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V.I. Minkin on his 80th anniversary

Ene Reaction of 4-Phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione with Dicyclopentadiene

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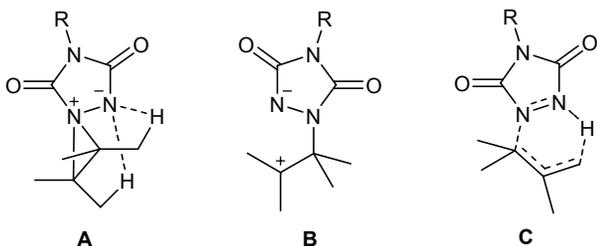
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Abstract—The kinetics of the ene reaction of *endo*-dicyclopentadiene with 4-phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione in benzene, toluene, acetonitrile, 1,2-dichloroethane, and chloroform have been studied. The reaction volumes and enthalpies have been determined, and the activation volume in toluene has been calculated from the pressure kinetic data. The “anomalous” ratio $\Delta V_{\text{corr}}^{\ddagger}/\Delta V_{\text{T}} = 1.34$ corresponds to a concerted cyclic transition state, though the addition product has acyclic structure.

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Addition of alkenes to the activated N=N bond of 4-phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione (**1**) has been the subject of many studies [1–15]. Grdina et al. [6] noted a high kinetic isotope effect in the reaction of **1** with *cis*-2-methyl-3-(trideuteriomethyl)but-2-ene, and subsequent studies provided experimental proofs for the formation of aziridinium imide in the first step of such reactions [12, 16]. Until present, a large number of experimental data have been accumulated, according to which ene reactions could involve different transition states, in particular aziridinium imide (**A**), dipolar (**B**), and concerted (**C**).



A dramatic difference is observed between the rates of the Diels–Alder reactions with dihydrotriazole **1** and its structural analog, *N*-phenylmaleimide [17]. Taking into account fairly similar π -acceptor properties of these dienophiles, the higher reactivity of compound **1**

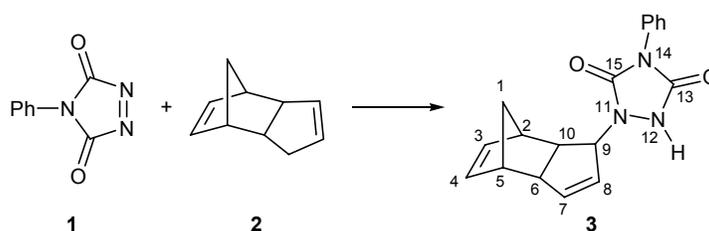
can be rationalized by the lower energy of rupture of the π -N=N bond compared to C=C bond [17].

Dienophiles with a C=C bond are weakly reactive in ene reactions with alkenes and unconjugated dienes under normal conditions, whereas analogous reactions with compound **1** are fast and irreversible [18]. For example, the reaction of **1** with 2,3-dimethylbut-2-ene in 1,2-dichloroethane at 25°C is complete immediately after mixing the reactants with a heat effect of -150 kJ/mol; $k_2 = 335$ l mol⁻¹ s⁻¹ [18].

1,3-Dienes possessing an allylic hydrogen atom are capable of reacting with a less active dienophile, diethyl azodicarboxylate, according to both Diels–Alder and Alder–ene patterns [19, 20]. The rate of the ene reaction of acyclic alkenes with dihydrotriazole **1** increases in parallel with the donor power of alkenes: $\ln k_2 = 74.24 - 8.26 IP$ [18]. Such relation between the reaction rate ($\ln k_2$) and ionization potential (*IP*) of diene is typical of Diels–Alder reactions with dienes belonging to the same structural series [21, 22].

Because of high exothermicity, no equilibrium in this process is observed under normal conditions. Ene reactions are characterized by high negative volumes of activation [23, 24]. Therefore, they should be considerably accelerated under high hydrostatic pressure.

Scheme 1.



Comparison of the volumes of activation (ΔV^\ddagger) and reaction (ΔV_r) makes it possible to judge how similar are their structures [20, 23].

The ene reaction of **1** with cycloalkenes involving C=C bond transfer is usually facile, whereas in the reaction with norbornene analogous double bond transfer to the bridging carbon atom is energetically unfavorable; therefore, this reaction requires more severe conditions and is accompanied by skeletal rearrangement [25].

