α-Cyano-β-(o-ethoxycarbonylphenyl)aminoacrylamide (XVIa). A mixture of 0.6 g (4.3 mmole) of the enamine (XV) and 2.5 g (15 mmole) of the ester (II) in 10 ml of glacial acetic acid was boiled for 6 h, cooled, and the solid filtered off and washed with water and alcohol to give 0.24 g (19%) of (XVIa), mp 227-229°C (from DMF). $M^{+\cdot}$ 259. Found: C 60.3; H 5.2; N 16.5%. $C_{13}H_{13}N_3O_3$. Calculated: C 60.2; H 5.0; N 16.2%.

α-Cyano-β-(o-carboxyphenyl)aminoacrylamide (XVIb). A mixture of 0.6 g (4.3 mmole) of the enamine (XV) and 2 g (15 mmole) of the ester (II) in 10 ml of glacial acetic acid was boiled for 6 h, cooled, and the solid filtered off and washed with water and alcohol to give 0.24 g (19%) of (XVIa), mp 227-229°C (from DMF). $M^{+\cdot}$ 259. Found: C 57.0; H 3.9; N 18.1%. Calculated: C 57.1; H 3.9; N 18.2%.

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SYNTHESIS OF 5-OXOINDENO[1,2-b]PYRIDINIUM SALTS

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When N-methylated 4-aryl-5-oxo-4,5-dihydroindeno[1,2-b]pyridines are oxidized with hydrogen peroxide in the presence of perchloric acid, in addition to the formation of the indenopyridinium perchlorates, cleavage of the dihydropyridine ring occurs, giving the 2-arylideneindan-1,3-dione.

We have previously converted the 1,4-dihydro-isomers of cyclic pyridine derivatives into the corresponding 1,2-isomers by reducing pyridinium salts [1, 2]. Similar conversions of polycyclic dihydropyridines such as dihydroindeno[1,2-b]pyridines have not been described. The aim of this investigation was to develop methods for the synthesis of N-methyl-5-oxoindeno[1,2-b]pyridinium salts. The starting materials were 5-oxoindeno[1,2-b]pyridines (I) or the N-methylated 5-oxo-4,5-dihydroindeno[1,2-b]pyridines (II) [3, 4]. In the case of pyridines (I), these were heated with methyl toluene-p-sulfonate or dimethyl sulfate. The use of this classical method for the synthesis of the salts was restricted by preparative difficulties, namely, resinification and the hygroscopicity of the products. When the salts (III) were obtained as the monosulfates or tosylates, therefore, they were converted into the perchlorates by ion exchange by treatment with $NaClO_4$, since pyridinium perchlorates are readily crystallizable compounds. A method used by us previously [1, 2] for the preparation of pyridinium salts by the oxidation of N-methylated 1,4-dihydropyridines with hydrogen peroxide in the presence of perchloric acid was complicated in the indenopyridine series by the occurrence of side reactions, i.e., in addition to salt formation, cleavage of the dihydro-

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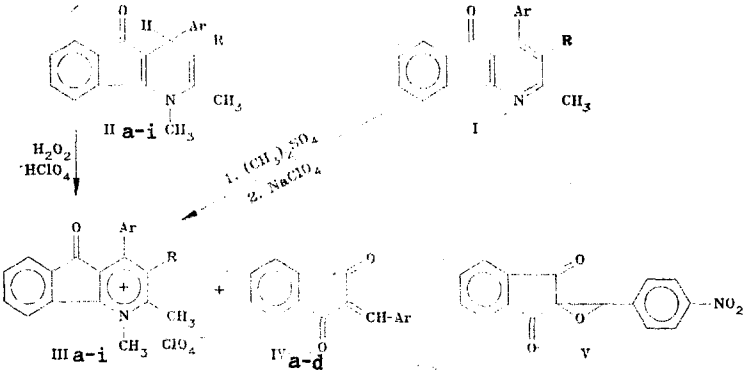
TABLE 1. Properties of Indenopyridinium Perchlorates (III)

