

BASE CATALYSED HYDROGEN EXCHANGE IN CYCLOPROPYLCYANIDE

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Abstract—The exchange of the α -hydrogen atom in cyclopropylcyanide has been studied in methanol and sodium methoxide as a base. The reaction is both first order in base and in cyclopropylcyanide. Using base concentrations from 0.01M up to 3.0M the logarithm of the exchange rate constant depends linearly on the H_- function. For the H/D exchange, the following activation parameters have been calculated: $\Delta H^\ddagger = 27.2 \pm 0.2$ kcal/mol, $\Delta S^\ddagger = 15.7 \pm 0.8$ e.u. (326°K). The kinetic isotope effect is found to be $k_D/k_T = 1.33$ and $k_H/k_D = 1.9$. This suggests that the slowest reaction step is not proton abstraction, but the exchange between labelled and unlabelled solvent molecules in a relatively rapidly formed solvated carbanion.

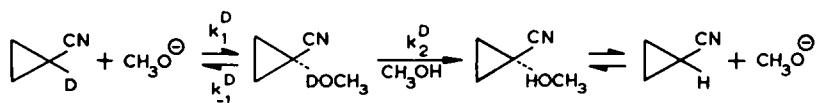
INTRODUCTION

WALBORSKY *et al.*^{1,2} have studied the base catalysed racemization and hydrogen exchange reactions of 2,2-diphenylcyclopropylcyanide with methanol and ether as the solvent. It has been observed that the pseudo-first order exchange in methanol is about 8,000 times faster than the racemization. This may point to a high degree of retention of configuration of the carbanionic transition state.

As part of investigations on the acidity of the α -hydrogen atom in cyclopropane derivatives we wish to report the results of the base-catalysed H/D and D/T exchange of cyclopropylcyanide in methanol with sodium methoxide as the base.

Kinetics

The discussion of the kinetics will be exemplified with the exchange of α -deuterio-cyclopropylcyanide (RD) in methanol:



The reaction is essentially irreversible by the excess of methanol. The kinetic expression for the exchange rate v_D is:

$$v_D = k_O^D a_{RD} a_{CH_3O^\ominus} \quad (1)$$

where a_{RD} and $a_{CH_3O^\ominus}$ = the activities of RD and CH_3O^\ominus

k_O = overall rate constant, in which the index D denotes the exchange of deuterium.

* Part of the forthcoming thesis of W. Th. van Wijnen.

¹ H. M. Walborsky, A. A. Youssef and J. M. Motes, *J. Am. Chem. Soc.* **84**, 2465 (1962).

² H. M. Walborsky and F. M. Hornyak, *J. Am. Chem. Soc.* **77**, 6026 (1955).

Applying the steady-state condition to the solvated substrate anions it can be deduced

$$k_0^D = \frac{k_1^D k_2^D}{k_{-1}^D + k_2^D} \quad (2)$$

During a kinetic run the amount of sodium methoxide remains virtually constant. Furthermore the concentration of α -deuteriocyclopropylcyanide is taken relatively low, and does not vary significantly in all series of experiments, thus $a_{RD} \approx [RD]$ and equation (1) reduces to

$$v_D = k^D [RD] \quad (3)$$

where

$$k^D = k_0^D \cdot a_{CH_3O^\ominus} \quad (4)$$

On integration, we find

$$k^D \cdot t = \ln \frac{[RD]_{t=0}}{[RD]_t} \quad (5)$$

The acidity function H_- , with respect to methanol as the standard state, is defined as³:

$$H_- = pK_{CH_3OH} + \log a_{CH_3O^\ominus} + \log \frac{f_{RD}}{f_{R^-}} - (n + 1) \log a_{CH_3OH} \quad (6)$$

where pK_{CH_3OH} = autoprotolysis constant of methanol

f_{RD} and f_{R^-} = activity coefficients of RD and of the solvated anion R^-

n = "effective solvation number" of the methoxide ion.

