Trifluoroacetylation of *O*-vinyl acetoxime

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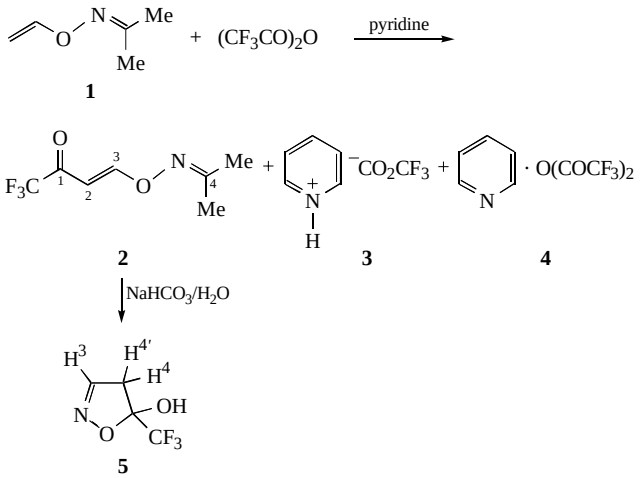
O-Vinyl acetoxime reacts with trifluoroacetic anhydride (pyridine, room temperature) to form (*E*)-*O*-[2-(trifluoroacetyl)vinyl] acetoxime or 5-hydroxy-5-trifluoromethyl-4,5-dihydro-1,2-oxazole.

Vinyl ethers,[1] *N*-vinyl amides[1] and vinyl sulfides[2,3] are known to be capable of undergoing the non-typical (for ordinary alkenes) electrophilic substitution at the β-vinylic carbon when treated with trifluoroacetic or trichloroacetic anhydrides. Note that under similar conditions, *N*-vinylpyrroles are trifluoroacetylated normally at the α-position of the pyrrole ring retaining their *N*-vinyl group intact.[4,5] Despite its extraordinary nature, synthetic and mechanistic importance, this type of vinylic electrophilic substitution still has not got the attention it deserves.

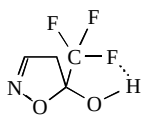
This note is a preliminary communication on the trifluoroacetylation of currently available[6,7] *O*-vinyl oximes, representing the first example of electrophilic substitution at the vinyl group adjacent to two directly linked heteroatoms, CH_2=CHON, wherein the basic nitrogen can be concurrently attacked by an electrophile.

We found that *O*-vinyl acetoxime **1** reacts readily with trifluoroacetic anhydride in the presence of pyridine at room temperature to give expected[1–3] (*E*)-*O*-[2-(trifluoroacetyl)vinyl] acetoxime **2** after direct distillation in 53% yield (not optimised yield) along with pyridinium trifluoroacetate **3** and incompletely reacted pyridine–trifluoroacetic anhydride complex **4**. However, when the reaction mixture is treated with aqueous $NaHCO_3$, 5-hydroxy-5-trifluoromethyl-4,5-dihydro-1,2-oxazole **5** is isolated as the only product in 65% yield (Scheme 1). The structure of oxazole **5** follows from the ^{1}H, ^{13}C, ^{19}F and ^{15}N NMR spectra as well as from the fragmentation under electron ionization.† The chemical shift of ^{15}N (–6.41 ppm) corresponds to the 1,2-oxazole structure (–12.0 to 2.2 ppm).[8,9]



Scheme 1

In the IR spectrum of a dilute solution of oxazole **5** in CCl_4 (0.001 M), only a narrow symmetric band at 3577 cm^{-1} is present in the region 3000–3700 cm^{-1}. This band can be attributed to the following intramolecular H-bond:



The similar H-bonding was observed earlier[10] in 2,6-difluorophenol (ν_{OH} = 3586 cm^{-1}).

The formation of **5** implies the hydrolysis of **2** *via* intermediate semi-acetal-like adduct **6** which decomposes to 3-oxo-4,4,4-trifluorobutyraldehyde **7** and acetoxime **8**. The two latter compounds undergo reoximation to result in corresponding aldoxime **9** and acetone (the hydroxylamine exchange between oximes and aldehydes or ketones under solvolytic conditions is a well-established fact[11]).

The intramolecular hydroxyl–carbonyl interaction in aldoxime **9** leads to the ring closure with the formation of oxazole **5** (Scheme 2).

