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RADICAL ADDITION REACTION OF ALCOHOLS TO 1-(4-NITROPHENYL)-5H-PYRROLIN-2-ONE

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Quantum chemical calculations of the parameters of the 1-(4-nitrophenyl)-5H-pyrrolin-2-one molecule have been carried out by the MNDO method. The radical addition reaction of aliphatic, alicyclic, and aromatic alcohols to 1-(4-nitrophenyl)-5H-pyrrolin-2-one with the formation of 3- and 4-substituted pyrrolidones has been investigated.

The behavior of aryl substituted pyrrolin-2-ones in radical addition reactions has not been studied previously. The radical addition of alcohols to functional derivatives of unsaturated compounds has been investigated in the greatest detail [1, 2], and also similar reactions involving furans [3]. In the latter case 2- and 3-substituted butanolides were obtained and an opinion was expressed regarding the direction (at position 2 or 3) of addition of α-hydroxyalkyl radicals to 2(5H)-furanone.

The behavior of 1-(4-nitrophenyl)-5H-pyrrolin-2-one (I) in radical addition reactions with aliphatic, alicyclic, and aromatic alcohols has been studied in the present work. In addition a quantum chemical calculation of the parameters of the (I) molecule by the MNDO method has been carried out (Table 1).

The values obtained for the torsion angles show that the pyrroline fragment is not planar and the benzene ring is inclined relative to the heterocycle at the $C_{(7)}-N_{(1)}$ bond at an angle of 52°. The bond lengths of $C_{(7)}-N_{(1)}$ and $C_{(2)}-N_{(1)}$ are close to one another and the $N_{(1)}$ nitrogen atom has a high negative charge. The results given indicate the insignificant conjugation of the unshared electron pair on nitrogen both with the benzene ring and with the carbonyl group. The presence of negative charges on the $C_{(3)}$ and $C_{(4)}$ carbon atoms in pyrroline (I) make it possible to calculate the participation of the $C_{(3)}=C_{(4)}$ double bond of this compound in free radical addition reactions with alcohols.

Di-tert-butyl peroxide (DTBP), which has a high solubility in alcohols, was used as initiator of the process. However, due to poor solubility of pyrrolinone (I) in alcohols the reaction was carried out in a large excess of alcohol [molar ratio (I):DTBP:alcohol was 1:0.2:15-20]. With high boiling alcohols reaction was effected at atmospheric pressure and 150-155°C by gradually introducing DTBP and a portion (1/3) of the alcohol into an excess (2/3) of the alcohol and pyrrolinone (I). For alcohols boiling below 150°C the addition process was carried out in an autoclave. The result of reacting pyrrolinone (I) with alcohols (ethanol, octanol, cyclohexanol) was a mixture of previously unknown substituted pyrrolidones (see Scheme 1) containing mainly 3- and 4-hydroxyalkylpyrrolidones (isomers A and B).

It was established chromatographically that isomers A predominated in the resulting compounds (II)-(IV) (Table 2).

One of the reasons for the low yields of product is the enforced requirement, due to its poor solubility, of placing the whole quantity of pyrrolinone (I) into the reaction vessel at one time, which causes major development of side reactions.

The structure of the substances obtained was established with the aid of PMR and IR spectra (Tables 2 and 3). Analysis of the IR spectra of compounds (II)-(IV) taken in dilute solution in dichloromethane showed that the addition of alcohols to the pyrrolinone molecule occurred in two directions (Scheme 1) with the formation of structures A and B. Bands were observed in the IR spectra of compounds (III) and (IV) in the region for stretching vibrations of the OH group both for unbonded OH groups at 3590-3600 cm^{-1} and for OH groups participating in intramolecular hydrogen bonds at 3450-3570 cm^{-1}. The presence of a mixture of isomers was confirmed by the splitting of the carbonyl group stretching vibrations at 1695-1715 cm^{-1},

