

## Trifluoroacetylation of Ketone *O*-Vinyloximes

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**Abstract**—Ketone oxime *O*-vinyl ethers having alkyl or phenyl radicals react with trifluoroacetic anhydride in ether in the presence of pyridine, yielding 43–54% of the corresponding ketone oxime *O*-(*trans*-4,4,4-trifluoro-3-oxo-1-butenyl) ethers with high stereoselectivity.

Trifluoro(or trichloro)acetylation of vinyl ethers with trifluoro(trichloro)acetic anhydride can be regarded as electrophilic substitution at the vinyl  $\beta$ -carbon atom. As a rule, the reaction proceeds smoothly under mild conditions and leads to formation of *trans*-trifluoro(trichloro)acetylvinyl ethers in high yields. These products are valuable synthons for preparation of potential biologically active heterocyclic compounds, specifically of perhaloacyl pyran derivatives [1–4].

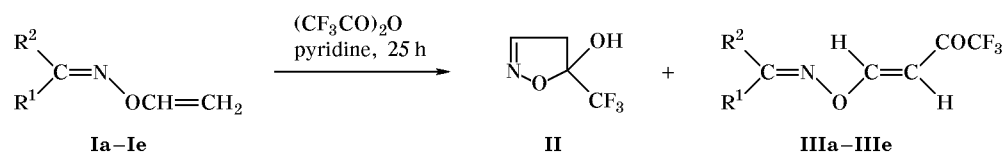
Ketone *O*-vinyloximes, which have become accessible in the recent time [5, 6], may also be regarded as vinyl ethers. However, the double bond in these compounds appears near the energy-rich ON group [6] in which the basic nitrogen atom can also be attacked by electrophile. The first attempt to effect trifluoroacetylation of acetone oxime *O*-vinyl ether (**Ia**) resulted in formation of not only expected trifluoroacetyl derivative but also of product of its further transformation, 5-hydroxy-5-trifluoromethyl-4,5-dihydro-1,2-oxazole (**II**) [7].

The goal of the present work was to get a deeper insight into specific features of the reaction of aliphatic and aromatic ketone *O*-vinyloximes with tri-

fluoroacetic anhydride. We also planned to find conditions under which the reaction can be stopped at the stage of formation of primary replacement products. We have found that thoroughly dehydrated *O*-vinyloximes **Ia–Ie** react with trifluoroacetic anhydride in dry diethyl ether in the presence of pyridine at room temperature as readily as common vinyl ethers do (the reaction conditions were almost identical to those described in [1]). As a result, expected *O*-(*trans*-4,4,4-trifluoro-3-oxo-1-butenyl)oximes **IIIa–IIIe** were isolated in 43–54% yield (Scheme 1). The yields, physical properties, and elemental analyses of compounds **IIIa–IIIe** are given in Table 1, and Tables 2 and 3 contain their NMR and IR spectral parameters.

In the  $^1\text{H}$  NMR spectra of oximes **IIIa–IIIe** the coupling constant  $^3J(1\text{-H}, 2\text{-H})$  was found to be 12.3 Hz. This value corresponds to *trans*-replacement of hydrogen at the  $\beta$ -carbon atom of the vinyl group with formation of the *trans* isomers. Introduction of a trifluoroacetyl group sharply changes  $^{13}\text{C}$  chemical shifts of unsaturated fragments, as compared to initial *O*-vinyloximes **Ia–Ie**, indicating strong redistribution of electron density. Signals from the  $\alpha$ - and  $\beta$ -carbon atoms shift downfield by  $\sim 11$  and 14 ppm, respec-

Scheme 1.



$\text{R}^1 = \text{R}^2 = \text{Me}$  (**a**);  $\text{R}^1 = \text{Me}$ ,  $\text{R}^2 = i\text{-Pr}$  (**b**);  $\text{R}^1 = \text{Me}$ ,  $\text{R}^2 = t\text{-Bu}$  (**c**);  $\text{R}^1 = \text{R}^2 = i\text{-Pr}$  (**d**);  $\text{R}^1 = \text{Me}$ ,  $\text{R}^2 = \text{Ph}$  (**e**).