From Eqns (3) and (6) it can be derived that

$$\log k^D = H_- - (n + 1) \log a_{CH_3OH} + \left\{ \log \frac{f_{RD}}{f_{R^-}} + \log k_0^D - pK_{CH_3OH} \right\} \quad (7)$$

Consequently, the sum of the terms between brackets is constant. As the activity coefficient of methanol becomes unity in dilute sodium methoxide solution, the H_- function (Eq. 6) approaches to

$$H_- = \log [CH_3ONa] + pK_{CH_3OH} \quad (8)$$

At low base concentrations Eq. (4) reduces to

$$k^D = k_0 [NaOCH_3] \quad (4a)$$

It is clear that similar expressions can be derived for the exchange of ordinary cyclopropylcyanide (RH) in CH_3OD .

RESULTS AND DISCUSSION

At base concentrations ranging from 0.01 M to 3.0 M the reaction is of first order in cyclopropylcyanide, in accordance with Eq. (3). The concentration of the substrate has been kept low (< 0.2 M) in order to avoid kinetic complications due to the

³ R. A. More O'Ferral and J. H. Ridd, *J. Chem. Soc.* 5030 (1963).

dilution of the hydrogen isotope in methanol-d. Some typical results are shown in Fig. 1.

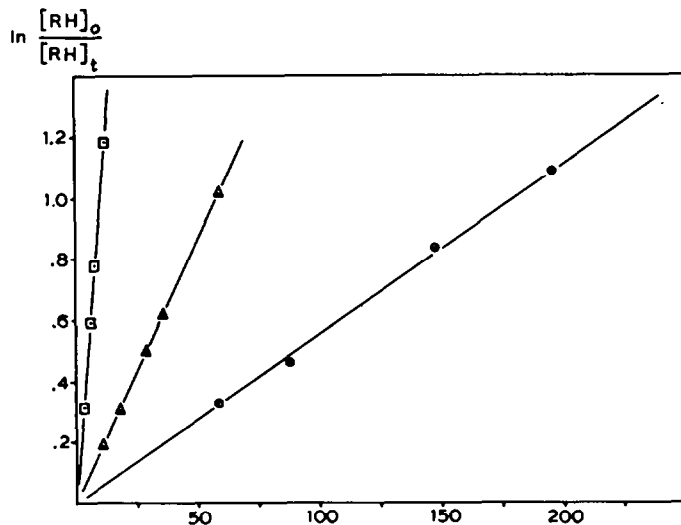


FIG. 1 Exchange reaction of cyclopropylcyanide in CH_3OD at 326.2°K . $[\text{CH}_3\text{ONa}] = 0.504\text{M}$ (\circ); 0.94M (Δ); 2.27M (\square).

The exchange rate is also found to be first order in sodium-methoxide up to 0.1 M .

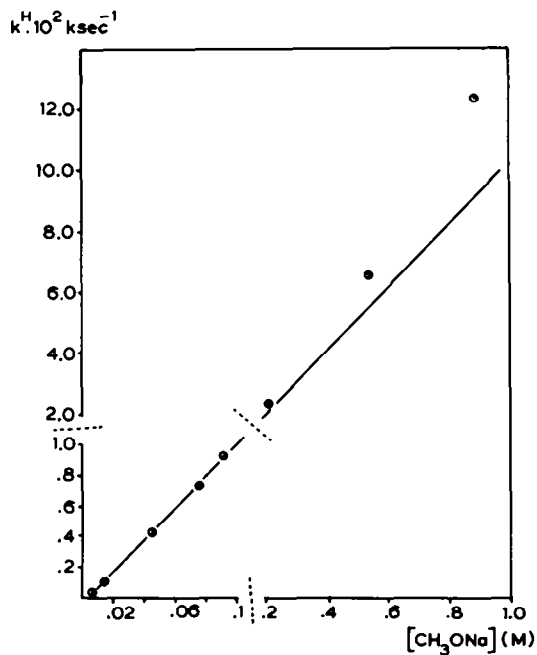


FIG. 2 Exchange reaction of cyclopropylcyanide in CH_3OD at 343°K . The rate constant k^H as a function of $[\text{CH}_3\text{ONa}]$.