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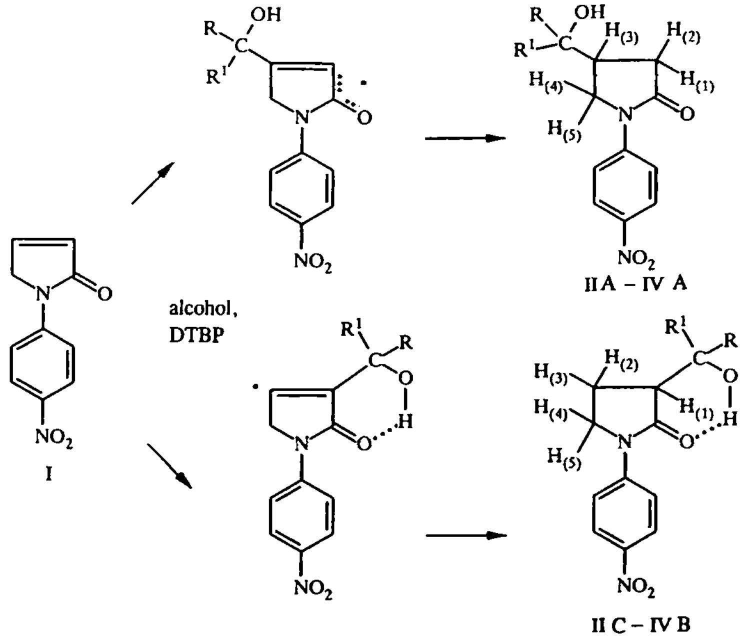


II R = Me, R^1 = H; III R = C_7H_{15}, R^1 = H; IV R + R^1 = $(CH_2)_5$

in which the shorter wave band may be assigned to the stretching vibration of a free C=O group and the longer wave band to C=O in structure B. Skeletal vibrations of the benzene ring at 1590-1595 and 1495-1500 cm^{-1} were recorded in the IR spectra of all compounds as were the stretching vibrations of the NO_2 group (ν_{as} 1515-1520, ν_s 1332-1337 cm^{-1}). Deformation of the benzene ring were superimposed and gave intense absorption at 843-847 cm^{-1}. Stretching vibrations of the $C_{sp3}-H$ bonds were at 2800-3000 cm^{-1} and of the $C_{sp2}-H$ at 3000-3100 cm^{-1}.

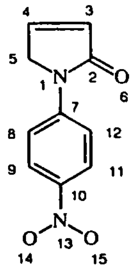
The complexity of the PMR spectra of the products investigated in the 1-3 ppm region is linked with the presence of mixtures of isomers A and B, of asymmetric carbon atoms, and of nonequivalent geminal protons in position 4 and possibly 3 also.

The presence in the addition products from ethanol and 1-octanol of two asymmetric carbon atoms in both isomers causes them to exist as erythro and threo forms and complicates interpretation of the spectra. The data obtained are given in Table 3.

It turned out to be possible to obtain information on the ratio of isomers A and B and of their erythro and threo forms by analysis of the spectra of a mixture of 4- and 3-(1-hydroxyethyl)pyrrolidone (II). In the spectrum of this product the signals of the methyl groups (not given in Table 3) were four doublets with coupling constant 7.0 Hz. As a result of the effect of the carbonyl the signals of the CH_3 group must be at lower field in isomer B than in isomer A. In this case the doublets with chemical shifts 1.38 and 1.35 ppm with an integrated intensity ratio of 70:30 may probably be assigned to the erythro and threo forms of isomer B and the doublets at 1.18 and 1.15 ppm with ratio 54:46 to the erythro and threo forms of isomer A. From the sum of the integrated intensities of the two pairs of doublets it may be concluded that isomer A comprises 80% and isomer B 20%. This is explained by the reaction proceeding through a radical stabilized by conjugation in the case of isomer A (see Scheme 1), which is excluded when forming isomer B.

