Use of PMR spectroscopy for quantitative measurements Kinetics of formation of 2-cyanoquinoxaline-1,4-dioxide from 2-acetoxyiminomethylquinoxaline-1,4-dioxide

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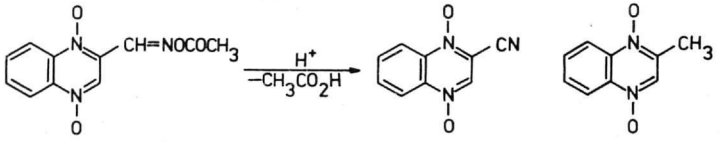
The elimination of acetic acid from 2-acetoxyiminomethylquinoxaline-1,4-dioxide and the formation of 2-cyanoquinoxaline-1,4-dioxide in trifluoroacetic acid is a first-order reaction. A novel experimental procedure of kinetic measurements using a direct recording of a height of signal selected from the spectrum of a reacting compound was found to be superior to the commonly used repeated recording of the corresponding part of the spectrum.

Удаление уксусной кислоты из 2-ацетоксииминометилхиноксалин-1,4-диокиси и образование 2-цианохиноксалин-1,4-диокиси в трифторуксусной кислоте представляет собой реакцию первого порядка. Описывается новый метод кинетического измерения, состоящий из прямого регистрирования высоты избранного сигнала из спектра реагирующего вещества. Метод является более удобным по сравнению с обычно применяемым методом повторной регистрации соответствующей части спектра.

The fact that the intensity of a p.m.r. signal is proportional to the number of protons responsible for that signal, enables to use p.m.r. spectroscopy in different quantitative determinations [1, 2], one of which is the measurement of reaction rates. To be of value, a p.m.r. method should be, naturally, more rapid and specific and at least as accurate as other possible procedures. For kinetic measurements, the p.m.r. spectroscopy is advantageous in particular, if any single sharp p.m.r. signal of the starting material is missing in the spectrum of the product and if the reaction in question takes place in a homogeneous medium not hindering the direct recording of the spectrum.

We have already observed [3] that decomposition of 2-acetoxyiminomethylquinoxaline-1,4-dioxide (*I*) to 2-cyanoquinoxaline-1,4-dioxide (*II*) occurred in

acid media. This reaction lowered the yield of *I* during acetylation of the corresponding oxime, and therefore, we studied its kinetics in order to eliminate the formation of the unwanted by-product (Scheme 1)



I *II* *III*

Scheme 1

Experimental

P.m.r. spectra of the investigated compounds were determined in about 10% solution in deuterated trifluoroacetic acid. The measurements were performed on a p.m.r. spectrometer Tesla BS 487C (80 MHz) using hexamethyldisiloxane (δ 0.05 p.p.m.) as internal standard. Chemical shifts of unresolved multiplets (m) were estimated from their centres. The p.m.r. chemical shifts of all compounds are in Table 1.

Table 1

PMR chemical shifts in δ p.p.m.

Compound	H-5,H-8	H-6,H-7	H-3	*CH*=N	*CH*$_3$
I	8.39 m	7.82 m	8.86 s	9.18 s	2.04 s
II	8.36 m	7.85 m	8.84 s	—	—
III	8.36 m	7.79 m	8.67 s	—	2.54 s

2-Acetoxyiminomethylquinoxaline-1,4-dioxide (*I*) was prepared from 2-hydroxyiminomethylquinoxaline-1,4-dioxide and acetic anhydride in acetic acid solution [3]; m.p. 187—188°C (acetic acid).

For $C_{11}H_9N_3O_4$ (247.2) calculated: 53.44% C, 3.67% H, 17.00% N; found: 53.10% C, 3.42% H, 17.15% N.

2-Methylquinoxaline-1,4-dioxide (*III*) was prepared from benzofuroxan-1-oxide and acetone [4]; m.p. 175—176°C (ethanol).

For $C_8H_8N_2O_2$ (176.2) calculated: 61.36% C, 4.58% H, 15.90% N; found: 61.33% C, 4.64% H, 16.24% N.

