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DEOXOFLUORINATION OF PYRIDINYLOXOACETATES BY SULFUR TETRAFLUORIDE

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An effective scalable method for the synthesis of α-, β-, and γ-pyridinyloxoacetates has been developed, based on the interaction of the respective bromopyridines with diethyl oxalate in the presence of isopropylmagnesium chloride. This method enables the preparation of all isomeric pyridinyl oxoacetates with preparative yields in multigram quantities. The deoxofluorination process of isomeric pyridinyl oxoacetates with sulfur tetrafluoride was investigated. It was established that the deoxofluorination of α- and γ-pyridinyloxoacetates with sulfur tetrafluoride leads to the formation of a mixture of α-/γ-pyridinyldifluoroacetic acid esters and α-/γ-pyridinyltetrafluorinated ethers, which can be separated chromatographically. It was found that when using an excess of sulfur tetrafluoride and prolonged heating of the reaction mixture, the fluorination of α-/γ-pyridinyl oxoacetates results in the exclusive formation of α-/γ-pyridinyltetrafluorinated ethers. On the other hand, in the case of deoxofluorination of β-pyridinyloxoacetate with sulfur tetrafluoride, varying the temperature and the amount of fluorinating reagent allows for the selective formation of β-pyridinyldifluoroacetic acid ester or β-pyridinyltetrafluorinated ether. α-/β-/γ-Pyridinyltetrafluorinated ethers are new representatives of the small group of hetaryltetrafluorinated ethers and have potential applications in medicine and agrochemistry.

Keywords: α-, β-, γ-pyridinyloxoacetates, deoxofluorination, sulfur tetrafluoride, α-, β-, γ-pyridinyldifluoroacetic esters, α-, β-, γ-pyridinyltetrafluorinated ethers.

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Introduction

Nitrogen-containing heterocycles are important objects in medical chemistry and biochemistry, while pyridine moiety is one of the most common ones in FDA-approved drugs [1]. At the same time, introduction of (poly)fluoroalkyl group into heterocyclic systems is a standard tool in the design of potential pharmaceuticals as it provides increased lipophilicity [2] and metabolic stability of molecules [3,4]. Thus, 3-aminopyrazinone derivatives with a (difluoromethyl)pyridinyl fragment act as thrombin inhibitors [3], and modification of the drug *itraconazole* with this moiety leads to improvement of its pharmacokinetic parameters [4]. Some piperidines with mono- and difluoromethyl groups found their application as biologically active drugs with anticancer activity [5]. Therefore, the search for synthetic approaches towards polyfluorinated derivatives of pyridines is a relevant task.

Deoxofluorination of carbonyl compounds with sulfur fluorides is a quite general method of introducing a difluoromethylene motif into organic molecules, which can be attributed to the relative availability of fluorinating reagents and the obviousness of the reaction course.

Reagents can vary from relatively available such as sulfur tetrafluoride (SF_4) [6], diethylaminosulfur trifluoride (DAST) [7] to less available and more expensive ones as (2-methoxyethyl)aminosulfur trifluoride (Deoxo-Fluor) [3]. The DAST-oriented strategy is the most typical approach to the deoxofluorination of ketones, although it usually requires harsh reaction conditions: prolonged heating, often without solvent, with large excesses of the reagent

[7]. However, the SF_4-oriented approach generally provides a more efficient course of deoxofluorination and has a number of advantages, such as shorter reaction time, room temperature, high yields, and adequate reagent ratios [6].

