SYNTHESIS OF N-METHYLPENTAFLUOROPHENYLPYRIDINIUM SALTS

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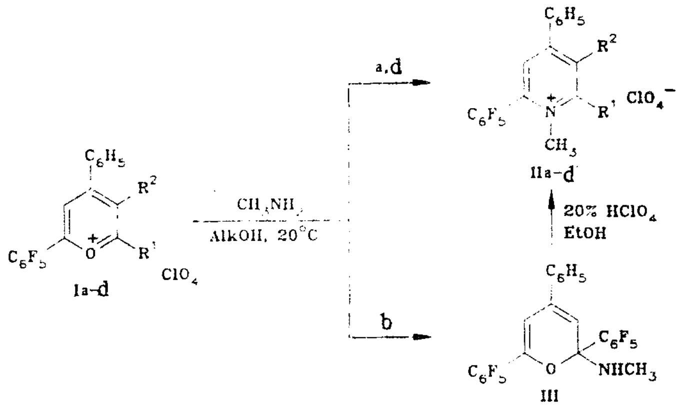
Di- and triaryl-N-methylpyridinium perchlorates bearing pentafluorophenyl groups have been obtained by reaction of the appropriate pyrylium salts with methylamine. In the case of 4-phenyl-2,6-bis(pentafluorophenyl)pyrylium perchlorate, a stable 2H-pyran intermediate was isolated.

N-Alkylpyridinium salts with aryl substituents in the heterocycle are of considerable practical value. They show high biological activity [1, 2], are strongly luminescent, and dyes derived from them have good generative properties, improved stability and solubility in aqueous alcoholic media [4].

The object of this study was to investigate possible ways of obtaining novel N-methylpyridinium salts bearing a pentafluorophenyl group in the heterocyclic moiety. The most frequently used method for the preparation of 2,4,6-trisubstituted pyridines and their N-alkyl derivatives is by reaction of pyrylium salts with ammonia (ammonium salts) and primary aliphatic amines [5]. This method has been used to obtain penta- and decafluorotriphenylpyridines from the appropriate pyrylium perchlorates [6]. There have been no reports of reactions of the latter with alkylamines.

We have now examined the reaction of di- and triphenylpyrylium salts (Ia-d) with methylamine in alcoholic solution. Compounds (Ia, c, d) readily give the N-methylpyridinium perchlorates (IIa, c, d) at room temperature, no replacement of fluorine atoms in the pentafluorophenyl rings taking place. The salt (Ib), which bears pentafluorophenyl groups in the 2- and 6-positions does not give the pyridinium compound under these conditions, but from the reaction mixture there was isolated a compound which was not a salt, M 519, which on the basis of spectral data was assigned the intermediate pyran structure (III).



I, II a $R^1=Ph$, $R^2=H$, Alk=Et; b $R^1=C_6F_5$; $R^2=H$, Alk=*t*-Bu; c $R^1=Me$, $R^2=H$, Alk=*t*-Bu; d $R^1-R^2=(CH_2)_4$, Alk=*t*-Bu

The IR spectrum of this compound showed strong absorption at ~3200 cm^{-1} for NH group vibrations. The presence of a methylamino-group was supported by the PMR spectrum (in $CDCl_3$), which contained a doublet at 3.12 ppm assigned to the methyl group protons, and a broadened signal at 4.35 ppm (NH proton). When CD_3OD was added to the solution, the signal at 4.35 ppm disappeared, and the doublet at 3.12 ppm was converted into a singlet. Apart from these signals, the PMR spectrum showed singlets at 5.80 (3-H) and 7.56 ppm (5-H) together with a signal at 7.10 ppm (C_6H_5). The ^{19}F NMR spectrum indicated that (III) contained two nonequivalent pentafluorophenyl groups.

