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THE ESTIMATION OF REACTION ENTHALPY FOR COMPLEX MOLECULES USING BENSON GROUPS
Comparison of different strategies

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Estimation methods developed over years by S. W. Benson and co-workers for calculation the thermodynamic properties of organic compounds in the gas phase are applied to a pharmaceutical real process with all type of non-idealities. The different strategies used to calculate the reaction enthalpy of a chemical process, in the absence of data for complex molecules, using the Benson group additivity method are presented and also compared with the experimental value of reaction enthalpy obtained using reaction calorimetry (Mettler-Toledo, RC1®). We demonstrate that there are some strategies that can be followed to obtain a good estimation of the reaction enthalpy in order to begin the safety assessment of a chemical reaction. This work is part of an industrial project [1] in which the main objective was the risk assessment of chemical real and complex processes using the commonly available tools for the SMEs (with limited resources).

***Keywords:** Benson groups, enthalpy, estimation, hazard assessment, heat of reaction, reaction calorimetry*

Introduction

In order to assess the chemical reaction hazards of a process it is necessary to have information on the heat of reaction. The heat of reaction is certainly the most important part of all the information needed to evaluate and calculate the hazards associated with the realization of a chemical reaction. Moreover, heats of reaction are used to calculate the temperature increase in a worst-case scenario, assuming loss of heat exchange with the surroundings. For example, the Maximum Temperature due to the main Synthesis Reaction (MTSR) developed by Gygax [1]. Data are usually obtained by specific calorimetric techniques including reaction calorimetry such as RC1®, ARC® or DSC.

However, for an initial assessment, it is often sufficient to use data obtained during the course of the process development together with calculated, estimated or literature data. Moreover, for various reasons, the experimental determination of reaction heats for processes is not always feasible or practical, especially in the Small and Medium Enterprises (SME). Predictive techniques are therefore a necessary part of the tools used in the assessment of overall energy release of a chemical reaction.

Theoretical background

A good initial estimate of the heat of reaction can be obtained by calculation from the heats of formation of the reactants and products using Hess's Law, thus:

$$\Delta_{\mathrm{r}} H = \sum \Delta H_{\mathrm{f\ Products}} - \sum \Delta H_{\mathrm{f\ Reactants}} \tag{1}$$

The precision of the results obtained relies on the accuracy of the heats of formation of the reactants and products and the level of completeness of the reaction, but it can be also affected by side reactions, changes of state or solution/dilution effects.

According to the literature [2, 3], the Benson method of group additivity is probably the most widely used and practical method for estimating thermodynamic data of organic species. This method estimates the heat of reaction with more precision and reliability than any other current methods available. So, this method can be used to estimate heats of formation of complex molecules for which data are usually not available. In addition, the heats of reaction can be estimated by analogous reactions using simpler species (where the heats of formation of these species can also be estimated using the Benson's method of group additivity).

This method was developed 30 years ago [4], introducing some improvements to the existing method (Average Bond Energy Summation). This method takes into account:

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- The linking envelope effect to the main group/atom
- The rings effect
- The isotopic effect (cis/trans, ortho/meta/para)
- The non-linking interactions.

The result is a more accurate method than the previous one (normally the uncertainty achieved by this method is from 9 to 13 kJ mol^{-1} for substances which contain the following atoms: C, H, N, O) [4]. On the other hand, the improved method is more complex to use and requires more data for parameterisation (due to the higher number of groups used) than the previous one. By means of this method, the gas-phase formation enthalpies of reactants and products or the reaction enthalpy can be calculated. Thus, the key point for an accurate estimation of the reaction enthalpy is the correct choice of the Benson groups to be used.

Perhaps the more widely spread computer program for the estimation of thermodynamic data and hazards assessment is CHETAH® [5], which possibly includes the most extensive available database of Benson groups. However, there are two important limitations of this method. The first one is the lack of accurate data for some organic functional groups, which are present in the complex molecules commonly used in the fine chemical industries. The second limitation is the fact that the majority of the methods for thermodynamic data estimation are only for gas species, whereas usually, the organic reactions are carried out in the condensed phase. Thus, to take full advantage of the CHETAH® computer program, some kind of strategy must be followed to get the most accurate estimation.

To show some of the possible strategies that can be followed when a necessary group is missing, we present the results obtained in the estimation of the reaction enthalpy of a real complex reaction (Scheme 1) using as a computing tool the program CHETAH® v.7.2. The accuracy of the results obtained was verified by means of Reaction Calorimetry RC1®.

$$R–OSO_2–R'+R''–SH \rightarrow R–S–R''+R'–SO_3H$$

Scheme 1 Reaction analysed

Results and discussion

For the estimation of the heat of this reaction in gas phase, all the necessary groups of Benson were not available in the current version of the computing program. In this reaction, the Benson groups which contain the molecular group SO_2, as the central group or as the 'environment' (The central group is to the left of the hyphen in the notation used in CHETAH® and the environment is to the right of the hyphen), are absent in the current literature because of the problems associated with their experimental determination [6].

