

Brief Communications

Nitration of alcohols by nitryl fluoride

B. S. Fedorov* and L. T. Eremenko

*Institute of Chemical Physics in Chernogolovka, Russian Academy of Sciences,
142432 Chernogolovka, Moscow Region, Russian Federation.
Fax: 007 (096) 515 3588*

A general method for the preparation of nitrates by treatment of alcohols with nitryl fluoride (FNO₂) in MeCN in the presence of KF has been developed.

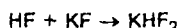
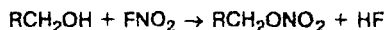
Key words: nitryl fluoride, nitration; alcohol nitrates.

Alcohol nitrates are of interest because they exhibit antianginal activity.¹ Therefore, the development of new general methods for their synthesis is an urgent task. Among the *O*-nitration reactions in aprotic media,^{2–4} nitration of alcohols with nitryl fluoride has remained almost unstudied. Only the nitration of ethanol cooled to –10 °C with bubbling gaseous FNO₂ has been described.⁵ Under these conditions, the process occurs ambiguously: significant amounts of acetaldehyde and acetic acid are formed along with ethyl nitrate (yield ~31%). It has been shown in the subsequent studies that the choice of the solvent plays a decisive role in nitration by nitryl fluoride. For example, to stop the reactions of FNO₂ with amines at the stage of the formation of primary nitramines, low-nucleophilic or nonpolar solvents (CCl₄, alkanes) should be used,^{6,7} while alcohol nitrates with the same number of carbon atoms are obtained in acetonitrile.⁸

In the present work, it is established that the reaction of EtOH with FNO₂ in anhydrous MeCN in the presence of KF with cooling (–20 to –30 °C) results in the formation of ethyl nitrate in 89–90% yield. Under these conditions, the process is complete after 10–15 min (increasing the duration of the reaction to 30–40 min and increasing the temperature to 0–5 °C decreases the yield of ethyl nitrate to 63–64%). The proposed

method for nitration of alcohols has a general character and was used by us for preparing nitrates from primary, secondary, monoatomic and multiatomic, nitro, polynitro, and fluoronitro alcohols of the aliphatic series, as well as the nitrate of an alicyclic alcohol, cyclohexanol (Table 1).

Nitrates of alcohols in which oxygen is less nucleophilic, as, *e.g.*, in the case of 2,2,2-trinitroethanol, can also be synthesized by this method. The role of KF is to bind HF, and the potassium difluoride formed is insoluble in MeCN and can be isolated quantitatively after the end of the reaction.



Experimental

Nitryl fluoride was obtained in the reaction of F₂ and N₂O₄ by the procedure described previously.⁹

Ethyl nitrate. Potassium fluoride (5.8 g, 100 mmol) was added to a solution of anhydrous EtOH (4.6 g, 100 mmol) in anhydrous MeOH (45 mL). Nitryl fluoride (6.5 g, 100 mmol) was bubbled through the mixture cooled to –20 to –30 °C for 10–12 min with vigorous stirring. The mixture was stirred for

Table 1. Yields and properties of alcohol nitrates synthesized

Initial alcohol	Product	B.p. /°C (p/Torr)	n_D^{20}	Yield (%)	Publ. data		Refer- ence
					B.p./°C (p/Torr)	n_D^{20}	
EtOH	EtONO ₂	88	1.3852	89	89	1.38528	10
Pr ⁿ OH	Pr ⁿ ONO ₂	40 (50)	1.3972	90	110	1.39725	11
Pr ⁱ OH	Pr ⁱ ONO ₂	30 (50)	1.3910	87.6	101–102	1.3910	12
(CH ₂ OH) ₂	(CH ₂ ONO ₂) ₂	63–64 (1.5)	1.4480	94.3	64 (1.5)	1.4480	13
HOCH(CH ₂ OH) ₂	CH(ONO ₂)(CH ₂ ONO ₂) ₂	108–110 (1.0)	1.4730	92.3	125 (2.0)	1.4732	14
C(CH ₂ OH) ₄	C(CH ₂ ONO ₂) ₄	140–141 ^b	—	87.4	141 ^b	—	15
O ₂ NCH ₂ CH ₂ OH	O ₂ NCH ₂ CH ₂ ONO ₂	67 (0.5)	1.4551	89.5	74 (1)	1.4550	16
FC(NO ₂) ₂ CH ₂ OH	FC(NO ₂) ₂ CH ₂ ONO ₂	35–36 (0.6)	1.4372	85.6	62 (5)	1.4377	17
C(NO ₂) ₃ CH ₂ OH	C(NO ₂) ₃ CH ₂ ONO ₂ ^a	50–51 (0.5)	1.4661	94.2	—	—	
MeC(F)(NO ₂)CH ₂ OH	MeC(F)(NO ₂)CH ₂ ONO ₂	45–46 (0.8)	1.4258	85.4	47–48 (1)	1.4256	18a
HOCH ₂ C(F)(NO ₂)CH ₂ OH	O ₂ NOCH ₂ C(F)(NO ₂)CH ₂ ONO ₂	38–39 ^b	—	86.0	38–39 ^b	—	18b
cyclo-C ₆ H ₁₁ OH	cyclo-C ₆ H ₁₁ ONO ₂	74–75 (15)	1.4560	95.6	53 (10)	1.4562	19