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TABLE 1. Physicochemical Properties and Yields of Polyfluorinated N-Methylpyridinium Perchlorates

Compound	Empirical formula	T_{decomp} (from alcohol)	UV spectrum, λ_{max}, nm (log ε)	PMR spectrum (in DMSO-D_6*), δ, ppm	^{19}F NMR spectrum (in DMSO-D_6*), δ, ppm	Yield, %
II a	$C_{24}H_{15}ClF_5NO_4$	215...218	320 (4,47)	3,94 (3H, s, N—CH_3); 7,53...8,20 (10H arom.); 8,66 (1H, 3-H); 8,86 (1H, 5-H)	2,16; 13,15; 26,20	69
II b	$C_{24}H_{10}ClF_{10}NO_4$	302...304	335 (4,40)	4,11 (3H, s, N—CH_3); 7,70 (3H); 8,18 (2H, Harom.); 9,12 (2H, 3-and 5-H)	4,42; 15,72; 26,20	60
II c	$C_{19}H_{13}ClF_5NO_4$	254...257	297 (4,39)	2,98 (3H, s, CH_3); 4,09 (3H, s, N—CH_3); 7,68 (3Harom.); 8,11 (2Harom.); 8,67 (1H, 3-H); 8,73 (1H, 5-H)	4,97; 13,65; 25,70***	78
IId	$C_{22}H_{17}ClF_5NO_4$	241...243	295 (4,30)	1,34...2,07 (4H); 2,64 (2H); 2,94 (8H, 5-H—8-H); 3,81 (3H, s, N—CH_3); 6,97...7,20 (5Harom.); 7,37 (1H, 3-H)	5,32; 17,70; 25,90	44

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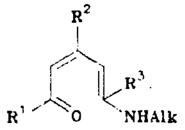
*The spectrum of (IId) was obtained in CF_3COOH.

**Intensity ratios 2:1:2.

***In CF_3COOH.

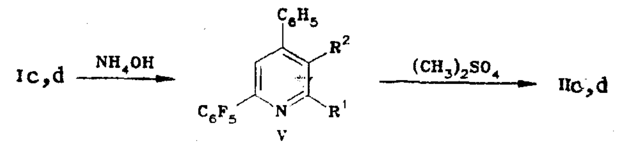
Pyrylium salts are known to react with alkylamines to give stable acyclic intermediates (IV) [7]. The spectral behavior of the intermediate obtained here, including the absence from its IR spectrum of carbonyl absorption, is not in accordance with structure (IV).



IV

So far as we are aware, this is the second example of the isolation of a stable pyranoid intermediate on reaction of pyrylium salts with primary aliphatic amines [8]. The enhanced stability of (III) appears to be due to the stabilizing effect of the pentafluorophenyl group on the reaction center at the sp^3-hybridized carbon of the pyran ring (cf. [9]). On heating (III) in alcohol with the addition of 20% perchloric acid, the pyridinium salt (IIb) was obtained.

An alternative route to pentafluorophenylpyridinium salts is by methylation of the appropriate pyridines with dimethyl sulfate [10], but this failed to give the expected compounds (II). On heating 2-pentafluorophenyl-4,6-diphenylpyridine [6] with an excess of dimethyl sulfate at 100°C, the starting material was recovered unchanged. Pyridines (Vc, d) likewise failed to undergo alkylation under these conditions.



I, V c $R^1=CH_3$, $R^2=H$; d $R^1-R^2=(CH_2)_4$

EXPERIMENTAL

IR spectra were obtained on a UR-20 in KBr disks, and UV spectra on a UV-VIS in dichloromethane. PMR and ^{19}F NMR spectra were obtained on Varian A56/60A (10 and 56.4 MHz), Bruker AC-200, and Bruker WP-

200SY (200 and 188 MHz) instruments. The internal standards used were HMDS, $CHCl_3$, and C_6F_6, respectively, chemical shifts being given on the δ scale for PMR, and in ppm from C_6F_6 for ^{19}F NMR. The molecular mass was obtained on a Finnigan MAT 8200 mass spectrometer.

The required pyrylium perchlorates were obtained by literature methods [6, 11], and the principal characteristics and yields of (IIa-d) are shown in Table 1.

The elemental analyses for C, H, Cl, F, and N were in agreement with the calculated values.

