Secondary deuterium kinetic isotope effects on the thermolysis of 1-pyrazolines

BASIL H. AL-SADER AND ROBERT J. CRAWFORD
Department of Chemistry, University of Alberta, Edmonton, Alberta

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Secondary kinetic isotope effects on four deuterated 1-pyrazolines support the formation of a trimethylene intermediate during gas phase thermolysis. Calculation of cyclization relative rate constants for the trimethylene intermediates reveals that substitution of hydrogen by deuterium has no effect when the terminal methylenes are substituted, but the rate constants are decreased when the central methylene's hydrogens are substituted. Explanations are advanced for all of the observed effects.

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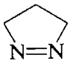
Introduction

Secondary deuterium kinetic isotope effects offer a useful method of characterizing the bond cleavages occurring in the rate-determining transition state of thermolysis reactions. Seltzer and co-workers (1) have established that the substitution of hydrogen by deuterium on the nitrogen bearing carbon of an azoalkane increases $\Delta G^{\ddagger}$ by 80 to 110 cal per deuterium (i.e. 12 to 15% per deuterium at 105°) when that carbon–nitrogen bond is breaking. A similar effect has been observed in solvolytic processes (2). Wolfsberg and Stern (3) suggest that the α-isotope effect arises from the difference in the initial and transition states of the force constants of the HCX bond, the major contribution arising from the bending force constant.

In earlier work it has been suggested that both carbon–nitrogen bonds are being cleaved in the rate-determining step of 1-pyrazoline thermolysis, and that a nitrogen free intermediate is produced (4). This interpretation arose from a progressive decrease in activation energy on going from 1-pyrazoline (**1**) to 3,3,5,5-tetramethyl-1-pyrazoline (**2**). The decrease per methyl group, approximately one kcal mole^{-1}, was that expected by analogy with azoalkane thermolysis (4). However one kcal mole^{-1} per methyl group is comparable to some conformational factors encountered in cyclic compounds, thus the increase in rate could arise from an increase in ground state energies. The replacement of hydrogen by deuterium leads to a predictable value for the kinetic isotope effect (1) and at the same time removes any conformational complications, or serious changes in non-bonded interactions.



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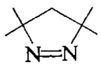

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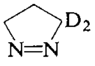

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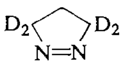

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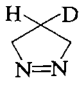

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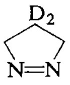

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Experimental

All samples of deuterated 1-pyrazolines were purified by gas–liquid chromatography (g.l.c.) using a Wilkens Aerograph Autoprep model A-700 with a 20 ft 10% Ucon-insoluble or Fluoropak column. Deuterium analyses were carried out on a Metropolitan–Vickers MS-2, single focussing mass spectrometer. The nuclear magnetic resonance (n.m.r.) spectra were measured using a Varian A-60 and an HR-100 spectrometer.

1,3-Dibromopropane-1,1,3,3-d_4

A solution of freshly distilled diethyl malonate (24.5 g, 0.15 mole) in dry ether (160 ml) was added dropwise to a well stirred solution of lithium aluminium deuteride (6.75 g, 0.16 mole) in dry ether (350 ml) at such a rate as to maintain steady reflux. After completion of addition, the refluxing was continued for an additional 3h, cooled to 0°, and water added slowly to decompose the excess deuteride. The solution was then acidified with dilute hydrobromic acid, the ether layer removed by distillation, and the crude product in the aqueous layer converted, without isolation, to the dibromide by the addition of 48% hydrobromic acid (116 g) and concentrated sulfuric acid (50 ml). The mixture was then refluxed for 7 h, and 10 to 15 ml of 48% hydrobromic acid were added at the end of each hour. The 1,3-dibromopropane was then distilled out of the solution, the organic layer was washed several times with a potassium carbonate solution, and dried over anhydrous sodium sulfate. Distillation gave 12.7 g (40% yield based on malonate), b.p. 165°.

1,3-Dibromopropane-1,1-d_2

A solution of freshly distilled β-propiolactone (14.4 g, 0.2 mole) in 160 ml dry ether was added, with stirring, to a solution of lithium aluminium deuteride (4.2 g) in 300 ml dry ether. The work-up and conversion to the dibromide was carried out in the same manner as for the aforementioned tetradeuterio sample.

