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Catalytic reductive hydrodefluorination of 1,1-difluoronaphthalen-2(1*H*)-one

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Abstract

An optimised method of 1,1-difluoronaphthalen-2(1*H*)-one hydrodefluorination leading to the formation of fluoronaphthol under mild conditions is proposed. The palladium-catalysed process is shown to involve carbonyl reduction followed by subsequent hydrogen fluoride (HF) elimination. The structure of the intermediate product and the effect of catalyst support material on hydrodefluorination selectivity have been determined.

Keywords: heterogeneous catalysis, palladium catalysis, hydrogenation, fluorinated aromatic compounds, reaction mechanism

Каталитическое восстановительное гидродефторирование 1,1-дифторнафталин-2(1*H*)-она

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Аннотация

Предложен оптимизированный метод гидродефторирования 1,1-дифторнафталин-2(1*H*)-она, приводящий к образованию фторнафтола в мягких условиях. Показано, что катализируемое палладием превращение заключается в восстановлении карбонильной группы с последующим отщеплением фтороводорода (HF). В ра-

боте установлена структура промежуточного продукта реакции, а также влияние носителя катализатора на селективность гидродефторирования.

Ключевые слова: гетерогенный катализ, палладиевый катализ, гидрирование, фторированные ароматические соединения, механизм реакции

INTRODUCTION

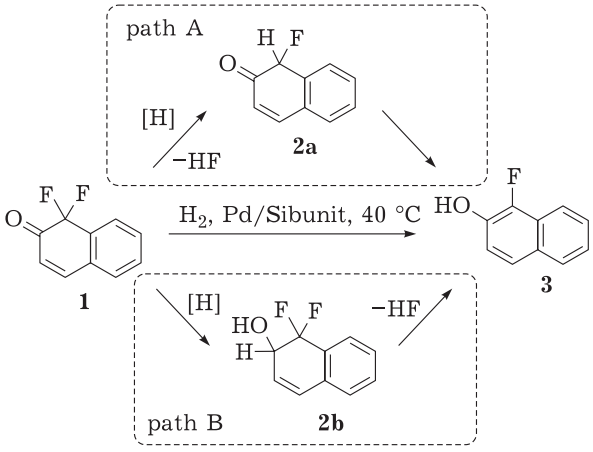
Organofluorine compounds are of great importance for the development of medicinal substances, polymers, and agrochemicals [1, 2]. Catalytic hydrodefluorination of α,α-difluoroketones allows one to obtain fluoronaphthols, which are used in the synthesis of liquid crystals [3], fluorescent probes [4], and biologically active compounds [5]. Reductive defluorination of condensed polycyclic difluoroketones can be used in the synthesis of organic semiconductors for molecular electronics [6]. The study of the mechanism of hydrodefluorination of polyfunctional organic compounds allows one to establish the features of the catalytic process and develop effective sustainable methods for the synthesis of organofluorine compounds.

In this work, we report reductive palladium-catalysed defluorination of 1,1-difluoronaphthalen-2(1*H*)-one with hydrogen (Scheme 1).

EXPERIMENTAL

Materials and methods

^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on Bruker AV-300, AV-400 and AV-600 spectrometers at room temperature, chemical shifts (δ) are given in ppm relative to TMS and $CFCl_3$, respectively. High resolution mass spectra (HRMS) were measured using a DFS instrument. All reactants were of commercial purity and used without further purification. 1,1-Difluoronaphthalenone **1** [7] and palladium catalysts [8, 9] were prepared according to procedures reported earlier. In the case of Pd on silica C-80, precipitation was performed in Cs_2CO_3 solution.



Scheme 1. Reductive defluorination of 1,1-difluoronaphthalen-2(1*H*)-one.

*General procedure for catalytic hydrogenation of **1***

To a degassed suspension of palladium catalyst (60 mg) in 2 mL EtOH, 240 mg (1.33 mmol) of 1,1-difluoronaphthalen-2(1*H*)-one **1** in EtOH (6 mL) was added under hydrogen atmosphere (1 bar). The mixture was stirred vigorously at 40 °C until the consumption of hydrogen stopped. The reaction mixture was then filtered through a silica pad, the latter was washed twice with EtOH. The combined solution was then evaporated on a rotary evaporator and analyzed by ^{19}F NMR spectroscopy.

*Reduction of **1** with sodium borohydride*

To a solution of 1,1-difluoronaphthalen-2(1*H*)-one **1** (1 mmol) in a mixture of ethanol (1.3 mL), tetrahydrofuran (0.6 mL) and water (0.1 mL), $NaBH_4$ (0.5 mmol) was added in small portions under vigorous stirring. The reaction mixture was stirred for another 3 h at 30 °C, cooled to room temperature and filtered. The solvent was removed under reduced pressure. The residue was diluted with water and Et_2O, and aq. HCl was added until pH of the aqueous phase was 3. The resulting mixture was extracted with Et_2O (3 × 3 mL). The combined organic phase was separated and dried over $MgSO_4$. The solvent was removed under reduced pressure, giving **2b**.