2-Cyanoquinoxaline-1,4-dioxide *(II):* a mixture of 2-hydroxyiminomethylquinoxaline-1,4-dioxide (2.05 g; 0.01 mole), acetic anhydride (1.5 ml), conc sulfuric acid (0.1 ml), and glacial acetic acid (4 ml) was refluxed for 15 min and poured into cold water (100 ml). Yellow crystals were filtered by suction and washed with water. Yield 85%; m.p. 209—210°C (acetic acid). IR ν(C≡N) 2260 cm^{-1}.

For $C_9H_5N_3O_2$ (187.2) calculated: 57.76% C, 2.69% H, 22.45% N; found: 58.01% C, 2.92% H, 22.40% N.

Procedure A

A mixture of *I* (123.6 mg; 5×10^{-4} mole) and *III* (88.1 mg; 5×10^{-4} mole) dissolved in trifluoroacetic acid (1 ml) in a p.m.r. tube was placed in thermostated water bath 80, 75, 70, 65, and 60°C ±0.1°C, respectively. In time periods 5—20 min, the reaction was discontinued by cooling the tube in an ice bath to 20°C. At that temperature the p.m.r. spectrum was recorded in the δ 9.25—8.50 p.p.m. range seven times, and the heights (in mm) of the singlets at δ 9.18 and 8.67 p.p.m. were determined. The maximum and minimum values for each signal were omitted and the mean of the remaining five values was calculated. The spectrometer setting for all other measurements was maintained the same. The mean height of the signal selected as standard (δ 8.67 p.p.m.) must also be kept constant. Should it, however, vary, due to homogeneity instabilities, the mean intensity of methine CH=N signal must be correspondingly corrected. Graphical presentation of these results is provided in Fig. 1.

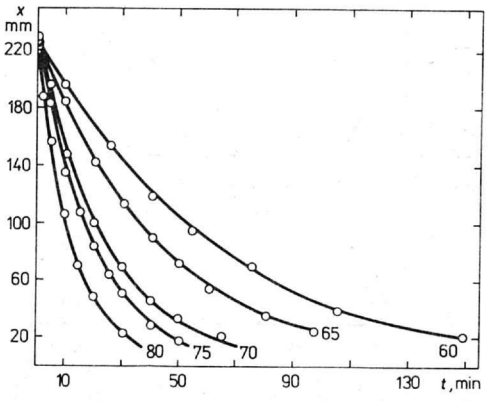


Fig. 1. Decrease of signal height with time.

Procedure B

1. A mixture of *I* (123.6 mg; 5×10^{-4} mole) and *III* (88.1 mg; 5×10^{-4} mole) dissolved in trifluoroacetic acid (1 ml) in a p.m.r. tube was heated at a programmed temperature (80, 75, 70, and 65°C ±0.5°C, respectively) directly in the temperature probe of a p.m.r. spectrometer. The height of the methine CH=N signal was recorded by the same way as used in the Indor technique [5]. During the experiment, the pen moved from left upper to right

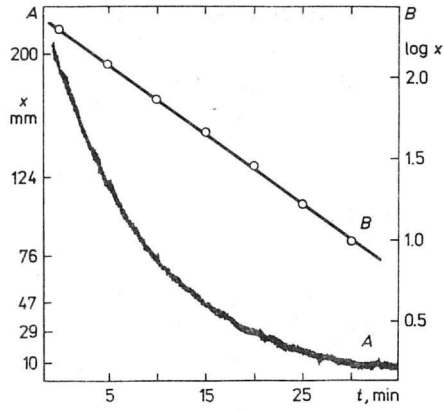


Fig. 2. Direct record of signal intensity decrease (A) and transformation to the logarithmical scale (B).

lower corner of the registration paper plotting the decrease of the signal intensity *vs.* time (Fig. 2, curve A).* Hexamethyldisiloxane was used as a field/frequency lock signal. The homogeneity was carefully adjusted and maintained by autoshim Y; its stability was continuously checked by a sensitive voltmeter connected to the output of the detector of absorption signal from the internal lock system. Amplification and sweep rate of the recorder were properly adjusted so as the full area of the paper was used. The RF power was kept low enough to avoid the saturation of the recorded signal. The zero line position of the pen was estimated at the proper frequency from the blank part of the spectrum. An appropriate number of signal amplitude data from the recorded exponential curve was transferred to the logarithmical scale and the linear plot B in Fig. 2 was constructed.