The different strategies tested for the determination of the reaction enthalpy are presented below:

Strategy one

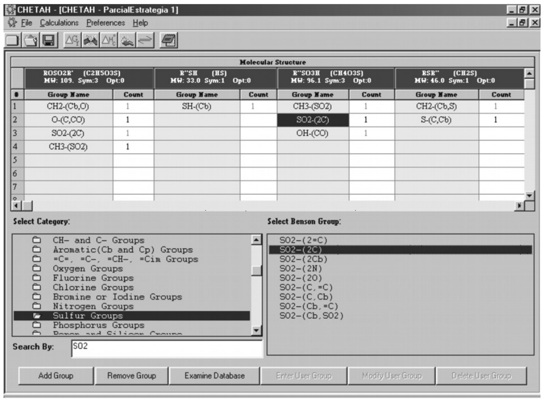
In the literature [4] it is recommended that, when dealing with an absent group, this can be substituted by another one of 'similar' nature. Substitutions in the 'environment' are allowable, but the environmental changes should be as similar as possible to the environment. Substitutions in the central group are NOT allowed in this technique.

This strategy is applied to the reaction considered as follows:

When the group SO_2 belongs to the environment, it can be replaced by the known and relatively 'similar' group CO. The absent Benson groups [O–(C,SO_2)] and [OH–(SO_2)] have to be replaced by the known groups [O–(C,CO)] and [OH–(CO)].

When the group SO_2 is the central group (which cannot be substituted), the environment groups have to be replaced by known and 'similar' Benson groups, while keeping the same central group. The absent Benson group [SO_2–(O,C)] is replaced by the known group [SO_2–(2C)]. Note that all the substitutions occur on the right-hand side of the 'dash' in the modified notation, which is the environment part of the group.

In Fig. 1 the introduction of the detailed groups of this strategy in the CHETAH® program is presented.



Molecular Structure

#	ROSO2R' (C2H5O3S) MW: 109. Sym:3 Opt:0		R"SH (HS) MW: 33.0 Sym:1 Opt:0		R"SO3H (CH4O3S) MW: 96.1 Sym:3 Opt:0		RSR" (CH2S) MW: 46.0 Sym:1 Opt:0	
#	Group Name	Count	Group Name	Count	Group Name	Count	Group Name	Count
1	CH2-(Cb,O)	1	SH-(Cb)	1	CH3-(SO2)	1	CH2-(Cb,S)	1
2	O-(C,CO)	1			SO2-(2C)	1	S-(C,Cb)	1
3	SO2-(2C)	1			OH-(CO)	1		
4	CH3-(SO2)	1						
5								
6								
7								

Search By: SO2

Fig. 1 Strategy one introduced in the CHETAH® program

Strategy two

The literature [4] also suggests that one can proceed by interpolation or extrapolation of known group values in a series of homologous groups in order to obtain a better accuracy of the estimated groups. It is important to realize that one should try to perform these operations in the 'environment'. If that fails, one can

Table 1 Estimation of SO_2–(C,O) group using strategy two

Strategy two		
SO_2–(2C)	–288	kJ mol^{-1}
SO_2–(2O)	–417	kJ mol^{-1}
Estimated group		
SO_2–(C,O)	–353	kJ mol^{-1}

interpolate in the central group, while keeping the environment constant, but with lower accuracy. Thus, interpolation or extrapolation in the environment is preferable because environmental group changes lead to values that are not very different and errors will be minimized, whereas central group changes lead to potentially larger errors.

Following this second strategy, the absent Benson group [SO_2–(O,C)] can be estimated by interpolation in the series [SO_2–(2C)] to [SO_2–(2O)] (presented in Table 1). From this value, known value of the formation enthalpy of the gas molecule ($CH_3SO_2OCH_3$), which contains the last absent Benson group [O–(SO_2,C)], and the knowledge of all the other Benson groups contained in this molecule, it is possible to estimate the value of the last absent Benson group [O–(SO_2,C)] (will be presented in Table 3, see below).

However, this strategy can only be applied if the property of bonding addition is fulfilled and, according to the literature [6], this is not the case in this example.

Strategy three

Finally, because the value of the formation enthalpy of methanesulfonic acid in the gas phase can be determined and the formation enthalpy of the compound CH_3SO_2OMe is known, it is possible to obtain the values of the necessary absent Benson groups ([SO_2–(O,C)] and [O–(SO_2,C)]) to calculate the reaction enthalpy presented in Scheme 1.

Application of this strategy to the reaction considered is as follows:

- Because the value of the formation enthalpy of $PhSO_3H$ in the gas phase is known and using the specific relation shown in Eq. 2 [6] (specific for a group SO_2 linked to benzene), it is possible to obtain the formation enthalpy in the gas phase of methanesulfonic acid.

$$\Delta H_f(g,CH_3SO_3H)=\Delta H_f(g,PhSO_3H)-127.1\ kJ\ mol^{-1} \quad (2)$$

- From this value and the knowledge of all the other groups which form this molecule (extracted from CHETAH®), it is possible to obtain the value of the unknown Benson group [SO_2–(C,O)] (presented in Table 2).

