

THE EFFECT OF SOLVENT, BASE STRENGTH AND ISOTOPIC SUBSTITUTION ON THE KINETICS OF NITRO GROUP REARRANGEMENT*

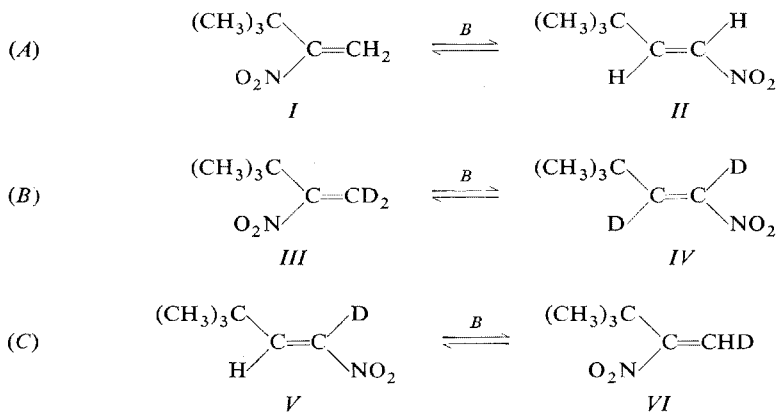
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The effect of solvent polarity, isotopic substitution and base strength on the rate of rearrangement of 2-nitro-3,3-dimethyl-1-butene (*I*) and 1-nitro-3,3-dimethyl-1-butene (*II*) has been studied. From the equilibration data at 13 temperatures the thermodynamic functions of the studied reaction have been determined.

The suggested mechanism of the nitro group rearrangement in conjugated nitro olefins presumes the formation of a delocalised anion as an intermediate¹ (a substrate-base complex) which is the rate determining step of the two-step reaction.



The reaction has now been studied on systems A, B and C. The equilibrium composition was determined over the temperature range 100°C in a series of aprotic solvents of various polarity (Table I), using triethylamine as catalyst. The measure-

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ments were carried out starting from both isomers, the experimental error being about 1%. The ΔH and ΔS values were determined graphically as well as by linear regression; the agreement between the results obtained by the two methods was very good. The thermodynamic data are as follows: $\Delta H = -4.20 \pm 0.23$ kcal mol⁻¹, $\Delta S = -5.56 \pm 0.26$ cal mol⁻¹ deg⁻¹, $\Delta G = -2.56 \pm 0.15$ kcal mol⁻¹. The straight line equation has the form $\log K = 0.9081/T - 1.22$, the correlation coefficient is 0.997. The thermodynamic parameters of the reaction of deuterated compounds $III \rightleftharpoons IV$ agree within the experimental error with that of the reaction $I \rightleftharpoons II$ (correlation coefficient 0.994), see Fig. 1.

Neither isotopic substitution nor polarity of solvent had any measurable effect on the equilibrium. The dependence of the reaction rate on temperature, solvent polarity and basicity of the catalyst was studied. The rate constants were calculated from the dependence of concentration of the isomers on time by substituting into the integrated rate equation². The error of the reaction rate determination was 3%. The results are summarised in Tables II and III.

In order to obtain information about the rate determining step and the structure of the transition state, we measured rates of the deuterated derivatives (Table IV). The rate constant varies with solvent in the range of more than two orders of magnitude (Table III). The stabilisation by solvation of the ground and the transition state is thus different in different solvents. Since the increase in the solvent polarity leads to the rapid increase in the reaction rate, we may consider the transition state to be substantially more polar than the ground state (*i.e.* it may have an ion-pair character). The value of the macroscopic dielectric constant does not express satisfactorily the situation in the immediate vicinity to the reacting species (the reaction in nitrobenzene is slower than in 1,2-dimethoxyethane although the dielectric constant of the former solvent is by one order of magnitude greater than that of the latter). The reaction is accelerated in solvents of the electron-donor character (basic solvents)

TABLE I
Equilibrium Constants, K , and Thermodynamic Functions, ΔG , of the Reaction $I \rightleftharpoons II$

K	T, K	$-\Delta G, \text{kcal mol}^{-1}$	K	T, K	$-\Delta G, \text{kcal mol}^{-1}$
11	395	1.90	38.0	323	2.35
15.1	383	2.08	49.0	313	2.43
17.0	373	2.10	50.1	310	2.43
19.9	359	2.15	53.6	307	2.45
23.5	353	2.22	64.5	298	2.48
27.6	343	2.27	79.5	293	2.56
32.4	334	2.32			

