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INTERACTION OF 4,5,7-TRIMETHYL-4,5,6,7-TETRAHYDROPYRROLO[3,2-*c*]PYRIDINES WITH ACETIC AND TRIFLUOROACETIC ANHYDRIDES

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The reactions of NH- and N-vinyl-4,5,7-trimethyl-4,5,6,7-tetrahydropyrrolo-[3,2-c]pyridines and their 2-substituted derivatives with acetic and trifluoroacetic anhydrides have been studied. Trifluoroacetylation of tetrahydropyrrolo-[3,2-c]pyridines occurs at the α-position of the pyrrole ring, whereas cleavage of the tetrahydropyridine ring with formation of 3-vinylpyrroles occurs with acetic anhydride. 2-Acetyl-4,5,7-trimethyl-1-vinyl-4,5,6,7-tetrahydropyrrolo[3,2-c]pyridine was synthesized by the Vilsmeier–Haack reaction.

Keywords: vinylpyrroles, tetrahydropyrrolopyridines, acetylation, cleavage of tetrahydropyridine, trifluoroacetylation.

Acetylation and trifluoroacetylation of pyrrole and its derivatives at the α-position of the pyrrole is carried out with the corresponding anhydrides and acid chlorides. The acetylation reaction almost always requires heating and the presence of Lewis acid type catalyst [1]. Trifluoroacetylation is more selective and occurs at room temperature or below. In some cases pyridine and other tertiary amines are used as a catalyst [2].

In attempting the functionalization of the pyrrole ring of 4,5,7-trimethyl-4,5,6,7-tetrahydropyrrolo-[3,2-*c*]pyridine (**1**) and its N-vinyl-substituted derivative **3** for biological screening, we studied their interaction with acetic and trifluoroacetic anhydrides. It was established that at 70°C in acetic anhydride cleavage of the tetrahydropyridine ring occurred with formation of 2-[(N-methylacetamido)propyl]-3-vinylpyrrole (**6**) and not the expected acetylation of the pyrrole unit in pyrrolopyridine **1**.

The N-vinylpyrrole **3** underwent analogous cleavage at 70°C. The reaction mixture contained 80% of 1,3-divinylpyrrole **8** according to chromato-mass spectrometry, but this compound could not be isolated pure from the reaction mixture. It is very labile and partially polymerized during chromatographic separation.

Three degradations of the piperidine ring are described in the literature – the Hofmann reaction (cleavage of the quaternary piperidinium bases), the von Braun reaction (cleavage of N-benzoylpiperidines under the influence of PX_5, where X = Cl or Br), and cleavage under the influence of cyanogen bromide. As a rule these reactions occur under relatively vigorous conditions. We did not find any information on the cleavage of tetrahydropyridines under the influence of acetic anhydride.

Tetrahydropyrrolo[3,2-*c*]pyridines substituted at position 2 (**2, 4, 5**) also underwent cleavage of the tetrahydropyridine ring under the influence of acetic anhydride. Cleavage of 2-trifluoroacetyl-substituted **4** was particularly difficult: at 70 and 90°C the yield of 3-vinylpyrrole **9** did not exceed 10%. The basic product of the reaction was a mixture of the isomeric acetates **11A'** and **11B** (isolated in 48% yield).

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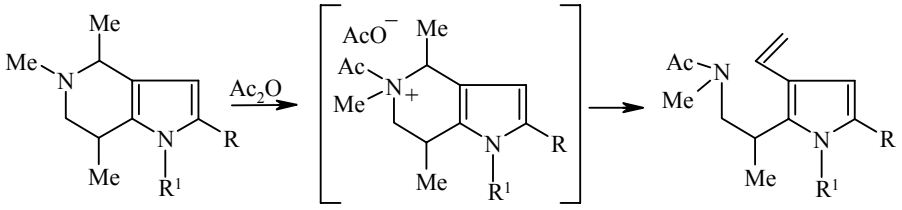
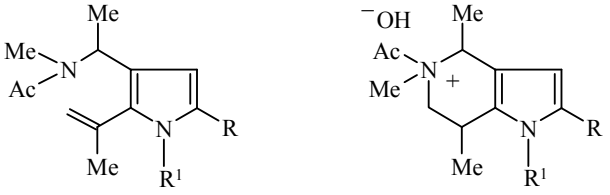