Table 2 Estimation of SO_2–(C,O) group using strategy three

Strategy three		
AHf (g, $PhSO_3H$)	–376	kJ mol^{-1}
Estimation using Eq. (2)		
AHf (g, $MeSO_3H$)	–503	kJ mol^{-1}
Known groups		
CH_3–(SO_2)	–42	kJ mol^{-1}
HO–(SO_2)	–159	kJ mol^{-1}
Estimated group		
SO_2–(C,O)	–302	kJ mol^{-1}

- Finally, from this value and the formation enthalpy of CH_3SO_2OMe it is possible to determine the last unknown group [O–(SO_2,C)] (presented in Table 3).

All these values of the Benson groups can be used to calculate the formation enthalpies in the gas phase of the reactants and products. Furthermore, these formation enthalpies can be used to calculate the reaction enthalpy (also in the gas phase) using Hess law (Eq.(1).

The values of the reaction enthalpy in the gas phase are corrected to obtain data under real process conditions, which is not described here [7]. These values (Table 4) are compared with the experimental value of the reaction enthalpy (–133±5%) obtained using reaction calorimetry (Mettler-Toledo, RC1®).

The analysis of the results presented in Table 4, show that strategy one generates a good approxima-

Table 3 Estimation of O–(SO_2,C) group using strategy two and three

Estimation of group O–(SO_2,C)			
AHf (lq, CH_3SO_2OMe)	–564		kJ mol^{-1}
AHvap (CH_3SO_3H)	89		kJ mol^{-1}
Estimation			
AHf (g, CH_3SO_2OMe)	–475		kJ mol^{-1}
Known groups	Str. 2	Str. 3	
CH_3–(SO_2)	–42	–42	kJ mol^{-1}
CH_3–(O)	–42	–42	kJ mol^{-1}
SO_2–(C,O)	–353	–302	kJ mol^{-1}
Estimated group			
O–(SO_2,C)	–38	–88	kJ mol^{-1}

Table 4 Results obtained. (a) Referred to mol of limiting reactant

Strategy	Reaction enthalpy/ kJ $mol^{-1(a)}$	Estimation error/%
one	–124	6.8
two	–182	37
three	–131.4	0.8

tion to the experimental value (only 7% error), which is satisfactory for preceding the next steps of the preliminary evaluation process of the reaction hazards. The accuracy of this estimate could come from the use of a similar functional group and the reliability of the data used to make this estimate. Strategy two generates an erroneous result (37% error), but at least it is an error by excess so the results obtained would be conservative. This error could come from the application of one of the estimation rules, which cannot be done in this case, as it is suggested in the literature [6]. Strategy three generates the most precise data (1% error). The low error is probably due to the reliability of the data used and the fact that, in this strategy, the central group remains constant. However, if the results obtained for the gas-phase reaction enthalpy were not corrected by the change of phase enthalpies, the error obtained would be greater (for example for strategy three the error would be around 80%).

Conclusions

When estimating a heat of reaction using the Benson's method, there are different strategies that can be followed when one or various Benson's groups are absent.

The proposed strategies applied with the Benson's group additivity method generate quite good data for the calculation of the heat of reaction.

The choice of an erroneous strategy, or an error in the correction of the data obtained with the Benson groups in the gas phase could generate erroneous results. The method has to be selected taking into account the reliability of the available data, the reaction and the available means.

References

1 Gygax, R., ISCRE 10th. Chemical Enginering Science, 43 (1988) 1759.
2 HarsBook, A technical guide for the assessment of highly reactive chemical systems, Nomen, R. (coordinator), Dechema, Frankfurt 2003 (ISBN 3-89 746-037-8), available at the HarsNet website or Chapter 2, 2001.
3 E. Domalski and E. D. Hearing, Estimation of the thermodynamic properties of carbon-hydrogen-nitrogen-oxygen-sulfur-halogen compounds at 298.15 K. Journal of Physical and Chemical Reference Data (1993), 22(4), 805-1159 (ISSN: 0047-2689).
4 D. J. Frurip, *et al*, Determination of Chemical Process Heats by Experiment and Prediction, International Symposium on Runaway Reactions and Pressure Relief Design, CCPPS/AICHE (ISBN 0-816669-0676-9), 95–149.
5 CHETAH 7.2, The ASTM Computer Program for Chemical Thermodynamic and Energy Release Evaluation; Prepared by ASTM E27.07 (NIST Special Database 16), 1998.
6 J. F. Liebman, In The Chemistry of Sulfonic Acids, Esters and Their Derivates; S. Patai and Z. Rappoport, Eds John Wiley & Sons Ltd. 1991, Chapter 8, 283-320.
7 X. Romero, 'Aplicació de HarsMeth v. 2.0 a procés Farmacèutic', IQS End of studies Project, Institut Quimic de Sarrià, Barcelona (2003).

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