In the region above 0.1 M however, the order deviates from unity (cf. Fig. 2). Keeping in mind, that activity terms rather than concentrations must be used, it is reasonable to apply the acidity function H_- for the stronger basic solutions. However, it has been shown, that some types of indicators give rise to H_- acidity functions, which differ appreciably in sodium methoxide solutions.³⁻⁵ These deviations may be attributed to differences in the solvation number n of the methoxide ion (cf. Eq. 6).

In accordance with Eq. 7, a plot of $\log k^H$ versus H_- gives straight lines with slopes, which only depend on the H_- scale used (cf. Fig. 3).

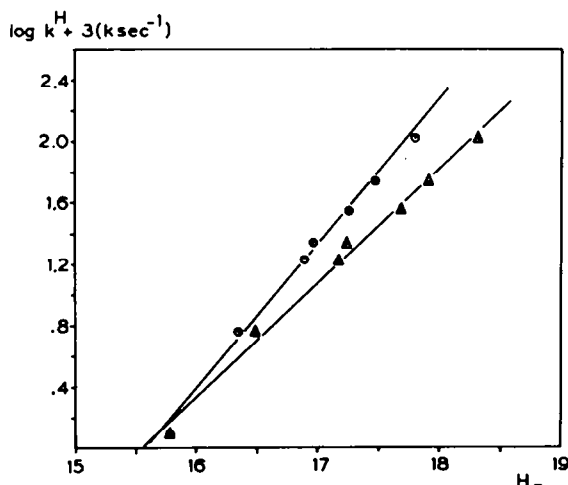


FIG. 3 Exchange reaction of cyclopropylcyanide in CH_3OD at 326.2°K . $\log k^H$ as a function of the acidity function H_- (eq. 7). H_- values of Rochester⁴ (\circ) and of More O'Ferrall and Ridd³ (Δ).

It is found that the relation $\log k = bH_- + c$, in which b and c are constants, holds over the whole range from dilute to concentrated solutions of sodium methoxide in methanol. Furthermore it turns out that the constant b is affected neither by the isotopic content of the solvent nor by the reaction temperature (cf. Table 1).

TABLE 1. THE RELATION $\log k = bH_- + c$, FOR THE H/D EXCHANGE IN CYCLOPROPYLCYANIDE

Solvent	Number of experiments	Temp $^\circ\text{K}$	H_- (Rochester) ⁴		H_- (More O'Ferrall) ³	
			b	c	b	c
CH_3OD	15	306.1	—	—	0.74 ± 0.07	-12.5 ± 1.4
CH_3OD	33	326.2	0.94 ± 0.01	-14.7 ± 0.4	0.75 ± 0.03	-11.6 ± 0.5
CH_3OD	19	343.0	0.94 ± 0.04	-13.7 ± 0.1	0.76 ± 0.04	-10.9 ± 0.3
CH_3OH^*	38	326.2	0.95 ± 0.03	-15.1 ± 0.3	0.78 ± 0.02	-12.5 ± 0.4

* The substrate was α -deuteriocyclopropylcyanide.

⁴ C. H. Rochester, *J. Chem. Soc.* 676, 2404 (1965); *Ibid.* 121 (1966).

⁵ K. Bowden, *Chem. Rev.* 66, 119 (1966).

The entropy of activation ΔH^* and the entropy of activation ΔS^* are calculated

$$\Delta H^* = 27.2 \pm 0.2 \text{ kcal/mole}$$

$$\Delta S^* = 15.7 \pm 0.8 \text{ e.u. (326.2}^\circ\text{K)}$$

We also carried out kinetic runs with the deuterated and the tritiated cyclopropylcyanide in ordinary methanol. The results are given in Table 2.