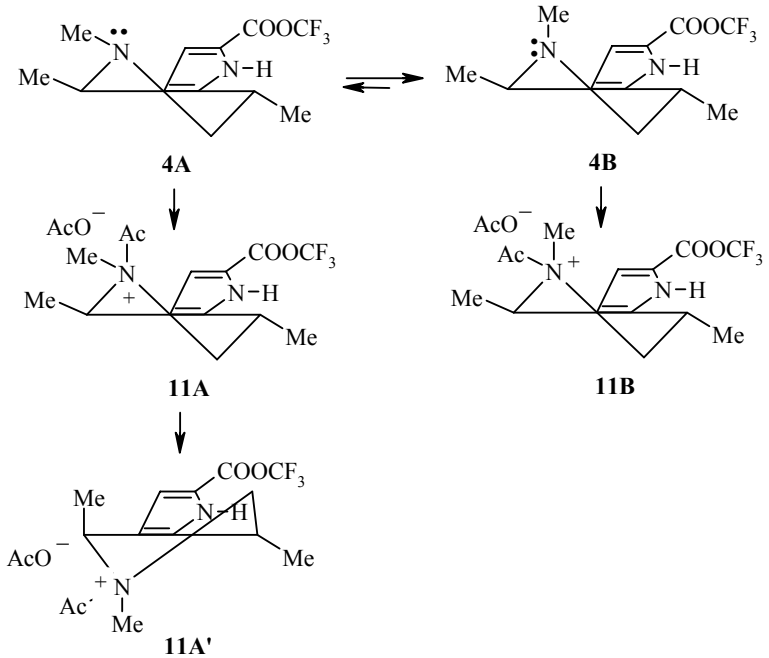
1–5 **A** **6–10**



B **12**, **13**

1 R = R^1 = H; **2** R = CHO, R^1 = H; **3** R = H, R^1 = CH=CH_2; **4** R = CF_3CO, R^1 = H; **5** R = CH=N–OH, R^1 = CH=CH_2; **6** R = R^1 = H; **7** R = CHO, R^1 = H; **8** R = H, R^1 = CH=CH_2; **9** R = CF_3CO, R^1 = H; **10** R = CN, R^1 = CH=CH_2; **12** R = CF_3CO, R^1 = H; **13** R = CN, R^1 = CH=CH_2

Their formation is explained by the existence of compound **4** as two isomers **4A** and **4B** with respect to the positions of N–Me and the unshared pair of the nitrogen atom as a result of inversion of the piperidine nitrogen atom in the tetrahydropyrrolopyridine **4**. Acetylation of this mixture leads to the isomeric acetates **11A** and **11B**. In **11A** with an axial acetyl group inversion of the tetrahydropyridine ring occurs and the compound is fixed in configuration **11A'** with the pseudo-*trans*-diaxial position of groups 4-Me and 7-Me. An analogous inversion was observed on benzoylation of 2*e*,5*e*-dimethylpiperidin-4*e*-ol [3]. The ^{1}H NMR spectrum of this mixture contains four singlets for AcO^- in the 2.01-2.06 ppm region, two singlets for N–Me (2.93 and 2.97 ppm), and also four doublets for the protons of the 4-Me (1.22 and 1.26 ppm) and 7-Me groups (0.92 and



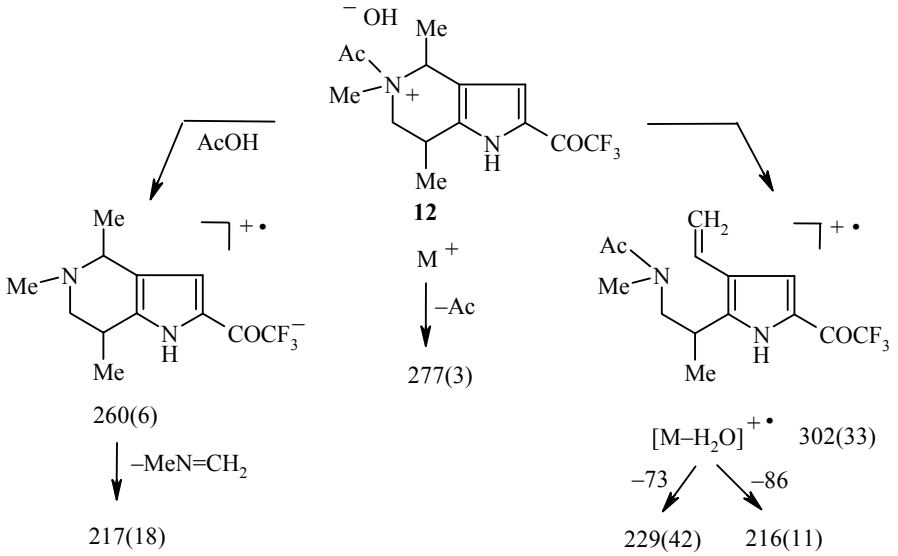
4A **4B**

11A **11B**

11A'

