Kinetic Studies of the High-pressure [6 + 4]π Cycloaddition of Tropone to Cyclohexa-1,3-diene

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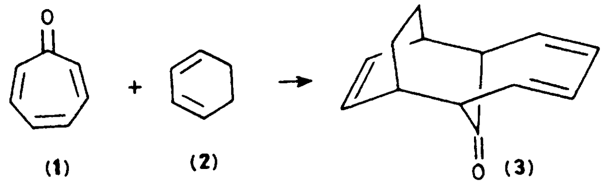
The kinetics of the [6 + 4]π cycloaddition of tropone to cyclohexa-1,3-diene have been studied in the temperature range 80—95 °C at pressures up to 2 000 bar in isopropylbenzene, *N,N*-dimethylformamide, and 1,4-dioxane. Activation parameters were in the range for a typical concerted intermolecular cycloaddition, and were mutually consistent in each solvent, but inconsistent with those reported for a high-pressure kinetic analysis of tropone and cyclopentadiene by le Noble. The effect of solvation on the cycloaddition reactions of tropone should be carefully re-evaluated.

Most of the concerted cycloaddition reactions previously studied by use of high-pressure kinetics have been Diels–Alder[1] and 1,3-dipolar cycloaddition reactions.[2] Large negative values (at least -20 cm^3 mol^{-1})[1,2] for the activation volume ($\Delta V^{\ddagger}$) and reaction volume (ΔV), with $0.5 < \Delta V^{\ddagger}/\Delta V < 1$, have been established.

However, high-pressure kinetic analysis[3] of the [6 + 4]π cycloaddition between tropone (**1**) and cyclopentadiene[4] revealed exceptionally low values for the activation volume and reaction volume (-7.5 and -4.3 cm^3 mol^{-1}) in dioxane at 60 °C; moreover, the ratio of these parameters was 1.7.[3] For this symmetry-allowed concerted reaction,[5] an explanation was provided in terms of strong electrostriction of tropone (**1**), a highly polar cycloaddend, in the initial state, reducing its partial molar volume (V_1). This proposal seems attractive, since tropone is regarded as a non-benzenoid aromatic compound, and a contribution of the polarised structure (oxidocycloheptatrienylium) should be favoured by Hückel's $4n + 2$ rule.[6]

The concerted nature of the [6 + 4]π cycloaddition of tropone to cyclopentadiene has already been established by Tanida *et al.*,[7] who carried out a kinetic analysis under the atmospheric pressure, and is predictable from the Woodward–Hoffmann rules.[5] Consequently, it seemed desirable to carry out a high-pressure analysis of Diels–Alder reactions of tropone, which might disclose some otherwise undetectable feature. We therefore carried out studies of the reaction of tropone with maleic anhydride[8] and norbornene,[9] typical dienophiles, and obtained 'normal' values for the V_1 (99.8 cm^3 mol^{-1} in isopropylbenzene and 97.0 cm^3 mol^{-1} in *N,N*-dimethylformamide at 60 °C). A discrepancy with le Noble's figure (85.6 cm^3 mol^{-1} in dioxane at 60 °C) was apparent, although the solvents used were different. The different data from high-pressure kinetics encouraged us to undertake an independent study of a [6 + 4]π cycloaddition reaction with tropone. Many examples of [6 + 4]π cycloadditions have been published,[10] with tropone as a 6π cycloaddend. We describe here the concerted [6 + 4]π cycloaddition of tropone to cyclohexa-1,3-diene (**2**)[11] to form the *exo*-cycloadduct (**3**) in 1,4-dioxane (the same solvent as in le Noble's experiment[3]), and cumene and dimethylformamide (DMF) (our previous solvents for the Diels–Alder reactions of tropone with dienophiles[8,9]).



(**1**) (**2**) (**3**)

Experimental

Materials.—Tropone (**1**) was prepared by Nozoe's method,[12] and purified by silica-gel column chromatography and distillation (Kugelrohr) *in vacuo* (to at least 99% purity). Cyclohexa-1,3-diene (**2**) (Aldrich) was distilled over $NaBH_4$ under N_2. The adduct (**3**)[11] was purified by recrystallizations from hexane; m.p. 140.0—141.0 °C (lit.,[11] 142—143 °C); $\nu_{max.}(CCl_4)$ 1 710 cm^{-1} (C=O); *m/z* 186 (M^+); $\delta_H(CDCl_3)$ 1.08—1.66 (2 H, m), 1.82—2.17 (2 H, m), 2.40—2.88 (2 H, m), 3.28—3.62 (2 H, m), 5.20—5.64 (2 H, m), 6.88—7.20 (2 H, m), and 7.15—7.40 (2 H, m); $\delta_C(CDCl_3)$ 21.7(t), 31.1(d), 59.9(d), 125.4(d), 125.5(d), 134.6(d), and 208.6(s). The solvents used were carefully purified; parity was monitored by g.l.c. or l.c. Cumene and dioxane were distilled over Na; DMF was dried over CaH_2 and distilled *in vacuo*.