TABLE 2. EXCHANGE RATE CONSTANT k_D AND k_T OF THE CORRESPONDINGLY LABELLED CYCLOPROPYLCYANIDE IN $\text{CH}_3\text{OH}/\text{CH}_3\text{ONa}$ AT 326.2°K

$[\text{CH}_3\text{ONa}]$	H ₋ (Rochester)	$k^D \times 10^3$ ksec ⁻¹	$k^T \times 10^3$ ksec ⁻¹	k^T/k^D
0.876	16.82	8.73 ± 0.3	6.82 ± 0.3	0.78 ± 0.03
1.02	16.95	10.27 ± 0.4	7.51 ± 0.3	0.73 ± 0.03
1.10	17.01	11.72 ± 0.4	8.80 ± 0.3	0.75 ± 0.03
1.14	17.04	13.31 ± 0.5	9.32 ± 0.3	0.72 ± 0.03

It is interesting to correlate the average value of $k_T/k_D (=0.74)$ with the k_H/k_D isotope effect. Applying the relation of Swain *et al.*⁶: $k_H/k_D = (k_D/k_T)^{2.26}$, we calculate $k_H/k_D = 1.9$. A similar result ($k_H/k_D = 1.9$) is obtained from corresponding experiments in CH_3OH and CH_3OD (cf. Table 1), if we assume as a first approximation that the H₋ function is the same in both alcoholic media.

It must be concluded from the observed small isotope effect, that the proton abstraction by base is not involved in the rate-determining step (k_1^D). Cram *et al.*⁷ interpreted such low values on the basis that $k_{-1}^D \gg k_2^D$ (cf. reaction scheme). This means that Eq. (2) simplifies to

$$k_0^D = k_1^D \cdot k_2^D/k_{-1}^D$$

Hence the rate-determining step, being associated with k_2^D , should be the diffusion of solvent molecules into the solvation shell around the cyclopropylcyanide anion.⁸

Both the isotope effect and the observed dependence of the exchange rate with the H₋ function are in accordance with the mechanism as outlined in the reaction scheme.

EXPERIMENTAL

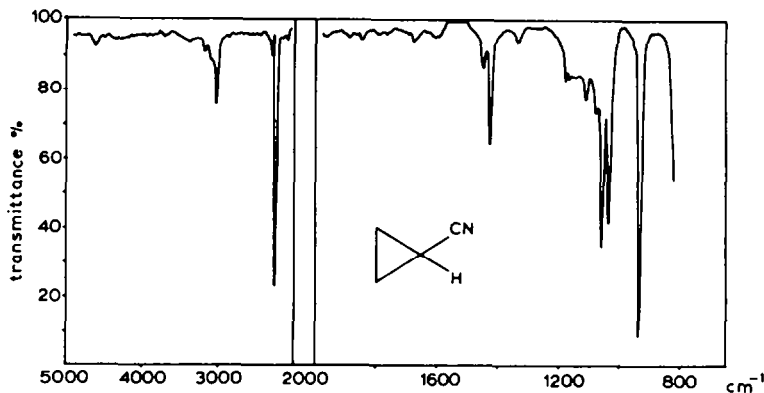
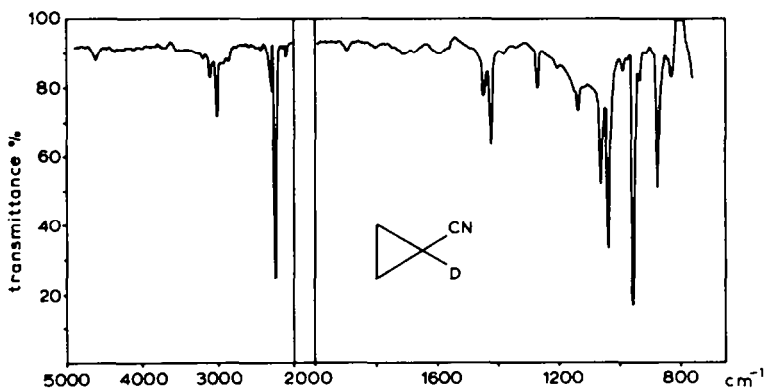
Deuterium analysis. The deuterium analysis of MeOH was determined on a Varian Associates Model A-60 NMR spectrometer, using benzene as a standard. The deuterium analysis of cyclopropylcyanide was carried out on a Perkin Elmer 125 IR spectrophotometer.