1.15 ppm). An isomeric mixture (1:1.5) of N-acetyl-N-methyltetrahydropyrrolo[3,2-*c*]pyridinium hydroxides **12** was isolated from chromatography of the acetates **11A'** and **11B** on aluminium oxide. The mixture was analysed by IR, ^{1}H NMR, and mass spectrometry. The IR spectrum of the mixture contained an intense band of the OH stretch at 3100-3500 cm^{-1} which overlapped the NH stretching vibration at 3300 cm^{-1}. In the ^{1}H NMR spectrum (Table 1) two signals were observed for each proton, except for NH and H-3, in comparison with the pyrrolopyridine **4**. The signals of all the protons underwent a low field shift, particularly noticeable for H-4 (by 1.68 ppm) and H-6 (by 1.82 ppm). In the major isomer, with $J_{6,7\text{-}trans}$ = 9.5 Hz, 7-Me is pseudoequatorial, whereas in the minor isomer, with $J_{6,7\text{-}trans}$ = 5.75 Hz, this methyl group is pseudoaxial.

The molecular ion is missing from the mass spectrum of compound **12**. The peak for the ion $[M - H_2O]^+$ with *m/z* 302* has an intensity of 33% which indicates that the Hofmann degradation occurs under mass spectrometric conditions. This ion then loses $[MeNHAc]^+$, to give an ion with *m/z* 73, and $CH_2=N^+MeAc$, to give an ion with *m/z* 86. Elimination of AcOH, and the radical Ac· from the ion $[M]^+$, may serve to confirm the ammonium structure of compound **12**.



Reaction of oxime **5** with acetic anhydride at 30°C was accompanied by dehydration of the oxime group to a nitrile group. As in the case of compound **4**, the ammonium base **13** was isolated by chromatography as the basic product of the reaction in a yield of 41%. According to its spectroscopic characteristics it was analogous to compound **12** and consisted of a mixture of isomers with respect to the positions of the 4-Me and 7-Me groups (ratio 1:1.4). The product of cleavage of the tetrahydropyridine unit – the 1,3-divinylpyrrole **10** – was formed in not more than 10% yield (^{1}H NMR) under these conditions and was not isolated pure.

The structures of the 3-vinylpyrroles **6**, **7**, and **9** were confirmed from a range of spectroscopic data. In the IR spectra the C=O stretching band of the amide was observed in the 1625-1630 cm^{-1} region and the stretching band of the pyrrole NH was observed in the 3280-3320 cm^{-1} range. The spectra of compounds **7** and **9** were characterized by the presence of the stretching vibration of the CO substituent in position 2 at 1650 and 1660 cm^{-1} respectively.

Signals for all the protons in the molecules were observed in the ^{1}H NMR spectra (Table 2). Spin-spin coupling constants for protons H-4 and H-5 with the NH proton characteristic for pyrrole [4] were observed for compounds **6**, **7**, and **9**. Signals of the vinyl group at $C_{(3)}$ were observed as three doublet of doublets with characteristic vicinal (8.9-11.0 and 17.4-17.7 Hz) and geminal (1.2-2.1 Hz) coupling constants.

* Here and below the values of *m/z* are given for the peaks

TABLE 1. [1]H NMR Spectra of the Tetrahydropyrrolopyridines **4**, **14**, **16**, and **17** and the Quaternary Bases **12** and **13**