We were the first to study the effects of solvent, temperature, and high hydrostatic pressure on the rate of the reaction of dihydrotriazole **1** with *endo*-dicyclopentadiene (**2**), leading to adduct **3** (Scheme 1). It was necessary to find out how active are other reaction centers in molecules **2** and **3**. The reaction rates were measured in five solvents, and the kinetic parameters are given in Table 1.

As follows from the data in Table 1, the reaction **1** + **2** \rightarrow **3** features large negative entropies of activation, which approach those typical of Diels–Alder reactions. Some proportionality is observed between the solvent effects on the rates of the ene reactions of **1** with dicyclopentadiene and 2-methylbut-2-ene ($r = 0.986$), as well as between the ene reaction **1** + **2** \rightarrow **3** and Diels–Alder reaction of **1** with anthracene [27] ($r = 0.970$). Calorimetric measurements in 1,2-dichloroethane at 25°C gave an enthalpy of -172 ± 2 kJ/mol

for the reaction **1** + **2** \rightarrow **3**. The large heat effect makes the process irreversible under ambient conditions. In order to estimate the volume of activation, we examined the effect of high hydrostatic pressure on the reaction rate (Table 2).

The rate of the reaction of dihydrotriazole **1** with dicyclopentadiene **2** in toluene at 25°C versus pressure is described by the equation

$$\ln(k_p/k_{p=1}) = -0.000000209p^2 + 0.001208651p; \\ R^2 = 0.9996.$$

The volume of activation corrected for the change of the reactant concentration due to solvent compression ($\Delta V_{\text{corr}}^\ddagger$) can be calculated by Eq. (1) [24], where β_t is the compressibility factor of toluene (91.9×10^{-6} 1/bar at 25°C [28]), and n is the kinetic order of the reaction. We thus obtained a $\Delta V_{\text{corr}}^\ddagger$ value of -27.6 ± 1.1 cm³/mol.

$$\Delta V_{\text{corr}}^\ddagger = -RT \partial \ln(k_p/k_{p=1}) / \partial P + (n-1)RT\beta_t. \quad (1)$$

Useful information can be provided by considering the ratio of the activation and reaction volumes $\Delta V_{\text{corr}}^\ddagger / \Delta V_r$. The volume of reaction is usually determined from the difference between the partial molar volumes of the products and initial reactants; however, more precise values can be obtained [29] from the dependence of the specific volume of the reactant

Table 1. Rate constants and activation parameters for the reaction of 4-phenyl-3H-1,2,4-triazole-3,5(4H)-dione (**1**) with *endo*-dicyclopentadiene (**2**) in different solvents at 25°C

| Solvent | $k_2 \times 100, \text{ l mol}^{-1} \text{ s}^{-1}$ | | | | | | | $\Delta H^\ddagger, \text{ kJ/mol}$ | $-\Delta S^\ddagger, \text{ J mol}^{-1} \text{ K}^{-1}$ | $\Delta G^\ddagger, \text{ kJ/mol}$ |
|--------------------|---|------|------|------|------|------|-------------------|-------------------------------------|---|-------------------------------------|
| | 15°C | 20°C | 25°C | 30°C | 35°C | 45°C | [26] ^a | | | |
| Toluene | | | 1.71 | | 3.19 | 5.88 | 64 | 46.0 | 125 | 83.2 |
| Benzene | | 2.08 | 2.70 | 3.65 | 5.08 | | 126 | 42.2 | 134 | 82.1 |
| Acetonitrile | | | 1.08 | | 2.08 | 3.29 | 57 | 41.4 | 142 | 83.7 |
| 1,2-Dichloroethane | 5.28 | 6.34 | 7.76 | | 11.1 | | 490 | 25.1 | 184 | 80.0 |
| Chloroform | | 10.0 | 12.9 | 15.8 | 19.9 | | 1430 | 31.3 | 155 | 77.5 |

^a Data of [26] for the ene reaction of triazole **1** with trimethylethylene at 10°C.