Compound	mp, °C	Found, %			Empirical formula	Calculated, %			Yield, %
		C	H	N		C	H	N	
IIIa	272—273	60,0	4,1	3,5	$C_{23}H_{20}ClNO_7$	60,3	4,4	3,1	55
IIIb	210—213	58,8	4,5	3,1	$C_{24}H_{22}ClNO_8$	59,1	4,6	2,9	42
IIIc	188—190	51,0	3,2	2,1	$C_{23}H_{19}BrClNO_7$	51,5	3,6	2,6	28
IIId	237—240	54,5	3,8	5,2	$C_{23}H_{19}ClN_2O_9$	54,9	3,8	5,6	19
IIIe	184—187	56,0	3,5	3,1	$C_{23}H_{19}Cl_2NO_7$	56,1	3,9	2,9	27
IIIf	230—232	54,5	3,5	3,0	$C_{24}H_{20}ClF_2NO_8$	55,0	3,9	2,7	38
IIIg	268—270	61,3	4,2	3,6	$C_{22}H_{18}ClNO_6$	61,8	4,2	3,3	14
IIIh	171—174	61,0	4,0	6,5	$C_{21}H_{15}ClN_2O_5$	61,4	3,7	6,8	48
IIIi	208—210	64,7	4,7	5,5	$C_{27}H_{21}ClN_2O_6$	64,2	4,2	5,6	35

pyridine ring took place, which will be the subject of a further communication. Preparatively, in addition to the salts (III), from the reaction mixture there were also isolated the acid hydrolysis products of (II) (in the case of (IIa), 3%, (IIb), 32%, and (IIc), 10%). In the oxidation of (IId), in addition to the expected 2-(p-nitrobenzylidene)indan-1,3-dione (IVd) there was isolated 2-spiro-(2'-indan-1',3'-dione)-3-(4'-nitrophenyl)oxirane (V).



II, III a-f R=$COOC_2H_5$, g R=$COCH_3$, h R=CN, i R=$CONHC_6H_5$; a,g—i Ar=C_6H_5, b Ar=4-$CH_3OC_6H_4$, c Ar=4-BrC_6H_4, d Ar=4-$NO_2C_6H_4$, e Ar=2-ClC_6H_4, f Ar=2-$F_2CHOC_6H_4$

Clearly, the electron acceptor group in the 2-arylideneindan-1-3-dione activates the >C=CH group, as a result of which addition of oxygen to this bond takes place under the reaction conditions, giving the oxirane (V). The structure of (V) was confirmed by ^1H and ^{13}C NMR, IR, and mass spectroscopy, as well as by direct synthesis. It is noteworthy that the synthesis of indan-1,3-dione derivatives of oxirane has hitherto been effected in basic media only [5].

N-Methyl derivatives of 5-oxo-4,5-dihydroindeno[1,2-b]pyridine (II) are fairly readily oxidized by atmospheric oxygen, since the salt (IIIa) was obtained in 55% yield on prolonged boiling of (IIa) in alcoholic solution acidified with $HClO_4$ (similarly, 28% of IIIb was obtained from IIb). The 4-(p-nitrophenyl) derivative of the indenopyridine (IId) did not afford the corresponding salt under these conditions, the reaction product being 2-(p-nitrobenzylidene)indan-1,3-dione (IVd) (yields 40-60%).

The IR spectra of the 5-oxoindenopyridinium salts (III) show strong absorption for the 5-CO group at 1735 cm^{-1}. The absorption due to the CO at $C_{(3)}$ in the esters (IIIa-f) merges with that for the 5-CO group, but in the 3-$COCH_3$ derivative (IIIg) the absorption at 1712 cm^{-1} is clearly separated. In the IR spectrum of (IIIh), two amide bands are seen at 1694 and 1668 cm^{-1}. The type of anion in the salts (III) has no effect on these IR bands.

EXPERIMENTAL

PMR spectra were obtained on a Bruker WH-90 spectrometer in DMSO-D_6, internal standard TMS, and IR spectra on a PE 580 B. The compounds (II) were synthesized as described in [4].

The properties of the indenopyridinium perchlorates are given in Tables 1 and 2.

