On the question of the correlation between kinetic Dimroth parameters and global electron density transfer in [4+2]-π-electron cycloaddition reactions

Karolina Kula[a*], Agnieszka Łapczuk[a], Przemysław Woliński[a] and Mikołaj Sadowski[a]

[a]Department of Organic Chemistry and Technology, Cracow University of Technology, Warszawska 24, 31-155 Cracow, Poland

| C H R O N I C L E	A B S T R A C T
	The correlation between coefficients from Dimroth equations and descriptors of global electron density transfer was explored based on the data available in the recent literature. We established that the obtained results should be very usable for the interpretation of the organic reactivity and molecular mechanisms.

1. Introduction

Cycloaddition processes are the most universal way for the preparation of many, different-type of carbo- and heterocyclic skeletons [1–5]. Mechanistic aspects of the [4+2]-p-electron cycloaddition reactions (with special participations of (3+2) and (4+2) processes) still pay the great attention of many scientists [6–10]. Even a few decades ago, the dogma about the concerted reorganization of the electron density, and synchronous formation of new sigma-bonds was treated as the most important fundament of the cycloaddition theory [11]. This view was however rapidly undermined after historical publications by Huisgen and Mloston at the 1986 [12,13]. At this moment, the general classification of cycloaddition mechanisms include two areas: polar and non-polar processes [9]. Within the first group, several scenarios are possible, such as polar, synchronous mechanisms, polar asynchronous (one step – two stage) mechanisms and stepwise mechanisms with the zwitterionic intermediate [14–17]. Alternatively, non-polar cycloadditions can be classified as polar, synchronous, non-polar asynchronous (biradicaloid) mechanisms and stepwise mechanisms with the biradical intermediate [18–20].

For the interpretation of mechanistic aspects of cycloaddition processes, different type theoretical and experimental, kinetic techniques are dedicated. In the framework we decided to do a short analysis of possible correlation between experimentally obtained reaction constants in the Dimroth equations [21–23] and theoretically calculated values of the global electron density transfer[24]. Dimroth constant E_T is a parameter characterizing polarity of the solvent. It is based on pyridinium N-phenolbetaine **X** as a test substance owing to a significant displacement of a solvatochromic band. Value of the E_T can be calculated using equation (1), which is the frequency of the absorption maximum in cm^{-1} in the examined solvent.

$$E_T = 2.859 \cdot 10^{-3} \cdot \tilde{v} \left[\frac{kcal}{mol}\right]$$

* Corresponding author
 E-mail address: karolina.kula@pk.edu.pl (K. Kula)
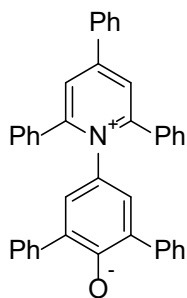
Global Electron Density Transfer (GEDT) during transition state is a good measure of the polar character of reaction [25]. GEDT takes place from nucleophile to electrophile, and can be obtained by sum of natural atomic charges of nucleophile fragments calculated through a natural population analysis (NPA)[26,27].

2. Results and discussion

Although, evidently most recent publications include the analysis of the solvent effects based on DFT computational results [28–31], in the literature are available some examples of experimental, kinetic study in this area. These results are especially interesting for the processes with the participation of NO_2-activated components [32,33]. So, the (3+2) cycloaddition with the participation of the nitrone – fluorenone derivative (**1**) as the TAC and E-3,3,3-trichloro-1-nitroprop-1-ene (**2**) is realized at the r.t and is realized with full selectivity yielded respective 4-nitroisoxazolidine with almost quantitatively yield [34,35]. The kinetic study regarding this transformation includes the analysis of the influence of the polarity solvent on the rate constants, as well as the estimation of activation enthalpy and entropy.
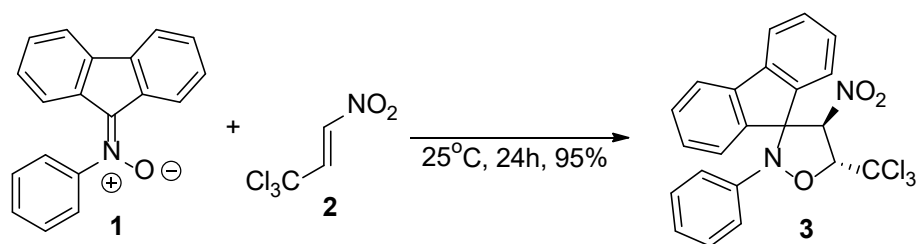