^a Found (%): C, 10.58; H, 0.83; N, 24.73. C₂H₂N₄O₉. Calculated (%): C, 10.62; H, 0.88; N, 24.78. IR, ν/cm^{-1} : 805 (C—NO₂); 822 (C—ONO₂); 1045 (C—O); 1280, 1695 (ONO₂); 1300, 1600 (C—NO₂); 2895, 2965 (CH₂). ¹H NMR (pure liquid), δ : 5.92 (s, 2 H, CH₂).

^b Melting point.

5 min at –25 °C, and KHF₂ was filtered off (quantitative yield). The filtrate was poured into ice-cold water (200 mL), and the oil that precipitated was extracted with CH₂Cl₂ (2×40 mL). The combined extract was dried with MgSO₄. After distilling off CH₂Cl₂ and distillation of the residue, ethyl nitrate (8.14 g, 89.4%) was obtained (see Table 1).

Nitrates of other alcohols were synthesized similarly. The yields and main parameters of the compounds obtained are presented in Table 1.

References

- V. I. Metelitsa and A. B. Davydov, *Preparaty nitratov v kardiologii* [Nitrate Preparations in Cardiology], Meditsina, Moscow, 1989 (in Russian).
- T. N. Montgomery, *J. Am. Chem. Soc.*, 1934, **56**, 419.
- B. M. L. Wolfrom and A. Rosenthal, *J. Am. Chem. Soc.*, 1953, **75**, 3662.
- G. Olah, S. Kuhn, and M. Stelke, *Chem. Ber.*, 1956, **89**, 2374.
- G. Hetherington and R. L. Robinson, *J. Chem. Soc.*, 1954, 3512.
- US Pat. 3 071 438, 1963; *Chem. Abstr.*, 1963, **59**, 447.
- B. S. Fedorov, Ph. D. (Chem.) Thesis, Inst. Chem. Phys. in Chernogolovka, Chernogolovka, 1976 (in Russian).
- R. G. Gafurov, B. S. Fedorov, and L. T. Eremenko, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1977, 383 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1977, **26**, 345 (Engl. Transl.)].
- G. A. Sokol'skii and I. L. Knunyants, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk* [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*], 1960, 779 (in Russian).
- P. Gray and S. Smith, *J. Chem. Soc.*, 1954, 769.
- A. Vogel, *J. Chem. Soc.*, 1948, 1847.
- R. D. Silva, *Ann.*, 1870, **154**, 256.
- J. Bolleau and M. Thomas, *Mém. poudres*, 1951, **33**, 155.
- Khimicheskaya entsiklopediya* [Chemical Encyclopedia], Bol'shaya Rossiiskaya Entsiklopediya, Moscow, 1992, **3**, 270 (in Russian).
- Spravochnik khimika* [Chemist's Handbook], Goskhimizdat, Moscow, 1963, **2** (in Russian).
- N. Levy, C. W. Scaife, and A. E. W. Smith, *J. Chem. Soc.*, 1946, 1096.
- L. T. Eremenko and F. Ya. Natsibullin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1968, 912 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1968, **17** (Engl. Transl.)].
- L. T. Eremenko and G. V. Oreshko, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1969, 384 (a); 320 (b) [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1969, **18**, No. 2 (Engl. Transl.)].
- Z. M. Soffer, E. W. Parrotka, and J. D. Domenico, *J. Am. Chem. Soc.*, 1952, **74**, 5301.

Received May 21, 1996;
in revised form January 29, 1997