NEW PYRYLIUM DERIVATIVES IN THE INDOLE SERIES

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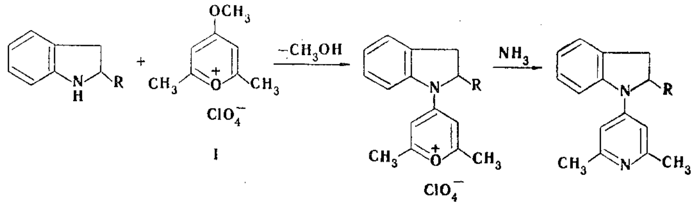
Nitrogen-unsubstituted 2,3-dihydroindole and its homologs, as well as 1,2,3,4-tetrahydro-β-carbolines, react with 2,6-dimethyl-4-methoxypyrylium perchlorates to give N-pyrylated derivatives of indole, which are converted to the corresponding pyridine bases by the action of ammonium salts and form 1-aminopyridinium derivatives with hydrazine hydrate.

It is known [1] that 2,4,6-trimethylpyrylium perchlorate has sedative activity. The aim of the present research was the synthesis of new analogs of this compound with residues of various indole derivatives attached to the pyrylium ring in place of one of the methyl substituents.

In agreement with [2], it was found that 2,3-dihydroindole (indoline) reacts with 2,6-dimethyl-4-methoxypyrylium perchlorate (I) [3] to give 2,6-dimethyl-4-(1-indolinyl)pyrylium perchlorate (II) [4]. Its structure is confirmed by IR spectroscopy and conversion to 2,6-dimethyl-4-(1-indolinyl) pyridine (III) by treatment with ammonium acetate (in acetic acid) or with ammonium carbonate (in alcohol) [4]. The structure of III is confirmed by IR and UV spectroscopy (its UV spectrum is similar to the UV spectra of other 4-indolinylpyridines [5]).



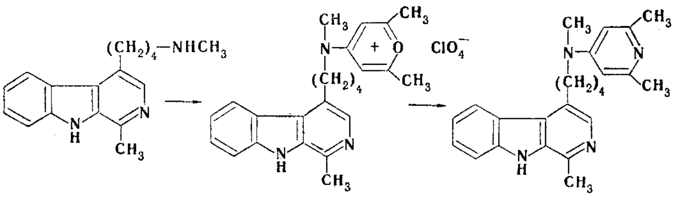
I

II, III R=H; IV R=CH$_3$ II, IV III

2-Methylindoline reacts like indoline with I to give a perchlorate (IV).

The possibility of the successful extension of this transformation to other indole derivatives containing a second basic nitrogen atom is worthy of attention. Brevicarine (V), the alkaloid from Carex parvus [6], forms a pyrylium derivative (VI), which is converted to a pyridine base (VII) on treatment with ammonium acetate in acetic acid. Under the conditions of this reaction, 1,2,3,4-tetrahydroharman forms 2,6-dimethyl-4-(1,2,3,4-tetrahydro-2-harmanyl)pyrylium perchlorate (VIII) in quantitative yield.

When II and VI are refluxed with excess hydrazine hydrate, they are converted to 1-aminopyridinium derivatives IX and X.



V VI VII

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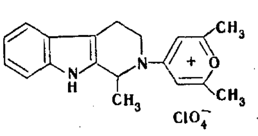
TABLE 1. Characteristics of the Compounds Obtained

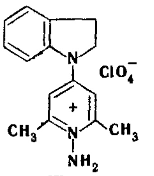
Comp.	mp, °C	Empirical formula	Found, %			Calc., %			IR spectra, ν_{max}, cm^{-1}	Yield, %
			C	H	N	C	H	N		
IV	183	$C_{16}H_{18}ClNO_5$	56,1	5,0	4,4	56,6	5,3	4,1	1660, 1550, 1470, 1360, 1100, 930^a	62
VI	176–177	$C_{24}H_{28}ClN_3O_5$	60,4	5,5	8,3	60,9	5,9	8,9	1660, 1585, 1100, 925, 850^b	85
VIII	246	$C_{19}H_{21}ClNO_5$	58,5	5,4	7,1	58,1	5,6	7,1	1660, 1560, 1100, 925, 725^b	100
VII	169—170	$C_{24}H_{28}N_4$	77,3	7,7	14,6	77,4	7,5	15,0	3250, 1645, 1600, 1550, 1450, 975^a	75
X	127	$C_{24}H_{30}ClN_5O_4$	58,6	6,4	14,0	59,1	6,2	14,3	3300, 1640, 1650, 1100, 935, 745^b	59

^{a}In a KBr pellet. ^{b}In mineral oil.