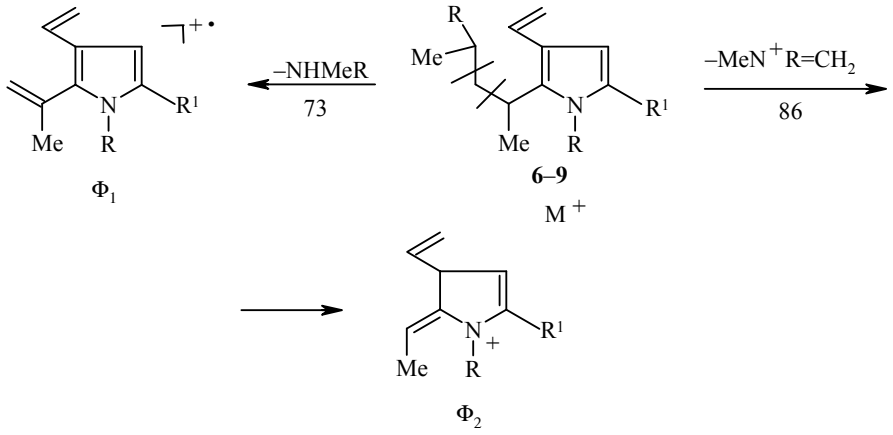
Compound	Chemical shifts, δ, ppm (SSCC, *J*, Hz)									
	NR[1]	H-3	H-4	Ha-6	He-6	4-Me	7-Me	H-7	5-Me	other protons
4	9.37 (br. s)	6.92 (q)	3.18 (q, *J* = 6.4)	2.24 (dd, *J* = 11.6, *J* = 10.4)	3.01 (dd, *J* = 11.6, *J* = 5.5)	1.37 (d, *J* = 6.4)	1.24 (d, *J* = 6.7)	3.12 (m)	2.42 (s)	
12										
major	10.6 (br. s)	7.18 (m)	4.96 (q, *J* = 6.4)	4.06 (dd, *J* = 13.7, *J* = 9.5)	3.32 (dd, *J* = 13.7, *J* = 7.3)	1.54 (d, *J* = 6.4)	1.34 (d, *J* = 7.0)	3.45-3.7 (m)	2.95 (s)	2.02 (s, Ac)
minor	10.6 (br. s)	7.18 (m)	4.92 (q, *J* = 6.4)	3.90 (dd, *J* = 13.7, *J* = 5.7)	3.29 (dd, *J* = 13.7, *J* = 7.0)	1.34 (d, *J* = 6.4)	1.33 (d, *J* = 7.0)	3.45-3.70 (m)	2.98 (s)	2.06 (s, Ac)
13										
major	5.37 (dd, *J* = 7.3, *J* = 1.5); 5.61 (dd, *J* = 15.6, *J* = 1.5); 6.95 (dd, *J* = 15.6, *J* = 7.3)	6.92 (s)	5.99 (q, *J* = 6.4)	3.15-3.95 (m)	1.48 (d, *J* = 6.4)	1.35 (d, *J* = 7.3)		3.15-3.95 (m)	2.76 (s)	2.03 (s, Ac)
minor	5.41 (dd, *J* = 7.3, *J* = 1.5); 5.62 (dd, *J* = 15.6, *J* = 1.5); 7.06 (dd, *J* = 15.6, *J* = 7.3)	6.91 (s)	5.95 (q, *J* = 6.4)	3.15-395 (m)	1.49 (d, *J* = 6.4)	1.31 (d, *J* = 8.3)		3.15-3.95 (m)	2.83 (s)	2.01 (s, Ac)
14	9.00 (br. s)	6.63 (d, *J* = 2.4)	3.17 (q, *J* = 6.4)	2.23 (dd, *J* = 11.0, *J* = 9.8)	2.9 (dd, *J* = 11.0, *J* = 5.2)	1.37 (d, *J* = 6.4)	1.19 (d, *J* = 6.4)	3.05-3.25 (m)	2.43 (s)	2.37 (s, Ac)
16	7.33 (dd, *J* = 15.6, *J* = 8.2); 5.30 (dd, *J* = 8.2, *J* = 0.6); 5.26 (dd, *J* = 15.6, *J* = 0.6)	7.00 (q, *J* = 1.8)	3.29 (q, *J* = 6.4)	2.24 (dd, *J* = 11.9, *J* = 8.2)	3.08 (dd, *J* = 11.9, *J* = 5.5)	1.34(d, *J* = 6.7)	1.21(d, *J* = 6.7)	3.02	2.43 (s)	
17	7.38 (dd, *J* = 15.9, *J* = 9.0); 5.16 (dd, *J* = 15.9, *J* = 0.9); 5.23 (dd, *J* = 9.0, *J* = 0.9)	7.03 (q, *J* = 1.8)	3.51 (s)	2.70-2.90	—	—		2.70-2.90		1.18 (t, *J* = 7.1, CH_3); 2.63 (q, *J* = 7.1, CH_2)

TABLE 2. ^{1}H NMR Spectra of the 3-Vinylpyrroles **6**, **7**, **9**, and **10**

