REACTIONS OF CYCLAMMONIUM CATIONS

XVIII.* REACTION OF N-ACYLPHENANTHRIDINIUM SALTS IN SITU WITH NUCLEOPHILIC AROMATIC AND HETEROAROMATIC COMPOUNDS

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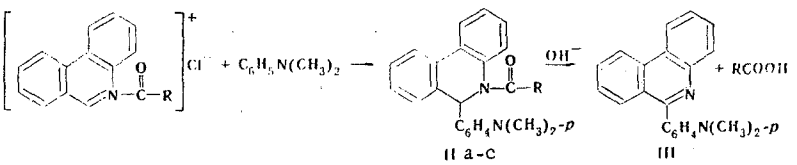
5-Acyl-6-substituted 5,6-dihydrophenanthridines are formed in the reaction of phenanthridine with nucleophilic organic compounds in the presence of alkyl halides. This method made it possible to introduce a phenanthridine residue into the ring of dialkylanilines, 1-alkyl-1,2,3,4-tetrahydroquinolines, 1-alkylindolines, 2-alkylindoles, pyrroles, indoline, and α-methylfuran, and also made it possible to obtain several ketones of the phenanthridine series.

In developing the hetarylation of organic compounds by N-acyl salts of six-membered nitrogen heterocycles [1-3], we found that the N-acylphenanthridinium cation can also be successfully used in this reaction.

Like other heteroaromatic cations (pyrylium, thiopyrylium, and their benzo derivatives), the aromatic N-acylcyclammonium cations (pyridinium and benzopyridinium) are to a considerable extent similar to aromatic carbonium ions (tropylium and benzotropylium). In this connection, it seemed of interest to make at least a qualitative comparison of the activity of N-acylphenanthridinium salts with the activity of N-acyl salts of other benzopyridinium compounds in reactions with various nucleophiles. It is known that the electrophilicity of the analogously constructed benzotropylium cations decreases in the linear order dibenzotropylium > benzotropylium > angular dibenzotropylium cations [4].

As it turned out, the N-acyl phenanthridinium salts in situ are less active in these reactions than other benzopyridinium salts. Thus we were unable to hetarylate furan, thiophene, and 2-methylthiophene, and the reaction with dialkylanilines also proceeded more poorly than with N-acylquinolinium, -isoquinolinium, and -acridinium salts. Moreover, the phenanthridinium salts proved to be active only with some acyl halides, while, for example, the quinolination of dialkylanilines [2] proceeds well in the presence of the acid halides of the most diverse aliphatic, aromatic, or heterocyclic carboxylic acids.



II a-c III

The steric requirements of the reaction are so great that apparently only the p position of the dialkylanilines undergoes electrophilic attack by the phenanthridinium cation. This was proved by conversion of II by alkaline or acid hydrolysis to the known [5] 6-(p-dimethylaminophenyl)phenanthridine (III). At-

* See [1] for communication XVII.

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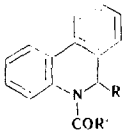
TABLE 1.



Compound	R	R′	Mp, °C*	R_f†	Found, % C	Found, % H	Found, % N	Empirical formula	Calc., % C	Calc., % H	Calc., % N	Yield, %
IIa	p-$(CH_3)_2NC_6H_4$	C_2H_5O	78—80	0,76	77,1	6,6	7,7	$C_{24}H_{24}N_2O_2$	77,4	6,5	7,5	71
IIb	p-$(CH_3)_2NC_6H_4$	2-Furyl	150—151	0,56	79,4	6,5	6,8	$C_{26}H_{22}N_2O_2$	79,2	5,6	7,1	84
IIc	p-$(CH_3)_2NC_6H_4$	C_6H_5	184—185	0,40	82,9	6,1	6,7	$C_{28}H_{24}N_2O$	83,1	6,0	6,9	65
IV	1-Methyl-1,2,3,4-tetrahydro-6-quinolyl	C_6H_5	184—186	0,58	83,5	6,3	6,7	$C_{30}H_{26}N_2O$	83,7	6,1	6,5	60
V	1-Methyl-1,2-dihydro-5-indolyl	C_6H_5	115—116	0,46	83,2	5,9	6,7	$C_{29}H_{24}N_2O$	83,6	5,8	6,7	62
VI	2-(5-Benzoyl-5,6-dihydro-6-phenanthridyl)-5-pyrryl	C_6H_5	237—239	0,22	83,1	4,7	6,6	$C_{44}H_{31}N_3O_2$	83,4	4,9	6,6	42
VII	1-Phenyl-2-pyrryl	C_6H_5	200—202	0,67	84,2	5,6	6,2	$C_{30}H_{22}N_2O$	84,5	5,2	6,6	61
VIII	2-Methyl-5-furyl	C_6H_5	117—118	0,56	81,9	5,5	3,5	$C_{25}H_{19}NO_2$	82,2	5,2	3,8	20
IXa	1-Methyl-3-indolyl	C_6H_5	229—230	0,74	84,3	5,6	6,9	$C_{29}H_{22}N_2O$	84,0	5,4	6,7	43
IXb	2-Methyl-3-indolyl	C_6H_5	262—263	0,41	84,2	5,5	7,1	$C_{29}H_{22}N_2O$	84,0	5,5	6,8	53
Xa	Phenacyl	C_6H_5	149—150	0,33	83,0	5,3	4,1	$C_{28}H_{21}NO_2$	83,3	5,3	3,8	19
Xb	2-Thenoylmethyl	C_6H_5	209—210	0,21	76,4	4,9	3,4	$C_{26}H_{19}NO_2S$‡	76,3	4,6	3,4	17

