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REDUCTION AND ALKALINE HYDROLYSIS OF 5-OXOINDENO[1,2-b]PYRIDINIUM SALTS

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UDC 547.665'821.3:
542.938'941

5,9b-Dihydro derivatives of indeno[1,2-b]pyridine were obtained by the reduction of the corresponding 1,2-dimethyl-4-aryl-5-oxoindeno[1,2-b]pyridinium perchlorates. 1,2-Dimethyl-3-ethoxycarbonyl-4-phenyl-5-oxoindeno[1,2-b]pyridinium perchlorate forms in alkaline medium with splitting, recyclization and deamination products.

In the monocyclic pyridine series, the transformation of 1,4-dihydro- to 1,2-dihydro-isomers is readily accomplished by the reduction of the corresponding pyridinium salts, but a similar transformation for condensed derivatives is not known. The reduction of pyridinium salts is often carried out in alkaline medium, or agents are used which produce such a medium in the course of the reaction. Therefore, the object of the present work was to study the reduction of indenopyridinium perchlorates and their transformations in alkaline medium.

To reduce the indenopyridinium salts I, we used catalytic hydrogenation and reduction by sodium borohydride and sodium bis(methoxyethoxy)-aluminum hydride. In the catalytic reduction of salts by Raney nickel and Pd/C catalysts, a mixture of 5,9b- and 4,5-dihydro-isomers of the corresponding indenopyridines is formed, as well as products of further reduction of the latter, which will be reported separately.

In the reaction of 5-oxoindeno[1,2-b]pyridinium perchlorates I with sodium borohydride in an acetonitrile solution, a selective reduction of the pyridinium ring takes place, as the result of which the corresponding 1,2-dimethyl-4-aryl-5-oxo-5,9b-dihydroindeno[1,2-b]-pyridines II are formed. The formation of the 5,9b-dihydro-isomer II structure was confirmed by spectral methods of investigation. The appearance in the PMR spectrum of a CH proton signal in the form of a singlet excludes the 2,5-dihydro-isomeric structure, while the 4H-indenopyridine isomers, for which the proton signal at the $C_{(4)}$ atom is also a singlet, are known compounds which we used for the synthesis of the starting indenopyridinium salts I [3]. The frequency of the IR vibrations of the 5-CO groups of compounds II is appreciably decreased (up to 1665 cm^{-1}), which is explained by the increase in the conjugation.

When 1,2-dimethyl-3-ethoxycarbonyl-4-phenyl-5-oxoindeno[1,2-b]pyridinium perchlorate (Ia) is reduced by sodium bis(2-methoxyethoxy)aluminum hydride, whose use is favorably affected by increase in the basicity of the medium [4], not only is 5,9b-dihydro-isomer IIa formed, but 1-methyl-2,5-dioxo-3-acetyl-4-phenylindeno[1,2-b]pyridine (III) is also formed, which indicates splitting of the pyridine ring during the reaction. The subsequently studied reaction of indenopyridinium perchlorate Ia with an aqueous-alcoholic solution of alkali is a special case of nucelophilic recyclization of the pyridine ring [5].

The sole path of formation of 1-methyl-3-acetyl-4-phenyl-2,5-dioxoindeno[1,2-b]pyridine (III) is recyclization of the intermediate formed as the result of cleavage of the $N–C_{(2)}$

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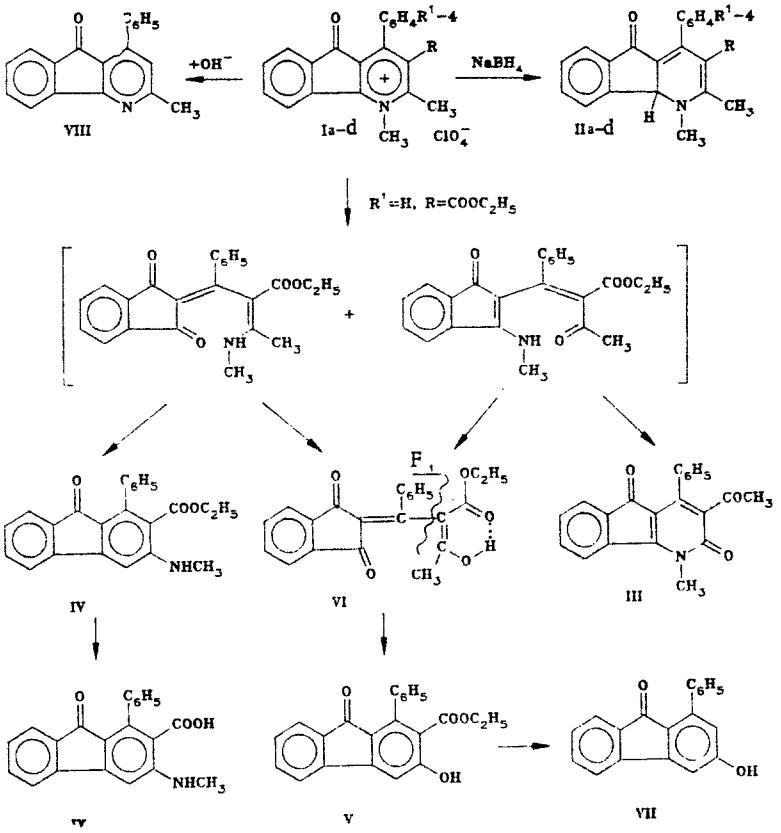
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp 86-89, January, 1987.
Original article submitted May 16, 1986.