Results and discussion

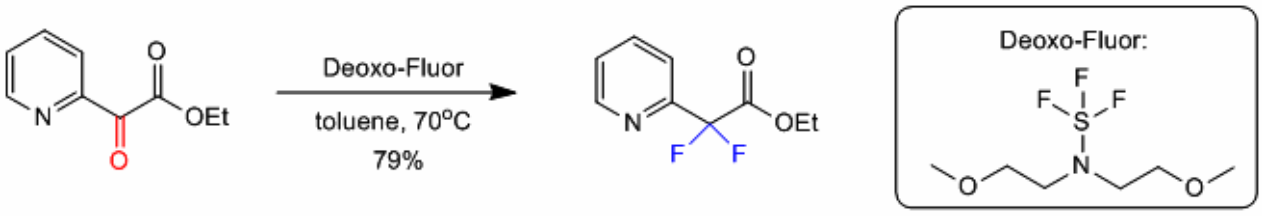
Pyridinyloxoacetates are attractive substrates to prepare side-chain fluorinated pyridinylacetate derivatives. However, they contain two carbonyl centers that can undergo deoxofluorination, so the direction of the reaction is not obvious. The only examples of deoxofluorination of a-substituted pyridinyloxoacetate known in the literature are reactions with DAST or Deoxo-Fluor [3]. The latter was carried out at prolonged heating in a toluene solution and led to the formation of exclusively a-pyridinyldifluoroacetic acid ester (Scheme 1). Nevertheless, there is no information on the deoxofluorination of α-pyridinyloxoacetate with sulfur tetrafluoride, other isomeric pyridinyloxoacetates were not involved in such transformations at all.

In this article, the results of the examination of the reaction of α-, β-, and γ-substituted pyridinyloxoacetates with sulfur tetrafluoride are given, and the correlation of the deoxofluorination course with the nature of the substrate and the substrate/reagent ratio is highlighted.

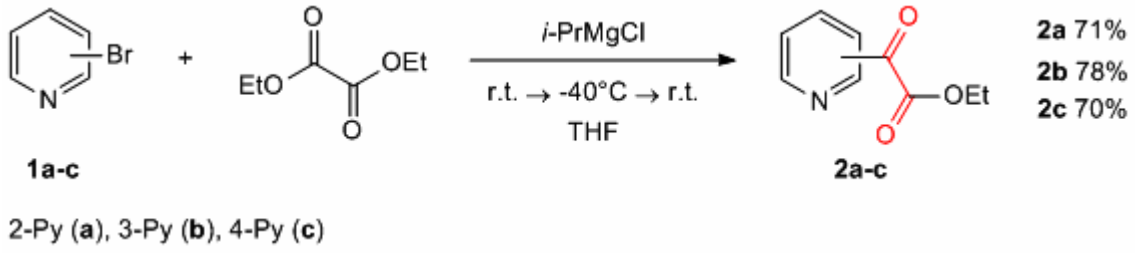
For the preparation of pyridinyloxoacetates **2a–c**, a general, efficient and easy-to-scale method was developed, based on the interaction of available bromopyridines **1a–c** with diethyl oxalate in the presence of isopropylmagnesium chloride. Thus, dropwise addition of *i*-PrMgCl to the solution of respective bromopyridine **1a–c** in THF at room temperature, followed by slow addition of diethyl oxalate at −40°C and subsequent stirring of the reaction mixture at room temperature for 24 hours, leads to the quantitative formation of pyridinyloxoacetates **2a–c**. *T*reatment of the reaction mixture with a saturated aqueous solution of NH_4Cl, extraction of the reaction products with ethyl acetate and their distillation *in vacuo* afforded analytically pure compounds **2a–c** with 70–78% yields in multigram quantities (Scheme 2).

It should be noted that oxoacetates **2a–c** were described in the literature earlier, but the methods of their synthesis differed significantly and were not preparative. Specifically, α-substituted oxoacetate **2a** was obtained as a side product after the acylation of 2-(trimethylstannyl)pyridine with diethyl oxalate with a 19% yield in an amount of 170 mg [8]. β-Substituted oxoacetate **2b** was synthesized from 3-lithiated pyridine, generated *in situ* by the reaction of β-bromopyridine with *n*-butyllithium, with a 15% yield in an amount of only 136 mg [9]. γ-Substituted oxoacetate **2c** was obtained by oxidation of 2-bromo-1-pyridin-2-yl-ethenone hydrobromide with selenium oxide in a 50% yield in an amount of up to 0.5 g [10]. Therefore, in contrast to the previously known synthetic approaches to pyridinyloxoacetates **2a–c**, our method of synthesis of these compounds has a general nature and allows to obtain the target products in preparative quantities with high yields and purity.