The similar package of kinetic measurements were collected for the (4+2) cycloaddition reaction between cyclopentadiene (**4**) and E-2-phenylnitroethene (**5**) [36]. In this case, the substituent effect was also experimentally evaluated for analogous reaction with the participation of other 2-arylnitroethenes.
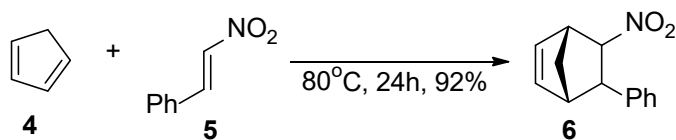
The next example of the comprehensive kinetic study is a cycloaddition of Z-C,N-diphenylnitrone (**7**) with mentioned above 3,3,3-trichloro-1-nitroprop-1-ene [37].
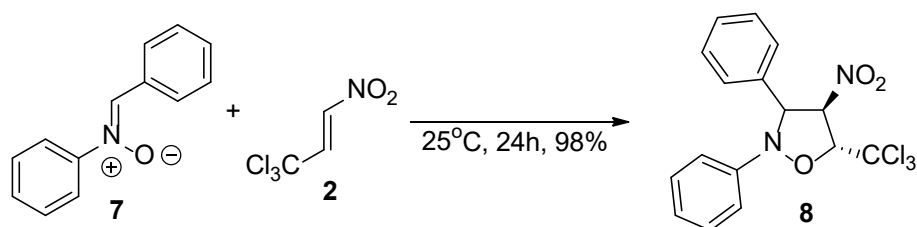
The seme nitrone was also tested as a component of the (3+2] cycloaddition to the gem-chloronitroethene (**9**) [38]. In this case, next to solvent effects, the substituent effects and the activation parameters were also estimated.
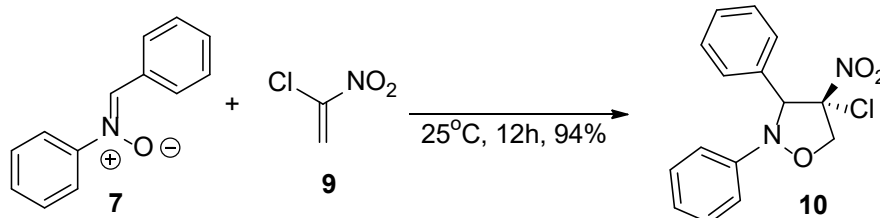
Lastly, in the recent literature, the kinetic study on the hetero Diels-Alder reaction of E-2-(4-carbomethoxyphenyl)-1-cyano-1-nitroethene (**11**) and ethyl-vinyl ether (**12**) are available [39,40]. This analysis was supported by estimation of the analysis of the substituent effects and the activation parameters.

Fortunately, for all mentioned processes, respective DFT mechanistic studies are additionally performed. So, it is possible to estimate the value of the electron density transfer between substructures. These descriptors, and experimental measured constants in Dimroth correlations are collected in **Table 1.**

Table 1. Key kinetic parameters for model cycloaddition processes

Reaction	Global electron density transfer (GEDT) [e]	Coefficient in the Dimroth equation
1+2	0.18	0.008
4+5	0.21	0.009
7+2	0.21	0.011
7+9	0.32	0.031
11+12	0.40	0.049

The correlation analysis exhibits the excellent [41,42] relationship (R>0.99) between coefficients from Dimroth equations and GEDT values.

$$GEDT = 5.13*E_T + 0.15 \quad (R=0.994)$$

So, in the evaluated range of Dimroth coefficients, this relation can be treated as general and usable for the prediction of the solvent effect based on theoretical estimated GEDTs.
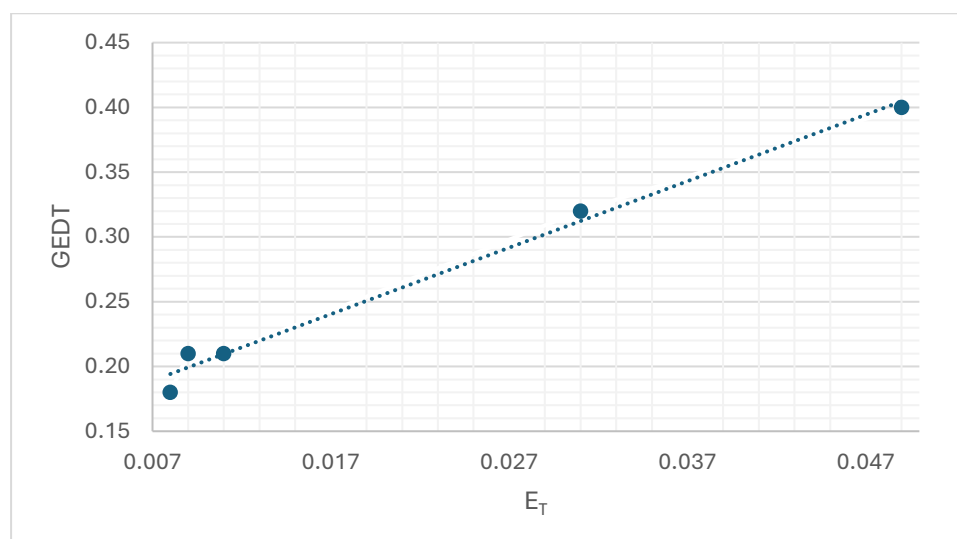

Fig. 1. The graphical illusstration of the correlation between coefficients from Dimroth equations and GEDT values.

3. Conclusion

Analysis of literature source exhibits, that independently of many theoretical works, in the recent time some valuable papers regarding the experimental kinetic studies were performed. Based on this information we decided to explore the theoretical background for the observed solvent effects. Our short analysis confirms without any doubts the existence of the correlation between coefficients from Dimroth equations and descriptors of global electron density transfer. In our opinion

this tool can be a simple and usable approach for the predictions of the organic reactivity and molecular mechanisms within cycloaddition reactions.

Grants and funding

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