 0009-3122/87/2301-0070$12.50

Scheme



I, II a—c R=$COOC_2H_5$, d, R=CN; a, d R^1=H, b R^1=NO_2, c R^1=OCH_3

bond of the pyridine ring. It should be noted that product III is identical with indenopyridine, isolated during acidic splitting of 1,2-dimethyl-3-ethoxycarbonyl-4-phenyl-5-oxo-4,5-dihydroindeno[1,2-b]pyridine [6].

Cleavage of the N—$C_{(9b)}$ bond in the indenopyridinium Ia molecule with subsequent recyclization leads to the formation of 1-phenyl-2-ethoxycarbonyl-3-methylamino-9-oxofluorene (IV). The indane-1,3-dione derivative VI isolated from the reaction mixture is a result of nucleophilic substitution of the $NHCH_3$ group by the OH group in the primary product of splitting, formed as the result of cleavage of the N—$C_{(9b)}$ bond. The derivative of the indane-1,3-dione, the ethyl ester of α-acetyl-β-(indane-1,3-dion-2-ylidene)-β-phenylpropionic acid (VI), has an enolized α-acetyl carbonyl group, which is stabilized by a strong intramolecular hydrogen bond, whose formation leads to elongation of the conjugation chain. The presence of an enol group was confirmed by the formation of a chelate ring in the reaction of compound VI with $FeCl_3$ and by the analysis of the IR spectra. In the 1700 cm^{-1} region, the absorption of compound VI is identical with that of 2-benzylideneindane-1,3-dione. These data, and also the discovery of fragment F_1 in the mass spectrum of derivative VI, confirmed its existence in the form with an enolized carbonyl group in the composition of the substituent at the $C_{(2)}$ atom of the indane ring, and thus excluded the alternative structure with an enolized carbonyl group in indanedione.

The intramolecular condensation of indanedione VI during the reaction leads to the formation of 1-phenyl-2-ethoxycarbonyl-3-hydroxy-9-oxofluorene (V), as confirmed by a separate experiment. 3-Hydroxyfluorene-9-one V is not the product of splitting 3-methylaminofluoren-9-one IV, since boiling of the latter in alcoholic alkali leads to hydrolysis of the ester group and 1-phenyl-3-methylamino-9-oxofluorene-2-carboxylic acid (IX) separates out from the reaction mixture.

Under the reaction conditions, the ester group of 3-hydroxyfluorenone V becomes partially hydrolyzed and decarboxylated, resulting in 1-phenyl-3-hydroxy-9-oxofluorene (VII). The discovery of 2-methyl-4-phenyl-5-oxoindeno[1,2-b]pyridine (VIII) among the reaction products is clearly explained by the dealkylation of the initial product, and also by the hydrolysis and decarboxylation of its carbethoxy group.

TABLE 1. Characteristics of Synthesized Compounds

Compound	mp, °C	Found, %			Empirical formula	Calculated,		
		C	H	N		C	H	N
IIa	174—176	77,2	5,4	3,9	$C_{23}H_{21}NO_3$	76,9	5,9	3,7
IIb	204—206	68,7	4,7	7.3	$C_{23}H_{20}N_2O_5$	68,3	5,0	6,9
IIc	184—186	74,2	5,7	3,5	$C_{24}H_{23}NO_4$	74,0	5,9	3,6
IId	210—212	80,9	5,2	9,5	$C_{21}H_{16}N_2O$	80,7	5,2	9.0
IV	153—155	77,0	5,6	4,2	$C_{23}H_{19}NO_3$	77,3	5,4	3,9
V	162—163	76,5	4,6	—	$C_{22}H_{16}O_4$	76,7	4,7	—
VI	113—115	73,1	5,0	—	$C_{22}H_{18}O_5$	72,9	5,0	—
VII	255—256	83,6	4,3	—	$C_{19}H_{12}O_2$	83,8	4,4	—
IX	206—208	76,4	4,7	4,4	$C_{21}H_{15}NO_3$	76,6	4,6	4,3