The synthesized ethyl pyridinyloxoacetates **2a–c** react with sulfur tetrafluoride at room temperature in the presence of a catalytic amount of hydrofluoric acid, generated in *situ* by adding the required amount of water directly to the reaction mixture. It was found



Scheme 1. Fluorination of α-pyridinyloxoacetate by Deoxo-Fluor [3]



Scheme 2. Synthesis of pyridinyl oxoacetates **2a–c** by the interaction of bromopyridines with diethyloxalate in the presence of isopropylmagnesium chloride

that the deoxofluorination of α- and γ-substituted ketoesters **2a,c** with sulfur tetrafluoride (2 equiv.) under these conditions occurs non-selectively and gives a mixture of products, namely, products of fluorination at keto function, pyridinyldifluoroacetates **3a,c**, and products of exhaustive fluorination at both keto- and ester groups, tetrafluorinated ethers **4a,c** (Scheme 3).

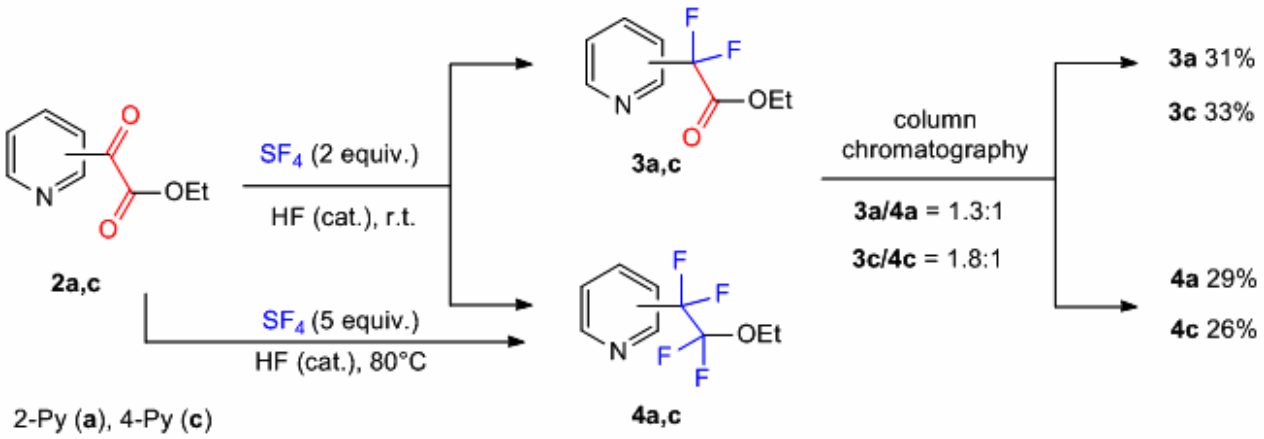
The ratio of deoxofluorination products, difluorides **3a,c** and tetrafluorides **4a,c** was 1.3:1 (**3a**:**4a**) and 1.8:1 (**3c**:**4c**), which can be easily determined from spectral monitoring of the reaction mixtures by ^{19}F NMR. Thus, chemical shifts of CF_2-groups of compounds **3a,c** are located at approximately −105 ppm and appear as singlets, while compounds 4a,c are characterized by the multiplicity of signals of CF_2-groups, which can be found at approximately −90...−110 ppm. Despite the moderate chemoselectivity of the reaction of pyridinyloxoacetates **2a,c** with sulfur tetrafluoride, all fluorination products were isolated in an individual state using column chromatography (Scheme 3).

It was found that, unlike α- and γ-substituted ketoesters **2a,c**, the process of deoxofluorination of β-substituted pyridinyloxoacetate **2b** with sulfur tetrafluoride occurs selectively. Thus, when using two equivalents of the fluorinating agent and carrying out the process at room temperature, only ethyl 2,2-difluoro-2-(pyridin-3-yl)acetate **3b** was formed, and it was isolated in an analytically pure form after distillation with a 60% yield (Scheme 4).

