ISOMERIZATION RECYCLIZATION OF PYRIDYLETHYLATED KETONES. NEW METHOD FOR THE SYNTHESIS OF QUINOLINE DERIVATIVES

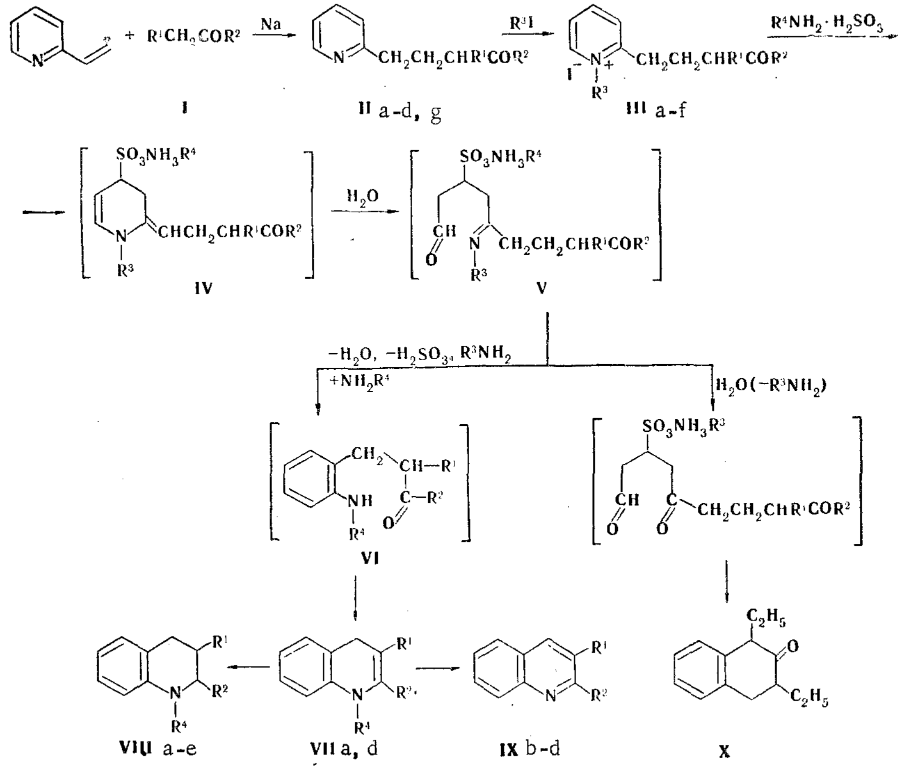
P. B. Terent'ev, Lieh T'i Ch'in,
and A. N. Kost*

UDC 547.821:543,51:542.952

Quinolines and 1,2,3,4-tetrahydroquinolines were obtained by heating quaternary salts of pyridylethylated ketones with sulfites of primary amines in an ampul. 1-Tetralone or substituted 2-tetralones are formed as side products. Substituted 1,4-dihydroquinolines were also identified among the reaction products by chromatographic mass spectrometry.

We recently reported that under the conditions of the Kost–Sagitullin rearrangement [1, 2] 5-(2-pyridyl)pentan-2-one is converted in high yield to 1,2-dimethyl-1,2,3,4-tetrahydroquinoline; 1,2-dimethyl-1,4-dihydroquinoline and 1-tetralone as a side product were also detected in the reaction medium [3].

In order to expand the scope of this reaction we studied the Kost–Sagitullin rearrangement of quaternary salts IIIa-g of pyridylethylated carbonyl compounds IIa-e, which we obtained by the method in [4] by the reaction of 2-vinylpyridine with ketones Ib-e in the presence of sodium† (see the scheme presented below).



II, III, VIII, IX a-d $R^3=R^4=CH_3$; a $R^1=H$, $R^2=CH_3$; b $R^1=C_2H_5$, $R^2=C_3H_7$; c $R^1=H$, $R^2=C_6H_5$; d $R^1=CH_3$, $R^2=C_6H_5$; e $R^1=H$, $R^2=CH_3$, $R^3=R^4=C_2H_5$; f $R^1=H$, $R^2=R^4=CH_3$, $R^3=C_4H_9$; g $R^1=COOC_2H_5$, $R^2=CH_3$

---

*Deceased.

†Compound IIa was obtained as a result of the acidic hydrolysis of IIg by the method in [5].