TABLE II

Rate Constants, k (h^{-1}), and Activation Parameters of the Reaction, Catalysed by Triethylamine, in Various Solvents

$T, ^\circ\text{C}$	Dioxan	Cyclohexane	EGDE ^a	THF ^a
40	0.0079	0.00025	0.035	0.0075
50	0.01	0.00051	0.055	0.016
61.2	0.025	0.00085	0.088	0.052
70	0.048	0.0023	0.17	—
80	0.065	0.005	0.25	—
k_{rel}	31.8	1	136	30
ΔH^\ddagger , kcal mol ⁻¹	12.4	16.66	10.8	14.64
ΔS^\ddagger , cal mol ⁻¹ deg ⁻¹	-28.4	-24.51	-32.07	-23.61
ΔG^\ddagger , kcal mol ⁻¹	20.8	24.0	20.3	21.7

^a EDGE ethyleneglycol dimethyl ether, THF tetrahydrofuran, NB nitrobenzene, DMSO dimethyl sulphoxide, HMPT hexamethylphosphoric triamide.

which assist in the ionisation of the C—H bond, lowering thus the activation energy of the reaction.

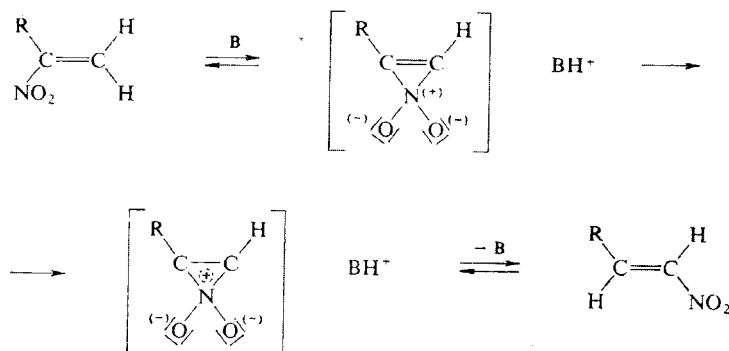
The transition state is formed by association of two molecules (the substrate and the base) and the resulting decrease in the number of translational and rotational degrees of freedom manifests itself by a negative activation entropy. In this case, the entropy term is composed of the following three negative contributions: association of the compound and the base in the transition state (this contribution is the same for all solvents), orientation of the solvent around the highly polar transition state (the highest contribution in cyclohexane), and specific solvation of the transition state which should have the greatest effect in dimethyl sulfoxide and hexamethylphosphoric triamide. We may justifiably assume that at least the two last solvents can be included into the transition state (Fig. 2).

The change of the free enthalpy of activation in going from one solvent to another is given by the free enthalpy of solvation, $\Delta \Delta G_s^\ddagger$. In the studied series of solvents, cyclohexane was chosen as the reference solvent, its solvation effect being taken as unity. The change of the free enthalpy of solvation reflects the effect of solvent, *i.e.* the difference between the energy of solvation of the ground and the transition state. In Table V the value $\Delta \Delta G_s^\ddagger = \Delta G_s^\ddagger - \Delta G_{\text{cyclohexane}}^\ddagger$ is compared with the most general empirical polarity parameter, E_T . As seen, the dependence is not linear, the deviations being due to specific solvations. The $\Delta \Delta G_s^\ddagger$ value include also the basicity contribution of the solvent whereas E_T is a measure of polarity³.

TABLE II
(Continued)

Dibutyl ether	Anisole	NB ^a	Ethyl acetate	DMSO ^a	HMPT ^a
0.008	0.0013	0.006	0.0022	0.148	0.174
0.015	0.005	0.009	0.005	0.4	0.49
0.037	0.0085	0.02	0.0088	0.73	0.91
0.058	0.02	0.055	0.015	0.98	1.2
0.098	0.05	0.08	0.045	1.4	1.8
32	5.2	24	8.9	593	697
13.5	16.43	15.1	15.7	8.87	9.24
-26.83	-21.08	-22.35	-22.27	-36.72	-33.72
21.5	22.7	21.8	22.4	19.8	19.3