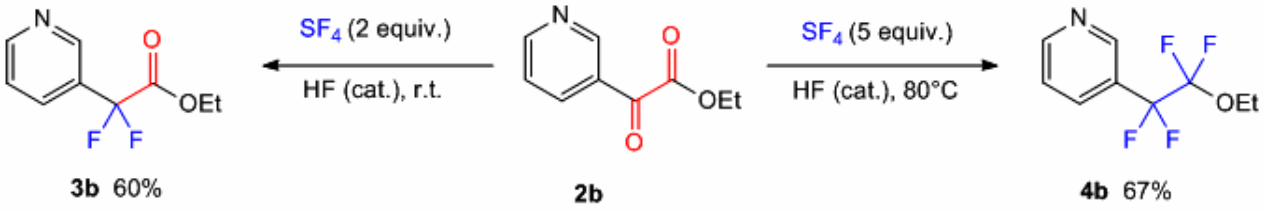
Moreover, exhaustive fluorination of b-substituted pyridine **2b** at keto- and ester-functions was also achieved through the addition of 5 equivalents of tetrafluoride and heating the reaction mixture at 80°C. As a result, a previously unknown tetrafluorinated ester **4b** was isolated in a pure form with a 67% yield after distillation (Scheme 4). It is worth noting that the use of similar fluorination conditions (5 equiv. SF_4, 80°C) for α- and γ-substituted ketoesters **2a,c** also leads to exclusive formation of tetrafluorinated ester **4a,c** isolated in a yields 69% and 71%, respectively (Scheme 3).

Note that esters of pyridinyldifluoroacetic acids **3a–c** were previously obtained by cross-coupling of the appropriate pyridinylhalide with bromodifluoroacetate catalyzed by copper iodide, as well as by electrophilic fluorination of the respective pyridinylacetates with N-fluorobenzenesulfonimide [11].

At the same time, pyridinyltetrafluoroethyl ethers **4a–c** were previously unknown, and they belong to a small group of representatives of tetrafluoroalkyl ethers of heterocyclic compounds and have the potential for utilization in medicine and agrochemistry [12]. The structure of tetrafluorinated ethers **4a–c** was confirmed by spectral data. In particular, the signals of



Scheme 3. Reactions of ethyl pyridinyloxoacetates **2a,c** with sulfur tetrafluoride



Scheme 4. Reaction of ethyl pyridinyl oxoacetate **2b** with sulfur tetrafluoride

CF_2-groups in the ^{19}F NMR spectra are triplets and they are located in their characteristic region of approximately −90 and −110 ppm (for the γ-isomer 4c, δ_F=−90.5 ppm ($^3J_{FF}$=4.5 Hz, CF_2OEt), δ_F=−114.6 ppm ($^3J_{FF}$=4.5 Hz, $PyCF_2$)). In the ^{13}C NMR spectra, their signals form triplet, due to the splitting of carbon atoms on both fluorine atoms with different spin-spin coupling constants (δ_{CF2}=113.5 ppm, $^1J_{CF}$=253.3 Hz, $^2J_{CF}$=41.1 Hz), δ_{CF2}=118.1 ppm, $^1J_{CF}$=271.2 Hz, $^2J_{CF}$=40.9 Hz) (Figure).

Conclusions

In summary, an efficient and easily scalable approach to α-, β-, and γ-pyridinyloxoacetates was developed, based on the interaction of the respective bromopyridines with diethyl oxalate in the presence of isopropylmagnesium chloride, which allows obtaining the respective pyridinyloxoacetates in multigram quantities. Deoxofluorination of α- and γ-pyridinyloxoacetates leads to the formation of a mixture of α-/γ-pyridinyldifluoroacetates and α-/γ-pyridinyltetrafluorinated ethers, which were separated chromatographically. The variation of the temperature regime and the amount of fluorinating reagent allowed to selectively obtain products of the reaction of β-pyridinyloxoacetate with sulfur tetrafluoride, β-pyridinyldifluoroacetate and β-pyridinyltetrafluorinated ether.