TABLE 2. Spectral Characteristics of Derivatives of 5,9b-Dihydroindeno[1,2-b]pyridine IIa-d

Compound	PMR spectrum (in $CDCl_3$), δ, ppm						IR spectrum, cm^{-1}	UV spectrum, nm (log ε)
	3-$COOCH_2CH_3$		2-CH_3 (s, 3H)	1-CH_3 (s, 3H)	9b-H (s, 1H)	other protons		
	(t, 3H)	(q, 2H)						
IIa	0,61	3,71	2,69	3,16	4,86	7,39 (m, 5H, 4-C_6H_5), 7,49--7,90 (m, 4H, of indane)	1685, 1665	444 (4,02)
IIb	0,86	3,76	2,74	3,19	4,87	7,44—7,87 (m, 6H, arom.), 8,20 (d, J = 9.5 Hz, 2H, arom.)	1685, 1665	450 (3,83)
IIc	0,70	3,77	2,67	3.13	4,83	3,83 (s, 3H, OCH_3), 6,89 (d, J=8,5 Hz, 2H) and 7,28—7,90 (m, 6H, arom.)	1680, 1665	444 (3,96)
IId	—	—	2,57	3,23	5,01	7,33—7,91 (m, 9H, arom.)	1670, 2200	445 (3,90)

EXPERIMENTAL

The PMR spectra were run on a WH-90 spectrometer relative to TMS as internal standard, UV spectra on a Specord UV-Vis spectrophotometer in ethanol, IR spectra on PE-580 B spectrophotometer in mineral oil, and the mass spectra on a AEI MS-50 spectrometer with a direct introduction of the sample into the ionic source at 70 eV. Indenopyridinium perchlorates Ia-d were obtained according to [3]. The compounds were recrystallized from ethanol.

The characteristics of the compounds synthesized are given in Tables 1 and 2.

1,2-Dimethyl-4-aryl-5-oxo-5,9b-dihydroindeno[1,2-b]pyridines IIa-d. Sodium borohydride (0.4 g, 10 mmoles) is added in two portions to a solution of 5 mmoles of indenopyridinium perchlorate I in 60 ml of acetonitrile, and the mixture is stirred for 10-15 min. Then 100 ml of water are added, and the mixture is extracted by ether (3 × 50 ml). The ether extracts are dried and evaporated. Yellow colored compounds are obtained, yield 43-54%.

Reaction of 1,2-Dimethyl-3-ethoxycarbonyl-4-phenyl-5-oxoindeno[1,2-b]pyridinium perchlorate (Ia) with Alkali. A solution of 1.1 g (20 mmoles) of KOH in 5 ml of water is added to 0.9 g (2 mmoles) of perchlorate Ia in 40 ml of ethanol, and the mixture is heated on a water bath for 1 h 30 min. The dark-orange solution is then diluted by 400 ml of water, acidified by dilute HCl to pH 4, and extracted by chloroform (2 × 100 ml). The chloroform solution is dried, evaporated to a volume of 3-4 ml, and preparatively chromatographed on a plate with silica gel L 40/100 (size of the plate 20 × 35 cm, thickness of nonstationary layer 2-3 mm). A chloroform—hexane—acetone (9:7:1) mixture is used as eluent. Zones are collected, counting from the front: A) a weakly yellow zone absorbing UV light; B) brightly yellow (orange fluorescence at UV light); C) yellow; D) almost colorless, absorbing UV light; and a brown zone before the starting line, from which after repeated chromatography, the orange zone E and yellow zone F are collected. After elution of the adsorbed material from silica gel by chloroform, compounds IV-IX are obtained.

1-Phenyl-2-ethoxycarbonylfluoren-9-one (V) (from Fraction A). PMR spectrum (DMSO-D_6): 0.84 (t, 3H, CH_3), 3.90 (q, J = 7.0 Hz, 2H, CH_2), 7.14-7.87 (m, 10H, arom. protons), 11.30

ppm (br. s, 1H, OH). IR spectrum: 1710, 1650 cm^{-1}. Mass spectrum, m/z (%): 344 (34) $[M]^{+\cdot}$, 298 (100) $[M - C_2H_5OH]^{+\cdot}$, 270 (69) $[M - COOC_2H_5, -H]^{+\cdot}$, 242 (12) $[M-COOC_2H_5, -H, -CO]^{+\cdot}$, 213 (36).

