MECHANISM OF THE STEREOISOMERIC CONVERSIONS OF NITROENAMINES CONTAINING A N—H BOND IN CHLOROFORM—METHANOL MIXTURES

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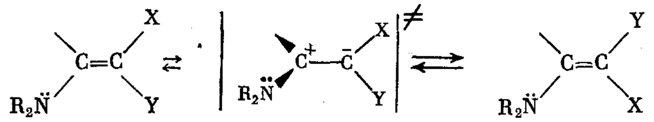
UDC 541.124:541.63:547.416

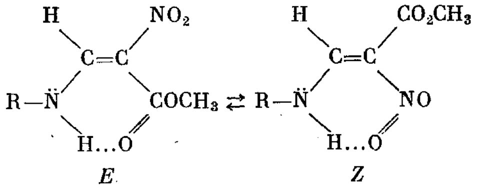
The rotation around the C=C bond (Z,E-isomerization) of enamines containing a tertiary amino group takes place by a thermal mechanism through a polar transition state [1].



(1)

The stereoisomeric conversions of enamines containing a secondary amino group may have a more complex mechanism due to the participation of the N—H bond in the reaction, the Z,E-isomerization of enamino ketones and enamino ethers containing a N—H bond being accompanied by proton-exchange reactions between the molecules of the compounds being isomerized [2, 3], while in proton-donor solvents the solvent molecules also participate in the exchange [4]. Consequently, the Z,E-isomerization of such compounds requires detailed study.

In this investigation we have studied the isomeric conversions in a proton-donor solvent of enamines containing a N—H bond, using as examples the nitroenamines (I) and (II)



(2)

$R = CH_3C_6H_4$ (I); CH_3 (II).

As solvents we chose the mixtures $CD_3OD—CDCl_3$ and $CH_3OH—CDCl_3$ in a ratio of 1:1 by volume, and we used dynamic PMR [5] as the method for studying the isomerization kinetics. Methanol was mixed with chloroform to increase the solubility of the compounds being studied and to increase the difference in the chemical shifts of the $COOCH_3$ groups in the Z- and E-isomers ($\Delta\delta_{CO_2Me}{}^{Z,E} = 6.6$ Hz for (I) and 5.8 Hz for (II)). The lifetime of the stereoisomers ($\tau_{Z,E}$) was determined by a total analysis of the line shape of the signals from this group in the PMR spectra according to a standard program for two-center exchange [5]. On studying the temperature dependence of the PMR spectra under conditions of slow Z,E-transitions it was found that the isomeric equilibrium constant of enamine (II) $K_e = [Z]/[E]$ (it was determined by integrating the CH signals, the difference in the chemical shifts of whose isomers is equal to 47.5 Hz) depends appreciably on temperature. Thus, the fraction of the Z-isomer increases with a decrease in the temperature of the specimen (Fig. 1). The relationship observed was therefore taken into account when calculating τ_E and τ_Z. In the case of enamine (I) this relationship is less well-defined; with a change in the temperature of the specimen from 14 to 51°C the value of K_e changes from 1.7 to 1.5. After calculating $\tau_{Z,E}$ from the temperature dependence of this parameter by the method of least squares the activation parameters of the Z,E-isomerization were found (Table 1). As follows from the data obtained on changing from enamine (I) to (II), i.e., with an increase in the electron-donor strength of the substituent R, the rate of the isomeric transitions ($1/\tau$) increases, while the quantities E_a, $\Delta H^{\neq}$, $\Delta S^{\neq}$ and $\Delta G^{\neq}$ decrease, which corresponds to a greater stability of the activated complex in case (II). This fact enables us to represent the isomerization of (I) and (II) within the framework of a thermal mechanism [1]. For the example of aromatic nitroenamines of

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A. N. Nesmeyanov Institute of Heteroorganic Compounds, Academy of Sciences of the USSR. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 8, pp. 1776-1780, August, 1981. Original article submitted January 19, 1981.

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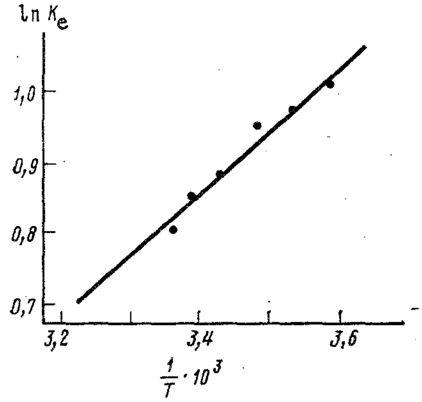


Fig. 1

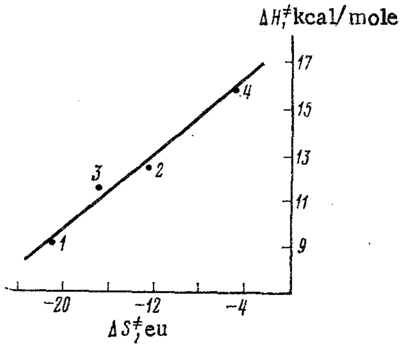


Fig. 2

Fig. 1. Temperature dependence of the isomeric equilibrium constant $K_e = [Z]/[E]$ of enamine (II) in CD_3OD–$CDCl_3$ solution in Arrhenius coordinates.