TABLE I

Rate constants and secondary kinetic isotope effects for α-deuterated 1-pyrazolines at 229.40 ± 0.05°

Compound		10^4k (s^{-1})	k_H/k_D Observed	k_H/k_D Corrected to 105°	$\Delta\Delta G^{\ddagger}$ per deuterium cal $mole^{-1}$
1		23.82			
		23.98			
		23.77			
	Avg.	23.86 ± 0.11			
3*		20.06			
		19.87			
	Avg.	19.96 ± 0.13	1.19 ± 0.01	1.26 ± 0.01	86 ± 6
4*		16.94			
		17.20			
	Avg.	17.07 ± 0.18	1.40 ± 0.02	1.55 ± 0.02	84 ± 6

*Mass spectral and nuclear magnetic resonance analyses indicate samples to have greater than 98% deuteration in the positions indicated.

1,3-Dibromopropane-2,2-d_2

Diethyl malonate-2,2-d_2 prepared by exchanging diethyl malonate with sodium ethoxide in ethanol-*O-d*, (four exchanges) was reduced as above using lithium aluminium hydride and converted to the dibromide without isolation of the glycol.

1,3-Dibromopropane-2-d_1

Deuterium bromide, prepared by the addition of phosphorus tribromide to deuterium oxide, was added to allyl bromide using the photochemical method of Kharasch and Mayo (5).

1-Pyrazolines

The deuterated 1-pyrazolines were prepared from the corresponding pyrazolidines which in turn were synthesized from the deuterated 1,3-dibromopropanes by the previously described method (6).

Kinetic Method

The apparatus used is essentially that described by Smith and Bagley (7). The thermocouple used for temperature measurements was a four-junction model, and was calibrated against roll sulfur, tin (analytical), and lead (analytical).

Product Analysis

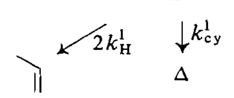
The exact product compositions were obtained by sealing degassed samples (2 μl) in small Pyrex bulbs (0.5 ml) and heating to 241 °C for greater than nine half-lives. The bulbs were placed in a bulb crusher and the products carried directly onto a 20 ft column of mineral oil on fire brick in tandem with a 20 ft column of 10% di-*n*-butyl malonate on Diatoport. Integrations were carried out using a planimeter.

Results and Discussion

The rate constants measured for each of the α-deuterated pyrazolines are recorded in Table I. The β-deuterated pyrazolines run at a different temperature are given in Table II. The results confirm that both carbon–nitrogen bonds are breaking in the rate-determining transition state.

The β-deuterium isotope effects are somewhat larger than those normally found (8). However, comparisons with other systems are difficult in that in the trimethylene species produced the hydrogens attached to the central methylene are β to both newly formed sp^2 centers. Hoffmann (9) has recently dealt with the singlet trimethylene species and hyperconjugative interactions play an important role in the stabilization of the species. It may be in fact just this hyperconjugative interaction that is giving rise to the enhanced β-deuterium isotope effects. Hodnett (10) has observed a value for the secondary β-tritium isotope effect on the isobutyl radical. This would tend to suggest 18 cal $mole^{-1}$ for the β-deuterium effect. A considerably smaller effect has been observed by Seltzer and Hamilton (11) for the 1-phenylethyl-2,2,2-d_3 radical; however, delocalization of the radical may account for the suppression of hyperconjugation in this case.

The proportion of cyclopropane and propylene produced on thermolysis of each of the pyrazolines is indicated in Table III. These proportions are controlled by the product-determining steps (Scheme 1) (4).



SCHEME 1

TABLE II

Rate constants and secondary kinetic isotope effects for β-deuterated 1-pyrazolines

Compound	Temperature		10^4k (s^{-1})	k_H/k_D Observed	k_H/k_D Corrected to 105°	$\Delta\Delta G^{\ddagger}$ per deuterium (cal $mole^{-1}$)
1	224.0		15.3			
	226.9		19.3			
5	224.0		14.76*			
			14.24			
		Avg.	14.50	1.05±0.01	1.06±0.01	52±10
6	226.9		17.00†			
			17.30			
		Avg.	17.15	1.12±0.01	1.14±0.01	56±10

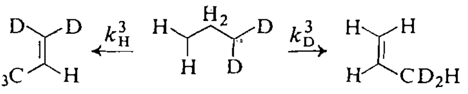
*Corrected for 4.9% $C_3H_6N_2$ (mass spectral analysis).
†Corrected for 11.3% $C_3H_5DN_2$ and 0.1% $C_3H_6N_2$ (mass spectral analysis).

