HYDROACRIDINES AND RELATED COMPOUNDS

XI.* 2,4-DIPHENYL-5,6-CYCLOALKENOPYRIDINE N-OXIDES AND THEIR BEHAVIOR TOWARD ACETIC ANHYDRIDE

G. A. Klimov, V. N. Ovsyannikova,
and M. N. Tilichenko

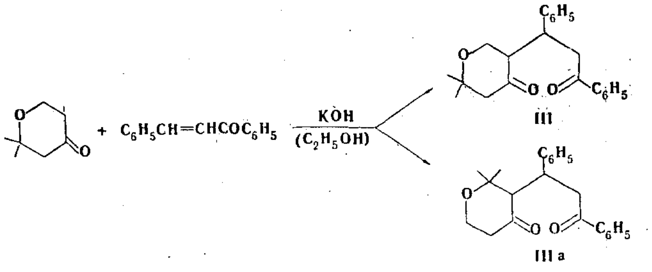
UDC 547.828.83.07:543.422.4

The N-oxides of 2,4-diphenyl-5,6,7,8-tetrahydroquinoline, 2,4-diphenylpyrindane, and 7,7-dimethyl-2,4-diphenyl-6-oxa-5,6,7,8-tetrahydroquinoline were synthesized. On heating with acetic anhydride, the N-oxides form, respectively, acetates of 2,4-diphenyl-5,6,7,8-tetrahydro-8-quinolinol, 2,4-diphenyl-7-pyrindanol, and 7,7-dimethyl-2,4-diphenyl-6-oxa-5,6,7,8-tetrahydro-8-quinolinol; hydrolysis of the acetates gives the alcohols.

The synthesis and some transformations of 2,4-diphenyl-5,6-cycloalkenopyridine N-oxides are described in this paper. It is known that systems of this sort find application in the synthesis of medicinal preparations and serve as key compounds in the total synthesis of heterocyclic steroids [1-3].

The bases (IV-VI) necessary for the synthesis of the N-oxides (VII-IX) were obtained by reaction of the appropriate 1,5-diketones (I-III) with hydroxylamine in n-propyl alcohol [4]. Base V was synthesized in high yield via the method in [5].

Diketone III is formed in high yield on treatment of a mixture of benzalacetophenone and 2,2-dimethyltetrahydro-4-pyrone with alcoholic alkali. The IR spectrum of the synthesized compound contains a split absorption band at 1695-1712 cm^{-1}, which is characteristic for unconjugated and conjugated carbonyl groups. In connection with the fact that there are two unequivalent α-methylene groups in 2,2-dimethyltetrahydro-4-pyrone, one should have assumed that the reaction with chalcone may proceed in different directions. The results of thin-layer chromatography (TLC) make it possible to conclude that the reaction gives only one product, the structure of which was proved by the following chemical transformations.



The oxidation of bases IV-VI with hydrogen peroxide in acetic acid gives the corresponding N-oxides (VII-IX). The reaction does not go to completion: small amounts of unchanged bases remain along with the expected N-oxides. This can apparently be explained by the effect of the phenyl groups which lower the electron density on the nitrogen atom and cause steric hindrance. The IR spectra of the synthesized compounds contain intense absorption bands at 1270-1310 cm^{-1}, which are characteristic for the N-oxide group.

---

*See [10] for communication X.

Far-Eastern State University, Vladivostok. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1547-1551, November, 1972. Original article submitted September 15, 1971.

TABLE 1. Properties of the Synthesized Compounds

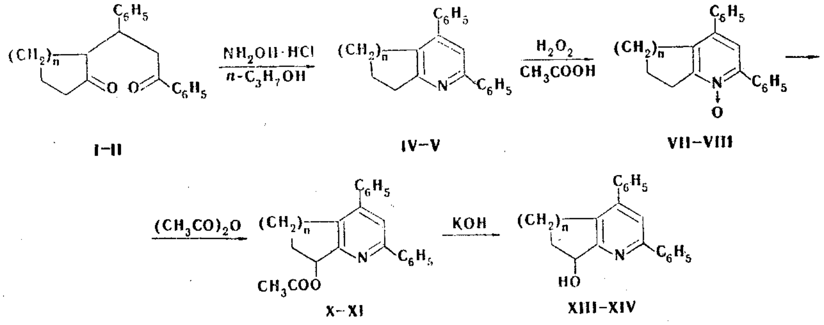
Compound	mp, °C (crystallization solvent)	R_f	Empirical formula	Found, %			Calc., %			Yield, %
				C	H	N	C	H	N	
III	147—148 (picrate)	0,50[a]	$C_{20}H_{24}O_3$	78,3	7,2		78,5	7,2		93,8
VI	80—82 (picrate)	0,75[b]	$C_{20}H_{21}NO$	83,6	6,9		83,8	6,8		94,3
VII	171—173 (dibutyl ether)	0,26[b]	$C_{20}H_{17}NO$	83,7	6,3	4,9	83,6	6,0	4,9	54,6
Picrate	155—156 (aqueous alcohol 1 : 10)		$C_{20}H_{17}NO \cdot C_6H_3N_3O_7$			10,8			10,8	
Hydrochloride	207—209 (aqueous alcohol 1 : 10)		$C_{20}H_{17}NO \cdot HCl$			3,7			4,3	
VIII	117—120 (aqueous alcohol 1 : 3)	0,35[b]	$C_{21}H_{19}NO$	83,0	6,8		83,7	6,4		43,9
Picrate	125—126 (alcohol)		$C_{21}H_{19}NO \cdot C_6H_3N_3O_7$			10,6			10,6	
IX	156—158 (acetone)	0,52[b]	$C_{22}H_{21}NO_2$	79,7	6,8	4,2	79,7	6,4	4,2	63,7
Picrate	117—118 (alcohol)		$C_{22}H_{21}NO_2 \cdot C_6H_3N_3O_7$			10,1			10,0	
X	130—132 (heptane)	0,55[b]	$C_{22}H_{19}NO_2$	79,9	6,1	4,4	80,2	5,8	4,2	91,5
Picrate	110—111 (methanol)		$C_{22}H_{19}NO_2 \cdot C_6H_3N_3O_7$			9,9			10,0	