The reaction rate (Table III) increases significantly with increasing base strength. The reaction can be separated into two steps (Scheme 1): 1) the base-induced proton abstraction with formation of the intermediate and the conjugated acid, 2) formation of the product. The effect of the base strength on the reaction rate is described quantitatively by Brønsted equation^{4,5}: $-\log k_B = x \cdot pK_B + C$, where $C = -\log G$. a , and x and G are temperature and solvent-dependent constants, characteristic for the given



SCHEME 1

Scheme of the Reaction Mechanism

reaction, and k_B is the rate constant for the given base. The equation was solved graphically (Fig. 3) and the results are as follows:

T, K	313	323	334	343	353
x	0.6	0.55	0.463	0.44	0.43
$C = 0.32$					

TABLE III

Rate Constants, k (h^{-1}), and Activation Parameters of the Reaction, Catalysed by Various Bases, in 1,2-Dimethoxyethane

The rate data are given as $10^3 k$.

$T, ^\circ\text{C}$	B1 ^a	B2 ^a	B3 ^a	B4 ^a	B5 ^a
40	33.9	5.5	0.0125	0.6	0.08
50	55.0	7.5	0.0575	1.75	0.175
61.2	87.0	17.5	0.164	3.75	0.625
70	170.0	30.0	0.504	5.0	0.95
80	248.0	55.0	0.9	17.0	3.2
k_{rel}	2.710	440	1	48	6.4
ΔH^\ddagger , kcal mol ⁻¹	10.81	14.20	24.0	16.59	20.61
ΔS^\ddagger , cal mol ⁻¹ deg ⁻¹	-32.07	-26.08	-9.95	-22.05	-17.37
ΔG^\ddagger , kcal mol ⁻¹	20.3	22.0	27.0	23.2	25.8
$\text{p}K_B$	3.28	4.07	8.94	6.30	7.44

^a B1 triethylamine, B2 tributylamine, B3 N,N-dimethylaniline, B4 N-ethylmorpholine, B5 N,N-diethylaniline.

TABLE IV

Rate Constants, k (hour⁻¹) of the Rearrangement of the Deuterated Compounds (triethylamine, 1,2-dimethoxyethane)

$T, ^\circ\text{C}$	40	50	61.2	70	80
Reaction III \rightleftharpoons IV	0.0055	0.0087	0.016	0.035	0.062
Reaction III \rightleftharpoons IV	$\Delta H^\ddagger = 13.37$ kcal mol ⁻¹ , $\Delta S^\ddagger = -30.01$ cal mol ⁻¹ deg ⁻¹ $\Delta G^\ddagger = 22.3$ kcal mol ⁻¹				
Reaction IV \rightleftharpoons III	$k_{70} = 0.0005$, $k_{80} = 0.00127$				
Reaction V \rightleftharpoons VI	$k_{80} = 0.00551$				

The activation energy, as well as the activation entropy, increases rapidly with the decreasing base strength.

The found primary kinetic isotope effect shows (Tables II and IV) that proton (or deuteron) abstraction is the rate determining step of the reaction. On the other hand, the magnitude of the isotope effect witnesses that in the transition state the C—H (C—D) bond is considerably weakened but not completely broken⁶. The secondary isotope effect, studied in the reaction $V \rightleftharpoons VI$, plays only a negligible role. The stretching and bending vibrations of the C—H and C—D bonds were determined from IR spectra and the theoretical value of isotope effect was calculated⁷.

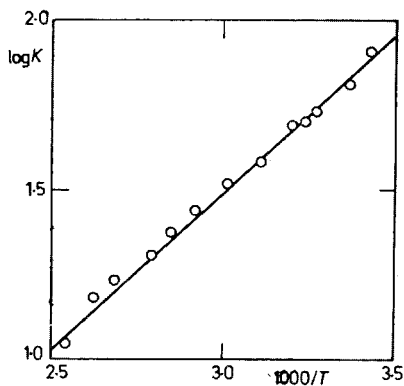


FIG. 1

The Dependence of $\log K$ on $1/T$ for the Reaction $I \rightleftharpoons II$

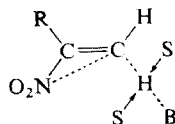


FIG. 2

The Assumed Structure of the Transition State

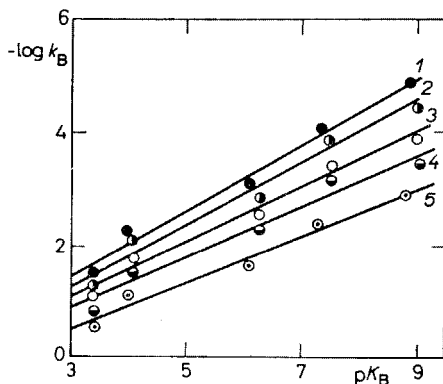


FIG. 3

The Dependence of $-\log k_B$ on pK_B at Various Temperatures
1 40°C, 2 50°C, 3 61.2°C, 4 70°C, 5 80°C.