**Table 1.** Yields, boiling points, refractive indices, and elemental analyses of *O*-(*trans*-4,4,4-trifluoro-3-oxo-1-butenyl)-oximes **IIIa–IIIe**

Comp. no.	Yield, %	bp, °C ( <i>p</i> , mm)	$n_D^{20}$	Found, %				Formula	Calculated, %			
				C	H	F	N		C	H	F	N
<b>IIIa</b>	53	60–63 (2)	1.4410	42.99	4.56	28.67	7.20	C <sub>7</sub> H <sub>8</sub> F <sub>3</sub> NO <sub>2</sub>	43.08	4.13	29.21	7.18
<b>IIIb</b>	53	62–64 (2)	1.4414	47.84	6.02	25.60	6.25	C <sub>9</sub> H <sub>12</sub> F <sub>3</sub> NO <sub>2</sub>	48.43	5.42	25.54	6.28
<b>IIIc</b>	52	70–72 (2)	1.4411	50.65	6.02	23.73	5.80	C <sub>10</sub> H <sub>14</sub> F <sub>3</sub> NO <sub>2</sub>	50.63	5.95	24.03	5.90
<b>III d</b>	54	78–80 (3)	1.4406	52.31	6.70	23.01	5.52	C <sub>11</sub> H <sub>16</sub> F <sub>3</sub> NO <sub>2</sub>	52.59	6.42	22.69	5.57
<b>IIIe</b>	43	116–119 (2)	1.5286	56.26	4.27	22.37	5.72	C <sub>12</sub> H <sub>10</sub> F <sub>3</sub> NO <sub>2</sub>	56.04	3.93	22.16	5.45

tively. In the former case this shift directly results from the substitution of hydrogen, and the downfield shift of the  $\beta$ -carbon signal reflects  $\pi$ -acceptor effect of the trifluoroacetyl fragment. The same factor is responsible for the downfield shift of the C=N signal by ~5–6 ppm (Table 2). In molecule **IIIe** the acceptor effect of the trifluoroacetyl group also extends to the *ortho*- and *para*-carbon atoms of the benzene ring: the corresponding signals shift downfield by 1.2 and 2.2 ppm, respectively.

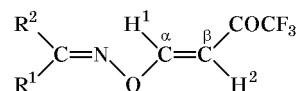
No thermal isomerization of the products about the double C=C bond was observed during vacuum distillation (60–119°C). However, the <sup>1</sup>H and <sup>13</sup>C NMR spectra of **IIIb** contain two sets of signals from the methyl and isopropyl groups, indicating the presence of *E* and *Z* isomers with respect to the C=N bond. The <sup>1</sup>H NMR data show that the isomer ratio of product **IIIb** is the same as in the initial *O*-vinyl-oxime **Ib** (*E*:*Z* = 7:1). In the other cases, i.e., with unsymmetrically substituted compounds **IIIc** and **IIIe**, no *Z* isomers were detected.

Trifluoroacetyl derivatives showed a quite different absorption pattern in the IR regions 1590–1715 and 2850–3100 cm<sup>-1</sup>, as compared with initial *O*-vinyl-oximes **I**. All products **IIIa–IIIe** are characterized by a very strong IR absorption band with its maximum at 1595–1598 cm<sup>-1</sup>,  $\nu$ (C=C). The CF<sub>3</sub> group gives rise to symmetric bending vibration band at 1307 cm<sup>-1</sup> and strong asymmetric vibration bands at 1195 and 1146 cm<sup>-1</sup>. The C=N vibration frequency differs only slightly from that observed for initial *O*-vinyl-oximes **Ia–Ie** [5, 6, 8]; it ranges from 1626 to 1652 cm<sup>-1</sup>, depending on the substituent in the ketone fragment. Carbonyl stretching vibrations appear as a doublet band at 1712/1692 cm<sup>-1</sup> with unusually low intensity. In order to assign IR bands more precisely, we have calculated vibration frequencies of the three double bonds in compound **IIIa** using Gaussian-98 program [9] assuming equilibrium geometry (6-31G basis set).

