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SHORT COMMUNICATIONS

Dedicated to Full Member of the Russian Academy of Sciences N.S. Zefirov on His 70th Anniversary

Microwave-Assisted Direct Solid-Phase Transformation of 3-Trimethylsilyl- and 3-Triethylgermyl-2-propynols into Imidazo[1,2-*a*]pyridine-3-carbaldehyde

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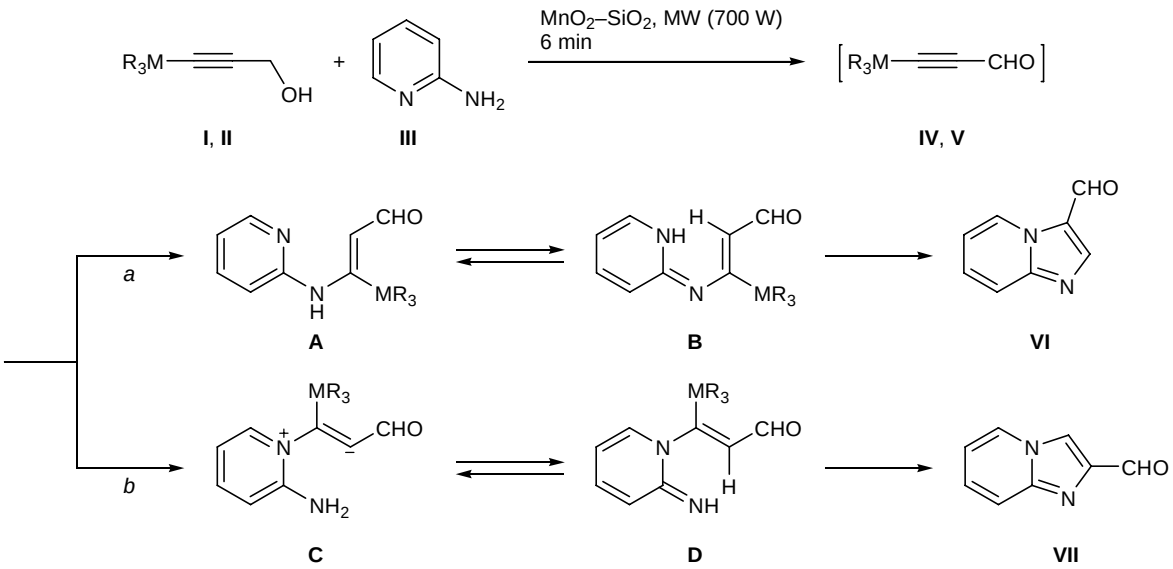
We recently developed a highly effective one-step procedure for solid-phase synthesis of heteroelement-containing 1,3-azaenynes from acetylenic alcohols and primary amines by the action of MnO_2–SiO_2 under microwave irradiation [1]. Surprisingly, in the reactions of 3-trimethylsilyl- and 3-triethygermyl-2-propynols **I** and **II** with 2-aminopyridine (**III**), which were performed under analogous conditions, we isolated 30% of imidazo[1,2-*a*]pyridine-3-carbaldehyde (**VI**) together with the expected Schiff bases $R_3MC{\equiv}C$–CH=N–Py-2 (R_3M = Me_3Si, Et_3Ge). Presumably, the formation of heterocyclic aldehyde **VI** is preceded by nucleophilic addition of 2-aminopyridine (**III**) at the triple bond of intermediate propynals **IV** and **V**. Next follows enamine–imine isomerization of β-aminoenal **A** into **B** and dehydrogenation according to path *a* in Scheme 1.

Taking into account that 2-aminopyridines may be regarded as 1,3-difunctional nitrogen-centered nucleophiles [2], another reaction path is possible (path *b* in Scheme 1). This path implies reaction of propynals **IV** and **V** at the ring nitrogen atom of 2-aminopyridine (**III**) to produce zwitterionic intermediate **C**, which can be converted into imine **D** via intramolecular proton

Scheme 1.