Compound	Chemical shifts, δ, ppm. (SSCC, *J*, Hz)								
	NH, br. s	3-CH=CH$_2$	H-4	H-5	N–CH$_3$, s	N–Ac, s	N–CH$_2$, m	CH–CH$_3$	2-R
6	9.04	6.63 (dd, *J* = 17.4, *J* = 8.9); 5.32 (dd, *J* = 17.4, *J* = 2.1); 4.92 (dd, *J* = 8.9, *J* = 2.1)	6.1 (t, *J* = 2.4, *J* = 2.4)	6.61 (t, *J* = 2.4, *J* = 2.4)	2.78	2.00	3.76	3.40 (m, CH); 1.21 (d, *J* = 6.7, CH$_3$)	—
7	10.03	6.57 (dd, *J* = 17.7, *J* = 11.3); 5.48 (dd, *J* = 17.7, *J* = 1.5); 5.08 (dd, *J* = 11.3, *J* = 1.5)	7.05 (d, *J* = 2.1)	—	2.75	2.02	3.70	3.30 (m, CH); 1.28 (d, *J* = 6.4, CH$_3$)	9.45 (s, CHO)
9	10.48	6.56 (dd, *J* = 17.4, *J* = 11.0); 5.54 (dd, *J* = 17.0, *J* = 1.2); 5.15 (dd, *J* = 11.0, *J* = 1.2)	7.25 (m)	—	2.84	2.04	3.82	3.52 (m, CH); 1.29 (d, *J* = 6.7, CH$_3$)	—
10	—*	6.2 (dd, *J* = 17.4, *J* = 10.2); 5.60 (dd, *J* = 17.4, *J* = 1.5); 5.20 (dd, *J* = 10.2, *J* = 1.5)	6.89 (s)	—	2.80	2.05	—*	CH* 1.29 (d, CH$_3$)	—

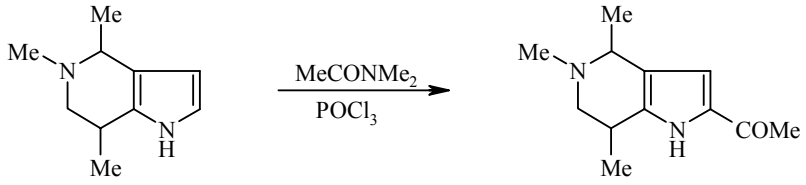
* The signals of the remaining protons overlap with those of the ammonium base **13**.

The mass spectra of the vinylpyrroles **6-9** were characterized by the presence of weak molecular ion peaks (1-8%), the ions $[M]^+$ corresponding to the molecular formula. The basic direction of splitting is characterized by α- and β-fission in the amidoisopropyl radical at position 2 which leads to the formation of fragments Φ_1 and Φ_2.



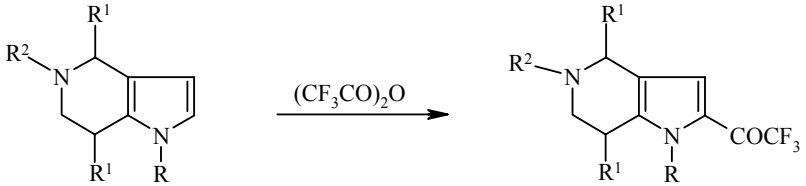
We suggest that conversion of the tetrahydropyrrolopyridines **1-5** into 3-vinylpyrroles occurs via a Hofmann reaction and begins with formation of N-acyl salts of type **A**. Subsequent attack of the acetoxy anion at the 4-Me group leads to rupture of the $C_{(4)}$–N bond and formation of the vinylpyrroles. The absence from the reaction mixture of the alternative 2-vinylpyrroles **B** is evidently explained by steric hindrance to attack of the acetoxy anion on the pseudo-axial proton H-7 (a second β-proton relative to the ammonium nitrogen).

The 2-acetyl-substituted pyrrolopyridine **14** was obtained from compound **1** in 75% yield by the Vilsmeier–Haack reaction.



1 **14**

In contrast to acetic anhydride, reaction of trifluoroacetic anhydride with the tetrahydropyrrolopyridines **1**, **3**, and **15** gave trifluoroacetylation at the α-position of the pyrrole ring. The corresponding 2-trifluoroacetyl substituted pyrrolo[3,2-*c*]pyridines **4**, **6**, and **17** were obtained in 60-70% yields.



