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Variable Activity of Reagents with C=C and N=N Bonds in Cycloaddition Reactions

O. V. Anikin^a, D. A. Kornilov^a, T. V. Nikitina^a, and V. D. Kiselev^{a, *}

^aButlerov Institute of Chemistry, Kazan (Volga Region) Federal University, Kazan, Tatarstan, Russia

*e-mail: vkiselev.ksu@gmail.com

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Abstract—Data on rates and enthalpies of the reactions of quadricyclane (**4**) and diadamantylidene (**5**) with *N*-phenylmaleimide (**1**), 4-phenyl-1,2,4-triazoline-3,5-dione (**2**), and tetracyanoethylene (**3**) are obtained for the first time. Reagent **2** with the N=N reaction center is found to be six orders of magnitude more active than its structural analog **1**. A strong π -acceptor **3** is 370 times more active than reagent **2** in the reaction with a strong π -donor substrate **4** but is less active than reagent **2** in many $[4\pi + 2\pi]$, $[2\pi + 2\pi + 2\pi]$, and $[2\pi + 2\pi]$ cycloaddition reactions, and, especially, in ene reactions. The possible causes of the strong difference and variable activity of compounds **1–3** with C=C and N=N bonds are discussed.

Keywords: reaction rate, enthalpy of reaction, cycloaddition reactions, ene reactions

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INTRODUCTION

There is keen interest in cycloaddition reactions, as they have a broad synthetic potential [1]. Furthermore, intense attention is paid to these reactions, and in particular to the Diels–Alder reaction, because these reactions occur in a quantitative yield and the data on the effect of various factors on their rates and equilibrium are reliable [2]. It has been demonstrated for a wide range of dienes and dienophiles with the C=C reaction centers that the rate of the Diels–Alder reaction ($\log(k_2, k_2/L \text{ mol}^{-1} \text{ s}^{-1})$) depends on the ionization potential (IP_D , eV) of a diene, electron affinity energy (E_A , eV) of a dienophile, the balance between the energy of bond rupture and formation (ΔH_{r-n} , kJ mol⁻¹), and the distance between the reaction centers **1–4** (see below) in a diene ($R_{C(1)-C(4)}$, Å) [2]:

$$\log k_2 = -28.81 + \frac{316.3}{IP_D - E_A} - \frac{69.9R_{C(1)-C(4)}}{IP_D - E_A} - 0.054\Delta H_{r-n}$$

This relationship permits the prediction of the rate of Diels–Alder reactions involving those C=C bonds that have not been studied yet and planning of the experimental conditions. However, the rate of Diels–Alder reactions involving N=N bonds is not described by this equation. Thus, activity of *N*-phenyl maleimide (**1**) with the C=C reaction center in Diels–Alder reactions with different dienes is five to six orders of magnitude lower than that of its structural analog, 4-phenyl-1,2,4-triazoline-3,5-dione (**2**) with the N=N reaction

center, although their E_A values are close (~ 1 eV) [2, 3]. Furthermore, in the Diels–Alder reactions with dienes having weak π -donating properties, the reaction rate of even tetracyanoethylene (**3**), one of the strongest π -acceptors ($E_A = 2.88$ eV [4]) and the most active dienophiles with the C=C reaction center, is usually lower than that of dienophile **2** [2, 3]. However, dienophile **3** was found to be more active than dienophile **2** in the Diels–Alder reaction with strong π -donating dienes, such as substituted anthracenes ($IP_D = 7.0–7.5$ eV) [3, 5].

In order to obtain novel data for the reactions involving the C=C and N=N bonds, we studied the kinetics and calorimetric parameters of the reactions of $[2\pi + 2\sigma + 2\sigma]$ cycloaddition of **1–3** to reagent **4** and $[2\pi + 2\pi]$ cycloaddition to reagent **5** (Fig. 1). The findings were compared to the results for the $[2\pi + 2\pi + 2\pi]$ and $[4\pi + 2\pi]$ cycloaddition reactions and ene reactions between reagents **1–3** and substrates **6–11** (Fig. 2).