Table 2. Pressure effect on the rate of the reaction of 4-phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione (**1**) with *endo*-dicyclopentadiene (**2**) in toluene at 25°C

| <i>P</i> , bar | <i>k</i> ₂ , l mol ⁻¹ s ⁻¹ | ln(<i>k</i> _{<i>P</i>} / <i>k</i> _{<i>P</i>=1}) |
|----------------|---|---|
| 1 | 0.0171 | 0 |
| 470 | 0.0293 | 0.538 |
| 983 | 0.0460 | 0.989 |
| 1050 | 0.0478 | 1.028 |
| 1448 | 0.0641 | 1.321 |

solution ($1/d$) on the product concentration (c_3) [Eq. (2); see figure).

$$1/d_\tau = 1/d_{\tau=0} + c_{3,\tau} \Delta V_r / 1000 d_{\tau=0}. \quad (2)$$

Here, d_τ is the density of the reactant solution at a moment τ , and $c_{3,\tau}$ is the concentration of adduct **3** at the same moment, calculated from the kinetic data.

From two series of measurements we obtained ΔV_r values of -20.2 and -21.0 cm³/mol. The ratio of the volume of activation to the average volume of the reaction **1** + **2** → **3** is considerably higher than unity (1.34 ± 0.08). This means that the volume of the activated complex is smaller than the volume of product **3** by 7 ± 1.1 cm³/mol. Taking into account weak and

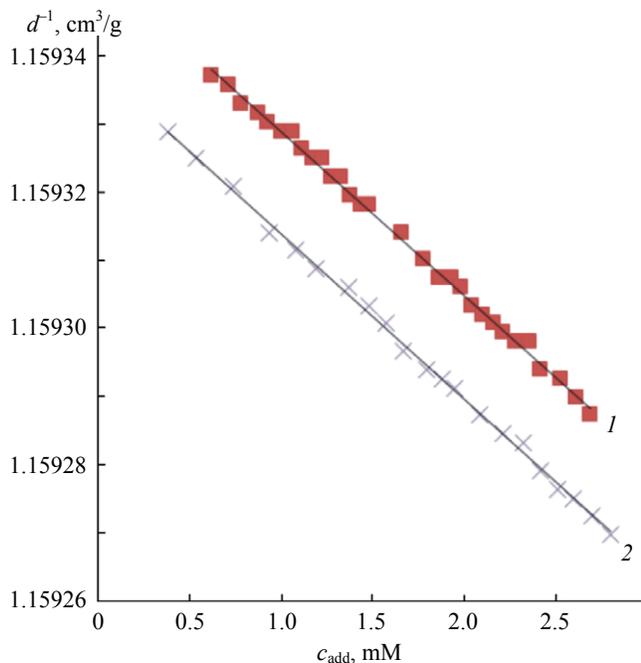
irregular effect of solvent polarity on the reaction rate (Table 1), electrostriction effect in the solvation of the activated complex cannot be regarded as a probable factor responsible for increased compactness of the activated complex. It is known that cyclic molecules are always more compact than linear ones [30]. For example, the transformation of alkenes into the corresponding cycloalkanes is characterized by reduction of the volume by more than 15 cm³/mol [30]. The “anomalous” ratio $\Delta V_{\text{corr}}^\ddagger / \Delta V_r = 1.34$ suggests concerted cyclic transition state **C** in the reaction **1** + **2** → **3**, whereas adduct **3** is acyclic. By special experiments we showed that there was no addition of **1** to the C³=C⁴ or C⁷=C⁸ bond of **3**.

EXPERIMENTAL

4-Phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione (**1**) (Aldrich) was purified by sublimation at 100°C/10 Pa, mp 165–170°C (decomp.), λ_{max} (ϵ), nm: 540 (248) in benzene; 527 (186) in 1,4-dioxane; 540 (245) in toluene. *endo*-Dicyclopentadiene (**2**) was purified by vacuum distillation, mp 32°C. The solvents used were purified according to standard methods [31].

