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INDOLOPYRIDINES WITH AN ANGULAR HETEROATOM.

11.* SYNTHESIS OF 12-ARYLIDENINDOLO-[2,1-*a*]ISOQUINOLINIUM SALTS

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The condensation of aromatic aldehydes with indolo[2,1-a]isoquinoline in a solution of trifluoroacetic acid yielded a series of 12-arylidenindolo[2,1-a]isoquinolinium trifluoroacetates. Analogous quaternary salts are formed with trichloroacetic and acetic acids as well as upon the reaction of indoloisoquinolinium hydrochloride with p-nitrobenzaldehyde or with p-nitrophenyldiazonium chloride in ethanol.

We studied the condensation of indolo[2,1-*a*]isoquinoline (I) with a series of aromatic aldehydes in acid media since 5-aryl-7,7-dimethylindolo[1,2-*a*]quinolinium perchlorates possess strong fluorescence and hold promise as laser dyes [2, 3], solvatochromic indicators, and dyes for epoxy resins [4]. The reaction was carried out in a mixture of tetrahydrofuran with trifluoroacetic, trichloroacetic, and acetic acids at room temperature over several hours. The corresponding 12-arylidenindolo[2,1-*a*]isoquinolinium acetates IIa-i were obtained in yields from 25 to 90%. These high-melting crystalline products range in color from yellow to dark green. Their physicochemical characteristics are given in Tables 1 and 2.

In comparison with the PMR spectrum of starting isoquinoline I, the spectra of compounds II show the doublet for 11-H shifted upfield by 0.2-0.6 ppm. This shift is probably related to shielding by the introduced arylidene fragment, which has the preferred *E*-configuration determined by steric hindrance evident from examination of the Dreiding models.

The signal of the vinyl proton 13-H is a singlet at 6.93-7.0 ppm in the case of an aryl moiety with an electron-donor substituent and in the vicinity of 7.4 ppm in the case of an electron-withdrawing *p*-nitrophenyl group. The ^{13}C NMR spectrum of compound IIa lacks the signal for 12-C seen for starting isoquinoline I at 93.0 ppm but displays new signals from the two quaternary carbon atoms 12-C (at 111.1 ppm) and 1′-C (at 129.0 ppm) and a set of signals from the five atoms of the introduced phenyl substituent. The NMR spectra of almost all the analytical samples obtained indicated that compounds II are isolated as one geometrical isomer or the magnetic equivalence of their *Z*- and *E*-isomers.

An exception is found for derivatives IIb and IIe, which have methoxyarylidene fragments. Thus, the PMR spectrum of IIb taken at 400 MHz shows OMe singlets at 3.80 and 3.89 ppm in ~9:1 ratio. The spectrum recorded before recrystallization shows that salt IIb is formed with a ~2:1 *E:Z* isomer ratio.

In order to establish the feasibility of obtaining analogous arylidene derivatives in a medium of less strong carboxylic acids, we studied the condensation in trichloroacetic and acetic acids. We chose *p*-nitrobenzaldehyde as the aldehyde component since its use in trifluoroacetic acid led to almost quantitative

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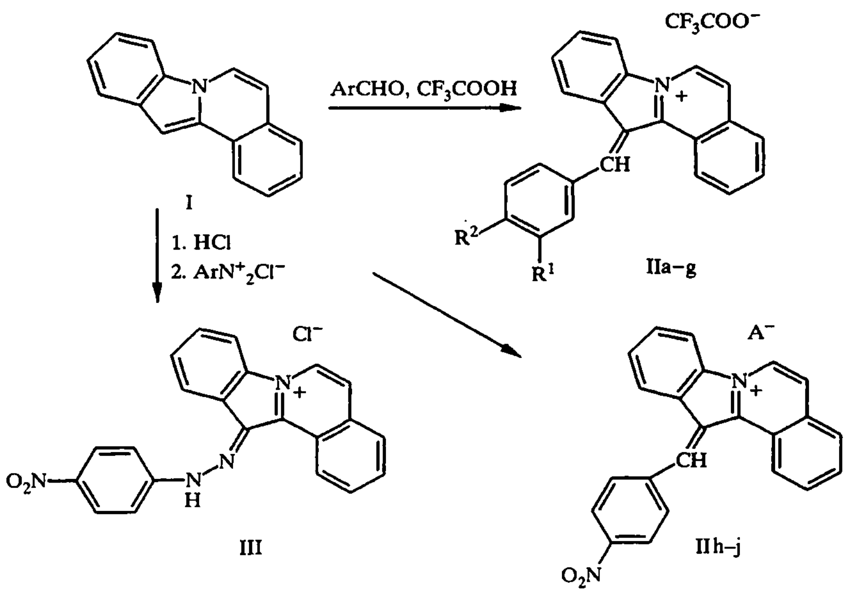

