Synthesis of 5-alkyl-4-polyfluoroacylpyrrole-2,3(1*H*)-diones

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Diacylation of fluoroalkyl-containing β-aminovinyl ketones with oxalyl chloride afforded 5-alkyl-4-polyfluoroacylpyrrole-2,3(1*H*)-diones.

Key words: pyrrole-2,3(1*H*)-diones, fluoroalkyl-containing β-aminovinyl ketones, oxalyl chloride.

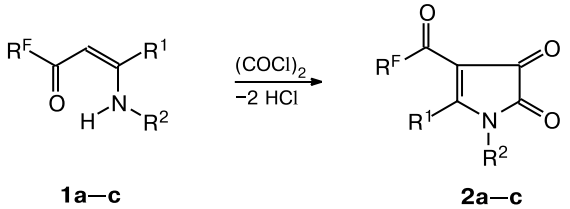
Substituted pyrrole-2,3(1*H*)-diones are widely used in organic synthesis, especially for the preparation of various N-containing heterocyclic compounds.[1—4] The unique reactivities of pyrrolediones and the biological activities of their derivatives motivate one to synthesize new representatives of this class.

The chemical properties of pyrrolediones significantly depend on the nature of substituents in the heterocycle, which vary broadly. However, as far as we know, pyrrolediones containing polyfluoroacyl substituents were not reported. The goal of the present study was to obtain such compounds.

The main preparative method for construction of the pyrrole-2,3-dione fragment is diacylation of β-aminovinyl ketones with oxalyl chloride. Fluoroalkyl-containing β-aminovinyl ketones **1a—c** were used as the starting compounds.

It was found that compounds **1a—c** react with oxalyl chloride under mild conditions to give 5-alkyl-4-polyfluoroacylpyrrole-2,3(1*H*)-diones **2a—c** (Scheme 1).

Scheme 1



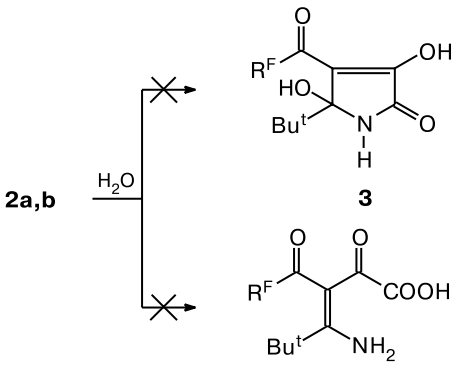
1a—c **2a—c**

	R^1	R^2	R^F
a	Bu^t	H	CF_3
b	Bu^t	H	$(CF_2)_4H$
c	Me	Ph	CF_3

Pyrrolediones **2a—c** are crystalline yellow substances; their spectroscopic characteristics agree with the literature data for known representatives of this class.[1—4]

Pyrrolediones containing electron-withdrawing substituents typically react with nucleophilic reagents. According to previous data,[3—5] the reactions of pyrrole-2,3(1*H*)-diones **2a—c** with water could be expected to follow two pathways, namely, addition of the nucleophile to the C(5) atom of the ring or decyclization through cleavage of the N—C(2) bond, to give substituted dihydroxypyrrolones **3** or 4-aminoalk-3-enoic acid derivatives **4**, respectively. However, compounds **2a,b** did not react with water at room temperature even at a multiple excess of the reagent while keeping the reaction mixture in an acetone—water (2 : 1) system for 48 h (Scheme 2).

Scheme 2



A number of factors can be responsible for the chemical stability of pyrrolediones **2a,b** to water. First, they contain a bulky *tert*-butyl group in position 5 of the het-

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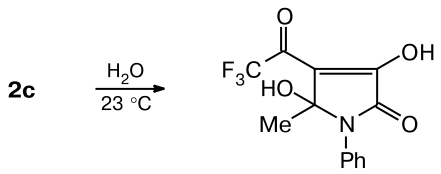
erocycle, which hinders the formation of a cyclic transition state postulated for reactions of 4-acylpyrrole-2,3(1*H*)-diones with nucleophiles.[5] Second, they are *N*-unsubstituted, which makes pyrrolediones less reactive in reactions with nucleophiles.[3]

Pyrroledione **2c**, in which the N atom bears a Ph substituent, easily adds water when kept in acetone—water (10 : 1) at room temperature for 15 min to give 3,5-dihydroxy-5-methyl-1-phenyl-4-trifluoroacetylpyrrol-2(1*H*,5*H*)-one (**5**) (Scheme 3).