Similar compounds, 5-amino-5-trifluoromethyl-3-substituted-4,5-dihydro-1,2-oxazoles (Δ^2-isoxazolines), have been recently synthesised by an entirely different reaction from 2-amino-2-trifluoromethyl-5,5-dimethyltetrahydro-4-pyrones and hydroxylamine.[12]

Thus, the perfluoroacylation of *O*-vinyl oximes promises to become a source of highly reactive perfluoroalkyl-substituted ketoaldehydes and 1,2-oxazole derivatives, new potent building blocks for the design of biologically active molecules.

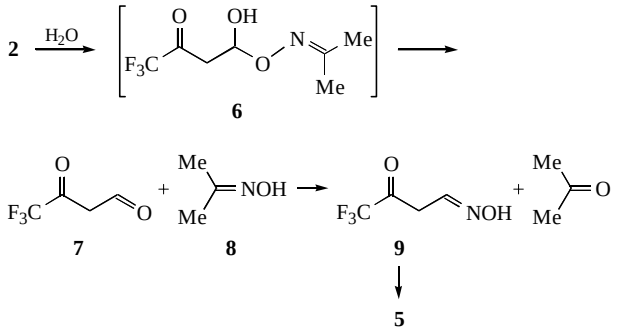
While the trifluoroacetylation of *O*-vinyl oximes originates a novel class of multifunctional compounds, the cyclization of trifluoroacetyl acetaldoxime is a useful supplement to the well-known syntheses[12–14] of 4,5-dihydro-1,2-oxazoles (apart from

† ^{1}H NMR (400.13 MHz), ^{13}C NMR (101.61 MHz) in $CDCl_3$, standard TMS; ^{19}F NMR (89.35 MHz) in $CDCl_3$, standard CCl_3F; ^{15}N NMR (40.56 MHz) in [$^2H_6$]DMSO, standard $MeNO_2$.

To a mixture of 1.98 g (20 mmol) of *O*-vinyl acetoxime **1** and 1.58 g (20 mmol) of pyridine in 15 ml of diethyl ether, 4.2 g (20 mmol) of trifluoroacetic anhydride was added dropwise for 1.5 h.

(*a*) Upon distillation of the reaction mixture in a vacuum, 2.07 g of oxime **2** (yield 53%) was isolated, bp 60–63 °C (2 mmHg). ^{1}H NMR, δ: 8.21 (d, H-2, $^3J_{2-3}$ 12.3 Hz), 6.18 (d, H-3, $^3J_{2-3}$ 12.3 Hz), 2.02, 2.00 (Me_2). ^{13}C NMR, δ: 180.36 (C=O, $^2J_{C-F}$ 35.1 Hz), 166.91 (C-2), 163.89 (C-4), 116.53 (CF_3, $^1J_{C-F}$ 290.6 Hz), 97.80 (C-3), 21.47, 16.73 (Me_2). ^{19}F NMR, δ: –78.73. IR (neat, ν/cm^{-1}): 571, 536, 582, 595, 683, 700, 726, 752, 826, 898, 972, 1055, 1145, 1195, 1257, 1279, 1308, 1371, 1435, 1598, 1650, 1688, 1711, 1793, 2852, 2926, 2964, 3001, 3052, 3086. Found (%): C, 42.99; H, 4.56; N, 7.20; F, 28.67. Calc. for $C_7H_8F_3NO_2$ (%): C, 43.08; H, 4.13; N, 7.18; F, 29.21.