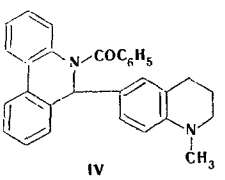
* Compounds VIII and X were recrystallized from ethanol, while the remaining compounds were recrystallized from amyl alcohol.

† In a thin layer of aluminum oxide [benzene–hexane–chloroform (6 : 1 : 30)].

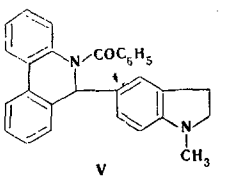
‡ Found: S 7.7%. Calculated: S 7.5%.

tempts to detect the presence of the ortho isomer in the reaction medium by means of thin-layer chromatography in six solvent systems were unsuccessful.

Ring fusion also proceeds through the 6 position of phenanthridine and in the p position relative to the amino group (IV, V) in the reaction of the N-acylphenanthridinium cation with 1-methyl-1,2,3,4-tetrahydroquinoline and 1-methyl-2,3-dihydroindole.

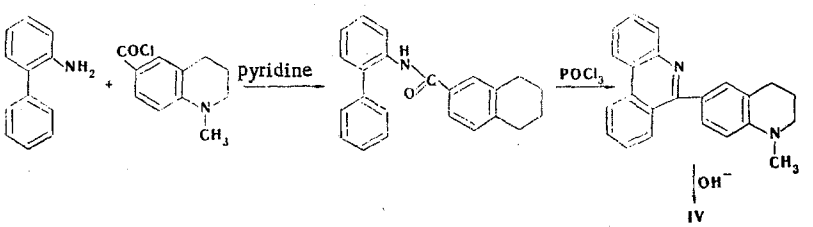


IV



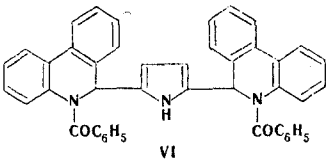
V

The structures of IV and V were proved by alternative synthesis.



The UV spectra of II, IV, and V are similar. The IR spectra of these compounds contain characteristic absorption bands at 1640-1650 cm^{-1}, which correspond to the stretching vibrations of the carbonyl group of amides, which also confirms their structures.

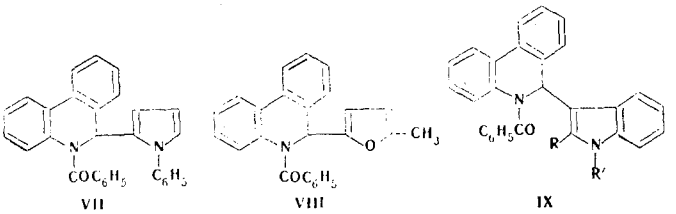
As in the case of isoquinoline and quinoline, in the reaction with pyrrole, two (α and β) isomers of monophenanthridinylpyrrole (which we detected by thin-layer chromatography) and a bis derivative (VI), which is the major reaction product, are formed in the reaction with pyrrole.



VI

Only monosubstituted derivatives VII and VIII are obtained with N-phenylpyrrole (as we did not increase the reaction time) and with 2-methylfuran.