EXPERIMENTAL

Quadricyclane was synthesized using the procedure described in [6], dried over sodium, and recondensed at lower pressure (600 Pa). Quadricyclane purity was determined by volumetric titration of the reagent with a bright red tetracyanoethylene solution in toluene, since the reaction between reagents **3** and **4** (hereafter, reaction **3 + 4**) occurs very rapidly and is seven orders of magnitude faster than reaction **3 + 6**. The titration results demonstrate that purity of the reagent **4** is $97 \pm 0.5\%$. Diadamantylidene was synthe-

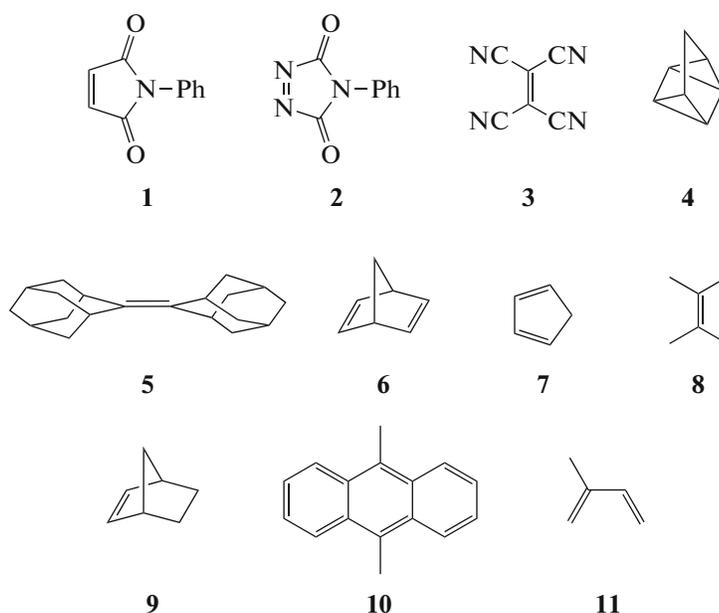


Fig. 1. Reagents in the cycloaddition and ene reactions.

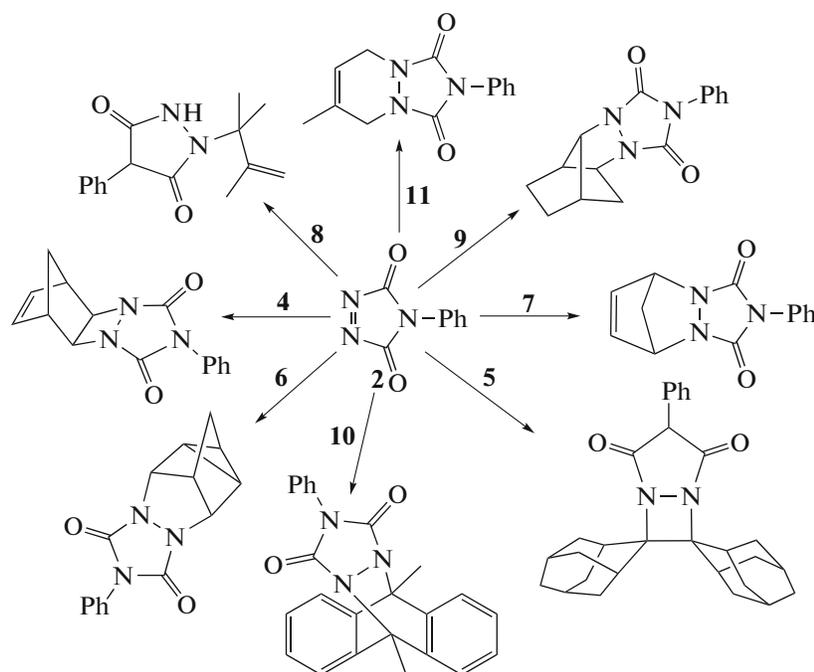


Fig. 2. Cycloaddition reactions: $[2\pi + 2\sigma + 2\sigma]$ ($2 + 4$), $[2\pi + 2\pi + 2\pi]$ ($2 + 6$), $[4\pi + 2\pi]$ ($2 + 7$, $2 + 10$, and $2 + 11$), $[2\pi + 2\pi]$ ($2 + 5$), the ene reaction ($2 + 8$), and the ene reaction with the Wagner–Meerwein rearrangement ($2 + 9$).