(*b*) The reaction mixture was poured into 30 ml of a saturated aqueous $NaHCO_3$ solution. The organic layer was separated, and the aqueous layer was extracted with diethyl ether (4×5 ml). The combined extract was washed with water (3×5 ml) and dried over $MgSO_4$. After the removal of ether and vacuum sublimation (1 mmHg) of the residue, 2.01 g (65%) of oxazole **5** was obtained, mp 41–42 °C. ^{1}H NMR, δ: 7.30 (nr. m, H-3, $^3J_{3-4}$ 1.7 Hz, $^3J_{3-4'}$ 1.5 Hz, $^5J_{H-F}$ 0.8 Hz), 3.72 (br. s, OH), 3.37 (dq, H-4, $^2J_{4-4'}$ 18.8 Hz, $^3J_{3-4}$ 1.7 Hz, $^4J_{H-F}$ 0.5 Hz), 3.18 (dq, H-4′, $^2J_{4-4'}$ 18.8 Hz, $^3J_{3-4'}$ 1.5 Hz, $^4J_{H-F}$ 1.5 Hz). ^{13}C NMR, δ: 146.58 (C-3, $^1J_{3-4}$ 34.8 Hz), 121.99 (CF_3, $^1J_{C-F}$ 283.7 Hz), 101.59 (C-5, $^2J_{C-F}$ 34.9 Hz, $^1J_{4-5}$ 41.8 Hz), 43.65 (C-4, $^1J_{3-4}$ 34.8 Hz, $^1J_{4-5}$ 41.8 Hz). ^{19}F NMR, δ: –83.65. ^{15}N NMR, δ: –6.41 ($^2J_{N-H}$ 15.8 Hz). IR (KBr, ν/cm^{-1}): 451, 471, 534, 576, 602, 700, 734, 800, 840, 886, 924, 980, 1010, 1057, 1130, 1182, 1199, 1256, 1304, 1330, 1416, 1430, 1628, 2861, 2930, 2957, 2991, 3100, 3577 (OH in CCl_4). MS, *m*/*z* (%): 155 (1.8, [M$^+$]), 138 (6.1, [M – OH$^+$]), 125 (14.7), 111(14), 97 (12.5, [CF_3CO^+]), 92 (14.7), 86 (100), 69 (36.1), 68 (19.8), 67 (8.4), 63 (17.5), 58 (21.6), 56 (19.3), 54 (15.3), 44 (22.7), 42 (61.3). Found (%): C, 30.65; H, 3.06; N, 8.51; F, 36.67. Calc. for $C_4H_4F_3NO_2$ (%): C, 30.18; H, 2.52; N, 8.81; F, 36.77.



Scheme 2

the above procedure,[12] also through the 1,3-dipolar addition of nitrile oxides to alkenes[13] and oximation of α,β-ethylenic carbonyl compounds[14]).

References

1 M. Hojo, R. Masuda, Y. Kokuryo, H. Shioda and S. Matsuo, *Chem. Lett.*, 1976, 499.
2 M. Hojo, R. Masuda and Y. Kamitori, *Tetrahedron Lett.*, 1976, 1009.
3 M. Hojo and R. Masuda, *J. Org. Chem.*, 1975, **40**, 963.
4 B. A. Trofimov and A. I. Mikhaleva, *N-Vinilpirroly* (*N-Vinylpyrroles*), Nauka, Novosibirsk, 1984, p. 127 (in Russian).
5 B. A. Trofimov, in *Pyrroles, Part Two: The Synthesis, Reactivity and Physical Properties of Substituted Pyrroles*, ed. R. A. Jones, Wiley, New York, 1992, p. 131.
6 B. A. Trofimov, A. I. Mikhaleva, A. N. Vasil'ev and M. V. Sigalov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1979, 695 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1979, **28**, 651).
7 O. A. Tarasova, S. E. Korostova, A. I. Mikhaleva, L. N. Sobenina, R. N. Nesterenko, S. G. Shevchenko and B. A. Trofimov, *Zh. Org. Khim.*, 1994, **30**, 810 (*Russ. J. Org. Chem.*, 1994, **30**, 863).
8 M. Witanovski, L. Stefaniak and G. A. Webb, in *Annual Reports on NMR Spectroscopy*, ed. G. A. Webb, Academic Press, London, 1981, vol. 11B, p. 502.
9 Ban Chin Chen and W. von Philipsborn, *Helv. Chim. Acta*, 1983, **66**, 1537.
10 D. A. K. Jones and J. G. Watkinson, *J. Chem. Soc.*, 1964, 2371.
11 P. A. S. Smith, *The Chemistry of Open-Chain Organic Nitrogen Compounds*, Benjamin, Inc., New York, 1966, ch. VII, p. 100.
12 V. Ya. Sosnovskikh, M. Yu. Mel'nikov and A. V. Zaitsev, *Mendeleev Commun.*, 1999, 40.
13 R. Huisgen, *Angew. Chem.*, 1963, **75**, 604.
14 A. Belly, R. Jacquier, F. Petrus and J. Verducci, *Bull. Soc. Chim. France*, 1972, 330.

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