Experimental

NMR spectra were recorded on Bruker Avance DRX 600 spectrometer (operating frequencies 600 MHz (^1H) and 470 MHz (^{19}F)); Bruker Avance DRX 500 spectrometer (operating frequencies 499.9 MHz (^1H), 125.7 MHz (^{13}C), and 376.5 MHz (^{19}F)); Varian Unity Plus 400 instrument (operating frequencies 399.9 MHz (^1H)). Chemical shifts are reported relative to internal TMS (^1H, ^{13}C) or $CFCl_3$ (^{19}F) standards. Starting materials were purchased from Merck, Fluka, and EnamineLdt. Melting points are uncorrected. Elemental analysis was carried out in the analytical laboratory of Institute of organic chemistry, NAS of Ukraine.

General procedure for pyridinyl oxoacetates ***2a–c***

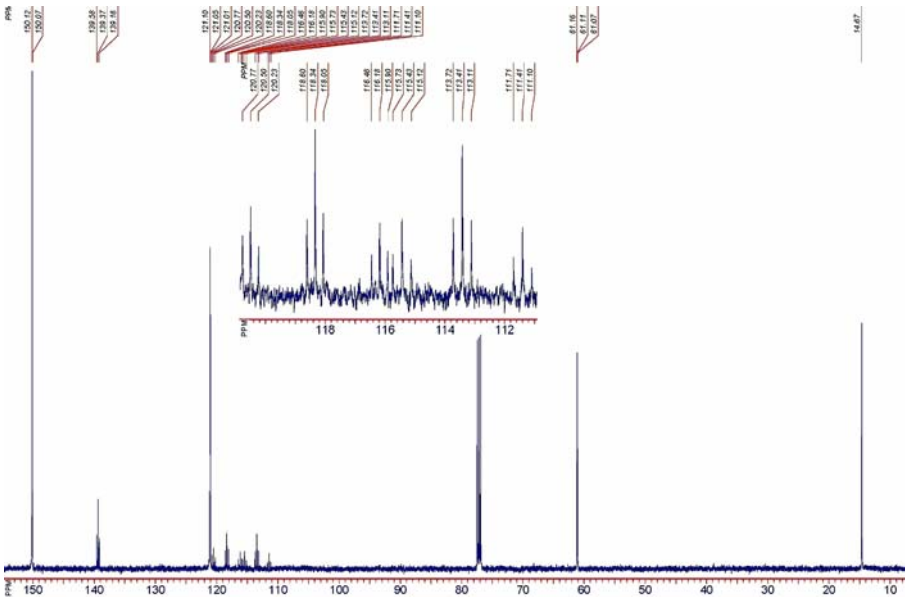
i-PrMgCl (2 M in THF, 62.5 mL, 125 mmol) was added dropwise to a stirring solution of respective bromopyridine **1** (20 g, 125 mmol) in THF (200 mL) at room temperature under argon atmosphere. Reaction mixture was stirred at room temperature for 40 minutes, then it was cooled to −40°C. A solution of diethyl oxalate (15.4 g, 105 mmol) in THF (100 mL) was added dropwise to the reaction mixture. The reaction mixture was allowed to warm up slowly to room temperature, then it was left at room temperature for 24 hours. A saturated aqueous solution of NH_4Cl (50 mL) was added to the reaction mixture, and the mixture was extracted with EtOAc (2×150 mL). Combined organic extracts were dried over $MgSO_4$, the solvent was evaporated, the residue was distilled *in vacuo* to afford compound **2**.

Ethyl 2-oxo-2-(pyridine-2-yl)acetate ***2a***

It was obtained as yellowish viscous liquid (15.9 g, 71%). bp=90−100°C/0.3 mm Hg (lit. 85−88°C/0.5 mm Hg [8]). Spectral data are identical to the literature [13].

Ethyl 2-oxo-2-(pyridin-3-yl)acetate ***2b***

It was obtained as yellowish viscous liquid



^{13}C NMR spectra of compound **4c**

(17.45 g, 78%). bp=90−95°C/0.3 mm Hg (lit. 153−155°C/20 mm Hg [14]). ^{13}C NMR (125.7 MHz, $CDCl_3$) d: 14.1 (s, CH_3), 62.9 (s, CH_2), 123.8 (s, C_{Py}), 128.5 (s, C(CO)), 137.2 (s, C_{Py}), 151.5 (s, C_{Py}), 154.8 (s, C_{Py}), 162.3 (s, C=O), 184.6 (s, C=O) ppm. The other spectral data are identical to the literature [9].