Synthesis of 1,2-Dimethyl-4-aryl-5-oxoindeno[1,2-b]pyridinium Salts (III). A. The indenopyridine (I) (10 mmole) was heated with 2 ml of dimethyl sulfate (until a neutral reac-

TABLE 2. PMR Spectra of 1,2-Dimethyl-4-aryl-5-oxoindeno[1,2-b] pyridinium Perchlorates (III)

Compound	1-CH_3 (s 3H)	2-CH_3 (s, 3H)	3-R	4-Ar	Protons at $C_{(6)}$–$C_{(9)}$
IIIa	4,47	2,84	0,86 (t 3H); 4,06 (q 2H)	7,27—7,60 (m, 5H)	7,78—7,60 (m 3H); 8,32—8,52 (m 1H)
IIIb	4,51	2,88	1,01 (t 3H); 4,19 (q 2H)	3,88 (s 3H); 7,12 (d 2H); 7,42 (d 2H)	7,79—8,10 (m 3H); 8,38—8,60 (m 1H)
IIIc	4,55	2,91	0,93 (t 3H); 4,12 (q 2H)	7,71 (d 2H) 8,36—8,61 (m 3H)	7,87—8,12 (m 3H)
IIId	4,52	2,90	0,99 (t 3H); 4,17 (q 2H)	7,38 (d 2H); 7,80 (d 2H)	7,87—8,09 (m 3H); 8,42—8,58 (m 1H)
IIIe	4,55	2,94	0,89 (t 3H); 4,08 (q 2H)	7,18—7,71 (m 4H)	7,83—8,09 (m 3H); 8,42—8,60 (m 1H)
IIIf	4,53	2,92	0,89 (t 3H); 4,10 (q 2H)	7,18 (t 1H) [Jh–f=72,0 Hz] 7,24—8,09 (m, 7H)	8,40—8,57 (m, 1H)
IIIg	4,54	2,80	2,09 (s 3H)	7,31—7,68 (m, 5H)	7,83—8,03 (m 3H); 8,40—8,58 (m 1H)
IIIh	4,51	3,10		7,57 (s 5H)	7,69—8,03 (m 3H); 8,38—8,53 (m 1H)
IIIi	4,62	2,94	7,49 (s 5H); 10,79 (s 1H)	7,07—7,43 (m, 5H)	7,84—8,31 (m 3H); 8,44—8,60 (m 1H)

tion was obtained) for 6-8 h at 60-80°C. The mixture was cooled, treated with ether, and the solid separated and dissolved in the minimum amount of water. The aqueous solution was saturated with $NaClO_4$, and the colorless or pale yellow indenopyridinium perchlorate which separated was filtered off and recrystallized from propan-2-ol. Yield 35-60%. (In the case of 1,2-dimethyl-3-acetyl-4-phenyl-5-oxoindeno[1,2-b]pyridinium monomethylsulfate, mp 250-253°C, yield 65%).

B. The indenopyridine (I) (3 mmole) and 1.5 g (8 mmole) of methyl toluene-p-sulfonate were heated at 130-140°C for 12 h. The cooled reaction mixture was treated with dry dioxane, filtered, and the tosylate recrystallized from chloroform–hexane. (In the case of 1,2-dimethyl-3-cyano-4-phenyl-5-oxoindeno[1,2-b]pyridinium tosylate, mp 220-223°C, yield 69%).

Exchange of the anion for ClO_4^- in the remaining tosylates was carried out by method A, yields 40-65%.

C. The N-methyl compound (II) (10 mmole) was boiled in 80 ml of ethanol with 20 mmole of hydrogen peroxide (30% aqueous solution) and 10 mmole of perchloric acid (57% aqueous solution) until the red color disappeared (1-4 h). The solvent was removed in vacuo, and the residue cooled and treated with ether. The perchlorate (III) which separated was filtered off and recrystallized. The ethereal solution was evaporated to give the 2-arylideneindan-1,3-dione (IV), which was recrystallized from acetic acid. The compound (IVa) was identical in its physicochemical properties with the authentic indan-1,3-dione derivative [6]. Following oxidation of (IId), the oxirane (V) was isolated from the ether solution (yield 35%).