Fig. 2. Relationship between the parameters $\Delta H^{\neq}$ and $\Delta S^{\neq}$ for Z,E-isomerization of (II) in CD_3OD (1), CD_3OD–$CDCl_3$ (2); that of (I) in CD_3OD (3) and CD_3OD–$CDCl_3$ (4).

type (I) Z,E-isomerization has previously been detected involving a preliminary and kinetically controllable stage of ionization of the N–H bond and a subsequent rapid rotation into the mesomeric ion being formed (a dissociative mechanism), this being observed in solutions of basic aprotic solvents [6]. In spite of the reverse effect of a substituent being characteristic of such isomerization, to confirm the conclusion of a thermal mechanism for the isomerization of the nitroenamines being studied in methanol solution it is necessary to make certain that the mechanism of the stereoisomeric conversions does not alter during the transition from (I) to (II). As follows from Fig. 2, a satisfactory linear correlation is observed between the parameters ΔH and ΔS, which indicates the existence of a compensation

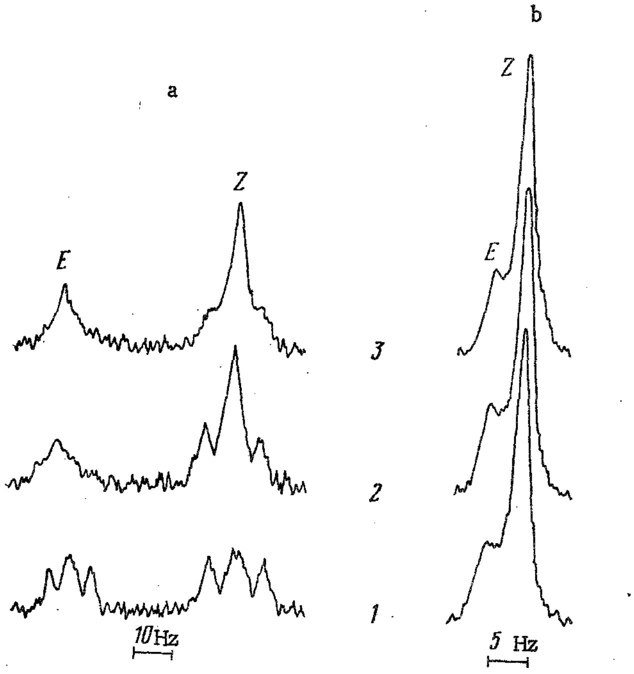


Fig. 3. PMR spectra of enamine (II) in CD_3OD–$CDCl_3$ solution in the region of the signals of CH = (a) and CO_2ME (b) recorded immediately after the preparation of the solutions (1) and over 1-2 min afterwards (2 and 3).

TABLE 1. Kinetic Parameters for the Z,E-Isomerization of Nitroenamines (I) and (II) in a $CDCl_3$—CD_3OD Mixture*

Compound	$\tau \cdot 10^2$ † sec		E_a, kcal/mole		$\Delta H^{\neq}$, kcal/mole		$\Delta S^{\neq}$, e.u.		$\Delta G^{\neq}_{298}$ kcal/mole	
	E	Z	E	Z	E	Z	E	Z	E	Z
(I)	12,8±0,6	20,2±1,2	16,6±1,2	16,6±1,2	16,0±1,1	16,0±1,1	−4,9±3,7	−5,8±3,8	17,5±0,5	17,8±0,5
(II)	2,2±0,1	4,1±0,2	13,0±0,6	14,8±0,6	12,4±0,6	14,2±0,6	−12,6±1,5	−8,0±1,2	16,1±0,4	16,6±0,4
(II)‡	0,81±0,04	1,5±0,06	9,7±0,6	11,1±0,6	9,1±0,6	10,5±0,6	−21,1±2,0	−18,0±1,8	15,4±0,3	15,9±0,3

*A variation in the concentration of the enamines from 0.19 to 0.29 M had no effect on the kinetics of the processes studied.
†At 50°C.
‡Z,E-isomerization in pure CD_3OD solution.