Ethyl 2-oxo-2-(pyridin-4-yl)acetate ***2c***

It was obtained as colorless crystalline solid (15.65 g, 70%). mp=52−53°C; bp=80−83°C/0.3 mm Hg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.42 (t, $^3J_{HH}$ 7.2 Hz, 3H, CH_3), 4.46 (q, $^3J_{HH}$ 7.2 Hz, 2H, CH_2), 7.83 (d, $^3J_{HH}$ 5.2 Hz, 2H), 8.86 (d, $^3J_{HH}$ 5.2 Hz, 2H) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$) δ: 14.2 (s, CH_3), 63.1 (s, CH_2), 122.6 (s, $2C_{Py}$), 138.7 (s, C(CO)), 151.2 (s, $2C_{Py}$), 162.1 (s, C=O), 185.2 (s, C=O) ppm. Anal. calcd. for $C_9H_9NO_3$: C 60.33, H 5.06, N 7.82, found: C 60.54, H 5.13, N 7.71 (%).

General procedure for pyridinyl difluoroacetates ***3a−c***

Respective pyridinyloxoacetate 2 (2 g, 10 mmol) and water (0.01 mL) were placed in an autoclave sleeve, the sleeve was placed in a stainless steel autoclave (V=250 mL). The autoclave was vacuumed, and then sulfur tetrafluoride (2.16 g, 20 mmol) was condensed into the autoclave cooled with liquid nitrogen. The reaction mixture was stirred at room temperature for 16 h. After the removal of volatile gaseous products the content of autoclave was poured into cold water (10 mL) and neutralized with a saturated aqueous solution of $NaHCO_3$ (10 mL). The reaction mixture was extracted with EtOAc (2×30 mL), organic layer was washed with water (10 mL), a saturated aqueous solution of $NaHCO_3$ (10 mL) and brine NaCl (10 mL), and dried over Na_2SO_4. The solvent was evaporated, the residue was distilled *in vacuo*. The mixture of fluorinated esters **3** and ethers **4** was separated by column chromatography (silica gel, EtOAc/hexane 1:1).

Ethyl 2,2-difluoro-2-(pyridin-2-yl)acetate ***3a***

It was obtained as yellow liquid (0.62 g, 31%, R_f=0.4 (EtOAc/hexane 1:1)). bp=85−87°C (0.5 mm Hg). Spectral data are identical to the literature [3].

Ethyl 2,2-difluoro-2-(pyridin-3-yl)acetate ***3b***

It was obtained as yellow liquid (1.21 g, 60%). bp=72°C (0.3 mm Hg). Spectral data are identical to the literature [15].

Ethyl 2,2-difluoro-2-(pyridin-4-yl)acetate ***3c***

It was obtained as yellow liquid (0.66 g, 33%, R_f=0.4 (EtOAc-hexane 1:1)). bp=45°C (0.3 mm Hg). Spectral data are identical to the literature [11].

General procedure for pyridinyltetrafluoroethyl ethers ***4a−c***

Pyridinyloxoacetate **2** (2 g, 10 mmol) and water (0.01 mL) were placed in an autoclave sleeve, the sleeve was placed in a stainless steel autoclave (V= 250 mL). The autoclave was vacuumed, and then sulfur tetrafluoride (5.4 g, 50 mmol) was condensed into the autoclave cooled with liquid nitrogen. The reaction mixture was stirred at 80°C for 7 days. The content of autoclave was poured into water (20 mL) and neutralized with a saturated aqueous solution of $NaHCO_3$ (30 mL) after the removal of volatile gaseous products. The reaction mixture was extracted with EtOAc (2r30 mL), organic extract was washed with water (30 mL), a saturated aqueous solution of $NaHCO_3$ (20 mL) and brine (30 mL), dried over Na_2SO_4. The solvent was evaporated, the residue was distilled *in vacuo* to afford **4.**