1-Methyl-2,4-diphenyl-6-pentafluorophenylpyridinium Perchlorate (IIa). To a suspension of 0.24 g (0.5 mmole) of the pyrylium perchlorate (Ia) in 5 ml of alcohol was added 0.4 ml of 12% alcoholic methylamine (1 mmole), and the mixture stirred for 5 h at room temperature. The solvent was removed in a rotary evaporator, and the residue was triturated with ether, filtered off, air-dried, dissolved in dichloromethane, and chromatographed on a column of alumina (grade II activity), eluent dichloromethane.

1,2-Dimethyl-4-phenyl-6-pentafluorophenylpyridinium Perchlorate (IIc). This was obtained as for (IIa), from the pyrylium salt (Ic) in tert-butanol. The mixture was poured into 25 ml of water, and the solid which separated was filtered off, washed with ether, and dried in air.

1-Methyl-4-phenyl-2-pentafluorophenyl-5,6,7,8-tetrahydroquinolinium Perchlorate (IId). This was obtained from (Id), as in the preceding preparation.

2-Methylamino-4-phenyl-2,6-bis(pentafluorophenyl)-2H-pyran (III, $C_{24}H_{11}F_{10}NO$). This was obtained from 0.57 g (1 mmole) of the pyrylium perchlorate (Ib) and 1 ml of 10% alcoholic methylamine (2.5 mmoles), as for (IIc). Mp 157-158°C (from benzene). IR spectrum: 3200-3350 cm^{-1} (N—H). The PMR spectral data are given in the general section. ^{19}F NMR spectrum ($CDCl_3$): 0.05, 0.65, 9.04, 9.43, 20.16, 23.72 ppm, intensity ratio 2:2:1:1:2:2. M$^+$ 519. Yield 0.33 g (63%).

1-Methyl-4-phenyl-2,6-bis(pentafluorophenyl)pyridinium Perchlorate (Ib). A mixture of 0.13 g (0.25 mmole) of the 2H-pyran (III) and 0.11 ml of 20% $HClO_4$ (0.25 mmole) in 5 ml of alcohol was stirred for 2 h at 25°C. The mixture was cooled to room temperature, poured into 25 ml of ether, and the solid which separated was filtered off, washed with water and ether, and dried in air.

2-Methyl-4-phenyl-6-pentafluorophenylpyridine (Vc, $C_{18}H_{10}F_5N$). To a suspension of 0.22 g (0.5 mmole) of the pyrylium perchlorate (Ic) in 10 ml of alcohol was added 1.5 ml of 25% aqueous ammonia, and the mixture stirred for 10 min at 3-5°C. It was then poured onto 50 g of ice, and the solid which separated was filtered off and washed with hexane. Mp 126-127°C [sublimed at 100°C (2 mm)]. PMR spectrum ($CDCl_3$): 2.64 (3H, s, N—CH_3), 7.51 ppm (7H, m, C_6H_5, 3- and 5-H). ^{19}F NMR spectrum ($CDCl_3$): —0.36, 7.43, 19.30 ppm, intensity ratio 2:1:2. M$^+$ 335. Yield 0.13 g (60%).

4-Phenyl-2-pentafluorophenyl-5,6,7,8-tetrahydroquinoline (Vd, $C_{21}H_{14}F_5N$). To a suspension of 0.24 g (0.5 mmole) of the pyrylium perchlorate (Id) in 10 ml of tert-butanol was added 1.5 ml of 25% aqueous ammonia, and the mixture stirred for 5 h, poured into 50 ml of water, and the solid which separated was filtered off and washed with hexane. Mp 107-108°C (from 50% aqueous alcohol). PMR spectrum ($CDCl_3$): 1.54-2.07 (4H), 2.67 (2H), 3.07 (8H, 5-H—8-H), 7.17 (1H, s, 3-H), 7.20-7.57 ppm (5H, C_6H_5). ^{19}F NMR spectrum ($CDCl_3$): —0.3, 6.9, 19.3 ppm, intensity ratio 2:1:2. M$^+$ 375. Yield 0.11 g (59%).

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