M. V. Lomonosov Moscow State University, Moscow 117234. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 800-802, June, 1981. Original article submitted October 20, 1980.

0009-3122/81/1706-0591$07.50

TABLE 1. Isolated Products of the Recyclization of Salts IIIa-e

Starting salt	Reaction conditions		Reaction products	mp, °C	Mass spectra of the bases: m/e (relative intensity, %)*	Yield, %
	temp., °C	Time, h				
IIIa	120	25	VIIIa	245—246† 204—205‡	161 (32), 146 (100), 131 (38), 118 (25), 91 (18), 77 (25), 72 (24), 71,5 (20), 65 (14)	48
IIIb	140	30	VIIIb	192—193**	217 (26), 174 (20), 148 (24), 132 (20), 120 (100), 106 (26), 97 (19), 83 (17), 77 (16)	28
			IXb	170—171‡[8]	199 (17), 184 (31), 171 (100), 168 (17), 143 (19), 142 (56), 127 (25), 115 (18), 77 (6)	26
IIIc	130	50	VIIIc	174—175 101—102‡[9]	223 (55), 149 (20), 146 (100), 131 (20), 111 (20), 98 (12), 91 (20), 77 (12), 65 (15)	5
			IXc	84—85 197—198‡	205 (100), 204 (85), 176 (28), 151 (15), 102,5 (20), 102 (45), 101,5 (30), 88 (65), 77 (45)	10
IIId	140	20	VIIId	Oil †† 182—183‡‡	237 (100), 236 (62), 221 (17), 220 (20), 165 (12), 118,5 (11), 110,5 (10), 109,5 (12), 77 (6)	40
			IXd	207—208‡ [10]	219 (100), 218 (30), 189 (5), 165 (5), 108,5 (25), 102 (20), 94,5 (15), 82 (10), 77 (5)	5
IIIe	120	30	VIIIe	254—255†, ***	175 (26), 160 (100), 146 (16), 132 (20), 130 (29), 118 (34), 91 (23), 77 (21), 65 (13)	11

---

*The molecular-ion peak and the eight most intense peaks are presented. †Boiling point. ‡The methiodide. **Found for the methiodide: C 53.3; H 7.5%. $C_{16}H_{26}IN$. Calculated: C 53.5; H 7.2%. ††Found: C 85.0; H 8.0%. $C_{17}H_{19}N$. Calculated: C 85.2; H 8.0%. ‡‡Picrate. ***Found: C 82.2; H 9.5%. $C_{12}H_{17}N$. Calculated: C 82.3; H 9.7%.

The rearrangement was accomplished by heating salts IIIa-f with an aqueous solution of the alkylammonium sulfite in a sealed ampul at 120-140°C for 25-50 h (see Table 1).

A preliminary evaluation of the composition of the reaction mixture was made on the basis of data from the chromatographic mass-spectral analysis of the chloroform extract of the reaction mass. The principal products isolated from the reaction mitures in all cases are 1,2,3,4-tetrahydroquinolines VIIIa-e (see the scheme and Table 1). In addition to them, in a number of cases we isolated quinolines IXb-d. We were unable to detect primary recyclization products VI in a single case, and 1,4-dihydroquinoline derivatives VIIa, d were identified only by mass spectrometry.

The structures of VIIIa-e were proved by comparison of their constants with the literature data (VIIIa, d) and also by analysis of their PMR spectra and the character of their fragmentation under electron impact. In the mass spectra of all tetrahydroquinolines VIIIa-e we observed intense peaks of molecular ions (see Table 1), the primary fragmentation of which is due above all to elimination of the R^2 radical; this is characteristic for the mass spectral behavior of α-substituted piperidines [6]. A multiplet of 12 protons of the $2\text{-}C_3H_7$ and $3\text{-}C_2H_5$ groups at δ 0.9-1.3 ppm, a quartet of two 4-H protons at 2.1 ppm, a multiplet of one 3-H proton at 2.6 ppm, a multiplet of one 2-H proton at 3.8 ppm, and a singlet of three protons of a $1\text{-}CH_3$ proton at 2.95 ppm are observed in the PMR spectrum of VIIIb at strong field. A multiplet of four aromatic protons at 6.5-7.1 ppm is found at weak field.