TABLE III

Cyclopropane and propylene yields on thermolysis of pyrazolines at 241°

Compound		Cyclopropane	Propylene
1		88.45	11.55
		88.34	11.66
		88.51	11.49
		88.40	11.60
	Avg.	88.43±0.07	11.57±0.07
3		87.98	12.02
		87.99	12.01
		87.99	12.01
	Avg.	87.99±0.01	12.01±0.01
4		87.29	12.71
		87.51	12.49
		87.49	12.51
	Avg.	87.43±0.17	12.57±0.17
5		89.23	10.77
		89.32	10.68
		89.07	10.93
	Avg.	89.21±0.13	10.79±0.13
6		90.43	9.57
		90.17	9.83
		90.29	9.71
		90.17	9.83
	Avg.	90.27±0.12	9.73±0.12

Integration of the n.m.r. spectrum of the propylene produced from **3** indicates a 52:48 ratio of $CD_2H—CH═CH_2$ to $CD_2═CH—CH_3$, thus an inverse intramolecular kinetic isotope effect for k^3_H/k^3_D of 0.92. This is consistent with the observed increase in propylene formed from **3** relative to **1**. Inverse isotope effects of this magnitude have been observed earlier in the change of hybridization of a deuterated carbon from sp^2 to sp^3 (12).



The further increase in propylene yield on going from **3** to **4** is consistent with an isotope effect of 0.92 in the product-determining step. Using the isotope effect data from the n.m.r. observations we can effectively calculate the isotope effect on the cyclization reactions. Assuming[1] that $k^1_H = k^3_H$ on the basis that the changes in

$$\text{e.g.}\quad \frac{k^1{}_{cy}}{2k^1{}_H} = \frac{88.43}{11.57}$$

and

$$\frac{k^3{}_{cy}}{k^3_H + k^3_D} = \frac{k^3{}_{cy}}{2.09k^3_H} = \frac{87.99}{12.01}$$

hybridization occurring are the same in each case then we find that $k^1{}_{cy} = 1.00k^3{}_{cy}$. Similarly by assuming that $k^3_D = k^4_D$ we find that $k^3{}_{cy} = 1.01k^4{}_{cy}$. This would suggest that there is little or no change in the CH force constants of the terminal methylene groups of the trimethylene intermediate on going to cyclopropane; a fact borne out by the very similar frequencies of the C—H stretching vibrations of cyclopropane (3075 and 3009 cm^{-1}) (13) and the terminal methylene stretching frequencies of propylene (3089 and 2991 cm^{-1}) (14). The CH_2 bending, wagging, and rocking modes for cyclopropane (1475, 975, and 854 cm^{-1}) (13) and the terminal CH_2 of propylene (1420, 963, and 912 cm^{-1}) (14) similarly have a compensatory effect such that the total change in force constant on going from sp^2 in the trimethylene species to cyclopropane is negligible.

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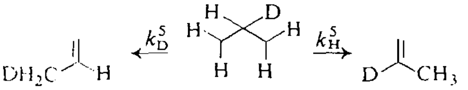
[1] This assumption seems justified on the basis that any secondary β-isotope effect would be expected to be smaller than the secondary α-isotope effect which is itself very small (see next paragraph).

The n.m.r. spectrum of propylene derived from **5** indicates that it is a 60:40 mixture of $CH_2{=}CD{-}CH_3$ to $CH_2{=}CH{-}CH_2D$, i.e. an isotope effect $k^5{}_H/k^5{}_D = 1.50 \pm 0.08$. There may be a small secondary isotope effect upon $k^5{}_H$, however, this is not expected to be greater than 1 to 2% since, using the Hammond hypothesis (15), one would expect the transition state to resemble strongly the intermediate rather than the propylene. Wiberg has shown that isotope effects of this



type are in the order of 1% (16). Assuming $k^1{}_H = 1.01\, k^5{}_H$ we can compare the cyclization rate constants $k^1{}_{cy}$ and $k^5{}_{cy}$. The analytical data in Table III indicate that:

$$\frac{k^1{}_{cy}}{2k^1{}_H} = \frac{88.43}{11.57} \quad \text{and} \quad \frac{k^5{}_{cy}}{k^5{}_H + k^5{}_D} = \frac{89.21}{10.79}$$

Using the aforementioned n.m.r. data we find that $k^1{}_{cy} = 1.13\, k^5{}_{cy}$. Similarly if we go through some type of calculations assuming that $k^5{}_D = 1.01\, k^6{}_D$ then we find that $k^5{}_{cy} = 1.13\, k^6{}_{cy}$. Thus deuterium substitution at the 4-position of the pyrazolines slows down the rate at which the intermediate cyclizes to cyclopropane. The quantity is exactly that observed for sp^3 carbons going to sp^2, in keeping with the previously mentioned characteristics of the cyclopropane structure.

It is evident that this study of secondary kinetic isotope effects is consistent with the proposed formation of the trimethylene intermediate in the thermolysis of 1-pyrazoline, and provides a strong case for the cleavage of both carbon–nitrogen bonds in the rate-determining transition state.

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