Adduct **3** was synthesized by mixing a solution of 100 mg (0.57 mmol) of triazole **1** in 5 mL of chloroform with 100 mg (0.76 mmol) of diene **2**. When the mixture turned colorless, the solvent was distilled off, and the residue was washed with hexane and recrystallized from benzene. Yield 110 mg (62%), white crystals, mp 153–154°C [17]. ¹H NMR spectrum (CDCl₃), δ , ppm: 1.36 and 1.59 (2H, 1-H, AB, ³J_{HH} = 8.4 Hz), 2.65 br.m (1H, 6-H), 2.84 br.m (1H, 2-H), 3.08 br.m (1H, 5-H), 3.38 br.m (1H, 10-H), 4.59 br.m (1H, 9-H), 5.45–6.07 m (4H, 3-H, 4-H, 7-H, 8-H), 7.36–7.53 m (5H, Ph), 8.27 s (1H, 12-H). ¹³C NMR spectrum (CDCl₃), δ , ppm: 44.71 (C⁶), 45.38 (C¹⁰), 47.48 (C²), 51.22 (C¹), 54.64 (C⁵), 64.42 (C⁹); 125.49, 128.23, 129.20, 131.37 (C_{arom}); 128.56 (C⁷), 132.37 (C³), 136.23 (C⁴), 141.35 (C⁸), 152.29 (C¹⁵), 153.60 (C¹³).

Normal pressure kinetic measurements. The rate of the reaction **1** + **2** → **3** was monitored by the absorbance of triazole **1**, $c_{0,1} = 3\text{--}5$ mM, in the region λ 530–570 nm using a Hitachi U-2900 spectrophotometer. The absorbance was measured both in the presence of a large excess of **2** and at equimolar ratio of **1** and **2**. In all cases, consistent values of the rate constants were obtained, which ruled out appreciable contribution of concurrent reactions of **1** at the C³=C⁴ and C⁷=C⁸ bonds of adduct **3**. We failed to obtain bis-adducts by keeping a solution of equimolar amounts of



Variation of the specific volume of the reaction mixture **1**+**2** versus concentration of adduct **3**; (1) $1/d_\tau = -0.023428c_3 + 1.15935$; $r = 0.9979$; $c_{0,1} = c_{0,2} = 4.37$ mM; $\Delta V_r = -20.2$ cm³/mol; (2) $1/d_\tau = -0.024319c_3 + 1.15934$; $r = 0.9993$; $c_{0,1} = c_{0,2} = 4.36$ mM; $\Delta V_r = -21.0$ cm³/mol.

compounds **1** and **2** in CDCl_3 for 7 days. The ^1H NMR spectrum of the resulting mixture showed the presence of adduct **3** with a small impurity. The available data confirm sharp reduction of the reaction rate upon formation of bis-adduct in the reaction of **1** with alkenes [8] and norbornene derivatives [32].

High pressure kinetic measurements. The reaction $\mathbf{1} + \mathbf{2} \rightarrow \mathbf{3}$ was carried out in toluene at 25°C on a high pressure setup equipped with an HP-500 high-pressure pump and a PCI-500 high-pressure optical cell with sapphire windows (Syn Ltd., Japan) compatible with a Scinco spectrophotometer (Korea). Stock solutions of **1** and **2** with the same concentration (0.0196 M) were prepared. Working solutions were prepared by mixing equal volumes (1 mL each) of the reactant solutions. The cell path length of a high-pressure quartz cell was 0.4 cm. In all cases, the kinetic dependences at high pressure were characterized by a correlation coefficient of higher than 0.999. The volume of activation at ambient pressure was calculated from $\partial \ln(k_P)/\partial P$ [Eq. (1)] and was $-29.9 \pm 1.1 \text{ cm}^3/\text{mol}$.

Calorimetric measurements of the heat of the reaction $\mathbf{1} + \mathbf{2} \rightarrow \mathbf{3}$ in 1,2-dichloroethane at 25°C were carried out by adding a known amount of crystalline compound **1** to a 0.1 M solution of **2**. As a result of three measurements, values of -150.6 , -151.1 , and -149.2 kJ/mol were obtained. After correction for the heat of dissolution of **1** (21.9 kJ/mol), the enthalpy of the reaction $\mathbf{1} + \mathbf{2} \rightarrow \mathbf{3}$ in 1,2-dichloroethane at 25°C was estimated at $-172 \pm 2 \text{ kJ/mol}$.

The density of reaction mixtures was measured at $25 \pm 0.001^\circ\text{C}$ using an Anton Paar DSA5000 M density and sound velocity meter (Austria). The measurements were carried out with equal concentrations of **1** and **2** (4.36 mM in the first series and 4.37 mM in the second). The current concentration of adduct (c_3) was calculated from the kinetic equation for the corresponding period of time. This procedure for the calculation of reaction volume does not require determination of partial volumes of all reaction participants.

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