1-Phenyl-2-ethoxycarbonyl-3-methylaminofluoren-9-one (IV) (from Fraction B). PMR spectrum (DMSO-D_6): 0.67 (t, 3H, CH_3), 3.70 (q, J = 7.0 Hz, 2H, CH_2), 2.94 (d, J = 5.0 Hz, 3H, $NHCH_3$), 6.82-7.60 (m, 10H), and 7.86 ppm (d, J = 7.0 Hz, 1H), NH and arom. protons. IR spectrum: 3370, 1700, 1672 cm^{-1}. Mass spectrum, m/z (%): 357 (100) $[M]^{+\cdot}$, 312 (38) $[M - C_2H_5O]^{+}$ 311 (74) $[M-C_2H_5OH]^{+\cdot}$, 310 (60), 254 (34).

Ethyl Ester of α-Acetyl-β-(indane-1,3-dion-2-ylidene)-β-phenylpropionic Acid (VI) (from Fraction C). PMR spectrum ($CDCl_3$): 0.92 (t, 3H, CH_2CH_3), 4.06 (q, J = 7.5 Hz, 2H, CH_2CH_3), 1.73 (s, 3H, CH_3), 7.41 (s, 5H, C_6H_5), 7.66-7.99 (m, 4H, of indane), 13.76 ppm (s, 1H, OH). IR* spectrum ($CHCl_3$, $5 \cdot 10^{-2}$ mole/liter, layer thickness 0.2 mm): 1728 (42), 1678 (95), 1645 cm^{-1} (60). Mass spectrum, m/z (%): 362 (5) $[M]^{+\cdot}$, 333 (20) $[M - C_2H_5O]^{+}$, 319 (6) $[M-COCH_3]^{+}$, 316 (100) $[M-C_2H_5OH]^{+\cdot}$, 315 (23) $[M - C_2H_5OH, -H]^{+}$, 301 (25) $[M - H_2O, -COCH_3]^{+}$, 287 (30), 273 (41) $[M-H_2O, -COCH_3, -CO]^{+}$, 260 (30), 246 (52), 233 (3) $[F_1]^{+}$.

2-Methyl-4-phenyl-5-oxoindeno[1,2-b]pyridine (VIII) (from Fraction D) is identical with the product obtained in the oxidation of 2-methyl-2-phenyl-5-oxo-4,5-dihydroindeno[1,2-b]-pyridine [7]. PMR spectrum ($CDCl_3$): 2.64 (s, 3H, CH_3), 7.00 (s, 1H, 3-H), 7.33-7.71 (m, 8H) and 7.86 ppm (d, J = 6.5 Hz, 1H) arom. protons.

1-Methyl-3-acetyl-4-phenyl-2,5-dioxoindeno[1,2-b]pyridine (III) (from Fraction E) does not give melting point depression with a known sample.

1-Phenyl-3-hydroxyfluoren-9-one (VII) (from Fraction F). PMR spectrum (DMSO-D_6): 7.18-7.84 (m, 11H, arom. protons), 12.07 (br. s, 1H, OH). IR spectrum: 1718 cm^{-1}. Mass spectrum, m/z (%): 272 (60) $[M]^{+\cdot}$, 271 (100), 255 (3) $[M-OH]^{+\cdot}$, 215 (9), 213 (9).

1-Phenyl-3-methylaminofluoren-9-one-2-carboxylic Acid (IX). A 0.1 g portion of compound IV and 0.1 g of KOH in a mixture of 4 ml of ethanol and 0.5 ml of water is boiled for 2 h. The mixture is diluted with 20 ml of water, acidified with dilute HCl, and a yellow precipitate is filtered, which is recrystallized and dried at 110°C. PMR spectrum (DMSO-D_6): 3.01 (br. s, 3H, NCH_3), 7.08-7.93 (m, 11H, arom. protons and NH), 12.65 (s, 1H, OH). IR spectrum: 3340, 1702, 1650 cm^{-1}.

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*IR spectrum of 2-benzylideneindane-1,3-dione: ($CDCl_3$, $5 \cdot 10^{-2}$ mole/liter): 1730 (51), 1688 cm^{-1} (95).