II a $R^1 = R^2 = H$; b $R^1 = H$, $R^2 = OMe$; c $R^1 = H$, $R^2 = NO_2$; d $R^1 = H$, $R^2 = OH$ (*ortho*); e $R^1 = OH$, $R^2 = OMe$; f $R^1 = R^2 = OMe$; g $R^1,R^2 = OCH_2O$; h $A^- = CCl_3COO^-$; i $A^- = MeCOO^-$; j $A- = Cl^-$

formation of salts II. These experiments showed that the expected arylidenes were also formed but the decrease in acid strength reduced the yield of trichloroacetate IIh to 52% and yield of IIi to 47%. On the other hand, the condensation of indoloisoquinoline hydrochloride I with *p*-nitrobenzaldehyde in abs. ethanol proceeded easily and the corresponding chloride IIj is formed in 71% yield. In this regard, Katritzky et al. [5] found that a substituted indolizinium hydrochloride (a fragment of which is found in starting I) does not undergo condensation with *p*-nitrobenzaldehyde.

TABLE 1. Characteristics of Synthesized Compounds IIa-j and III

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	R_f	IR spectrum, ν, cm^{-1}	[M-anion]$^+$*	Yield, %
		C	H	N					
IIa	$C_{25}H_{16}F_3NO_2$	$\frac{70.9}{71.6}$	$\frac{4.0}{3.8}$	$\frac{3.3}{3.3}$	224-227	0.53	1700, 1600 1520	306	36
IIb	$C_{26}H_{18}F_3NO_3$	$\frac{69.1}{69.5}$	$\frac{3.9}{4.0}$	$\frac{3.3}{3.1}$	220-222	0.58	1690, 1600 1520	336	61
IIc	$C_{25}H_{15}F_3N_2O_4$	$\frac{64.2}{64.7}$	$\frac{3.0}{3.2}$	$\frac{5.8}{6.0}$	>300	0.41	1695, 1600 1525, 1355	351	90
IId	$C_{25}H_{16}F_3NO_3$	$\frac{68.7}{69.0}$	$\frac{3.6}{3.7}$	$\frac{3.0}{3.2}$	219-221	0.35	3455, 1700 1600, 1520	322	25
IIe	$C_{26}H_{18}F_3NO_4$	$\frac{67.3}{67.1}$	$\frac{3.8}{3.9}$	$\frac{2.9}{3.0}$	226-228	0.37	3600, 1690 1600, 1520	352	36
IIf	$C_{27}H_{20}F_3NO_4$	$\frac{67.4}{67.6}$	$\frac{3.9}{4.2}$	$\frac{3.0}{2.9}$	240-243	0.29	1700, 1630 1520	366	43
IIg	$C_{26}H_{16}F_3NO_4$	$\frac{67.5}{67.4}$	$\frac{3.6}{3.5}$	$\frac{2.9}{3.0}$	166-168	0.43	1700, 1600 1520	350	40
IIh	$C_{25}H_{15}Cl_3N_2O_4$	$\frac{58.3}{58.8}$	$\frac{2.7}{2.9}$	$\frac{5.2}{5.5}$	>300	0.42	1700, 1600 1520, 1345		52
IIi	$C_{25}H_{18}N_2O_4$	$\frac{74.0}{73.2}$	$\frac{4.1}{4.4}$	$\frac{7.0}{6.8}$	240-242	0.47	1690, 1630 1520, 1345		47
IIj	$C_{23}H_{15}ClN_2O_2$	$\frac{71.7}{71.5}$	$\frac{4.0}{3.9}$	$\frac{7.1}{7.3}$	281-283	0.6		386	71
III	$C_{22}H_{15}ClN_4O_2$	$\frac{66.0}{65.7}$	$\frac{3.8}{3.7}$	$\frac{13.1}{13.9}$	260-262	0.4	3385, 1620 1535, 1355		33

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* By mass spectrometry.

