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N-HETARYLETHYLENES.

1.* SYNTHESIS AND ISOMERIZATION OF 10-ALLYL- AND 10-PROPENYLPHENOXAZINES

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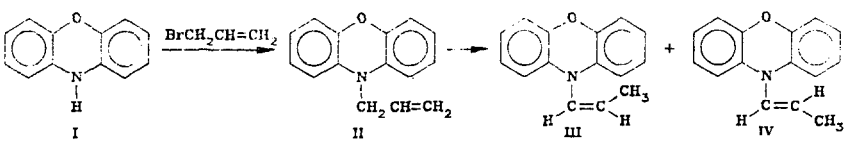
Alkylation of phenoxazine with allyl bromide has given 10-allylphenoxazine. The prototropic isomerization of 10-allylphenoxazine in DMSO on treatment with t-BuOK, KOH, and NaOH has been examined. At elevated temperatures, mixtures of cis- and trans-10-propenylphenoxazines are formed, but at room temperature in the presence of t-BuOK isomerization proceeds stereoselectively to give cis-10-propenylphenoxazine. The influence of temperature and reaction times on the isomeric composition of the 10-propenylphenoxazines has been studied. The cis-propenylphenoxazine obtained in the kinetically controlled reaction isomerizes under the reaction conditions to the equilibrium mixture of cis- and trans-isomers of 10-propenylphenoxazine.

Phenoxazines find extensive application, primarily as dyes [2]. Polymers derived from phenoxazine are used in electrophotography and related areas [3, 4]. There have, however, been no literature reports of the preparation of N-unsaturated phenoxazines, which might find applications for example in the preparation of polymers.

Enamines are commonly obtained preparatively by the base-catalyzed isomerization of N-allylamines (see [5] and citations therein), but the use of the reaction to obtain phenoxazines has not been reported.

We have examined the alkylation of phenoxazine (I) with allyl bromide, and studied the prototropic isomerization of the resulting 10-allylphenoxazine (II) in DMSO on treatment with t-BuOK, KOH, and NaOH.

Alkylation of (I) with allyl bromide was carried out with phase-transfer catalysis [6] in the system toluene–33% aqueous KOH–tetrabutylammonium bromide (10% of the weight of phenoxazine).



*For preceding communication, see [1]. The series "N-Hetarylethylenes" comprises 9-alkenylcarbazoles, 10-alkenylphenothiazines, and 10-alkenylphenoxazines.

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TABLE 1. Dependence of the Relative Amounts of Isomers (III) and (IV) on Temperature and Time (solvent DMSO, potassium tert-butoxide concentration 0.15 M)

T, °C	Time, min	Isomer content, %		$K^*_{III \rightleftarrows IV}$
		III	IV	
25	40	100	0	—
	300	81	19	
50	30	83	17	—
	300	79	21	
70	20	79	21	—
	60	70	30	0,46±0,04
	180	67	33	
	300	69	31	
80	10	67	33	0,51±0,03
	120	65	35	
	300	67	33	
100	10	61	39	0,61±0,06
	120	65	35	
	300	61	39	

*The values of the equilibrium constants are given with their standard deviations.

The reaction proceeds under mild conditions, at 50-60°C. According to TLC, when an excess (1.5 moles) of allyl bromide is used the reaction is complete in 40 min, showing that phenoxazine is quite reactive toward alkylation in the two-phase system ([7], p. 88).

The structure of (II) was proved by its IR and PMR spectra, and elemental analysis. The IR spectrum showed absorption for stretching vibrations of the C=C bond, and for deformational vibrations of the =C–H bond at 1650 and 930 cm^{-1}, respectively, absorption for the stretching vibrations of the free amino group in the starting phenoxazine being absent. In the PMR spectrum, the methylene group signal lies at 4.1 ppm, the protons for the $=CH_2$ and –CH= groups giving two signals with chemical shifts 5.2 and 5.8 ppm, respectively. All the signals are multiplets characteristic of the allyl group. The signals for the aromatic protons of the phenoxazine ring are seen as a complex multiplet at 6.2-6.8 ppm.

The prototropic isomerization of (II) in DMSO in the presence of t-BuOK gives a mixture of the 10-propenylphenoxazine isomers (III) and (IV), no other products being found. The time required for completion of the reaction is highly dependent on catalyst concentration and reaction temperature. At ambient temperature and a t-BuOK concentration of 0.15 M, the reaction is complete in less than one hour, isomerization proceeding selectively to give the cis-isomer (III) exclusively. Increasing the reaction time results in the accumulation in the products of the trans-isomer (IV). For example, after 5 h at 25°C, the ratio of propenylphenoxazines (III) and (IV) in the reaction products is 8:2 (Table 1). As the temperature is raised, the stereoselectivity of the reaction also decreases. For instance, at 50°C, after 0.5 h the ratio of isomers (III) and (IV) in the products is 83:17, respectively. Further increases in temperature and increasing the duration of the reaction result in the establishment of thermodynamic equilibrium between the cis- and trans-isomers of 10-propenylphenoxazine in the reaction mixture.