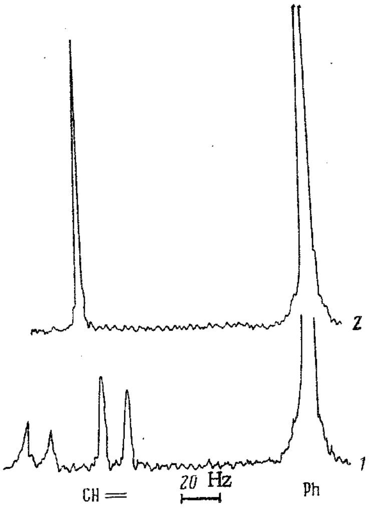
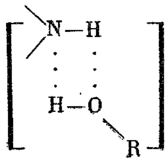


Fig. 4. PMR spectrum of enamine (I) in CH_3OH (1) and with added methanolic solution of sodium methylate (2) at 24°C.

effect [7] and, consequently, no change in the mechanism of the reaction with a change in R and the solvent. The activation parameters for (I) in methanol are taken from [4]. As follows from [6], a primary isotope effect is characteristic of a dissociative mechanism for Z,E-isomerization with a change from an enamine containing a N—H bond to its N-deutero analog. Consequently, we have studied the temperature dependence of the PMR spectra of (I) and (II) in $CH_3OH—CDCl_3$ and $CD_3OD—CDCl_3$ solutions. It was found that on changing from solutions of (I) and (II) in methanol to their deuteromethanol solutions the disappearance of the spin—spin coupling constant $J_{NH-CH} = 15$ Hz is observed in the PMR spectra, which indicates the replacement of a proton by a deuteron. However, in the region of the signals from the COOMe group the PMR spectra for different temperatures are virtually the same, both in methanol solution and in a solution of its deuterated derivative. Consequently, in the present case there is virtually no isotope effect in the reaction. The absence of an isotope effect is well illustrated by the PMR spectra (Fig. 3) recorded successively at 24°C over the 1-2 min immediately after dissolving (II) in a $CD_3OD—CDCl_3$ mixture. As may be seen from the spectra presented, the multiplicity of the CH— signals varies from a doublet of doublets to a doublet, which indicates a gradual replacement of a proton by a deuteron. Here the shape of the line from the COOMe group, which depends on the lifetime of the stereoisomers (fractions of a second), does not change. Thus, in our opinion the data presented indicate conclusively that the principal mechanism for the Z,E-isomerization of (I) and (II) in a mixture of chloroform and methanol is a thermal mechanism. It also follows from Fig. 3 that the rate of proton—deuteron exchange is appreciably lower than the rate of the stereoisomeric transitions of the enamine (II). This fact can be explained by the reactions proceeding through different transition states (3) [8] and (1), respectively



(3)

after the rupture of the intramolecular hydrogen bonds which is necessary both for proton exchange and for isomeric transformations.

The low basicity of methanol apparently does not enable the Z,E-isomerization of the compounds studied to be directed by a dissociative mechanism. However, this mechanism is probably realized on adding one drop of a 1 N methanolic solution of sodium methylate to a solution of enamine (I) in methanol. As follows from the PMR spectra (Fig. 4) the addition of a strong base leads to an abrupt acceleration of the stereoisomeric transitions with the disappearance of a spin—spin interaction in the NH—CH fragment. It should be noted that the rate of the isomeric transitions in the presence of sodium methylate is so high that it is not fixed in the time scale of the PMR method, even on cooling the specimen to —60°C. A similar action of sodium methylate is also found in the isomerization of the nitroenamine (II).

EXPERIMENTAL

The PMR spectra were recorded on a RYa-2309 spectrometer (90 MHz) in the internal stabilization regime against the signal from TMS in the solvent $CDCl_3:CD_3OD = 1:1$ by volume at 24°C. The accuracy of the thermostatting was ±0.5°C. PMR spectra of (I) (δ, ppm, E- and Z-): 3.87 and 3.78 (CO_2Me), 2.32 (CH_3), 7.11 and 7.14 (Ph), 8.91 and 8.40 (CH).

PMR spectra of (II) (δ, ppm, E- and Z-): 3.71 broad (CO_2Me), 8.57 and 8.03 (CH), 3.26 broad (NCH_3). The spectra from the COOMe groups under conditions of Z,E-transitions were calculated on a PDP-12 computer. The range of variation in temperature was 5-51°C. The solvents were purified by standard procedures [9]. Immediately prior to an experiment CH_3OH and CD_3OD were redistilled over $LiAlH_4$ and $LiAlD_3$, respectively. The samples were prepared under an argon atmosphere. Compounds (I) and (II) were synthesized by K. K. Babievskii.

CONCLUSIONS

1. The Z,E-isomerization of α-nitro-β-methylaminoacrylic ether and α-nitro-β-tolylaminoacrylic ether in a mixture of methanol and chloroform has been studied by dynamic PMR; the activation parameters of the process have been obtained.

2. The nature of the effect of substituents on the rate and energy parameters of Z,E-isomerization, the absence of a kinetic isotope effect, as well as the lower rate of proton exchange indicate that the isomeric transformations take place by a thermal mechanism.

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