2-(2-Ethoxy-1,1,2,2-tetrafluoroethyl)pyridine ***4a***

It was obtained as yellowish liquid from pyridinyl oxoacetate 2a and excessive amount of SF_4 (1.4 g, 69%); after column chromatography (0.65 g, 29%, R_f=0.5 (EtOAc-hexane 1:1)). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.25 (t, $^3J_{HH}$ 7.4 Hz, 3H, CH_3), 4.01 (q, $^3J_{HH}$ 7.4 Hz, 2H, CH_2), 7.42 (dd, $^3J_{HH}$ 7.8 Hz, $^3J_{HH}$ 5 Hz, 1H), 7.66 (d, $^3J_{HH}$ 7.8 Hz, 1H), 7.84 (t, $^3J_{HH}$ 7.8 Hz, 1H), 8.73 (d, $^3J_{HH}$ 5 Hz, 1H) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ: −89.5 (t, $^3J_{FF}$ 4.5 Hz), −117.5 (t, $^3J_{FF}$ 4.5 Hz) ppm. Anal. calcd. for $C_9H_9F_4NO$: C 48.44, H 4.07, N 6.28, found: C 48.56, H 4.17, N 6.11 (%).

3-(2-Ethoxy-1,1,2,2-tetrafluoroethyl)pyridine ***4b***

It was obtained as yellowish liquid from pyridinyl oxoacetate 2b and excessive amount of SF_4 (1.49 g, 67%). bp=30°C/1 mm Hg. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.03−1.14 (m, 3H, CH_3), 3.78−3.88 (m, 2H, CH_2), 7.22 (dd, $^3J_{HH}$ 7.9 Hz, $^3J_{HH}$ 4.9 Hz, 1H), 7.71 (d, $^3J_{HH}$ 7.9 Hz, 1H), 8.58 (d, $^3J_{HH}$ 4.9 Hz, 1H), 8.66 (s, 1H) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$) δ: 14.7 (s, CH_3), 61.0 (t, $^3J_{CF}$ 6 Hz, CH_2), 113.9 (tt, $^1J_{CF}$ 255.3 Hz, $^2J_{CF}$ 39.4 Hz, CF_2OEt), 118.5 (tt, $^1J_{CF}$ 271 Hz, $^2J_{CF}$ 35.1 Hz, CF_2Py), 123 (c, C_{Py}), 127.3 (t, $^2J_{CF}$ 24.8 Hz, CCF_2), 134.5 (t, $^3J_{CF}$ 6.2 Hz, C_{Py}), 148 (t, $^3J_{CF}$ 6.8 Hz, C_{Py}), 152.1 (s, C_{Py}) ppm. ^{19}F NMR (470 Hz, $CDCl_3$) δ: −90.52 (t, $^3J_{FF}$ 5.1 Hz), −114.6 (t, $^3J_{FF}$ 5.1 Hz) ppm. Anal. calcd. for $C_9H_9F_4NO$: C 48.44, H 4.07, N 6.28, found: C 48.23, H 4.24, N 6.36 (%).

4-(2-Ethoxy-1,1,2,2-tetrafluoroethyl)pyridine ***4c***

It was obtained as yellowish liquid from pyridinyl oxoacetate 2c and excessive amount of SF_4 (1.6 g, 71%); after column chromatography (0.58 g, 26%, R_f=0.5 (EtOAc-hexane 1:1)). ^{1}H NMR (400 MHz,

$CDCl_3$) δ: 1.25 (t, $^3J_{HH}$ 7.1 Hz, 3H, CH_3), 3.99 (q, $^3J_{HH}$ 7.1 Hz, 2H, CH_2), 7.49 (d, $^3J_{HH}$ 5.1 Hz, 2H), 8.75 (d, $^3J_{HH}$ 5.1 Hz, 2H) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$) δ: 14.7 (s, CH_3), 61.1 (t, $^3J_{CF}$ 6 Hz, CH_2), 113.4 (tt, $^1J_{CF}$ 253 Hz, $^2J_{CF}$ 38 Hz, CF_2OEt), 118.3 (tt, $^1J_{CF}$ 271 Hz, $^2J_{CF}$ 34 Hz, CF_2Py), 121.1 (t, $^3J_{CF}$ 5.5 Hz, C_{Py}), 139.4 (t, $^2J_{CF}$ 26 Hz, $\underline{C}CF_2$), 150.1 (s, C_{Py}) ppm. ^{19}F ЯМР (470 MHz, $CDCl_3$) δ: −90.0 (t, $^3J_{FF}$ 4.5 Hz), −116.2 (t, $^3J_{FF}$ 4.5 Hz) ppm. Anal. calcd. for $C_9H_9F_4NO$: C 48.44, H 4.07, N 6.28, found: C 48.31, H 4.15, N 6.17 (%).