2-Spiro-(2'-indan-1',3'-dione)-3-(4'-nitrophenyl)oxirane (V). 2-(4'-Nitrobenzylidene)-indan-1,3-dione (2.8 g, 10 mmole) was boiled for 4 h in 50 ml of ethanol with 2.3 ml of 30% H_2O_2 and 1.3 ml of 57% perchloric acid. The reaction mixture was diluted with water, and the colorless solid which separated was filtered off and recrystallized from ethanol. The yield of the oxirane (V) was 1.19 g (65%), mp 217-219°C. IR spectrum: 1756, 1723 cm^{-1} (CO). PMR spectrum: 5.16 (s, 1H, 3-H), 7.67-8.11 (m, 6H) and 8.33 ppm (d, 2H) — aromatic protons. ^{13}C NMR spectrum: 63.1 ($C_{(3)}$), 65.7 ($C_{(2)}$), 192.1 (CO), 190.7 ppm (CO). Mass spectrum: 295 (6) $[M]^{+\cdot}$, 278 (15) $[M - OH]^+$, 182 (18) $[M - CO]^+$, 104 (100). Found: C 64.9; H 3.2; N 4.5%. $C_{16}H_9NO_5$. Calculated: C 65.1; H 3.1; N 4.7%; M 295.

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AZAINDOLE DERIVATIVES.

67.* SYNTHESIS OF N-SUBSTITUTED 1-BENZYL-4-METHYL-5-CYANO-6-AMINO-7-AZAINDOLES

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N-substituted 1-benzyl-4-methyl-5-cyano-6-amino-7-azaindoles have been synthesized from the respective 1-benzyl-4-methyl-5-cyano-6-chloro(and 6-hydroxy)-7-azaindoles. The effect of the 5-cyano group on the oxidation-reduction processes accompanying nucleophilic replacement of chlorine in 6-chloro-7-azaindoles by primary and secondary amines has been considered. 7-Azaindoline compounds were dehydrogenated by chloranil to N-substituted 1-benzyl-4-methyl-5-cyano-6-amino-7-azaindoles.

The selective effect of various 6-amino derivatives of 1-benzyl-7-cyano-azaindoles on central serotoninergic systems has been described in [2]. In order to broaden the study of the antiserotonin effects of isomeric azaindoles it was of interest to obtain the hitherto unknown 6-amino derivatives of 1-benzyl-5-cyano-7-azaindoles (I). The starting material for the synthesis of compounds Ia-g was 1-benzyl-4-methyl-5-cyano-6-chloro-7-azaindoline (II) [1].

We have shown [3, 4] that the nucleophilic replacement of chlorine at position 6 in the 7-azaindoline system is a serious problem. For these reactions in such a system, because of the electron density distribution extremely severe conditions are needed, e.g., 6-chloro-7-azaindolines that do not contain a cyano group react with amines only at temperatures of at least 250°. Under such severe conditions, normal nucleophilic replacement is accompanied by redox processes, so that along with the 6-amino-7-azindolines there are formed the respective 6-amino-7-azaindoles and 7-azaindoles unsubstituted at position 6. The amounts of the latter are determined by the nucleophilicity of the amine and the redox potential of the azoindoline compound [3, 4].

The presence of a cyano group ortho to chlorine in 1-benzyl-6-chloro-7-cyano-5-azaindoline, which is distinguished by a higher redox potential than would be expected, increased the reactivity of the chlorine, and enabled it to undergo nucleophilic substitution by various other amines at lower temperature (180-185°) without the occurrence of redox reactions [2].

An analogous effect of an ortho-cyano group was observed in our case. The chlorine in compound II undergoes nucleophilic substitution with most primary and secondary aliphatic and heterocyclic amines at 180-185° to form N-substituted 1-benzyl-4-methyl-5-cyano-6-amino-7-azaindolines (IIIa-e) in high yield (77-87%). Only in the case of the sterically more hindered di-n-butylamine is the substitution less complete (55%) under these conditions, and about 35% of the starting chloroderivative II is recovered unchanged. With still weaker nucleophiles — aromatic amines of the aniline type — compound II does not react at all, not only at 180-185°, but is recovered practically unchanged even at 250°. Raising the temperature to 280-290° causes significant thermal decomposition of II. However with a stronger nucleophile — viz., hydrazine — II reacts already at 110-120° to form 1-benzyl-4-methyl-5-cyano-6-hydrazino-7-azaindoline (IV).

*For communication 66, see [1].

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