Kinetic Measurements.—The apparatus for the kinetic runs was the same as used in our previous studies.[8,9] The reaction was analysed as a pseudo-first-order reaction of (**1**); *i.e.* the initial concentrations were *ca.* 0.007 mol kg^{-1} for (**1**) and 0.14 mol kg^{-1} for (**2**). The reaction temperature was controlled to within ±0.5 °C. The progress of the reaction was monitored by h.p.l.c. [Nippon Waters 244 apparatus; Micropolasil column (3.9 mm diam. × 300 mm length)] by following the increase of the product (**3**), which showed extensive decomposition under g.l.c. conditions.

Measurement of Partial Molar Volume.—The partial molar volume of each substrate (V_i) was determined by extrapolation of the apparent molar volume (Φ_i) to infinite dilution; densities were measured with an Ostwald pycnometer at 60 ± 0.01 °C. For each substrate, Φ_i was almost constant in a particular solvent [equation (1), where i represents the solute; M is the

$$\Phi_i = [(1\,000 + M_i m_i)/d_{mi} - 1\,000/d]/m_i \qquad (1)$$

molecular weight, d_m and d are the densities of solution and pure solvent, respectively, and m is the molality].

Results and Discussion

Since cyclopentadiene dimerises very quickly and is very acid-sensitive, its suitability for kinetic study is questionable. On the other hand, cyclohexa-1,3-diene (**2**) is known to react stereo-

Table 1. Rate constants for the reaction of tropone with cyclohexadiene at various temperatures (10^6k/kg mol^{-1} s^{-1})

	T/K			
Solvent	353.2	358.2	363.2	368.2
Cumene	2.67 ± 0.05	3.85 ± 0.06	5.43 ± 0.01	6.59 ± 0.09
Dioxane	2.98 ± 0.03	3.57 ± 0.03	5.01 ± 0.02	6.85 ± 0.03
DMF	2.15 ± 0.03	2.96 ± 0.06	3.86 ± 0.04	5.13 ± 0.01

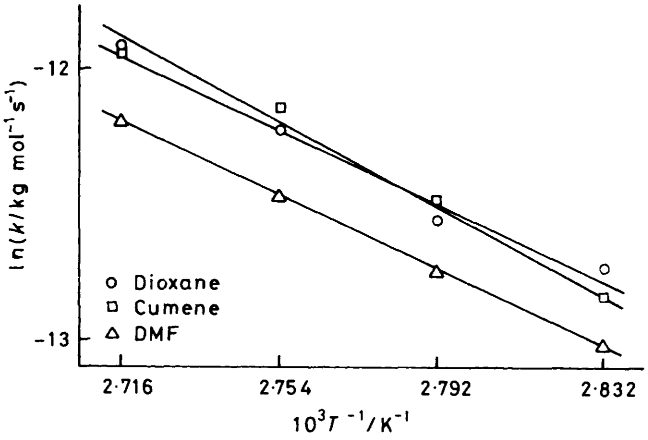


Figure 1. Arrhenius plots for the reaction of (**1**) with (**2**)

specifically to afford a [6 + 4]π cycloadduct (**3**) with tropone,[11] and is much more stable under comparable conditions.

In le Noble's paper[3] the small activation volume and reaction volume were interpreted on the basis of an unusually small partial molar volume of (**1**) (V_1) in dioxane (85.6 cm^3 mol^{-1}; smaller than that calculated from parachor listings by *ca.* 20 cm^3 mol^{-1}), which might be attributable to the polarised oxidocycloheptatrienylium structure. Furthermore, the large $\Delta V^{\ddagger}/\Delta V$ value was explained in terms of a secondary orbital interaction.[3] On these grounds, le Noble and his colleague concluded that the [6 + 4]π cycloaddition of tropone with cyclopentadiene was concerted under high-pressure conditions.