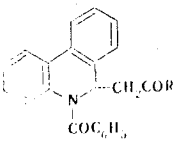
Phenanthridine also reacts similarly with indoles (IX), as was first demonstrated in [6]. It was found that a methyl group in the 2 position of indole does not hinder the reaction, which probably indicates that the process possibly occurs through an intermediate charge-transfer complex of the indoles (and apparently also of other organic nucleophile-electron donors) with the electrophilic N-acylphenanthridinium cation.



VII VIII IX

IX R = R' = H, CH_3

We were also able to carry out the reaction of N-acylphenanthridinium salts with several ketones to form the corresponding 5-acyl-5,6-dihydrophenanthridine derivatives (X).



X R = phenyl; 2-thienyl

EXPERIMENTAL

Reaction of Phenanthridine with Dimethylaniline and Acyl Chlorides. A 2.42 g (0.02 mole) sample of dimethylaniline and 0.01 mole of the acyl chloride were added to a solution of 1.79 g (0.01 mole) of phenanthridine in 10 ml of anhydrous dimethylformamide, and the mixture was heated at 100-105° for 10 h, after which it was steam distilled. The residue from the distillation was separated, dried, chromatographed, and recrystallized. The yields and characteristics of the compounds are presented in Table 1. The reactions with pyrroles, indoles, α-methylfuran, and ketones were carried out similarly.

6-(p-Dimethylaminophenyl)phenanthridine. A 4.5 g sample of solid potassium hydroxide was added to a solution of 1 g of II in 36 ml of 76% ethanol, and the mixture was refluxed for 2 h, after which it was diluted to twice its volume with water, the alcohol was removed by distillation, and the residue was extracted several times with benzene. The benzene extracts were dried, the benzene was removed by distillation, and the residue was recrystallized from hexane to give a product with mp 179-181° [5] and R_f 0.86 [chromatography in a thin layer of activity II aluminum oxide with elution with benzene–hexane–chloroform (6 : 1 : 30) and development with iodine vapors or UV light]. The picrate had mp 232-233° (from glacial acetic acid).

6-(1-Methyl-1,2,3,4-tetrahydro-6-quinolyl)phenanthridine. A. As described above, 6-(1-methyl-1,2,3,4-tetrahydro-6-quinolyl)phenanthridine containing starting compound IV was obtained by hydrolysis of 1 g of IV with alcoholic alkali. The product was purified through the picrate, which had mp 209-210° (from glacial acetic acid). Found: C 62.6; H 4.5; N 12.9%. $C_{23}H_{20}N_2 \cdot C_6H_3N_3O_7$. Calculated: C 62.9; H 4.2; N 12.8%. Decomposition of the picrate with alkali gave a pure sample with mp 119-120° (from hexane) and R_f 0.59 (one spot with self-generating bright-blue luminescence). Found: C 85.1; H 6.2; N 8.6%. $C_{23}H_{20}N_2$. Calculated: C 85.2; H 6.0; N 8.5%.

B. A 0.25 g (1.5 mmole) sample of 1-methyl-1,2,3,4-tetrahydroquinoline-6-carboxylic acid chloride (mp 204-205°) was added gradually to an ice-cooled solution of 0.31 g (1.5 mmole) of 2-aminodiphenyl in

24 ml of anhydrous pyridine, and stirring was continued for another 30 min. The pyridine was removed by steam distillation, and the residual N-(o-diphenylyl)-1-methyl-1,2,3,4-tetrahydroquinoline-6-carboxamide was separated, dried, and recrystallized from glacial acetic acid to give a product with mp 230-232°. Found: C 80.8; H 6.5; N 8.4%. $C_{23}H_{22}N_2O$. Calculated: C 80.7; H 6.5; N 8.2%. A mixture of 0.1 g (0.3 mmole) of the amide and 0.18 g (1.2 mmole) of phosphorus oxychloride was refluxed for 2 h. The excess phosphorus oxychloride was removed by distillation, and the residual resin was refluxed with 2 N alkali solution and then with excess 2 N sulfuric acid. The insoluble, resinous residue was separated, and the filtrate was neutralized with ammonium hydroxide. The resulting precipitate was separated and recrystallized from hexane to give a product with mp 118-119° and R_f 0.59. The spot on the chromatogram was identical to the spot of 6-(1-methyl-1,2,3,4-tetrahydro-6-quinolyl)phenanthridine with respect to the R_f value and the bright-blue fluorescence in UV light. The picrate had mp 209-210° (from glacial acetic acid). This product did not depress the melting point of the sample described above, and their IR spectra were identical.

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