1, 3, 15 **4, 16, 17**

1, **4** R = H; **3**, **15**–**17** R = CH=CH_2; **1**, **3**, **4**, **16** $R^1 = R^2$ = Me; **15**, **17** R^1 = H, R^2 = Et

TABLE 3. Characteristics of the Compounds Synthesized

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		C	H	N		
4	$C_{12}H_{15}F_3N_2O$	55.43 / 55.39	5.75 / 5.77	10.34 / 10.77	132-133	52
5	$C_{13}H_{23}N_3O$	70.21 / 69.95	7.92 / 8.15	17.83 / 18.02	140-142	91
6	$C_{12}H_{18}N_2O$	69.43 / 69.87	8.75 / 8.78	13.44 / 13.58	Oil	7
7	$C_{13}H_{18}N_2O_2$	66.53 / 66.67	7.75 / 7.69	12.01 / 11.96	Oil	18
9	$C_{12}H_{15}F_3N_2O$	55.01 / 55.39	5.60 / 5.77	10.43 / 10.77	Oil	9
12	$C_{14}H_{19}F_3N_2O_3$	53.43 / 52.50	5.89 / 5.98	8.44 / 8.75	Amorphous	48
13	$C_{15}H_{22}N_3O_2$	65.15 / 65.45	7.81 / 7.64	15.11 / 15.27	Oil	41
14	$C_{12}H_{18}N_2O$	69.35 / 69.9	8.51 / 8.70	13.68 / 13.6	122-124	42
16	$C_{14}H_{17}F_3N_2O$	58.86 / 58.74	6.10 / 5.94	9.52 / 9.79	Oil	55
17	$C_{13}H_{15}F_3N_2O$	57.10 / 57.35	5.75 / 5.51	10.35 / 10.29	Oil	65

Products of degradation of the tetrahydropyridine ring were not isolated on trifluoroacetylation which is explained by the low basicity of the trifluoroacetoxy anion.

So we have observed a new reaction of the cleavage of the tetrahydropyridine ring. It is of interest to determine whether this reaction is characteristic of tetrahydropyrrolo[3,2-*c*]pyridines alone or whether it can occur in other cases of heterocyclic compounds containing the tetrahydropyridine fragment.

EXPERIMENTAL

IR spectra were recorded on a UR-20 spectrometer in KBr disks (for crystalline compounds) or as films (for liquids). Mass spectra were recorded with a Kratos MS-2 SFR instrument with direct injection of the sample into the ion source with an ionizing current of 70 eV. Chromato-mass spectra were obtained with an HPMS 5988 instrument. ^{1}H NMR spectra of ~3% $CDCl_3$ solutions of the synthesized compounds were recorded at 20°C on a Bruker WM-200 (200 MHz) spectrometer. Chemical shifts were measured relative to TMS as internal standard. Alufol and Silufol UV-254 plates were used for thin-layer chromatography (development with iodine vapor). Brockman activity II Al_2O_3 was used for column chromatography. Physicochemical characteristics, yields, and elemental analyses are sited in Table 3.

The syntheses of compounds **1-3** are described in [5,6], of compound **5** in [7], and of compound **15** in [8].

4,5,7-Trimethyl-2-trifluoroacetyl-4,5,6,7-tetrahydropyrrolo[3,2-*c*]pyridine [4]. Pyridine (1.16 g, 14.6 mmol) was added to a solution of pyrrolopyridine **1** (0.5 g, 3 mmol) in methylene chloride, then trifluoroacetic anhydride (2.56 g, 12 mmol) in methylene chloride (10 ml) was added dropwise. The mixture was boiled for 2 h (controlled by TLC), made alkaline to pH 9-10 with aqueous soda solution, and extracted with methylene chloride. The extract was dried over $MgSO_4$, the solvent was evaporated, and the residue was recrystallized from a hexane–ethyl acetate mixture to give yellow crystals of compound **4** (0.4 g), R_f 0.4 (Alufol, ethyl acetate). IR spectrum, ν, cm^{-1} 1650 (CO). Mass spectrum, *m/z* (I_{rel}, %): 260 $[M]^+$(2), 245 (100), 217 (18), 202 (16).

2-[(N-Acetamido-N-methyl)isopropyl]-3-vinylpyrrole (6). A solution of pyrrolopyridine **1** (0.5 g, 3 mmol) in acetic anhydride (13 ml) was heated for 30 min at 70°C (monitored by TLC). The acetic anhydride was distilled off, the residue was chromatographed with ethyl acetate as eluent to give pyrrole **6** (45 mg) as a clear crystallizing oil which become red on standing, R_f 0.2 (Alufol, 1:2 hexane–ethyl acetate). IR spectrum, ν, cm^{-1}: 1625 (CO), 3280 (NH). Mass spectrum, *m/z* (I_{rel}, %): 206 $[M]^+$ (5), 120 (23), 133 (13).

