Synthesis of 1,3,4-trifluoroisoquinoline by copyrolysis of 2,3,5,6-tetrafluoropyridine-4-sulfonyl chloride with butadiene

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The reaction of 2,3,5,6-tetrafluoropyridine-4-sulfonyl chloride with butadiene in a flow system at 510—520 °C afforded 1,3,4-trifluoroisoquinoline. A scheme of this process is proposed.

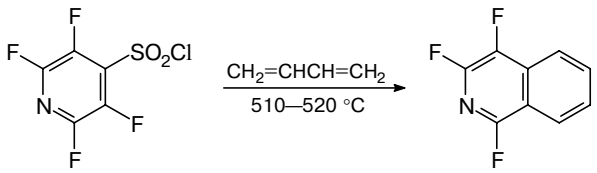
Key words: copyrolysis, 1,3,4-trifluoroisoquinoline, 2,3,5,6-tetrafluoropyridine-4-sulfonyl chloride, butadiene.

The known isoquinolines containing only F atoms as substituents include all monofluoro derivatives,[1—3] 1,3-difluoroisoquinoline,[4] and 3,7-difluoroisoquinoline.[5] Isoquinolines containing three, four, or five F atoms are unknown. 3,4,5,6,7,8-Hexafluoroisoquinoline[6] and heptafluoroisoquinoline[7] were also reported. In the present work, we developed a procedure for the synthesis of a previously unknown trifluoroisoquinoline.

Recently, we have described the synthesis of 1,2,3,4-tetrafluoronaphthalene by copyrolysis of perfluorobenzenesulfonyl chloride with butadiene.[8] We thought it reasonable to extend this approach, which has been used previously for compounds of the benzene series, to polyfluorinated pyridine derivatives with the aim of synthesizing fluoroisoquinolines.

Copyrolysis of 2,3,5,6-tetrafluoropyridine-4-sulfonyl chloride (**1**) with butadiene afforded 1,3,4-trifluoroisoquinoline (**2**) as the major fluorine-containing product (Scheme 1).

Scheme 1



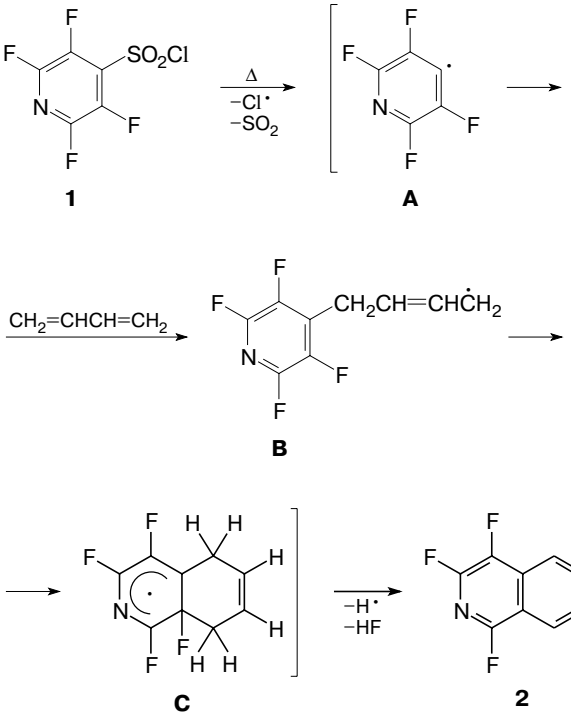
1 **2** (21%)

According to the data from GLC-mass spectrometry and GLC, small amounts of 2,3,5,6-tetrafluoropyridine and 2,3,5,6-tetrafluoro-4-chloropyridine (2—4% each) were obtained along with trifluoroisoquinoline **2**.

The formation of compound **2** can be rationalized as follows (Scheme 2):

Apparently, the 2,3,5,6-tetrafluoropyridyl radical (**A**) generated upon pyrolysis of compound **1** reacts with butadiene to form the corresponding allylic radical **B**.

Scheme 2



Its intramolecular cyclization gives rise to radical σ-complex **C** from which 1,3,4-trifluoroisoquinoline (**2**) is formed as a result of elimination of an H atom and HF.