Scheme 3



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The absence of a signal for the C(3)—OH enol group from the ^{1}H NMR spectrum of compound **5** and a comparatively low frequency of the stretching vibrations of the lactam CO group in its IR spectrum suggest the strong hydrogen bonding between these groups, which is characteristic of 3,5-dihydroxypyrrol-2-ones.[6]

Experimental

The syntheses of β-aminovinyl ketones **1a—c** were described earlier.[7—9] The course of the reaction was monitored by TLC on Silufol UV-254 plates with $CHCl_3$ as the eluent; spots were visualized with aqueous solutions of copper acetate and $KMnO_4$ and the iodine vapor. ^{1}H NMR spectra were recorded on a Bruker DRX-400 spectrometer (400 MHz) in $CDCl_3$ with Me_4Si as the internal standard. ^{19}F NMR spectra were recorded on a Tesla BS-587A spectrometer (75.3 MHz) in $CDCl_3$ with C_6F_6 as the internal standard. IR spectra were recorded on a Spectrum One FTIR-spectrometer (Perkin Elmer) in Nujol.

5-*tert*-Butyl-4-trifluoroacetylpyrrole-2,3(1*H*)-dione (2a). Oxalyl chloride (1.37 g, 10.8 mmol) was added to a solution of compound **1a** (2.00 g, 10.2 mmol) in 6 mL of anhydrous $CHCl_3$. The reaction mixture was kept at ~20 °C for 48 h and one third of the solvent was removed *in vacuo*. The precipitate that formed was filtered off and recrystallized from anhydrous $CHCl_3$ to give compound **2a** (1.90 g, 75%), m.p. 131—133 °C. Found (%): C, 48.12; H, 3.97; F, 22.61; N, 5.38. $C_{10}H_{10}F_3NO_3$. Calculated (%): C, 48.20; H, 4.05; F, 22.87; N, 5.62. IR, ν/cm^{-1}: 1786, 1729, 1650 (C=O), 3264 (N—H). ^{1}H NMR, δ: 1.50 (s, 9 H, Bu^t); 8.78 (br.s, 1 H, NH). ^{19}F NMR, δ: 85.9 (s, CF_3).

5-*tert*-Butyl-4-octafluorovalerylpyrrole-2,3(1*H*)-dione (2b) was synthesized analogously from compound **1b** (2.00 g, 6.1 mmol) and oxalyl chloride (0.82 g, 6.46 mmol). The yield of compound **2b** was 1.16 g (50%), m.p. 111—113 °C. Found (%): C, 40.86; H, 2.88; F, 40.19; N, 3.41. $C_{13}H_{11}F_8NO_3$. Calculated (%): C, 40.96; H, 2.91; F, 39.87; N, 3.67. IR, ν/cm^{-1}: 1774, 1729, 1697 (C=O), 3284 (N—H). ^{1}H NMR, δ: 1.46 (s, 9 H, Bu^t); 6.16 (tt, 1 H, $(CF_2)_4H$, $^2J_{H,F}$ = 52 Hz, $^3J_{H,F}$ = 5.5 Hz); 8.60 (br.s, 1 H, NH).

5-Methyl-1-phenyl-4-trifluoroacetylpyrrole-2,3(1*H*)-dione (2c). Oxalyl chloride (0.88 g, 6.93 mmol) was added to a solution of compound **1c** (1.50 g, 6.54 mmol) in 10 mL of anhydrous dichloroethane. The reaction mixture was refluxed for 50 min, concentrated by removing the solvent (3 mL), and cooled. The precipitate that formed was filtered off and recrystallized from chloroform—hexane (2 : 1) to give compound **2c** (0.37 g, 20%), m.p. 144—146 °C (decomp.). Found (%): C, 55.17; H, 2.92; F, 20.16; N, 4.97. $C_{13}H_8F_3NO_3$. Calculated (%): C, 55.14; H, 2.85; F, 20.12; N, 4.95. IR, ν/cm^{-1}: 1775, 1700, 1650 (C=O). ^{1}H NMR, δ: 2.69 (s, 3 H, Me); 7.23—7.25 (m, 2 H, H arom.); 7.56—7.60 (m, 3 H, H arom.).

3,5-Dihydroxy-5-methyl-1-phenyl-4-trifluoroacetylpyrrol-2(1*H*,5*H*)-one (5). Compound **2c** (0.1 g, 0.35 mmol) was dissolved in acetone (1 mL) and water (0.1 mL) was added. The reaction mixture was kept at ~20 °C for 15 min and the precipitate that formed was filtered off and recrystallized from acetone—water (10 : 1) to give compound **5** (0.09 g, 85%), m.p. 170—172 °C (decomp.). Found (%): C, 51.70; H, 3.43; F, 18.88; N, 4.34. $C_{13}H_{10}F_3NO_4$. Calculated (%): C, 51.84; H, 3.35; F, 18.92; N, 4.65. IR, ν/cm^{-1}: 1795, 1638 (C=O), 3128 (O—H). ^{1}H NMR, δ: 2.44 (s, 3 H, Me); 7.35—7.50 (m, 3 H, H arom.); 7.55—7.60 (m, 2 H, H arom.).

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