sized [7] from adamantanone, recrystallized from ethanol, and purified using a column packed with alumina, with hexane used as an eluent. The melting point of this compound T_{melt} is 181–183°C (according to the data reported in [7], $T_{\text{melt}} = 180–183^\circ\text{C}$). Tetracyanoethylene (Aldrich, 97%) and 4-phenyl-1,2,4-triazoline-3,5-dione (Aldrich, 97%) were purified by

sublimation (100°C, 100 Pa); T_{melt} of reagent 3 was 200–201°C (according to the data reported in [8], $T_{\text{melt}} = 201^\circ\text{C}$). Reagent 2 undergoes incongruent melting at 165–170°C (according to the data reported in [9], the incongruent melting point is 165–170°C). Imide 1 (Aldrich, 99%) was used without additional purification. The ^1H and ^{13}C NMR spectra of the

Table 1. The rate constants (k_2 , L mol⁻¹ s⁻¹) and enthalpies (ΔH_{r-n} , kJ mol⁻¹) of the cycloaddition and ene reactions at 25°C

Reaction	k_2	$-\Delta H_{r-n}$	Reaction	k_2	$-\Delta H_{r-n}$
[2 π + 2 σ + 2 σ]			[2 π + 2 π]		
4 + 1	3.70×10^{-7a}	— ^c	5 + 1	— ^c	— ^c
4 + 2	2.82×10^{-1b}	255 ^d	5 + 2	1.75×10^{-2b}	86 ^d
4 + 3	1.04×10^{2b}	236 ^d	5 + 3	— ^c	— ^c
[2 π + 2 π + 2 π] ^e			[ene] ^g		
6 + 1	— ^c	— ^c	8 + 1	— ^c	— ^c
6 + 2	3.95×10^{-3}	218	8 + 2	3.35×10^{2d}	150 ^d
6 + 3	1.30×10^{-5}	180	8 + 3	— ^c	— ^c
[4 π + 2 π] ^f			[ene] ^h		
7 + 1	8.70×10^{-2}	129	9 + 1	— ^c	— ^c
7 + 2	1.60×10^5	134	9 + 2	1.28×10^{-4}	170
7 + 3	4.78×10^2	113	9 + 3	— ^c	— ^c
[4 π + 2 π] ^f			[4 π +2 π] ^e		
10 + 1	3.0×10^{-2}	117	11 + 1	1.5×10^{-4i}	182 ⁱ
10 + 2	1.2×10^4	118	11 + 2	46	170
10 + 3	8.9×10^4	88	11 + 3	7.4×10^{-2}	166

^aIn quadricyclane. ^bIn toluene. ^cThe reaction rate is extremely low. ^dIn 1,2-dichloroethane. ^eAccording to data reported in [3]. ^fAccording to data reported in [2, 3, 5]. ^gAccording to the data reported in [19]. ^hEne reaction with the Wagner–Meerwein rearrangement [20]. ⁱFor the reaction with maleic anhydride [3].

adducts obtained in the reactions with reagents **4** and **5** completely coincided with the ones reported earlier [10–14]. The solvents were purified using the known procedures [15].

The rate of the fast reaction **3** + **4** was monitored according to changes in absorbance in the reagent solution using the stopped flow technique on a Cary 50 Bio spectrophotometer equipped with an RX 2000 stopped flow unit. The rates of all slower reactions were determined on a Hitachi U-2900 spectrophotometer.