The calculation results (Table 3) were fully consistent with the experimental data, including both vibration frequencies and band intensities.

The increased intensity and reduced frequency of the C=C bond vibrations in trifluoroacetyl derivatives may be explained by *p*, $\pi$ -conjugation involving double bonds and heteroatoms, for the molecule is planar. Introduction of a bulky isopropyl or *tert*-butyl group into the ketone fragment distorts the planar structure, which results in splitting of the symmetric bending vibration of methyl C–H bonds. Therefore, the IR spectra of compounds **IIIb–III d** contain doublet absorption bands at 1385/1371, 1399/1370, and 1388/1370 cm<sup>-1</sup>, respectively. In the IR spectrum of trifluoroacetyl derivative **IIIe**, the monosubstituted benzene ring is characterized by bands at 1766 cm<sup>-1</sup> (overtone) and 692 and 761 cm<sup>-1</sup> (out-of-plane bending vibrations). Characteristic frequencies in the regions 1600–1580 and 1500–1450 cm<sup>-1</sup> are obscured by the C=C and C=N bond vibrations. The results of calculations of molecule **IIIa** show that IR absorption in the region 892–905 cm<sup>-1</sup> belongs to stretching vibrations of the N–O bond. According to published data [10], the HC=CH vibration band at 960 cm<sup>-1</sup>, which characterizes *trans* configuration of the double bond, should have a high intensity. However, the band at 972 cm<sup>-1</sup> in the IR spectra of trifluoroacetyl derivatives **III** is medium. The IR spectra of compounds **IIIa** and **IIIe** are also characterized by low intensity (at the background level) of stretching vibrations of C–H bonds in the substituents.

Trifluoroacetyl *O*-vinyl-oxime derivatives **IIIa–III d** are light yellow liquids (compound **IIIe** is light red) with a specific odor, which are soluble in most organic solvents. Unlike initial *O*-vinyl-oximes **I** which are capable of decomposing with explosion on heating to 145–155°C [6], trifluoroacetyl derivatives **IIIa–IIIe** are more thermally stable (no explosions occurred while working with these compounds). The low yields

**Table 2.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of *O*-(4,4,4-trifluoro-3-oxo-1-butenyl)oximes **IIIa–IIIe**<sup>a</sup>

Comp. no.	$^1\text{H}$ NMR spectrum, $\delta$ , ppm				$^{13}\text{C}$ NMR spectrum, <sup>b</sup> $\delta_{\text{C}}$ , ppm						
	1-H	2-H	R <sup>1</sup>	R <sup>2</sup>	C=O	C=N	C <sup><math>\alpha</math></sup>	C <sup><math>\beta</math></sup>	CF <sub>3</sub>	R <sup>1</sup>	R <sup>2</sup>
<b>IIIa</b>	8.21	6.18	2.00	2.02	180.36	163.90 (157.26) <sup>b</sup>	166.91 (152.32)	97.80 (86.79)	116.53	21.47 (21.23)	16.73 (15.63)
<i>E</i> - <b>IIIb</b>	8.22	6.15	1.93	2.58 (CH), 1.12 (2Me)	180.20	170.44 (164.65)	167.08 (152.61)	97.66 (86.99)	116.42	17.51 (11.82)	34.44, 19.36 (34.29, 19.62)
<i>Z</i> - <b>IIIb</b>	8.22	6.15	1.88	3.38 (CH), 1.07 (2Me)	180.20	170.44 (165.51)	167.08 (152.57)	97.66 (86.95)	116.42	18.89 (15.14)	27.36, 18.89 (27.07, 18.95)
<b>IIIc</b>	8.23	6.15	1.95	1.16	180.17	172.11 (166.00)	167.28 (152.76)	97.61 (86.92)	116.45	11.70 (10.94)	37.99, 27.21 (37.36, 27.49)
<b>III d</b>	8.23	6.13	3.07 (CH), 1.17 (2Me)	2.58 (CH), 1.12 (2Me)	179.78	176.69 (171.34)	167.04 (152.87)	96.97 (86.72)	116.05	31.27, 20.27 (31.46, 21.06)	29.13, 18.51 (28.86, 19.12)
<b>IIIe</b>	8.33	6.30	2.40	7.68 (2-H), 7.49–7.23 (3-H, 4-H)	180.12	162.93 (157.13)	166.90 (152.78)	98.33 (88.11)	116.45	13.91 (13.21)	133.85 C <sup><i>i</i></sup> , 131.05 C <sup><i>p</i></sup> , 128.79 C <sup><i>o</i></sup> , 126.81 C <sup><i>m</i></sup> (135.86 C <sup><i>i</i></sup> , 129.26 C <sup><i>p</i></sup> , 126.32 C <sup><i>o</i></sup> , 128.42 C <sup><i>m</i></sup> )