The starting sulfonyl chloride **1** was prepared by oxidation of 2,3,5,6-tetrafluoropyridine-4-thiol with chlorine in acetic acid (*cf.* the preparation of perfluorobenzenesulfonyl chloride[9]).

The structures of compounds **1** and **2** were established by elemental analysis, high-resolution mass spectrometry, and NMR spectroscopy.

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The assignment of the signals in the ^1H and ^{19}F NMR spectra was made by comparing the chemical shifts and the spin-spin coupling constants of compound **2** with the corresponding values for isoquinoline[10] and perfluoroisoquinoline,[11] respectively. In the ^{19}F NMR spectrum of compound **2**, the signals are to a first approximation doublets of doublets. The $J_{F(1),F(4)}$, $J_{F(3),F(4)}$, and $J_{F(1),F(3)}$ values for trifluoroisoquinoline are close to the corresponding characteristics of perfluoroisoquinoline. The spin-spin coupling constants of the heterocyclic fragment of both fluoroisoquinolines change in the order $J^p_{F,F} > J^o_{F,F} > J^m_{F,F}$, which differs from that observed for fluorinated compounds of the benzene series ($J^o_{F,F} > J^p_{F,F} > J^m_{F,F}$).[12]

Experimental

The ^{19}F and ^1H NMR spectra were recorded on Bruker WP-200SY and Bruker DRX-500 instruments. The spectra of the individual compounds were obtained for solutions in CCl_4 and $(CD_3)_2CO$ (~10 mol.%). Hexafluorobenzene and hexamethyldisiloxane were used as the internal standards.

The high-resolution mass spectra were obtained on a Finnigan MAT 8200 instrument. The temperature of the inlet system was 50—270 °C. The energy of ionizing electrons was 70 eV. Mass spectrometry was used for determining the precise molecular weights and molecular formula.

GLC-mass spectrometry was carried out on a chromatograph equipped with an HP G1801A mass-selective detector. The energy of ionizing electrons was 70 eV. The compounds were separated on a 30-m capillary column with the inner diameter of 0.25 mm coated with a 0.25-μm thick film of HP-5 copolymer (helium as the carrier gas at a flow rate of 1 mL min^{-1}). The column temperature varied from 50 to 280 °C, the evaporator temperature was 280 °C, and the temperature of the ion source was 173 °C.

The GLC analysis was performed on an LKhM-72 instrument equipped with a katharometer using linear programming of the temperature (10 deg min^{-1}; 4000×4 mm columns, Chromosorb W as the solid carrier, SKTFT-803 and SKTFT-50 silicone as the liquid phases, helium as the carrier gas, the flow rate of helium was 10 mL min^{-1}).

The compounds were identified by GLC using authentic samples prepared according to a procedure reported previously.[13,14]

Synthesis of 2,3,5,6-tetrafluoropyridine-4-sulfonyl chloride (1). Gaseous chlorine was passed through a solution of 2,3,5,6-tetrafluoropyridine-4-thiol[15] (29.6 g, 0.16 mol) in AcOH (75 mL) at a rate of ~40 g h^{-1} for 9 h 20 min at ~20 °C (the rheometer was calibrated by the weight method based on adsorption of Cl_2 with a ~10% NaOH solution). After completion of the reaction, the acidic fraction was distilled off *in vacuo* using a water-aspirator pump. The residue was distilled *in vacuo* and a fraction with b.p. 68—72 °C (1—2 Torr) was collected. Compound **1** was obtained in a yield of 33.86 g (82.4%) (according to GLC, the purity was 98.1%). Found: *m/z* 248.9283 $[M]^+$. $C_5ClF_4NO_2S$. Calculated: M = 248.9274. ^{19}F NMR (CCl_4), δ: 78.9 (2 F, F(2), F(6)); 26.8 (2 F, F(3), F(5)).