The heat effects were measured using the procedure described previously [16]. Weighed samples of reagents **1**–**3** (20–30 mg each) were placed into air-proof containers whose ends were hermetically capped with Teflon septa. After temperature equilibration in the calorimeter and solutions of reagents **4** or **5**, the septa were cut off. The enthalpies of the reactions were calculated using the data obtained, with an adjustment for the heat of dissolution of reagents **1**–**3**.

RESULTS AND DISCUSSION

For reagents with the C=C bonds, there is usually symbathic dependence between changes in donor–acceptor properties of dienes and dienophiles and charge on their reaction sites. This dependence is probably not obeyed in the reagents with heteroatomic

reaction centers. We found (Table 1) that reagent **4**, which has a low ionization potential ($IP_{D4} = 7.40$ eV) and lower energy of formation ($\Delta H_{\text{form}} = 339.1$ kJ mol⁻¹) than its precursor, norbornadiene (**6**) ($IP_{D6} = 8.69$ eV, $\Delta H_{\text{form}} = 247.6$ kJ mol⁻¹ [10, 17, 18]), reacts with tetracyanoethylene (which has better π -accepting properties) 370 times faster than with 4-phenyl-1,2,4-triazoline-3,5-dione. The π -accepting properties of reagents **1** and **2** are comparable ($E_A \sim 1$ eV); however, the lower bond rupture energy of the N=N bond compared to that of C=C makes the rate constants of the reactions **2** + **4** and **1** + **4** differ by 6 orders of magnitude (Table 1). The ene reaction involving reagent **5** is forbidden according to the Bredt's rule, while the [2 π + 2 π] cycloaddition reaction **2** + **5** occurs easily in a quantitative yield. We were not able to conduct reactions **1** + **5** or **3** + **5** at room or elevated temperatures.

Formation of a strained four-membered cycle in reaction **2** + **5** is accompanied by a moderate exothermic heat effect (–86 kJ mol⁻¹). The [2 π + 2 σ + 2 σ] cycloaddition reactions involving quadricyclane are accompanied by opening of two cyclopropane rings, resulting in the highest heat effects among other known reactions (Table 1). Even higher exothermicity should be expected for the reactions involving maleimide [2]; however, the rate of the reaction between reagent **4** and a weak π -acceptor dienophile **1** turned out to be extremely low.

As it follows from the data listed in Table 1, tetracyanoethylene is more active than 4-phenyl-1,2,4-triazoline-3,5-dione only in the reactions with strong π -donors **4** and **10**. The inversion of the activity of dienophiles **2** and **3** is observed for all other reactions involving partners with moderate π -donor properties (Table 1). The Diels–Alder reaction **2** + **7** had the highest rate. It is noteworthy that reagents **1** and **3** with the C=C bonds cannot be inserted into compound **5** via the $[2\pi + 2\pi]$ cycloaddition reaction and to compounds **8** and **9** via the ene reaction.

CONCLUSIONS

The findings obtained in this study explain the drastic difference in the reactivities of dienophiles with similar acceptor properties, **1** and **2** ($E_A \sim 1$ eV). The difference in activities for all the studied reactions involving these reagents (Table 1) is controlled by the much lower rupture energy of the N=N bond than that of the C=C bond, while the contributions of intermolecular stabilization energy are small and comparable. In reactions between the compounds with strong donating properties, **4** and **10** ($IP_D = 7.40$ and 7.04 eV, respectively) and a strong acceptor tetracyanoethylene ($E_A = 2.88$ eV), the contribution of intramolecular stabilization energy controls the enhanced activity of tetracyanoethylene as compared to activities of 4-phenyl-1,2,4-triazoline-3,5-dione and 4-phenylmaleimide. In the remaining reactions, where the contribution of intramolecular stabilization energy is moderate, the variation in the reaction rate is again controlled by the lower N=N bond rupture energy in reagent **2**.

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