These results show that in the kinetically controlled reaction, the allylphenoxazine (II) undergoes prototropic isomerization to (III), which isomerizes under the reaction conditions to the equilibrium mixture of the cis- and trans-isomers (III) and (IV).

We have examined the effects of reaction temperature on the (III) $\rightleftarrows$ (IV) isomerization equilibrium. The ratio of isomers (III) and (IV) in the equilibrium mixture of products was found from the integral intensities of the CH_3 group signals in the PMR spectra (see below). The equilibrium constant at each temperature was calculated as the mean of three measurements (Table 1). The (III) $\rightleftarrows$ (IV) equilibrium was attained after 1-5 h, and at elevated temperatures the equilibrium constant increased slightly, being 0.61 ± 0.06 at 100°C (ΔG_{373} = 1.56 ± 0.31 kJ/mole). Using the equation $-R \ln K = \Delta H/T - \Delta S$, the enthalpy (10.0 ± 0.7 kJ/mole) and entropy [22.6 ± 2.0 J/(mole·K)] were calculated by least squares.

Similar results have been obtained by us previously [8] in a study of the isomerization of 10-allylphenothiazine to cis- and trans-10-propenylphenothiazines.

The greater thermodynamic stability of (III) as compared with its isomer (IV) distinguishes the 10-propenylphenoxazines from the previously-examined 9-propenylcarbazoles, in which it has been shown that the cis-isomer is thermodynamically less stable than the trans-isomer, as a result of the occurrence of steric interaction between the methyl group and the planar carbazole ring [9].

Phenoxazines are known to possess a planar structure [10] which is similar to that of phenothiazine [11]. In N-substituted derivatives of these heterocycles, the substituent at nitrogen has a quasiequatorial orientation (the extra-configuration, see [12, 13] and citations therein), and the lone pair of electrons of the nitrogen atom is little involved in the general π-electronic conjugation of the heterocycle [12]. Applying the method described in [8] to 10-propenylphenoxazines, it will be seen that in the extra-configuration, steric interactions between the cis-methyl group and the nonplanar heterocyclic moiety in (III) are less pronounced than in the planar cis-9-propenylcarbazole.

These findings show 10-propenylphenoxazines to be "anomalous" olefins, in which the cis-isomers are thermodynamically more stable than the trans-isomers [8], despite the obvious steric stresses. The reasons for this are not entirely clear.

The prototropic isomerization of the allylphenoxazine (II) into (III) and (IV) is efficiently catalyzed in DMSO by KOH and NaOH. At 60°C and a substrate–catalyst ratio of 1:0.7-1 (moles), the times for complete conversion of (II) into 10-propenylphenoxazines is 2-3 h. According to the PMR spectra, the reaction takes place stereoselectively with the preferential formation of the cis-isomer (III) [more than 90% in admixture with (IV)]. The catalytic activity of KOH and NaOH is much less than that of t-BuOK, but the use of KOH or NaOH is preferred in view of their ready availability and convenience in use. These results are in good agreement with the findings reported above, and indicate the greater mobility of the cis-trans isomerization equilibrium in 10-propenylphenoxazines as compared with 1-propenylphenothiazines [8].

The structures of (III) and (IV) were proved by their elemental analyses, IR and PMR spectra (see Experimental), and chemically, by their hydrolysis in acidic media to give phenoxazine and propionaldehyde [1]. The assignment of (III) and (IV) as the cis- and trans-isomers was made from the vicinal coupling constants for the vinyl group protons, equal to 7 and 13 Hz, respectively. The poorly resolved doublet for the methyl group in the cis-isomer (III) is seen at 1.64 ppm, the corresponding signal for the trans-isomer (IV) in the PMR spectrum of the mixture of (III) and (IV) being descreened by 0.22 ppm, as would be expected in view of the fact that the methyl group in the cis-isomer (III) falls within the anisotropic cone of the heterocyclic part of the molecule.

EXPERIMETNAL

PMR spectra were obtained on a BS-497 instrument in CCl_4 [(II) in $CDCl_3$], and IR spectra on an IKS-29 in thin films [(II) in Vaseline oil]. TLC was carried out on Silufol plates, eluent a 6:1 mixture of n-hexane and diethyl ether.