2[(N-Acetamido-N-methyl)isopropyl]-5-formyl-3-vinylpyrrole (7) was obtained analogously to compound **6** from pyrrolopyridine **2** (3 mmol) in acetic anhydride (13 ml). Vinylpyrrole **7**, is a yellow oil, R_f 0.2 (Alufol, ethyl acetate). IR spectrum, ν, cm^{-1}: 1630 (COMe), 1650 (CHO), 3305 (NH). Mass spectrum, *m/z* (I_{rel}, %): 234 $[M]^+$ (8), 148 (12), 161 (18).

2[(N-Acetamido-N-methyl)isopropyl]-1,3-divinylpyrrole (8). A solution of pyrrolopyridine **3** (0.2 g, 1 mmol) in acetic anhydride (2 ml) was kept for 2 weeks at 30°C (monitored by TLC). The solution was basified to pH 9 with 50% aqueous soda and extracted with ether. The extract was dried over $MgSO_4$. The extract (0.172 g, 75%) after removal of the ether in vacuum, contained 80% of compound **8** according to chromato-mass spectrometry. After chromatography of this residue on aluminum oxide with 1:10 ethyl acetate–hexane as eluent , 60 mg (26%) of compound **8** was isolated, loaded with polymers, as a yellow oil, R_f 0.52 (Alufol, 4:1 hexane–ethyl acetate). IR spectrum, ν, cm^{-1}: 1625 (N–CH=CH_2). Mass spectrum, *m/z* (I_{rel}, %): 232 $[M]^+$ (18), 159 (25), 146 (100), 132 (10), 131 (9), 130 (7), 118 (5), 117 (7), 91 (5), 86 (4), 77 (5), 56 (3), 44 (30), 43 (25).

2-[(N-Acetamido-N-methyl)isopropyl]-5-trifluoroacetyl-3-vinylpyrrole (9) and 5-Acetyl-4,5,7-trimethyl-2-trifluoroacetyl-4,5,6,7-tetrahydropyrrolo[3,2-*c*]pyridinium Hydroxide (12). A solution of 2-trifluoroacetylpyrrolopyridine **4** (0.22 g, 0.85 mmol) in acetic anhydride (8 ml) was heated for 5 h at 90°C (monitored by TLC). The acetic anhydride was evaporated in vacuum and the residue was chromatographed on a silica gel column. A 1:2 mixture of hexane and ethyl acetate washed out 3-vinylpyrrole **9** (30 mg, 9%), a yellow oil with R_f 0.5 (Silufol, ethyl acetate). IR spectrum, ν, cm^{-1}: 1630 (COMe), 1660 ($COCF_3$), 3320 (NH). Mass spectrum, *m/z* (I_{rel}, %): 260 $[M]^+$ (8), 229 (23), 216 (100).

Then a 1:1 mixture of hexane–ethyl acetate washed out a mixture (0.15 g, 48%) of N-acetyl-N-methyltetrahydropyrrolopyridinium acetates **11A**[1] and **11B**. This mixture was chromatographed for a second time on aluminum oxide, activity IV, with 1:1 hexane–ethyl acetate as eluent to give the pyrrolopyridinium hydroxide **12** (0.10 g) as a yellow amorphous substance, R_f 0.11 (Alufol, 1:1 hexane–ethyl acetate). IR spectrum, ν, cm^{-1}: 1680 ($COCF_3$), 3100-3500 (OH, NH). Mass spectrum, *m/z* (I_{rel}, %): 302 [M^+ - H_2O] (33), 277 (3), 260 (6), 235 (9), 233 (9), 232 (9), 217 (18), 216 (11), 214 (8), 202 (6), 160 (8), 148 (8), 146 (8), 119 (10), 118 (9), 117 (6), 86 (43), 44 (100), 43 (13).