2. A solution of I (123.6 mg) in trifluoroacetic acid (1 ml) was investigated by the same procedure as described above.

3. A solution of I (123.6 mg) in trifluoroacetic acid—acetic acid mixture (4:1 vol.) (1 ml) was studied as above.

Results and discussion

The p.m.r. signal of the methine CH=N proton of I is a sharp singlet at δ 9.18 p.p.m. not overlapped by other signals. Therefore, the decrease of its intensity during the reaction is easy to follow and it may be used for the calculation of kinetic parameters.

The highest accuracy in p.m.r. signal intensity measurement can be achieved by repeated recording of a signal and calculating the mean value of its height [2] from

* It is evident that also an increase of the p.m.r. signal of the reaction product is possible to record but, naturally, some time is necessary to wait till the signal develops in a proper intensity to enable an accurate setting of the irradiating frequency.

several measurements. The reaction has to be discontinued by cooling the sample to the temperature at which the reaction rate is negligible. However, a frequent quenching of the reaction decreased the calculated reaction rate (Fig. 3; procedure

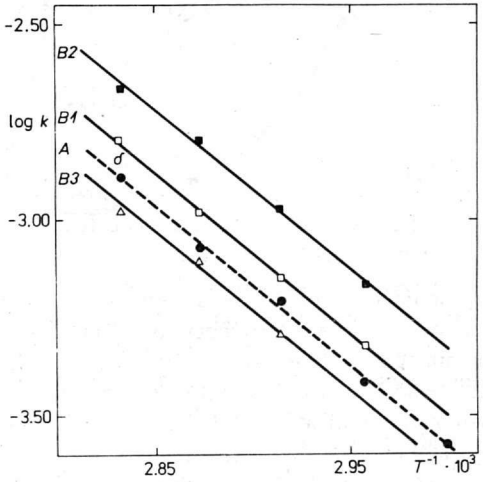


Fig. 3. Comparison of kinetics for different experimental procedures.

A). When the procedure *A* was repeated with only two measurements — one before the beginning of the reaction and the other at the time required to decompose about 80% of acetyl derivative *I* — the calculated rate constant was higher and agreed with accuracy ±2% with the value from the experiment made by procedure *B* at the same temperature.

For that reason, our experimental procedure *B*, the continuous measurement of decrease of the selected signal from the p.m.r. spectrum of reacting component by plotting the signal intensity on the recorder, gives more exact results. Furthermore, there is no need to use any standard for the correction of errors caused by rapid fluctuations of homogeneity. In this experimental arrangement, the homogeneity instabilities are manifested only as a noise on the registered monotonous curve which can be suppressed by filtration.

The investigated elimination of acetic acid from *I* is a first-order reaction as evidenced in Fig. 2 by the linear dependence of log *x* values (intensity in mm) on the time. Calculated rate constants and their log values together with log *A* values are listed in Table 2. From the average slope of the linear dependence of log *k* value on $1/T$ in Fig. 3, *i.e.*, $-E/2.303\ R$, the mean activation energy of the reaction $E = 78$ kJ mol^{-1} was calculated.

As the investigated reaction is acid catalyzed, its reaction rate decreases by addition of compound *III* which acts like a base and competes with acetyl

Table 2

Calculated kinetic parameters

Experimental procedure	T °C	$k \cdot 10^{-4}$ s^{-1}	log k	log A^a
A	80	12.90	−2.889	
	75	8.44	−3.074	8.65 ± 0.02
	70	6.20	−3.208	
	65	3.89	−3.410	
	60	2.66	−3.575	
B1	80	16.40	−2.785	
	75	10.30	−2.987	8.72 ± 0.02
	70	6.92	−3.160	
	65	4.68	−3.330	
B2	80	19.20	−2.717	
	75	16.00	−2.796	8.90 ± 0.02
	70	10.80	−2.967	
	65	6.68	−3.175	
B3	80	10.40	−2.979	
	75	8.33	−3.079	8.61 ± 0.04
	70	5.90	−3.229	

[a] Values of log A for each experiment were obtained from the graphical estimate in Fig. 3.

derivative I in protonation (procedure *B1*). Similarly, the rate of reaction is lowered by changing the strength of acid by substituting 20% of trifluoroacetic acid by weaker acetic acid (procedure *B3*).

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