10-Allylphenoxazine (II). To a mixture of 20 g (108 mmoles) of phenoxazine, 160 ml of toluene, 100 g of KOH, 2 g of tetrabutylammonium bromide, and 200 ml of water was added dropwise with vigorous stirring at 50-60°C a solution of 14.2 ml (164 mmoles) of allyl bromide in 40 ml of toluene. The reaction was complete 40 min after the disappearance of the spot on TLC corresponding to the starting phenoxazine. The toluene layer was separated, washed with water (3 × 50 ml), dried over KOH, and the solvent removed. Vacuum fractionation at 184-185°C (5 mm) gave 17.5 g (71%) of (II) as a yellow oil which solidified on standing. Crystallization from ethanol afforded colorless crystals, mp 69-70°C. Found, %: C 80.8; H 5.6; N 6.9. $C_{15}H_{13}NO$. Calculated, %: C 80.7; H 5.9; N 6.3.

cis-10-Propenylphenoxazine (III). A mixture of 3 g (13.5 mmoles) of 10-allylphenoxazine, 13.3 ml of DMSO, and 4.2 ml of an 0.73 N solution of potassium tert-butoxide in tert-butanol was kept at 20°C for 1 h (followed by TLC). The mixture was poured into 150 ml of water, extracted with benzene (5 × 30 ml), and the extracts washed with water (3 × 50 ml), dried over KOH, and the solvent removed. The residue was kept for 70 h under reduced pressure (20 mm) to give 2.85 g (95%) of (III) as a yellow oil, n_D^{20} 1.6465, bp 160-161°C (1 mm). IR spec-

trum: $\nu_{C=C}$ 1670, $\delta_{=C-H}$ 925 cm^{-1}. PMR spectrum: δ: 1.64 (3H, d.d, CH_3, $J_{=CHCH_3}$ = 5, $J_{CH=CCH_3}$ = 1 Hz), 5.7 (1H, m, $=CHCH_3$), 5.84 (1H, d.d, —CH=, $J_{CH=CH}$ = 7, $J_{HC=CCH_3}$ = 1 Hz), 6.2-6.8 ppm (8H, m, heterocyclic protons). Found, %: C 80.5; H 5.9; N 7.0. $C_{15}H_{13}NO$. Calculated, %: C 80.7; H 5.9; N 6.3.

Mixture of cis- and trans-Isomers of 10-Propenylphenoxazine (III, IV). A mixture of 3 g (13.5 mmoles) of (II), 15 ml of DMSO, and 0.55 g (9.8 mmoles) of powdered KOH was kept for 2 h at 60°C. The mixture was then poured into 150 ml of water, extracted with benzene (5 × 30 ml), and the extract washed with water (3 × 50 ml) and dried over KOH. The solvent was removed, and the residue fractionated in vacuo at 164-165°C (3 mm) to give 2.6 g (88%) of 10-propenylphenoxazine as a yellow oil. According to its PMR spectrum, the sample contained ~10% of the trans-isomer (IV). The IR spectrum of the mixture of (III) and (IV) was identical with that of the cis-isomer (III). PMR spectrum of (IV), δ: 1.86 (3H, d.d, CH_3, $J_{=CH-CH_3}$ = 5, $J_{CH=CCH_3}$ = 1 Hz), 5.7 (1H, m, $=CHCH_3$), 5.86 (1H, d.d, —CH=, $J_{CH=CH}$ = 13, $J_{CH=CCH_3}$ = 1 Hz), 6.2-6.8 ppm (8H, m, heterocyclic protons).

Similarly, from 13.5 mmoles of (II) in the presence of 13.8 mmoles of NaOH at 60°C after 3 h there was obtained 2.6 g (88%) of 10-propenylphenoxazine [from PMR, (III):(IV) = 9:1].

Thermodynamics of the Isomerization of 10-Propenylphenoxazine (III ⇄ IV). In a flask were placed 3.9 g (17.5 mmoles) of 10-allylphenoxazine and 20 ml of DMSO. The mixture was thermostated for 0.5 h, and 6.8 ml of an 0.59 N solution of potassium tert-butoxide in tert-butanol added. Samples (volume 1 ml) were withdrawn when all the 10-allylphenoxazine had reacted (according to TLC), and subsequently at fixed time intervals. Each sample was poured into 10 ml of water and extracted with benzene (5 × 10 ml). Completeness of extraction of (III) and (IV) was checked by TLC. The extract was washed with water (3 × 10 ml), and dried over K_2CO_3. The solution was concentrated to a volume of 1 ml, transferred to the cell of a PMR spectrometer, and spectrum recorded with an external standard in the region 0-3 ppm. The ratio of isomers (III) and (IV) in the samples was found from the integral intensities of the signals for the CH_3 groups (see above). The results are given in Table 1.

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