The calculated and experimental values are given in Table VI, together with the vibration frequencies employed in the calculations.

The intramolecular mechanism of the reaction was proved by carrying out the isomerisation $I \rightleftharpoons II$ in the presence of potassium nitrite containing 57% ^{15}N . Mass spectrometry showed no incorporation of ^{15}N into the product. The reaction was carried out in tetrahydrofuran containing 5% of water (in order to dissolve the potassium nitrite) and in hexamethylphosphoric triamide. In both cases the isomerisation was complete and the arising isomer II was isolated.

TABLE V
Comparison of $\Delta\Delta G_s^\ddagger$ with Parameter E_T

Solvent	HMPT ^a	DMSO ^a	EGDE ^a	Dioxane	Dibutyl ether
$\Delta\Delta G_s^\ddagger$, kcal mol ⁻¹	4.7	4.2	3.7	3.2	2.5
E_T , kcal mol ⁻¹	40.9	45.0	38.2	36.0	33.4

Solvent	THF ^a	NB ^a	Ethyl acetate	Anisol	Cyclohexane
$\Delta\Delta G_s^\ddagger$, kcal mol ⁻¹	2.3	2.2	1.6	1.3	0
E_T , kcal mol ⁻¹	37.4	42.0	38.1	37.2	31.2

^a HMPT hexamethylphosphoric triamide, DMSO dimethyl sulphoxide, EGDE ethylene glycol dimethylether, THF tetrahydrofuran, NB nitrobenzene.

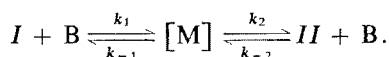
TABLE VI
Experimental and Theoretical Values of the Kinetic Isotope Effect and Stretching and Bending Vibrations of the C—H and C—D Bonds, Used in the Calculations

$T, ^\circ\text{C}$	40	50	61.2	70	80
$k_{\text{H/D}}\gamma$ calc.	6.03	5.71	5.382	5.15	4.92
$k_{\text{H/D}}\gamma$ exp.	6.20	6.35	5.51	4.86	4.07

Vibration	Bending			Stretching		
Isomer <i>I</i>	1 385	1 132	860	699	3 100	3 050
Isomer <i>III</i>	1 010	850	665	496	2 318	2 318

Kinetic measurements on the reaction $I \rightleftharpoons II$ demonstrated that the decrease in the concentration of the isomer I is faster than the corresponding increase in the concentration of the isomer II . This concentration difference ($c_0 - c_I - c_{II} \neq 0$) was greatest at the beginning of the reaction and after certain time it attained a value which was practically constant till the equilibrium was achieved. Such behaviour is caused by the formation of an intermediate (postulated in previous studies¹) which is of ionic character and cannot be detected chromatographically. The dependence of the concentration of the intermediate, $c_M = c_0 - c_I - c_{II}$, on time in various solvents shows that the maximum value of c_M was observed in dimethyl sulphoxide.

Kinetically, the rearrangement is a system of subsequent reversible reactions:



The rate constants were found by solution of a system of differential equations, valid for this system, using an analog computer. Following results were obtained. The constant k_1 is by two to three orders of magnitude smaller than k_2 , showing thus that the formation of an intermediate is the rate-determining step. The overall reaction rate is affected mainly by the magnitude of k_1 . The values of k_1 and k_2 depend on the solvent and base strength, the ratio of these constants being temperature- and solvent-dependent.

The ratio k_2/k_{-1} , which shows the probability of formation of I and II from the intermediate, equals three. The same conclusions hold also for the reverse reactions (the principle of microscopic reversibility). The concentration of the intermediate was also calculated and the result obtained was in accord with the value determined indirectly by gas-liquid chromatography. The fact that the concentration of the intermediate increases with the increasing dielectric constant of the solvent, can be considered as a proof of the ionic nature of the intermediate.