1,1-Difluoro-1,2-dihydronaphthalen-2-ol (2b). Yield 80 mg (78 %). Yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 4.63 (m, 1H, H^2), 5.90–6.10 (m, 1H, H^3), 6.50 (m, 1H, H^4), 7.16 (m, 1H, H^8), 7.28–7.46 (m, 2H, $H^{6,7}$), 7.70 (m, 1H, H^5). ^{13}C NMR (151 MHz, $CDCl_3$), δ: 69.4 (dd, J = 30.1, 23.1 Hz), 118.8 (dd, J = 243.9, 240.4 Hz), 124.4–125.0 (m), 127.1 (s), 127.8 (br. s), 128.0–128.2 (m), 128.4 (br. s), 129.0 (t, J = 23.1 Hz), 131.1–131.3 (m), 133.0 (t, J = 5.8 Hz). ^{19}F NMR

(282 MHz, $CDCl_3$), δ: (−113.1)−(−110.7) (ABX-system, 2F, diastereotopic). HRMS, *m/z*: calculated for $C_{10}H_8OF_2$ 182.0538, found 182.0537.

*Aromatization of **2b** with triethylamine*

To a solution of 1,1-difluoro-1,2-dihydronaphthalen-2-ol **2b** (80 mg, 0.43 mmol) in 1.5 mL of chloroform, NEt_3 was added (1.2 mL, 8.6 mmol), and the resulting mixture was stirred at 25 °C overnight. The solvent was removed on a rotary evaporator, and the residue was diluted with chloroform, washed twice with aq. HCl and water. The organic phase was separated, concentrated under reduced pressure, and analysed by ^{19}F NMR spectroscopy.

RESULTS AND DISCUSSION

Catalytic hydrogenation of 1,1-difluoronaphthalen-2(1H)-one

The initial hydrogenation of 1,1-difluoronaphthalen-2(1*H*)-one **1** was performed in the stationary mode under mild conditions (1 bar H_2, 40 °C, EtOH, **1** (0.16 M), Pd/Sibunit 159K 2.5 wt%). Hydrogen consumption stopped after 10 min, and complete conversion of **1** to 1-fluoro-2-naphthol **3** was achieved according to ^{19}F NMR spectral data of the reaction mixture (δ −101.5 (s) for **1**, (−113.1)−(−110.7) (ABX-system, diastereotopic) for **2b**, −144.6 (s) for **3**). Alternative routes to **3** can be found in literature, including solid-phase fluorination of a sixfold excess of 2-naphthol with *N*-fluorobenzenesulfonimide [10], decarboxylative fluorination of 2-hydroxy-1-naphthoic acid with Selectfluor [11] or fluorination of 2-naphthol with *N*,*N*′-difluoro-2,2′-bipyridinium salts in liquid CO_2 at room temperature with subsequent hydrogenation of intermediate **1** over palladium catalysis [12]. In most of those cases, prolonged reaction time or harsher conditions are required to obtain **3**.

Two possible mechanistic pathways may be proposed for this process: direct hydrogenolysis of C−F bond followed by fast tautomerisation of the resulting keto form **2a** (path A) or reduction of C=O bond resulting in secondary alcohol **2b**, which then undergoes HF elimination (path B). Ketone **1** was reduced with sodium borohydride for determination of the structure of possible intermediate, and 1,1-difluoro-1,2-dihydro-2-naphthol **2b** was obtained with 78 % preparative yield. Fluorinated compounds are known to undergo base-promoted β-elimination of HF [13]. To confirm the ability of secondary alcohol **2b** to transform into **3**, we treated **2b** with triethylamine and observed the formation of **3** with 30 % conversion according to ^{19}F NMR spectroscopy. Also, **2b** can be found in the reaction mixture (10 % conversion detected by ^{19}F NMR spectroscopy) if hydrogenation is performed with a lower concentration of **1** (0.016 M) and lower palladium content (1 wt%). These findings support our hypothesis of catalytic hydrodefluorination proceeding via path B.

*The effect of catalyst support on hydrodefluorination of **1***

In case of heterogeneous catalysis, the ability of catalyst support material or metal surface to adsorb HF may facilitate the elimination process. The effect of catalyst support material on hydrodefluorination selectivity was studied with 0.5 wt% of palladium (Table 1). Generally, silicon containing materials ($CaSiO_3$, kieselguhr and silica) demonstrate high selectivity, and a significant amount of intermediate **2b** is observed in other cases. This may indicate the participation of support material in HF elimination from **2b** with silicon containing materials having particularly high affinity to fluoride ion.

CONCLUSIONS

Catalytic hydrogenation of 1,1-difluoronaphthalen-2(1*H*)-one using palladium catalysts under mild conditions results in the formation of 1-fluoro-2-naphthol with a high conversion within ten

TABLE 1

Support material effect on the selectivity of 1,1-difluoronaphthalen-2(1*H*)-one hydrogenation

Entry	Support material	Conversion of **1** to **3**	Conversion of **1** to **2b**
1	$CaSiO_3$	70	25
2	$CaCO_3$	58	34
3	Sibunit 159K	100	0
4	α-Al_2O_3	71	22
5	Kieselguhr MN-3	84	8
6	C-80 silica	85	11
7	ZrO_2	60	30

Note. Conditions: 0.16 M **1** in EtOH, 0.5 wt% Pd on support, 1 bar H_2, 40 °C, 30 min. Conversions determined by ^{19}F NMR spectroscopy.

minutes. The plausible reaction mechanism includes hydrogenation of C=O bond with the subsequent elimination of hydrogen fluoride from secondary alcohol intermediate. Silicon-containing support materials facilitate HF elimination. The described method of α,α-difluoroketone moiety reduction can potentially be used for the synthesis of fluorinated aromatic compounds.

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