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ДЕОКСОФТОРУВАННЯ ПІРИДИНІЛОКСОАЦЕТАТІВ ТЕТРАФТОРИДОМ СІРКИ

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Розроблено ефективний масштабований метод синтезу α-, β- та γ-піридинілоксоацетатів, основою якого є взаємодія відповідних бромопіридинів із діетилоксалатом у присутності ізопропілмагнійхлориду. Даний метод дозволяє одержувати всі ізомерні піридинілоксоацетати з препаративними виходами в мультиграмових кількостях. Досліджено процес деоксофторування ізомерних піридинілоксоацетатів тетрафторидом сірки. Встановлено, що деоксофторування α- та γ-піридинілоксоацетатів тетрафторидом сірки приводить до утворення суміші α-/γ-піридинілдифторооцтових естерів та α-/γ-піридинілтетрафторованих етерів, яка може бути розділена хроматографічно. З'ясовано, що при використанні надлишку тетрафториду сірки і тривалому нагріванні реакційної маси фторування α-/γ-піридинілоксоацетатів приводить до виключного утворення α-/γ-піридинілтетрафторованих етерів. Натомість, при деоксофторуванні тетрафторидом сірки β-піридинілоксоацетату варіювання температурного режиму та кількості фторуючого реагенту дозволяє селективно одержувати β-піридинілдифторооцтовий естер та β-піридинілтетрафторований етер. α-/β-/γ-Піридинілтетрафторовані етери є новими представниками малочисельної групи гетарилтетрафторованих етерів та мають потенціал для використання в медичній та агрохімії.

Ключові слова: α-, β-, γ-піридинілоксоацетати, деоксофторування, тетрафторид сірки, α-, β-, γ-піридинілдифторооцтові естери, α-, β-, γ-піридинілтетрафторовані етери.

DEOXOFLUORINATION OF PYRIDINYLOXOACETATES BY SULFUR TETRAFLUORIDE

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An effective scalable method for the synthesis of α-, β-, and γ-pyridinyloxoacetates has been developed, based on the interaction of the respective bromopyridines with diethyl oxalate in the presence of isopropylmagnesium chloride. This method enables the preparation of all isomeric pyridinyl oxoacetates with preparative yields in multigram quantities. The deoxofluorination process of isomeric pyridinyl oxoacetates with sulfur tetrafluoride was investigated. It was established that the deoxofluorination of α- and γ-pyridinyloxoacetates with sulfur tetrafluoride leads to the formation of a mixture of α-/γ-pyridinyldifluoroacetic acid esters and α-/γ-pyridinyltetrafluorinated ethers, which can be separated chromatographically. It was found that when using an excess of sulfur tetrafluoride and prolonged heating of the reaction mixture, the fluorination of α-/γ-pyridinyl oxoacetates results in the exclusive formation of α-/γ-pyridinyltetrafluorinated ethers. On the other hand, in the case of deoxofluorination of β-pyridinyloxoacetate with sulfur tetrafluoride, varying the temperature and the amount of fluorinating reagent allows for the selective formation of β-pyridinyldifluoroacetic acid ester or β-pyridinyltetrafluorinated ether. α-/β-/γ-Pyridinyltetrafluorinated ethers are new representatives of the small group of hetaryltetrafluorinated ethers and have potential applications in medicine and agrochemistry.

Keywords: α-, β-, γ-pyridinyloxoacetates; deoxofluorination; sulfur tetrafluoride; α-, β-, γ-pyridinyldifluoroacetic esters; α-, β-, γ-pyridinyltetrafluorinated ethers.

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