An unusually fast nucleophilic addition of amidoximes to acetylene

Boris A. Trofimov, Elena Yu. Schmidt,* Al'bina I. Mikhaleva, Alexander M. Vasil'tsov and Andrey V. Afonin

Irkutsk Institute of Chemistry, Siberian Branch of the Russian Academy of Sciences, 664033 Irkutsk, Russian Federation. Fax: +7 3952 39 6046; e-mail: lschmidt@irioch.irk.ru

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The addition of amidoximes to acetylene in the presence of the KOH–DMSO superbase system afforded *O*-vinylamidoximes in 26–59% yields.

The oxime function is capable of adding to the carbon–carbon triple bond at its either oxygen or nitrogen site depending on the structure of the reactant and on the reaction conditions.[1–4] In the presence of superbases such as the KOH–DMSO system, ketoximes react with acetylene to form *O*-vinylketoximes which are further rearranged to pyrroles (the Trofimov reaction),[1,2,5,6] whereas aldoximes are dehydrated to nitriles under the same conditions.[1,2] However, the nucleophilic addition of amidoximes to acetylenes has not been adequately studied.

Thus, amidoximes react with propiolates to form imidazole derivatives *via* O-adducts.[7] Diacetylene, in the presence of KOH in aqueous DMSO, adds amidoximes at 22–36 °C to give unstable *O*-1-but-1-en-3-ynyl ethers in 21–24.5% yields.[8] Consequently, only very reactive ('activated') acetylenes are able to add amidoximes. At the same time, the reaction of amidoxime multident anions with simpler acetylenes might contribute both to a better understanding of nucleophilic addition at triple bonds and to the chemistry of building blocks.

Our study of these compounds has shown that amidoximes **1a**,**b** are able to readily add to acetylene in a short contact (5–7 min) at about 75 °C under a pressure of 12–14 atm in the KOH–DMSO superbase system to afford *O*-vinylamidoximes **3a**,**b** in 26 and 59% yields, respectively.†

The structure of adducts **3a**,**b** unambiguously follows from an excellent agreement between the ^{1}H and ^{13}C NMR and IR spectra of these adducts and *O*-vinylketoximes.[3,4]

The ^{1}H and ^{13}C NMR spectra of **1a** and **3a** show only a signal due to methyl groups, whereas there is a set of signals corresponding to a phenyl ring in the spectra of **1b** and **3b**. This suggests the presence of only one configurational isomer.

In order to identify the isomers of amidoximes **1a**,**b**, the direct ^{13}C–^{13}C coupling constants involving the oxime group carbon (53.0 and 67.2 Hz, respectively) were measured and compared to the coupling constants in acetamides and benzamides (49.5 and 62.4 Hz, respectively). In amidoximes **1a**,**b**, an increase in the ^{13}C–^{13}C coupling constant by 3.5 and 4.8 Hz, respectively, with respect to the isostructural amides was observed. This result is in good agreement with the *Z*-form of compounds **1a**,**b**.[9]

To support this conclusion, a ^{1}H NMR spectrum of acetamidoxime **1a** was recorded in the presence of the broadening paramagnetic reagent Gd(fod)$_3$. An additive of Gd(fod)$_3$ causes an abrupt broadening of the Me group signal due to paramagnetic relaxation proportional to r^{-6} (where r is the distance from the paramagnetic centre to the proton observed) and due to Gd(fod)$_3$ coordination to the iminic nitrogen in the *cis*-arrangement of the paramagnetic centre with respect to the Me group (*Z*-isomer);[10] the NH$_2$ group signal remained unaffected.

In the spectra of *O*-vinylamidoximes, the methyl group chemical shift and the ^{13}C–^{13}C coupling constants $^1J_{1\text{-Me}}$ in **3a**, as well as the chemical shift of the phenyl ring *ipso*-carbon and the ^{13}C–^{13}C coupling constants $^1J_{1\text{-ipso}}$ in **3b**, changed only slightly. This indicates that *O*-vinylamidoximes **3a**,**b** exhibit the same configuration as the initial amidoximes **1a**,**b**.[9,11]

Therefore, neither nitrogen-centred anionic species of the starting amidoximes, nor those of their apparent tautomers **2** are able to successfully compete with the oxygen-centred anions during the nucleophilic addition to acetylene under the above conditions. Heterocycles **4**–**6**, which were expected from cyclizations of adducts **3**, were not detected in the reaction mixture, probably, because of a relatively low temperature (as compared

† ^{1}H NMR (400.13 MHz), ^{13}C NMR (101.61 MHz) in $CDCl_3$, TMS as a standard.