Determination of the isomer ratio for compound (III) was unsuccessful due to the complexity of the spectrum. The PMR spectrum of compound (IV) at 1.1-2.0 ppm is complex due to the superimposition of the signals of the cyclohexane ring protons (not given in Table 3) and of the 2-H and 3-H protons of structure B. There were two closely located triplets at 2.17 ppm assigned to the 1-H proton of isomer B. A doublet for the 1-H and 2-H protons of structure A falls in the same region. The complex multiplet at 2.28 ppm was assigned to the 3-H proton of isomer A. The 4-H and 5-H protons of both structures A and B were nonequivalent which leads to complication of the spectral character. They are located at 2.89 ppm for structure B. The interaction of the 4-H and 5-H protons is displayed as a doublet with coupling constant 18.00 Hz and each signal of this doublet is split into a triplet by the influence of the two vicinal protons (2-H, 3-H of structure B). The signals of the 4-H and 5-H protons in structure A (2.50 ppm) are also split into doublets with coupling constant 18.0 Hz due to geminal interaction. Each signal of the doublet in its turn is split into a doublet due to vicinal interaction with the 3-H proton.

TABLE 1. Quantum Chemical Data of the 1-(4-Nitrophenyl)-5H-pyrrolin-2-one Molecule



Atom	Charge	Bond	Length. Å	Torsion angle	ω, deg
$N_{(1)}$	-0,428	$N_{(1)}—C_{(2)}$	1,43	$C_{(9)}—C_{(8)}—C_{(7)}—N_{(1)}$	-179,02
$C_{(2)}$	0,383	$C_{(2)}—C_{(3)}$	1,50	$C_{(8)}—C_{(7)}—N_{(1)}—C_{(2)}$	52,11
$C_{(3)}$	-0,105	$C_{(3)}—C_{(4)}$	1,35	$C_{(8)}—C_{(7)}—N_{(1)}—C_{(5)}$	-112,69
$C_{(4)}$	-0,074	$C_{(4)}—C_{(5)}$	1,51	$C_{(7)}—N_{(1)}—C_{(2)}—C_{(3)}$	-169,68
$C_{(5)}$	0,186	$C_{(5)}—N_{(1)}$	1,48	$N_{(1)}—C_{(2)}—C_{(3)}—C_{(4)}$	2,90
$O_{(6)}$	-0,311	$C_{(2)}—O_{(6)}$	1,22	$C_{(7)}—N_{(1)}—C_{(2)}—O_{(6)}$	12,35
$C_{(7)}$	0,160	$C_{(7)}—N_{(1)}$	1,42	$C_{(9)}—C_{(8)}—C_{(7)}—C_{(12)}$	-0,01
$C_{(8)}$; $C_{(12)}$	-0,830	$C_{(8)}—C_{(7)}$	1,41	$C_{(10)}—C_{(9)}—C_{(8)}—C_{(7)}$	-0,57
		$C_{(12)}—C_{(7)}$	1,41	$N_{(13)}—C_{(10)}—C_{(9)}—C_{(8)}$	179,96
$C_{(9)}$; $C_{(11)}$	0,024	$C_{(9)}—C_{(8)}$	1,40	$O_{(15)}—N_{(13)}—C_{(10)}—C_{(9)}$	0,48
		$C_{(11)}—C_{(12)}$	1,40	$O_{(15)}—N_{(13)}—C_{(10)}—C_{(11)}$	179,61
$C_{(10)}$	-0,093	$C_{(10)}—C_{(9)}$	1,41		
		$C_{(10)}—C_{(11)}$	1,41		
$N_{(13)}$	0,488	$N_{(13)}—C_{(10)}$	1,49		
$O_{(14)}$; $O_{(15)}$	-0,343	$O_{(14)}—N_{(13)}$	1,21		
		$O_{(15)}—N_{(13)}$	1,21		

The signals of the OH group protons have the shape of singlets broadened somewhat, which might be explained by the formation of hydrogen bonds, intramolecular for structure B and intermolecular (dimeric) for structure A. The signal at lower field for the OH group proton is assigned to structure B and that at high field to structure A.

The signals for the benzene ring protons of isomers A and B are found at 7.71 and 8.25 ppm as doublets with coupling constant 8.7 Hz. From the ratio of the integrated intensities for the mixture of isomers of compound (IV) it was concluded that isomer A comprised 57% and isomer B 43%.