2-Cyano-4,5,7-trimethyl-1-vinyl-4,5,6,7-tetrahydropyrrolo[3,2-*c*]pyridinium Hydroxide (13). A solution of oxime **5** (0.15 g, 0.6 mmol) in acetic anhydride (2 ml) was kept at 30°C for 2 weeks monitored by TLC). The acetic anhydride was removed in vacuum. Water (10 ml) was added to the residue which was then basified to pH 8 with a saturated solution of Na_2CO_3. It was then extracted with ether (4 × 50 ml) and the extract was dried with $MgSO_4$. The residue after evaporation of the ether was chromatographed on a column (1 × 30 cm) of Al_2O_3 (activity IV) with 1:4 ethyl acetate–hexane as eluent to give compound **13** (70 mg, 41%) as a colorless oil, R_f 0.23 (Alufol, ethyl acetate). IR spectrum, ν, cm^{-1}: 1632 (N–CH=CH_2), 2230 (CN), 3100-3500 (OH). Mass spectrum, *m/z* (I_{rel}, %): 257 $[M]^+$ (2),187 (2), 184 (14), 171 (10), 157 (10), 156 (8), 142 (8), 86 (42), 44 (100), 43 (36).

2-Acetyl-4,5,7-trimethyl-4,5,6,7-tetrahydropyrrolo[3,2-*c*]pyridine (14). Phosphorus oxychloride (0.92 g, 6 mmol) was added dropwise to N,N-dimethylacetamide (DMA) (1.66 g, 1.8 mmol) cooled to -5°C, and the mixture was stirred for 40 min at 20°C. It was cooled to 10°C and a solution of pyrrolopyridine **1** (0.5 g, 3 mmol) in DMA (4 ml) was added dropwise. The reaction mixture was stirred for 7 h at 40°C (monitored by TLC). Ice water (20 ml) was added and the mixture was basified with 10% aqueous sodium hydroxide. The mixture was extracted with ether (3 × 100 ml) and the extract was dried over $MgSO_4$. The residue (0.52 g) after removal of ether and DMA was recrystallized to give compound **14** (0.26 g, 42%) as rosy crystals, R_f 0.6

(Silufol, 25% NH_3–isopropanol, 1:10). IR spectrum, ν, cm^{-1}: 1650 (COMe). Mass spectrum, *m/z* (I_{rel}, %): 206 $[M]^+$ (5), 191 (100), 175 (10), 163 (26), 148 (33), 133(4), 118 (3), 91 (3), 43 (6).

4,5,7-Trimethyl-2-trifluoroacetyl-1-vinyl-4,5,6,7-pyrrolo[3,2-*c*]pyridine (16). Trifluoroacetic anhydride (0.66 g, 3.2 mmol) in methylene chloride (2 ml) was added dropwise at -5°C to a solution of 1-vinylpyrrole **3** (0.15 g, 0.9 mmol) and pyridine (0.07 g, 0.9 mmol) in methylene chloride (5 ml). The reaction mixture was kept at 30°C until the reaction was complete (monitored by TLC). The mixture was cooled, basified to pH 8 with 10% soda solution, extracted with ether (3 × 50 ml), and the extract was dried over $MgSO_4$. The residue after evaporation of the solvent was chromatographed on a column (1.2 × 17 cm) of Al_2O_3 with 2:1 ethyl acetate–hexane to give compound **16** (0.12 g, 55%) as a yellow oil, R_f 0.34 (Silufol, ethanol). IR spectrum, ν, cm^{-1}: 1663 ($COCF_3$). Mass spectrum, *m/z* (I_{rel}, %): 286 $[M]^+$ (0.5), 271 (100), 255 (15), 243 (8), 228 (23), 174 (7), 132 (5), 131 (9), 42 (7).

5-Ethyl-2-trifluoroacetyl-1-vinyl-4,5,6,7-tetrahydropyrrolo[3,2-*c*]pyridine (17). Trifluoroacetic anhydride (7.4 g, 35 mmol) was added to a solution of 1-vinylpyrrole **15** (0.62 g, 3.5 mmol) in absolute toluene (10 ml) and the mixture was kept for 5 h at 20°C (monitored by TLC). The toluene and trifluoroacetic anhydride were distilled off in vacuum. The residue was treated with a saturated solution of Na_2CO_3, extracted with ether (3 × 100ml), and the extract was dried over $MgSO_4$. The residue after evaporation of the ether was chromatographed on a column (2 × 40 cm) of Al_2O_3 with 1:5 ethyl acetate–hexane as eluent to give compound **17** (0.4 g, 65%) as a light-yellow oil, R_f 0.8 (Alufol, 1:1 hexane–ethyl acetate). IR spectrum, ν, cm^{-1}: 1650 ($COCF_3$). Mass spectrum, *m/z* (I_{rel}, %): 272 $[M]^+$ (40), 270 (26), 257 (11), 215 (100), 146 (14), 118 (14).

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