EXPERIMENTAL

All solvents were dried and purified using standard procedures^{8,9}. The kinetic measurements and gas-liquid chromatographic analyses were performed similarly as described in ref.¹.

2-Nitro-3,3-dimethyl-1-butene¹⁰ (I)

Condensation of 1-nitro-2,2-dimethylpropane¹¹ with paraformaldehyde afforded 2-nitro-3,3-dimethyl-1-butanol, b.p. 83°C/1 Torr, in 53% yield (ref.¹⁰ gives b.p. 82°C/1 Torr, yield 56%). The alcohol was transformed into its acetate, b.p. 112°C/11 Torr, in 80% yield (ref.¹⁰ states 110°C/10 Torr, yield 80%). The acetate was pyrolysed in the presence of sodium acetate and gave the olefin of 95% purity, b.p. 75°C/52 Torr. Rectification under nitrogen led to the product of 98% purity.

1-Nitro-3,3-dimethyl-1-butene¹² (*II*)

The condensation conditions were analogous to that described in ref.¹³. A mixture of freshly distilled trimethylacetaldehyde¹⁴ (17.2 g) and nitromethane (12.2 g) in water (50 ml) was cooled to 0°C and 33% aqueous potassium hydroxide solution (26 ml) added portionwise. The mixture was extracted with ether, the aqueous layer cooled and acidified. The product was taken up into ether, the ethereal layer dried over sodium sulphate and taken down. Distillation of the residue afforded 13 g (44%) of 1-nitro-3,3-dimethyl-2-butanol, b.p. 85°C/6 Torr. For C₆H₁₃NO₃ (147.2) calculated: 48.98% C, 8.84% H, 9.52% N; found: 48.88% C, 8.91% H, 9.45% N. This compound was transformed into the acetate which was pyrolysed in the liquid phase⁶ to give the product *II*, b.p. 45°C/3 Torr. The overall yield was 38%, purity 99% (ref.¹² states b.p. 30°C/1 Torr.)

(1,1-²H₂)-2-Nitro-3,3-dimethyl-1-butene (*III*)

(²H₂)-Paraformaldehyde¹⁵ (2 g) and 30% potassium deuterioxide in deuterium oxide (0.1 ml) was added to a solution of 1-nitro-2,2-dimethylpropane¹¹ (6 g) in ethyl acetate (10 ml) and the mixture was heated under stirring till it became homogeneous. The solution was cooled, acidified with dilute hydrochloric acid, dried and the solvent distilled off.

In an alternative procedure, the (²H₂)-paraformaldehyde (2 g) was dissolved in 2-propanol under stirring and catalysis with potassium fluoride¹⁶. 1-Nitro-2,2-dimethylpropane (6 g) was added at 30°C and the mixture was stirred for 4 hours. Both these procedures afforded (1,1-²H₂)-2-nitro-3,3-dimethyl-1-butanol, b.p. 89°C/1 Torr, in the respective yields 52% and 59%. The corresponding nitro olefin was obtained by dehydration of the nitro alcohol with phthalic anhydride¹. The product was fractionated under nitrogen, purity 98%, b.p. 40°C/10 Torr. For C₆H₉D₂NO₂ (131.1) calculated: 55.00% C, 6.87% H, 3.06% D, 10.86% N; found: 55.20% C, 6.97% H, 2.70% D, 10.71% N. The isotopic purity was 86%.

(1,2-²H₂)-1-Nitro-3,3-dimethyl-1-butene (*IV*)

The compound *III* was isomerised in tetrahydrofuran solution under catalysis with triethylamine. After the equilibrium had been attained, the solvent was evaporated and the product isolated by fractionation under nitrogen. For C₆H₉D₂NO₂ (131.1) calculated: 55.00% C, 6.87% H, 3.06% D, 10.65% N; found: 55.25% C, 6.99% H, 2.71% D, 10.70% N.

(1-²H)-1-Nitro-3,3-dimethyl-1-butene (*V*)

The condensation of (²H₃)-nitromethane with trimethylacetaldehyde was carried out similarly as in the case of the non-deuterated compound, and the desired *V*, b.p. 35°C/1 Torr, was obtained in 43% yield; isotopic purity 91% (according to PMR spectra and elemental analysis). For C₆H₁₀DNO₂ (130.1) calculated: 55.35% C, 7.69% H, 1.53% D, 10.71% N; found: 55.52% C, 7.85% H, 1.40% D, 10.76% N.

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