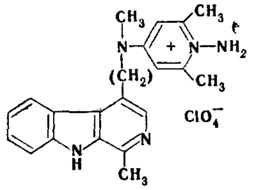
The IR spectra of pyrylium derivatives II, IV, VI, and VIII contain the intense absorption bands of the pyrylium cation at 1650 and 1550 cm^{-1} and of the ClO_4^- ion at 1100 cm^{-1} [7]. The individuality of the compounds obtained was verified by chromatography in a thin layer of aluminum oxide.



VIII



IX



X

EXPERIMENTAL

The melting points (uncorrected) were determined with a Koffler block, and the IR spectra were recorded with a UR-10 spectrophotometer.

2,6-Dimethyl-4-(1-indolinyl)pyrylium Perchlorate (II). A 1.79-g (15 mmole) sample of indoline was added to a suspension of 3.57 g (15 mmole) of perchlorate I in 50 ml of methanol, and the mixture was refluxed until all of the material had dissolved (about 15 min), after which it was concentrated to about half its original volume. The resulting precipitate was removed by filtration and washed with ether to give 4.5 g (92%) of yellow crystals with mp 247°. IR spectrum (KBr pellet), cm^{-1}: 1660, 1550, 1470, 1360, 930, and 770.

2,6-Dimethyl-4-(2-methyl-1-indolinyl)pyrylium (IV), 2,6-dimethyl-4-[N-methyl-N-(δ-harmanyl-4-butyl)amino]pyrylium (VI), and 2,6-dimethyl-4-(1,2,3,4-tetrahydro-2-harmanyl)pyrylium (VIII) perchlorates (Table 1) were similarly obtained.

2,6-Dimethyl-4-(1-indolinyl)pyridine (III). A mixture of 1.3 g (4 mmole) of II, 1 g (excess) ammonium acetate, and 20 ml of acetic acid was refluxed for 1 h, cooled, and poured into water. The aqueous mixture was neutralized with aqueous alkali and extracted with benzene. The extract was washed with water and dried with sodium sulfate. The solvent was removed by distillation, and the residue was crystallized from aqueous alcohol to give 0.8 g (100%) of a product with mp 117°. Found, %: C 80.6; H 7.1; N 12.3. $C_{15}H_{16}N_2$. Calculated, %: C 80.4; H 6.7; N 12.5. The hydrochloride had mp 112°. λ_{max} (CH_3OH): 295 and 318 nm, log ε 4.17 and 4.31.

Perchlorate VI was similarly converted to 2,6-dimethyl-4-[N-methyl-N-(δ-harmanyl-4-butyl)amino]pyridine (VII) (Table 1).

1-Amino-2,6-dimethyl-4-(1-indolinyl)pyridinium Perchlorate (IX). A 0.3-g (6 mmole) sample of hydrazine hydrate was added to 0.5 g (1.5 mmole) of II in 10 ml of methanol, and the mixture was refluxed for 1 h and cooled. The resulting needles were removed by filtration to give 0.2 g (100%) of a product with mp 208°. Found, %: C 52.6; H 5.4; N 11.9. $C_{15}H_{18}ClN_3O_4$. Calculated, %: C 52.9; H 5.3; N 12.4. λ_{max} (CH_3OH): 212, 240, and 338 nm; log ε 4.32, 4.38, and 4.76. IR spectrum (KBr pellet), cm^{-1}: 1640, 1520, and 1100.

1-Amino-2,6-dimethyl-4-[N-methyl-N-(δ-harmanyl-4-butyl)amino]pyridinium perchlorate (X) (Table 1) was similarly obtained from VI.

LITERATURE CITED

1. G. N. Dorofeenko, Yu. A. Zhdanov, A. N. Narkevich, N. I. Nikolaeva, and A. P. Ordyntseva, Summaries of Papers Presented at the Conference on the Problems of Directed Research for Physiologically Active Substances [in Russian], Erevan (1968), p. 68.
2. R. M. Anker and A. N. Cook, J. Chem. Soc., 117 (1946).
3. A. Baeyer, Ber., 43, 2337 (1911).
4. G. I. Zhungietu, B. P. Sukhanyuk, D. D. Buburuz, and G. N. Dorofeenko, Khim. Geterotsikl. Soedin., 1437 (1970).
5. A. K. Sheinkman, A. N. Kost, I. V. Komissarov, A. O. Ginzburg, K. A. Arnol'dova, and L. P. Makhno, Khim.-Farmats. Zh., No. 9, 29 (1968).
6. I. V. Terent'eva, T. I. Shirshova, A. F. Sholl', and V. I. Kovalenko, in: Brevicolline [in Russian], Kishinev (1969), p. 36.
7. J. A. Durden and D. G. Crosby, J. Org. Chem., 30, 1684 (1965).