XI	111—113 (heptane)	0,50[b]	$C_{23}H_{21}NO_2$	80,1	6,3	4,1	80,4	6,2	4,1	93,2
Picrate	173—176 (methanol)		$C_{23}H_{21}NO_2 \cdot C_6H_3N_3O_7$			9,7			9,8	
XII	133—135 (hexane)	0,58[c]	$C_{24}H_{23}NO_3$	77,4	6,5	3,5	77,2	6,2	3,8	94,0
Picrate	143—145 (methanol)		$C_{24}H_{23}NO_3 \cdot C_6H_3N_3O_7$			9,2			9,3	
Hydrochloride	128—130 (dibutyl ether)		$C_{24}H_{23}NO_3 \cdot HCl$			4,1			3,4	
XIII	156—157 (heptane)	0,20[b]	$C_{20}H_{17}NO$	83,1	6,2	5,6	83,6	6,0	4,9	93,7
Picrate	215—217 (methanol)		$C_{20}H_{17}NO \cdot C_6H_3N_3O_7$			11,0			10,8	
XIV	110—112 (heptane)	0,60[b]	$C_{21}H_{19}NO$	83,8	6,6	4,6	83,7	6,4	4,6	91,3
Picrate	183—184 (methanol)		$C_{21}H_{19}NO \cdot C_6H_3N_3O_7$			10,3			10,6	
XV	119—121 (hexane)	0,55[b]	$C_{22}H_{21}NO_2$	79,7	6,6	3,8	79,7	6,4	4,2	88,1
Picrate	175—176 (methanol)		$C_{22}H_{21}NO_2 \cdot C_6H_3N_3O_7$			9,8			10,0	
Hydrochloride	150—151 (benzene—hexane 10 : 1)		$C_{22}H_{21}NO_2 \cdot HCl$			3,3			3,8	

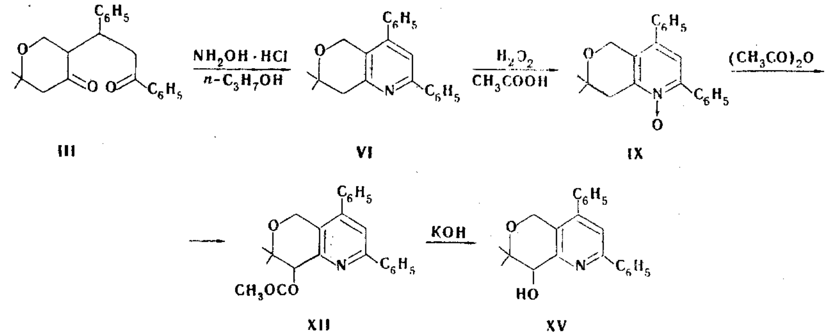
---

[a] Chloroform—carbon tetrachloride (2 : 1). [b] Chloroform. [c] Ether—petroleum ether (1 : 2).

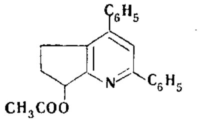
The NMR spectrum of oxide IX contains, in addition to other signals (protons of the gem methyl groups and aromatic protons), two singlets at 3.08 ppm (signal from the C_8 protons) and 4.73 ppm (signal from the C_5 protons); this attests to the presence of isolated methylene groups attached to C_5 and C_8. The results make it possible to suppose that the product of the addition of 2,2-dimethyltetrahydro-4-pyrone to chalcone has the 2,2-dimethyl-5-phenacylobenzyltetrahydro-4-pyrone structure (III).