O-Vinylacetamidoxime **3a**: n_D^{20} 1.5682. A mixture of 3.7 g (50 mmol) of amidoxime **1a** and 2.7 g (48 mmol) of KOH in 100 ml of DMSO was saturated with acetylene (12–14 atm), heated to 75 °C and immediately cooled to room temperature. The mixture was diluted with 200 ml of water and extracted with diethyl ether (4×20 ml). The extract was washed with water (4×5 ml) and dried over $MgSO_4$. After the removal of diethyl ether and purification of the residue by column chromatography (SiO_2, diethyl ether:pentane, 1:3), 1.3 g (26%) of *O*-vinylamidoxime **3a** was obtained. ^{1}H NMR, δ: 6.72 (dd, 1H, H$_\alpha$, $^3J_{\alpha-\beta}$ 14.0 Hz, $^3J_{\alpha-\beta'}$ 6.8 Hz), 4.62 (br. s, 2H, NH$_2$), 4.55 (dd, 1H, H$_\beta$, $^3J_{\alpha-\beta}$ 14.0 Hz, $^2J_{\beta-\beta'}$ 1.6 Hz), 4.01 (dd, 1H, H$_{\beta'}$, $^3J_{\alpha-\beta'}$ 6.8 Hz, $^2J_{\beta-\beta'}$ 1.6 Hz), 1.85 (s, 3H, Me). ^{13}C NMR, δ: 153.44 [C(1), $^1J_{1-\text{Me}}$ 52.6 Hz], 153.23 [C(2), $^1J_{2-3}$ 80.2 Hz], 85.70 [C(3), $^1J_{2-3}$ 80.2 Hz], 16.55 (Me). IR (neat, ν/cm^{-1}): 3475, 3340 (NH$_2$), 3085 (=CH$_2$), 1655 (C=N), 1630, 1615 (C=C), 1190 (C–O), 1170 (C=C), 960 (CH=CH), 835 (C=CH).

O-Vinylbenzamidoxime **3b** was prepared analogously in 59% yield, n_D^{20} 1.5806. ^{1}H NMR, δ: 7.65, 7.39 (m, 5H, Ph), 6.88 (dd, 1H, H$_\alpha$, $^3J_{\alpha-\beta}$ 14.0 Hz, $^3J_{\alpha-\beta'}$ 6.8 Hz), 4.95 (br. s, 2H, NH$_2$), 4.66 (dd, 1H, H$_\beta$, $^3J_{\alpha-\beta}$ 14.0 Hz, $^2J_{\beta-\beta'}$ 1.6 Hz), 4.13 (dd, 1H, H$_{\beta'}$, $^3J_{\alpha-\beta'}$ 6.8 Hz, $^2J_{\beta-\beta'}$ 1.6 Hz). ^{13}C NMR, δ: 154.37 [C(1), $^1J_{1-ipso}$ 65.7 Hz], 153.23 [C(2), $^1J_{2-3}$ 80.2 Hz], 133.08 (C$_{ipso}$, $^1J_{1-ipso}$ 65.7 Hz), 130.70 (C$_{para}$, $^1J_{para-meta}$ 55.4 Hz), 129.07 (C$_{meta}$, $^1J_{meta-ortho}$ 56.4 Hz), 126.91 (C$_{orto}$, $^1J_{ortho-ipso}$ 58.8 Hz), 87.36 [C(3), $^1J_{2-3}$ 80.2 Hz]. IR (neat, ν/cm^{-1}): 3490, 3390 (NH$_2$), 1645 (C=N), 1620 (NH$_2$), 1600 (C=C), 1185 (C–O), 1160 (C=C), 960 (CH=CH), 845 (C=CH).

with other nucleophilic additions to acetylene) and a short contact time. The latter are also supposed to be the factors that allow the O-vinylation to compete with the anticipated nucleophilic substitution of the amino group in amidoximes **1** (hydrolysis of anion **7**) or deoximation.

At the same time, the moderate yields of adducts **3** can also result from the above hydrolytic processes.

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