroxyisoquinoline [5154-02-9], whose structural formulae are represented in figure 1.

This paper reports the standard ($p^\circ = 0.1$ MPa) molar enthalpies of combustion, $\Delta_c H^\circ_m$ in oxygen at $T = 298.15$ K, determined by static-bomb calorimetry, as well as their standard molar enthalpies of sublimation measured by Calvet microcalorimetry, at the same temperature. The derived values of the standard molar enthalpies of formation for the compounds in the gaseous state are analysed in terms of enthalpic increments due to the entrance of the hydroxy group into the isoquinoline rings.

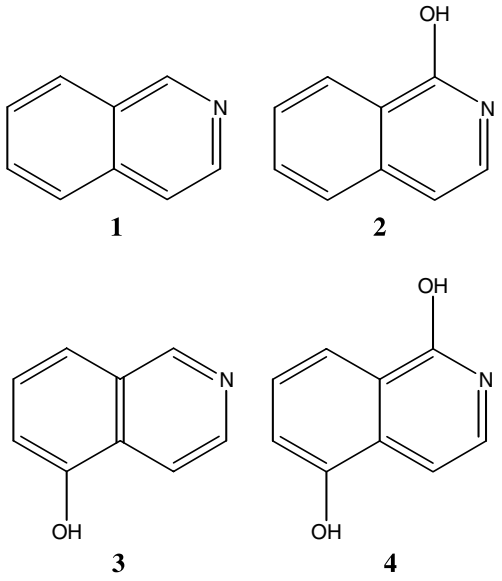

FIGURE 1. Structural formula for isoquinoline (**1**), 1-hydroxyisoquinoline (**2**), 5-hydroxyisoquinoline (**3**) and 1,5-dihydroxyisoquinoline (**4**).

2. Experimental

2.1. Compounds and purity control

The compounds, obtained commercially from Aldrich Chemical Co., were purified by vacuum sublimation until the combustion results were consistent and the carbon-dioxide recovery ratios were satisfactory. The average ratios, together with the standard deviations of the mean, of the mass of carbon dioxide recovered to that calculated from the mass of sample were: 1-hydroxyisoquinoline, (1.0002 ± 0.0002); 5-hydroxyisoquinoline (1.0002 ± 0.0002); 1,5-dihydroxyisoquinoline (0.9996 ± 0.0006), where the uncertainties are the standard deviations of the mean. The combustion experiments were performed with an isoperibolic static-bomb calorimeter; apparatus and technique have been described [8,9].

2.2. Combustion calorimetry

Benzoic acid (Bureau of Analysed Samples, Thermochemical Standard CRM-190p) was used for calibration of the bomb. Its massic energy of combustion, under standard bomb conditions, is $-(26431.8 \pm 3.7)\ \mathrm{J \cdot g^{-1}}$. The calibration results were corrected to give the energy equivalent ε_{calor} corresponding to the average mass of water added to the calorimeter: 3119.6 g. The energy equivalent of the calorimeter was determined, by other investigator [10], as $\varepsilon_{calor} = (16010.5 \pm 2.3)\ \mathrm{J \cdot K^{-1}}$, where the uncertainty quoted is the standard deviation of the mean. The compound, 5-hydroxyisoquinoline was studied in a different time so the value $\varepsilon_{calor} = (16015.9 \pm 0.7)\ \mathrm{J \cdot K^{-1}}$ [11] was used. For all experiments, ignition was made at $T = (298.150 \pm 0.001)$ K. Combustion experiments were made in oxygen at the pressure 3.04 MPa, with a volume 1 $\mathrm{cm^3}$ of water added to the bomb. The crystalline compounds were burnt in pellet form. The 1,5-dihydroxyisoquinoline (hygroscopic compound) was enclosed in polyester bags made of Melinex® (0.025 mm thickness), using the technique described by Skinner and Snelson [12], who determined the specific energy of combustion of dry