Temperature Effect.—The second-order rate constants for the reaction of tropone (**1**) with (**2**) at various temperatures in each solvent are listed in Table 1. The Arrhenius plots are shown in Figure 1; correlation coefficients (*r*) were 0.993 in cumene, 0.991 in dioxane, and 1.000 in DMF. The activation enthalpy ($\Delta H^{\ddagger}$), activation entropy ($\Delta S^{\ddagger}$), and activation free energy ($\Delta G^{\ddagger}$) at 100 °C are listed in Table 2. The relatively small values of $\Delta H^{\ddagger}$ and large negative values of $\Delta S^{\ddagger}$ observed are commonly exhibited by typical Diels–Alder reactions;[13–15] in a kinetic analysis of the [6 + 4]π cycloaddition of tropone with cyclopentadiene under atmospheric pressure this was also the case.[7] Consequently, on the basis of the effect of temperature, the [6 + 4]π cycloaddition should be considered as a concerted process, and no particular interaction between tropone and solvents was detected. Moreover, if the reaction obeyed a mechanism compatible with le Noble's analysis, $\Delta S^{\ddagger}$ might be expected to show a considerably smaller negative value than that obtained by us in dioxane; it is notable that $\Delta S^{\ddagger}$ related to $\Delta V^{\ddagger}$ in many examples.[16]

Pressure Effect and Volume Profile.—The rate constants (*k*) at various pressures (*P*) are listed in Table 3. From the pressure dependence of ln *k*, $\Delta V^{\ddagger}$ at atmospheric pressure was determined [equation (2)].

Table 2. Activation parameters for the reaction of tropone with cyclohexadiene at 373.2 K

Solvent	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J mol^{-1} K^{-1}	$\Delta G^{\ddagger}$/kJ mol^{-1}
Cumene	63 ± 8	−175 ± 20	128 ± 15
Dioxane	58 ± 8	−188 ± 21	128 ± 16
DMF	59 ± 2	−188 ± 5	129 ± 3

$$\Delta V^{\ddagger} = -RT(\delta \ln k/\delta P)_T \qquad (2)$$

As illustrated in Figure 2, the plots of ln *k vs. P* are linear in dioxane (*r* 1.000), but show a slight curvature in cumene and in DMF; in cumene, linearity was observed only below 1 500 bar (*r* 1.000). To express the pressure dependence of the rate constant, we can use equation (3).

$$\ln k = \mathrm{a} + \mathrm{b}P + \mathrm{c}P^2 \qquad (3)$$

The foregoing equations give $\Delta V^{\ddagger}$ values of −37.6 ± 1.1 (in cumene), −28.2 ± 2.0 (in dioxane), and −32.6 ± 0.6 cm^3 mol^{-1} (in DMF).[*] Although this widely used treatment tends to overestimate $\Delta V^{\ddagger}$,[†] fitting with the figures obtained from the present experiment is satisfactory.

Table 4 shows values of V_i for each substrate, ΔV at 60 °C, $\Delta V^{\ddagger}$ at 80 °C, and values of $\Delta V^{\ddagger}/\Delta V$.

Examination of volume change and volume profile reveals a resemblance to the Diels–Alder reaction of tropene with norbornene; $\Delta V^{\ddagger}$ is almost equal to ΔV, that is, the transition state is very product-like. In cumene, $\Delta V^{\ddagger}$ is little more negative than ΔV, but the difference is too small to conclude that the transition state is smaller than the product. It is noteworthy that V_1 is 99.1 cm^3 mol^{-1} in dioxane; this is in accord with our V_1 values in cumene and in DMF,[8,9] but not with the V_1 value of le Noble.[3] Therefore, we conclude that the solvation effect on (**1**) enables little contribution to the volume change. Consequently, the [6 + 4]π cycloaddition reaction of (**1**) falls in the category of concerted reactions, like the Diels–Alder reaction, even under high-pressure conditions. The discrepancy with le Noble's results is beyond experimental error.

A secondary orbital interaction was invoked by le Noble to explain his large $\Delta V^{\ddagger}/V$ value. Eckert has proposed that the large $\Delta V^{\ddagger}/\Delta V$ values ($\gg 1$) sometimes observed in Diels–Alder reactions with dienophiles having a strong *endo*-orientation effect might be due to such an effect; *i.e.* this interaction might cause constriction of the volume in the transition state. Even if this were also the case in the reaction of tropone with cyclopentadiene, which behaves as strongly stereospecific, with an *exo*-orientation effect, it has been shown that in Diels–Alder reactions simultaneously produced *endo*- and *exo*-adducts show little difference in $\Delta V^{\ddagger}$.[18] Thus, we cannot find a reasonable explanation for the reported data. Recently, a small negative $\Delta V^{\ddagger}$ value (*ca.* −8 cm^3 mol^{-1}) for the effect of pressure on the *retro*-Diels–Alder reaction was reported, and was explained in terms of transannular attractive forces.[19] If this explanation were to account for the $\Delta V^{\ddagger}/\Delta V$ value of the reaction of tropone with cyclopentadiene (1.7), the value of $\Delta V^{\ddagger}$ (−7.5 cm^3 mol^{-1}) would be almost entirely attributable to that attractive force, rather than to any volume change with bond-making.