On comparing the IR spectra of cyclopropylcyanide and of α -deuteriocyclopropylcyanide, we were able to assign the band at 934 cm^{-1} and at 957 cm^{-1} to the C—H and C—D deformation vibration respectively. It was not possible to base an accurate quantitative analysis on these two bands without using another absorption band as an internal standard. As such the band at 1044 cm^{-1} is suitable because it is insensitive for the deuterium percentage of the sample. Good straight lines could be obtained when the ratio E_{957}/E_{1044} or E_{934}/E_{1044} was plotted versus the percentage deuterium in cyclopropylcyanide. The accuracy of the analysis was about 3% absolute.

⁶ C. G. Swain, E. C. Stivers, J. F. Reuwer Jr. and L. J. Schaad, *J. Am. Chem. Soc.* **80**, 5885 (1958).

⁷ D. J. Cram, D. A. Scott and W. D. Nielsen, *J. Am. Chem. Soc.* **83**, 3696 (1961).

⁸ We learned from an abstract of Motes' thesis, that this mechanism also might underly the base-catalysed hydrogen exchange of 2,2-diphenylcyclopropylcyanide, J. M. Motes, *Diss. Abstr.* **26**, 6375 (1966).

FIG. 4. IR spectrum of cyclopropylcyanide in CCl_4 .FIG. 5. IR spectrum of α -deuteriocyclopropylcyanide (90 atom % D) in CCl_4 .

Determination of the activity of α -tritiocyclopropylcyanide. The activity of α -tritiocyclopropylcyanide was determined with an internal flow proportional counter operating at 150° and connected with a Wilkens Aerograph 90-P gas chromatograph with katharometer detection using He/CH_4 (85:15) as a carrier gas.* The specific activity of cyclopropylcyanide was calculated as the ratio of the number of counts and the recorded peak area, the latter being directly proportional to the amount of cyanide.

Synthesis of deuteriated and tritiated methanol. Mg (80 g) was dissolved in 1 l MeOH. The excess MeOH was distilled off and the magnesium methylate was dried *in vacuo* for 8 hr at 200° . D_2O (75 g) was then added and the mixture was allowed to stand overnight at room temp. CH_3OD was then distilled *in vacuo*, yield = 80–90%; 97–99 D-atom %. Tritiated MeOH was prepared in a similar way, using tritiated water (0.2 mC/ml), yield = 80–90%; activity 0.1 mC/ml.

Synthesis of deuteriated and tritiated cyclopropylcyanide. Cyclopropylcyanide (1 g) was heated in 5 ml 2M MeONa in MeOD for 8 hr at 50° . The reaction mixture was poured into a cold mixture of 25 ml H_2O and 5 ml ether. The water layer was extracted with ether (3×2 ml). The combined supernates were washed with sat NaCl(aq) (20 ml) and dried (MgSO_4). The ether was distilled and the residue was subjected to preparative gas chromatography, yield = 0.5 g; 70–80 D-atom %.

Cyclopropylcyanide was tritiated in a similar way using tritiated MeOH.

Preparation of sodium methoxide-methanol solutions. A stock soln of MeONa in MeOH (4M) was prepared according to More O'Ferral.⁹ It was stored in sealed soft-glass ampoules at -35° . The less concentrated

* W. Th. van Wijnen, Thesis, to be published.

⁹ R. A. More O'Ferral, Ph.D. Thesis, London (1962).

sols were prepared by dilution with a given amount of MeOH. The base strength was found by titration with acid.

Kinetic measurements. About 0.1 g of cyclopropylcyanide and a given amount of MeONa in 5 ml MeOH was heated in soft-glass ampoules at the desired temp. The reaction was stopped by cooling the ampoule down to -35° . The cyanide was isolated as described in the synthetic part. It was collected in CCl_4 (150 μl).

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