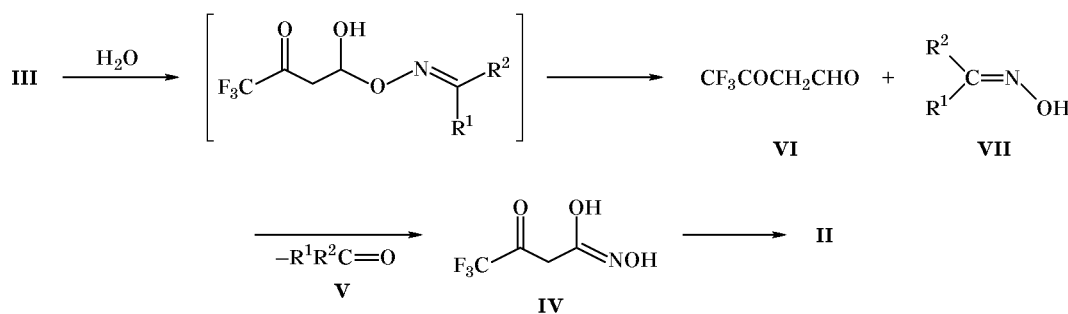
<sup>a</sup> For all the compounds,  $^3J(1\text{-H}, 2\text{-H}) = 12.3$  Hz,  $^1J(\text{C}, \text{F}) = 290.6$  Hz,  $^2J(\text{C}, \text{F}) = 35.1$  Hz.

<sup>b</sup> In parentheses are given the chemical shifts for the corresponding initial *O*-vinyloximes.

of products **III**, as compared to trifluoroacetyl derivatives of common vinyl ethers [1], may be attributed to side polymerization processes: Their distillation resulted in formation of a considerable amount of tars.

Due to the presence of activated C=C bond compounds **IIIa–IIIe** readily undergo hydrolysis to give 5-hydroxy-5-trifluoromethyl-4,5-dihydro-1,2-oxazole

(**II**) (Scheme 2; see also [7]). This scheme is supported by the  $^1\text{H}$  NMR spectra of samples exposed to atmospheric moisture (3 days, 18–20°C). The spectra contained signals belonging to compounds **III**, dihydrooxazole **II**, intermediate 4,4,4-trifluoro-3-oxobutylaldehyde oxime (**IV**), and also ketones **V**. In the  $^1\text{H}$  NMR spectrum of a mixture obtained by partial

**Scheme 2.**

**Table 3.** Absorption bands ( $\nu$ ,  $\text{cm}^{-1}$ ) in the IR spectra of *O*-(*trans*-4,4,4-trifluoro-3-oxo-1-butenyl)oximes **IIIa–IIIe**