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[*] If one assumes a linear relationship between ln *k* and *P*, $\Delta V^{\ddagger}$ values of the reaction may be calculated to be: in cumene, −31.0 ± 2.2 (*r* 0.998) up to 2 000 bar, but −33.1 ± 0.7 below 1 500 bar; in dioxane, −27.1 ± 0.9; and in DMF, −26.9 ± 2.1 cm^3 mol^{-1}.

[†] For more precise treatment of the relation of ln *k vs. P*, see ref. 17.

Table 3. Rate constants for the reaction of tropone with cyclohexadiene under various pressures at 353.2 K (10^6k/kg mol^{-1} s^{-1})

	p/bar				
Solvent	1	500	1 000	1 500	2 000
Cumene	2.67 ± 0.05	4.88 ± 0.07	8.29 ± 0.01	14.6 ± 0.2	21.6 ± 0.02
Dioxane	2.98 ± 0.03	4.70 ± 0.01	7.30 ± 0.05	12.1 ± 0.1	18.4 ± 0.01
DMF	2.15 ± 0.03	3.43 ± 0.02	6.07 ± 0.09	9.04 ± 0.04	13.1 ± 0.01

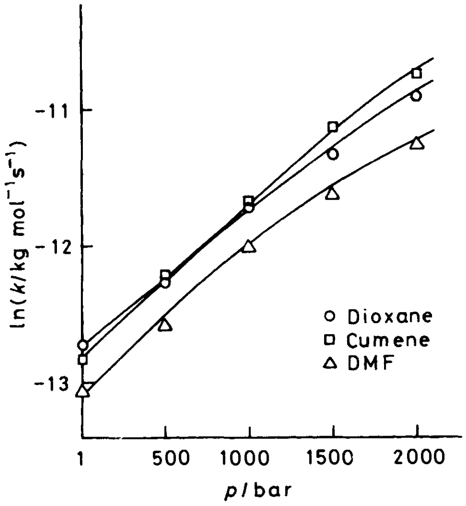

Figure 2. Pressure dependence of ln *k* for the reaction of (**1**) with (**2**) at 353.2 K

Solvent Effect.—There were no significant solvent effects on the reaction; solvent effects on $\Delta V^{\ddagger}$ and ΔV resembled those of a typical Diels–Alder reaction. In the preliminary report,[8] we suggested that only a special type of interaction between (**1**) and dioxane could explain the kinetics. However, our V_1 values in cumene and in DMF were almost the same (99.8 and 97.0 cm^3 mol^{-1}, respectively), in spite of the large difference in polarities of the solvents, in accord with expected values from parachor listings. If such an interaction were operative, the small negative values of $\Delta V^{\ddagger}$ and ΔV for the reaction of (**1**) with cyclopentadiene in dioxane observed by le Noble could be attributable to a small V_1 value in dioxane. In this sense, indeed dioxane has been known to behave as a solvent having a large dielectric constant, more than its macroscopic value; *e.g.* 1,4-dioxane strongly solvates tetrabutylammonium bromide.[20] However, such a rationale is hardly convincing in relation to a covalent compound like (**1**), having a small dipole moment (4.17 D in ref. 21; 4.30 D in ref. 22). The present data unambiguously eliminate this possibility.

In conclusion, the present results for the [6 + 4]π cycloaddition of tropone with cyclohexadiene are fully consistent with those expected for concerted reactions like the Diels–Alder reaction. Since mutually consistent data were obtained from three solvents of different polarity, the postulate of an extraordinary solvation property for tropone[1-3] should be reassessed. Finally, in view of recent interest in high-pressure reactions for organic synthesis,[23] it is noteworthy that the present study indicates the feasibility of [6 + 4]π cycloadditions with troponoids.

Table 4. Volume parameters for the reaction of tropone with cyclohexadiene (cm^3/mol)[a]

Solvent	V_1	V_5	V_6	ΔV	$\Delta V^{\ddagger}$	$\Delta V^{\ddagger}/\Delta V$
Cumene	99.8	97.6	161.3	−36.1	−37.6	1.04
Dioxane	99.1	99.1	166.4	−31.8	−28.2	0.89
DMF	97.0	97.5	160.3	−34.2	−32.6	0.95

[a] V_i and ΔV were measured at 333.15 K; $\Delta V^{\ddagger}$ at 353.2 K.

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