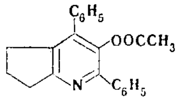
I, IV, VII, X, XIII $n=1$; II, V, VIII, XI, XIV $n=2$



The formation of two isomeric acetates of the X and Xa type, as described previously in the case of 5,6,7,8-tetrahydroquinaldine N-oxide [6], might have been expected when VII-IX were refluxed with acetic anhydride. However, only one substance is formed as a result of the reaction of VII-IX with acetic anhydride; this attests to an unambiguous rearrangement. The IR spectra of the synthesized compounds contain absorption bands at 1745 cm^{-1} and 1245 cm^{-1}, which are characteristic for the ester grouping.



X



X a

Alkaline hydrolysis of acetates X-XII gives the corresponding amino alcohols (XIII-XV). Absorption bands at 3485-3590 cm^{-1}, caused by the presence of an intramolecularly bonded hydroxyl group, are present in the IR spectra of the compounds obtained. Considering this and the fact that the 3 position is shielded to a considerable degree by the phenyl groups, one should have assumed the formation of amino esters with an acetoxy group attached to C_8. This assumption is confirmed by the NMR spectrum of XV, which contains the following signals: 4.32 ppm (signal from the proton attached to C_8), 4.65 ppm (signal from the protons of the methylene group attached to C_5), and 7.33 ppm (signal of the C_3 pyridine proton).

EXPERIMENTAL

The IR spectra were recorded with a UR-20 spectrophotometer with NaCl and LiF prisms. The NMR spectra were obtained with a ZKR-60 spectrometer with an operating frequency of 60 MHz. Activity II aluminum oxide was used for the chromatography with development with iodine vapors. The picrates were obtained by mixing hot methanol solutions of the substances and picric acid. The hydrochlorides were isolated by bubbling dry hydrogen chloride through ether (XII, XV) or benzene (VII) solutions of the compounds.

2,2-Dimethyl-5-phenacylobenzyltetrahydro-4-pyrone (III). A 4-g (0.03 mole) sample of 2,2-dimethyltetrahydro-4-pyrone [8] and 1.7 ml of 40% potassium hydroxide solution were added to a solution of 2.1 g (0.01 mole) of benzalacetophenone [7] in 33 ml of alcohol. The precipitated crystals were removed by filtration, washed successively with alcohol and water (until they were neutral), and dried.

2,4-Diphenyl-5,6,7,8-tetrahydroquinoline (V). This compound was obtained by refluxing a mixture of 24.6 g (0.08 mole) of diketone II, 123.2 g (1.6 mole) of ammonium acetate, and 160 ml of acetic acid for 3 h. Free base V was isolated by alkalization with saturated potassium carbonate solution.

2,4-Diphenylpyrindane (VII), 2,4-Diphenyl-5,6,7,8-tetrahydroquinoline (VIII), and 7,7-Dimethyl-2,4-diphenyl-6-oxa-5,6,7,8-tetrahydroquinoline (IX) N-Oxides. These compounds were obtained from 0.01 mole of the corresponding base, 0.025 mole of hydrogen peroxide, and 7 ml of acetic acid via a previously described method [9].

Acetates of 2,4-Diphenyl-7-pyrindanole (X), 2,4-Diphenyl-5,6,7,8-tetrahydro-8-quinolinol (XI), and 7,7-Dimethyl-2,4-diphenyl-6-oxa-5,6,7,8-tetrahydro-8-quinolinol (XII). These compounds were obtained by refluxing 0.01 mole of the corresponding N-oxide with 10 ml of acetic anhydride for 1 h. The free amino esters were isolated by the method in [9]. The acetates were hydrolyzed by heating 0.01 mole of the ester with 15.4 ml of 20% alcoholic potassium hydroxide for 1.5 h.

The properties of the synthesized compounds and the results of elementary analysis are presented in Table 1.

LITERATURE CITED

1. US Patent No. 3,366,635 (1968); Chem. Abstr., 69, 10,372 (1968).
2. British Patent No. 1,059,701 (1967); Chem. Abstr., 67, 3001 (1967).
3. M. A. Sluyter, V. K. Pandit, W. N. Speckamp, and H. O. Huisman, Tetrahedron Lett., 87 (1966).
4. H. Stobbe, J. Prakt. Chem., 86, 232 (1912).
5. M. Weiss, J. Am. Chem. Soc., 74, 200 (1952).
6. E. Ochiai, M. Takahashi, and R. Tanabe, Chem. Pharm. Bull., 15, 1385 (1967).
7. Organic Synthesis, Vol. 1 [Russian translation], IL, Moscow (1954), p. 77.
8. I. N. Nazarov, Zh. Obshch. Khim., 20, 2179 (1950).
9. G. A. Klimov, M. N. Tilichenko, and L. A. Timofeeva, Khim. Geterotsikl. Soedin., 1218 (1971).
10. V. I. Vysotskii, V. A. Stonik, and M. N. Tilichenko, Khim. Geterotsikl. Soedin., 984 (1972).