Copyrolysis of 2,3,5,6-tetrafluoropyridine-4-sulfonyl chloride with butadiene. Compound **1** (5.95 g) was passed for 13 min together with butadiene (the flow rate was ~5 L h^{-1}) through a quartz tube (400×20 mm) heated to 510—520 °C placed into a tube furnace. The reaction mixture was collected into a receiver cooled with a mixture of ice and salt and then steam-distilled. The distillate was extracted with CH_2Cl_2, and the extract was dried with $CaCl_2$ and analyzed by GLC-mass spectrometry and GLC. It was found that the solution contained 33% of compound **2**, ~5% of 2,3,5,6-tetrafluoropyridine, ~3% of 4-chlorotetrafluoropyridine, and a mixture of unidentified compounds with the maximum component content of no higher than 10%. After removal of CH_2Cl_2, the mixture was obtained in a yield of 2.72 g. According to the GLC data, compound **2** was obtained in 21% yield. The product that partially precipitated was filtered off, sublimed, and recrystallized from aqueous methanol. The purified product had m.p. 49—50 °C. Found (%): C, 59.09; H, 2.54; F, 31.12; N, 7.40; *m/z* 183.0295 $[M]^+$. $C_9H_4F_3N$. Calculated (%): C, 59.03; H, 2.20; F, 31.12; N, 7.64; M = 183.0296. ^1H NMR ($(CD_3)_2CO$), δ: 8.15 and 8.18 (both d, 1 H each, H(5), H(8), $J_{H(5),H(6)} = J_{H(7),H(8)} = 8.5$ Hz); 8.02 and 7.82 (both dd, 1 H each, H(6), H(7), $J_{H(6),H(7)} = 6.9$ Hz, $J_{H(5),H(6)} = J_{H(7),H(8)} = 8.5$ Hz). ^{19}F NMR (CCl_4), δ: 88.7 (dd, 1 F, F(1), $J_{F(1),F(3)} = 10$ Hz, $J_{F(1),F(4)} = 32$ Hz); 62.6 (dd, 1 F, F(3), $J_{F(1),F(3)} = 10$ Hz, $J_{F(3),F(4)} = 16$ Hz); 2.5 (dd, 1 F, F(4), $J_{F(3),F(4)} = 16$ Hz, $J_{F(1),F(4)} = 32$ Hz). The signal for the F(4) atom is characterized by additional doublet splitting with the constant $J_{F(4)—H} = 1.8$ Hz.

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References

1. A. Roe and C. E. Teague, Jr., *J. Am. Chem. Soc.*, 1951, **73**, 687.
2. M. Bellas and H. Suschitzky, *J. Chem. Soc.*, 1964, 4561.
3. PCT Int. Appl. WO 96 19456; *Chem. Abstrs.*, 1996, **125**, 114513z.
4. Brit. Pat. 845062; *Chem. Abstrs.*, 1961, **55**, 5543i.
5. Eur. Pat. Appl. EP 48539; *Chem. Abstrs.*, 1982, **97**, 55703q.
6. R. D. Chambers, M. Hole, W. K. R. Musgrave, R. A. Storey, and B. Iddon, *J. Chem. Soc. (C)*, 1966, 2331.
7. R. D. Chambers, M. Hole, B. Iddon, W. K. R. Musgrave, and R. A. Storey, *J. Chem. Soc. (C)*, 1966, 2328.
8. V. E. Platonov, O. I. Osina, A. M. Maksimov, and V. G. Kolechkina, *J. Fluorine Chem.*, 1999, **96**, 191.
9. P. Robson, T. A. Smith, R. Stephens, and J. C. Tatlow, *J. Chem. Soc.*, 1963, 3692.
10. T. J. Batterham, in *NMR Spectra of Simple Heterocycles*, J. Wiley, New York, 1973, 313.
11. R. S. Matthews, *Org. Magn. Reson.*, 1976, **8**, 628.
12. L. N. Pushkina, A. P. Stepanov, V. S. Zhukov, and A. D. Naumov, *Zh. Org. Khim.*, 1972, **8**, 586 [*J. Org. Chem. USSR*, 1972, **8** (Engl. Transl.)].
13. R. E. Banks, J. E. Burgess, W. M. Cheng, and R. N. Haszeldine, *J. Chem. Soc.*, 1965, 575.
14. K. V. Dvornikova, A. M. Maksimov, and V. E. Platonov, *12th Eur. Symp. of Fluorine Chemistry (29 August—2 September, 1998)*, Berlin, Germany, 1998, P II-89.
15. L. S. Kobrina, G. G. Furin, and G. G. Yakobson, *Zh. Obshch. Khim.*, 1968, **38**, 514 [*J. Gen. Chem. USSR*, 1968, **38** (Engl. Transl.)].

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