TABLE 2. PMR Spectra of Synthesized Compounds

Compound	Chemical shifts*, δ, ppm, (coupling constant, *J*, Hz)					
	1-H, br. d	5-H, d	6-H, d	8-H, br. d	11-H, br. d	13-H, s	other protons
IIa*2	7.82 (7.8)	6.72 (7.4)	8.15*	8.12* (7.8)	7.15 (8.2)	6.93*	7.5-7.2 (8H, m); 6.93* (2H, m)
IIb	E: 7.81 (8.2) Z: 7.86 (8.2)	6.68 (7.4)	8.12* (7.4)	8.09* (8.2)	7.53 (8.0)	6.98*	7.4-7.23 (5H, m, arom.); 6.98* (4H, m, arom.); 3.89 and 3.8 (3H, s, OMe; *E*:*Z* = 9:1)
IIc	7.97 (8.2)	6.75 (7.4)	8.18* (7.4)	8.13* (8.2)	7.86 (8.2)	7.41*	7.56 (2H, m); 7.35 (1H, m); 7.28 (1H, m); 6.95 (2H, m)
IIe	7.72 (7.5)	*	8.03 (7.4)	7.97 (7.8)	7.6 (8.0)	7.0	9.9 (1H, s, OH); 7.46-6.34 (9H, m); 3.86 and 3.82 (3H, s, OMe, E:Z = 3:1)
IIf	7.78 (8.0)	6.63 (7.4)	8.08	8.0	7.48 (7.8)	6.95	7.5-6.7 (8H, m); 3.86 (3H, s); 3.55 (3H, s)
IIg	7.78 (8.0)	6.65 (7.4)	8.02*	8.05* (8.2)	7.48 (m)	7.0	7.5-6.8 (6H, m); 7.12 (1H, s, 2'-H); 6.78 (1H, d, J = 8.0 Hz, 5'-H) 5.88 (2H, s, O–CH_2–O)
IIh	8.0 (8.2)	6.77 (7.4)	8.21*	8.18* (8.2)	7.88 (8.2)	7.43*	7.7-7.3 (7H, m); 7.0 (2H, m)
IIj	7.79 (8.0)	6.77 (7.4)	8.19*	8.14* (8.2)	7.67 (8.2)	7.39	7.58 (2H, m); 7.43-7.23 (5H, m); 7.0 (2H, m)

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* Signals overlap.

*2 ^{13}C NMR spectrum of the salt IIa (the corresponding shifts for starting compound I are given in square brackets): 108.7 (13-C), 109.3 (5-C), 120.8, 121.4, 121.8, 122.2, 125.4, 126.6, 126.9, 128.6 and 129.9 (all CH), 111.1 (12-C), 129.0, 130.5, 130.6, 130.9, 148.4 (all quat. C) [93.0, 108.7, 109.7, 120.7, 122.3, 123.7, 126.9, 127.4, 127.6 (all CH), 126.1, 128.8, 129.2, 131.4 and 134.8 (all quat. C)].

Furthermore, we attempted to carry out the condensation of chloride I with a *p*-nitrophenyldiazonium salt. The hydrazone III was isolated chromatographically in low yield (33%). The structure of III was proved by elemental analysis and its IR spectrum.

EXPERIMENTAL

The products obtained were purified by chromatography on silica gel L-60(40/100) columns. The purity of these products were monitored by TLC on Silufol UV-254 using 1:1 heptane–ether as the eluent and visualization with iodine vapor. The mass spectra were taken on an MX-1303 mass spectrometer. The ionizing voltage was 70 eV. The PMR spectra were taken on Bruker WP-250 and WP-400 spectrometers for solutions in $CDCl_3$ with TMS as the internal standard. The IR spectra were taken on a UR-20 spectrometer for KBr pellets.

12-Arylidenindolo[2,1-*a*]isoquinolinium Trifluoroacetates (IIa-g), Trichloroacetate (IIh), and Acetate (IIi). A sample of aromatic aldehyde (4.6 mmol) was added with stirring over 5 min to a mixture of indoloisoquinoline I (4.6 mmol) in anhydrous THF (25 ml) and trifluoroacetic acid (10 ml) cooled in a ice bath. After the mixture was maintained at room temperature for 6 h, the solvent and excess of trifluoroacetic acid were removed in vacuum. The solid mass formed was crystallized from ethanol or fractionated on a silica gel column to give colored, crystalline trifluoroacetates IIa-g. Trichloroaceate IIh and acetate IIi were analogously obtained by replacing CF_3CO_2H with CCl_3CO_2H and CH_3CO_2H, respectively.

12-(4-Nitrophenyl)indolo[2,1-*a*]isoquinolinium Chloride (IIj). Gaseous HCl was bubbled through a solution of indoloisoquinoline I (0.16 g, 0.74 mmol) in dry benzene (20 ml) for 10 min. The precipitate formed was separated and a solution of 4-nitrobenzaldehyde (0.13 g, 0.82 mmol) in abs. ethanol (25 ml) and three drops of piperidine were added to it. The mixture was maintained with stirring for 4 h at 20°C and then cooled to 0°C. The precipitate was separated and recrystallized from ethanol to give 0.2 g of yellow crystalline chloride IIj.

(4-Nitrophenylhydrazino)indolo[2,1-*a*]isoquinolinium Chloride (III). A solution of the diazonium salt obtained from *p*-nitroaniline (0.69 g, 5 mmol), HCl (1:1, 0.5 ml), and sodium nitrite (0.35 g, 5 mmol) was added to a solution of indoloisoquinoline I (1 g, 4 mmol) in ethanol (30 ml) at 0-5°C. Three drops of piperidine were added and the mixture was maintained with stirring for 2 h at 20°C. After cooling to 0°C, the precipitate formed was separated, washed with ethanol, and dried to give red crystalline hydrazone III (0.52 g, 33%).

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