Comp. no.	$\nu\text{C}=\text{O}$	$\nu\text{C}=\text{N}$	$\nu\text{C}=\text{C}$	$\delta\text{CF}_3$	$\tau\text{HC}=\text{CH}$	$\delta\text{R}^1, \text{R}^2$	$\nu\text{HC}=\text{CH}, \nu\text{R}^1, \text{R}^2$
<b>IIIa</b>	1711 s-m, 1691 m, 1680 m, 1700 <sup>a</sup> (75) <sup>b</sup>	1652 m, 1638 <sup>a</sup> (116) <sup>b</sup>	1598 v.s, 1598 <sup>a</sup> (880) <sup>b</sup>	1195 v.s, 1146 v.s	972 m	1433 m, 1372 m	3089 w, 3000 w, 2970 w, 2927 w
<b>IIIb</b>	1712 s-m, 1692 m	1643 m	1594 v.s	1196 v.s, 1147 v.s	972 m	1469 m, 1420 m, 1385 m, 1371 m	3093 w, 3052 w, 2975 s, 2938 m, 2879 m
<b>IIIc</b>	1712 s-m, 1692 m	1638 m	1597 v.s	1197 v.s, 1146 v.s	972 m	1480 m, 1465 m, 1399 w, 1370 s-m	2975 s, 2943 m, 2912 m, 2875 m
<b>III d</b>	1712 s-m, 1693 m	1642 m	1593 v.s	1195 v.s, 1146 v.s	971 m	1470 m, 1388 m, 1370 m	3086 w, 3052 w, 2974 s, 2939 m, 2879 m
<b>IIIe</b>	1712 s-m, 1691 m	1626 m	1592 v.s	1198 v.s, 1145 v.s	985 m	761 s, 692 s	3059 m, 2930 w, 2855 v.w

<sup>a</sup> Calculated frequency.<sup>b</sup> Relative intensity.

hydrolysis of oxime **IIIe** we observed a triplet at  $\delta$  6.48 ppm (=CH) and a doublet at  $\delta$  3.51 ppm ( $\text{CH}_2$ ,  $^3J = 5.68$  Hz), which can be assigned to intermediate **IV**; also, a singlet from the methyl protons of acetophenone was present at  $\delta$  2.60 ppm. The absence of signal from aldehyde proton of 4,4,4-trifluoro-3-oxobutyraldehyde (**VI**) in the downfield region of the spectrum ( $\delta$  9–10 ppm) suggests that the stages of water addition and cyclization are much slower than transoximation of ketone oxime **VII** with aldehyde **VI** (exchange of the oxime moiety between carbonyl compounds **VII** and **VI** is well known [11]).

### EXPERIMENTAL

The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker-400DPX instrument operating at 400.13 and 100.61 MHz, respectively; chloroform-*d* was used as solvent, and HMDS, as internal reference. The IR spectra were obtained on a Bruker ISF25 spectrometer from samples prepared as thin films.

*O*-Vinyloximes **Ia–Ie** were synthesized by vinylation of the corresponding ketone oximes with acetylene in the system KOH–DMSO under pressure [5, 6]. The *E/Z*-isomer ratio of compound **Ib** (7:1) was determined by  $^1\text{H}$  NMR spectroscopy; the assignment of *E*- and *Z*-configurations was made on the basis of the  $^{13}\text{C}$  NMR data [12].

***O*-(*trans*-4,4,4-Trifluoro-3-oxo-1-butenyl)oximes III (general procedure).** A solution of 6.30 g (30 mmol) of trifluoroacetic anhydride in 5 ml of diethyl ether was added dropwise with stirring at 18–20°C to a solution of 10 mmol of appropriate ketone *O*-vinyloxime **I** and 0.87 g (11 mmol) of pyridine in 5 ml of diethyl ether. The time of addition was 30 min. The mixture was then stirred for 2.5 h, the solvent was distilled off, and the residue was distilled in vacuo. In the synthesis of compounds **IIIb–IIIe**, pyridinium trifluoroacetate was preliminarily removed by flash chromatography on a dry column charged with silica gel (5–40  $\mu\text{m}$ ) containing an LL<sub>254</sub> luminescent indicator (the adsorbent was calcined for 5 h at 140°C; eluent diethyl ether).

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