EXPERIMENTAL

The IR spectra were taken on a LOMO IKS-29 instrument for solutions of concentration 1-5% in chloroform or dichloromethane. Layer thickness was 0.1-1 mm. The PMR spectra were taken on Bruker AM 300 and Tesla BS 587A instruments in $CDCl_3$ and DMSO-D_6, internal standard was TMS. Quantum chemical calculations were carried out by the MNDO method with the MOPAC-6 program using an IBM PC AT 486. Thin layer chromatography was carried out on Silufol UV 254 plates, the eluent was acetone–CCl_4–petroleum ether 2:1:0.5. Visualization was with 2,4-dinitrophenylhydrazine and iodine vapor.

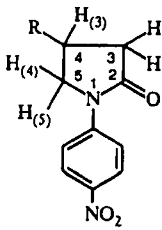
Procedure for Obtaining Compounds (III), (IV). The appropriate alcohol (1.5 mole) and 1-(4-nitrophenyl)-5H-pyrrolin-2-one (0.074 mmole) were placed in a two-necked flask fitted with a stirrer, reflux condenser, and thermometer. The mixture was heated with vigorous stirring to 150 ± 3°C and DTBP (0.014 mole) in the alcohol (0.15 mole) were added dropwise uniformly during 6 h. The reaction mixture was then heated for 1 h at the same temperature. At the end of the reaction the alcohol was distilled off. After cooling, the precipitated crystals were filtered off, dissolved in ether, and precipitated with hexane. The characteristics of the obtained compounds (III) and (IV) are given in Table 2.

Preparation of Compound (II). The synthesis was carried out in an autoclave, in which was placed ethanol (1.5 mole), DTBP (0.014 mole), and 1-(4-nitrophenyl)-5H-pyrrolin-2-one (0.074 mole). The mixture was kept at 155°C for 6 h and

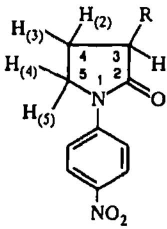
TABLE 2. Characteristics of 4- and 3-Hydroxyalkyl(cyclohexyl)pyrrolidones

Compound	R	Empirical formula	mp, °C	IR spectrum, cm^{-1}							Yield, %
				ν_{OH} free	ν_{OH} bounded	ν_{C-O} free	ν_{C-O} bounded	ν_{NO2}	ν_{ar}	δ_{NO2}, δ_{ar}	
II	CH_3CHOH	$C_{12}H_{14}O_4N_2$	145	3590	3420	1715	1700	ν_{as} 1515 ν_s 1332	1590 1495	847	30,0
III	$C_7H_{15}CHOH$	$C_{18}H_{26}O_4N_2$	155	3600	3450	1710	1695	ν_{as} 1515 ν_s 1337	1590 1495	843	27,5
IV	$C_5H_{10}COH$	$C_{16}H_{20}O_4N_2$	101	3590	3570	1715	1705	ν_{as} 1520 ν_s 1333	1590 1500	845	25,0

TABLE 3. Data of PMR Spectra of 4- and 3-Substituted Pyrrolidones



A



B

Compound	R	Structure	δ, ppm							J, Hz		
			H(1)	H(2)	H(3)	H(45)	OH	Ar	CHOH	H(13)	H(34)	H(45)
II	CH_3CHOH	A	2,19	2,19	2,29	2,51	3,46	7,71, 8,25	—	7,50	7,00	18,0
		B	2,19	1,50...2,00	1,50...2,00	2,84	3,61	7,71, 8,25	—			
III	$C_7H_{15}CHOH$	A	2,13	2,17	2,30	2,53	3,67	7,71, 8,25	3,54	7,40	7,00	17,0
		B	2,13	2,19	1,83	2,85	3,81	7,71, 8,25	3,54			
IV	$C_6H_{10}COH$	A	2,17	1,50...2,00	2,28	2,50	3,63	7,71, 8,25	3,50	7,50	7,00	18,0
		B	2,17	2,17	1,50...2,00	2,89	3,75	7,71, 8,25	3,50			

a pressure of 15 atm. Product (II) was isolated analogously to compounds (III) and (VI). The characteristics of compound (II) are given in Table 2.

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