The preponderant formation of tetrahydroquinolines VIII as compared with dihydroquinolines VII can evidently be explained by reduction of the latter by excess alkylammonium sulfite, as well as by their disproportionation, which leads to the simultaneous formation also of aromatized quinolines IX. This sort of process, which is catalyzed by acids, has been described previously [7]. Quinolines IXb-d are isolated from the reaction medium in the form of their hydrochlorides. The constants of the methiodides or picrates obtained from them were in agreement with the literature data (see Table 1).

We have previously noted [3] that among the products of recyclization of salt IIIa we detected 1-tetralone (in 24% yield), the formation of which was associated with the possibility of partial hydrolysis of the intermediately formed enamine V to the corresponding diketo aldehyde with its subsequent double condensation.

Our chromatographic mass-spectral study of the reaction mixtures obtained in the recyclization of salts IIIb-f made it possible only in the case of salt IIIb to detect and to subsequently isolate in 5% yield a ketone, which, according to the data from its IR and mass spectra and the results of an analysis of its 2,4-dinitrophenylhydrazone, corresponds to 1,3-diethyl-2-tetralone (X). Its IR spectrum contains an absorption band at 1720 cm^{-1}, and peaks of [M — H], [M — OH], and [M — C_2H_5] ions, which are characteristic for alkylcyclanones [6], are observed in its mass spectrum along with a molecular-ion peak.

EXPERIMENTAL

The PMR spectra of solutions of the compounds in CCl_4 (with hexamethyldisiloxane as the standard) and trifluoroacetic acid (with tetramethylsilane as the standard) were recorded with a PMR spectra. The chromatographic mass spectra were recorded with a Varian MAT-111 spectrometer; the column length was 1.5 m (with an inner diameter of 3.5 mm), the liquid phase was 5% SE-30 on Poropak, the carrier gas was helium, and the analysis was carried out with programmed heating of the thermostat from 100 to 250°C at a rate of 10 deg/min. The mass spectra were recorded at an energy of 80 eV. The mass spectra of the solid compounds were obtained with an MKh-1303 mass spectrometer at an ionization energy of 50 eV.

Quaternary salts IIIa-f were obtained by refluxing bases IIIa-d in benzene with excess methyl iodide (or with ethyl iodide and butyl iodide, respectively, in the case of IIIe, f). Compounds IIIb, IIId, and IIIf were oils. Compounds IIIa, IIIc, and IIIe had mp 102-103, 116-118, and 99-100°C (from alcohol), respectively.

General Method of Recyclization. A 10-ml sample of an aqueous solution of methylamine and 5 ml of the same solution saturated with sulfur dioxide were added to a solution of 20 mmole of salt III in the minimum amount of water, and the mixture was heated in a sealed ampul at 120-140°C for 25-50 h. It was then cooled, the precipitated hydriodide of the corresponding quinoline IX was separated, and the filtrate was neutralized with 20% sodium hydroxide solution and extracted with ether and benzene. The combined extracts were evaporated, and the residue was analyzed with a chromatographic mass spectrometer and separated with a column [on L 40/100 silica gel in benzene and benzene—methanol (9:1) systems], as a result of which tetrahydroquinolines VIII and the residual quinolines IX were isolated.

LITERATURE CITED

1. Ya. P. Stradyn', Khim. Geterotsikl. Soedin., No. 11, 1567 (1979).
2. R. S. Sagitullin, S. P. Gromov, and A. N. Kost, Dokl. Akad. Nauk SSSR, 243, 931 (1978).
3. P. B. Terent'ev, Lieh T'i Ch'in, and A. N. Kost, Khim. Geterotsikl. Soedin., No. 4, 564 (1980).
4. R. Levine and M. H. Wielt, J. Am. Chem. Soc., 74, 342 (1952).
5. W. E. Doering and R. A. N. Weil, J. Am. Chem. Soc., 69, 2461 (1947).
6. H. Budzikiewicz, C. Djerassi, and D. Williams, Mass Spectrometry of Organic Compounds, Holden Day, New York (1967), p. 315.
7. V. H. Gogte, K. M. More, and B. O. Tilak, Indian J. Chem., 12, 327 (1974).
8. V. I. Minkin, P. E. Nivorozhkin, and V. A. Bren', Zh. Obshch. Khim., 35, 1270 (1965).
9. R. C. Elderfield and B. H. Wark, J. Org. Chem., 27, 543 (1962).
10. J. M. F. Gagan and D. Lloyd, J. Chem. Soc., No. 18, 2488 (1970).