I, **IV**, R_3M = Me_3Si; **II**, **V**, R_3M = Et_3Ge.

transfer from the amino group to the α-carbon atom with rupture of the pyridine aromatic system. Oxidative cyclization of **D** could give rise to isomeric imidazo[1,2-*a*]pyridine-2-carbaldehyde (**VII**). It is known that 2-amino-3-hydroxypyridine reacts with ethyl 3-trifluoromethylpropynoate at the triple bond of the latter to afford adduct like **D** [3].

The structure of product **VI** was studied by IR and NMR spectroscopy (^{1}H, ^{13}C; COSY, COSYLR, NOESY, HMBC, HSQC) and mass spectrometry. The HMBC spectrum revealed a cross peak between 2-H and C^{8a} while no cross peak with C^5 was present. These data indicate that the product has structure **VI** rather than **VII**.

When the reaction of 3-trimethylsilyl-2-propynol (**I**) with 2-aminopyridine (**III**) and MnO_2–SiO_2 was carried out under classical conditions (by heating for 8 h in boiling methylene chloride), only traces of aldehyde **VI** were detected by ^{1}H NMR spectroscopy, while the major product was the corresponding Schiff base. We previously showed that under conventional conditions silicon- and germanium-containing propynals and their carbon analog, 3-*tert*-butylpropynal, chemoselectively take up primary amines at the aldehyde group to give acetylenic Schiff bases in almost quantitative yield [4]. Ebetino *et al*. described a three-step procedure for the synthesis of imidazo[1,2-*a*]pyridine-3-carbaldehyde (**VI**) from 2-aminopyridine and chloroacetaldehyde in no more than 30% yield while preparing 2-hydroxy-3-(imidazo[1,2-*a*]pyridin-3-yl)-2-phosphonopropionic acid which is an efficient antiphlogistic agent [5].

Imidazo[1,2-*a*]pyridine-3-carbaldehyde (VI). A mixture of 0.8708 g (4 mmol) of alcohol **II** and 0.3432 g (3.65 mmol) of amine **III** was thoroughly ground with 6.8 g (20 mmol) of MnO_2–SiO_2, and the resulting mixture was placed in a 20-ml Teflon reactor with a screw cap (the volume of the reaction mixture should not exceed 1/10–1/12 of the reactor volume). The mixture was irradiated in an LG MS-1904H microwave furnace at a power of 700 W over a period of 6 min in 1-min pulses with subsequent cooling to room temperature. The mixture was then treated with 40 ml of a 10:1 $CHCl_3$–MeOH mixture. The extract was evaporated under reduced pressure, and the solid residue was analyzed by ^{1}H NMR spectroscopy. The yield of compound **VI** was 30% (calculated on initial amine **III**). By preparative chromatography on aluminum oxide (eluent $CHCl_3$–MeOH, 200:1, by volume) we isolated 85 mg of **VI** as an orange–red crystalline substance, mp 103–104°C (from $CHCl_3$). IR spectrum (KBr), ν, cm^{-1}: 1645 (C=O), 1615 (C=C). ^{1}H NMR spectrum, δ, ppm: 7.15 d.d (1H, 6-H, $^3J_{5,6}$ = 6.6, $^3J_{6,7}$ = 7.0 Hz), 7.59 d.d (1H, 7-H, $^3J_{7,8}$ = 8.9 Hz), 7.85 d (1H, 8-H), 8.33 s (1H, 2-H), 9.52 d (1H, 5-H), 9.98 s (1H, CH=O). ^{13}C NMR spectrum, δ_C, ppm: 115.55 (C^6), 117.95 (C^8), 125.06 (C^3), 128.77 (C^5), 130.19 (C^7), 146.92 (C^2), 149.45 (C^{8a}), 177.93 (CH=O). Mass spectrum, *m*/*z* (I_{rel}, %): 146 (100) $[M]^+$, 117 (17) $[M - CHO]^+$, 90 (40), 78 (15), 63 (39), 51 (37), 39 (50). Found, %: C 65.10; H 4.17; N 18.73. $C_8H_6N_2O$. Calculated, %: C 65.75; H 4.14; N 19.17.

The IR spectrum was recorded on a Specord 75IR spectrometer. The ^{1}H and ^{13}C NMR spectra were measured on a Bruker DPX-400 instrument using $CDCl_3$ as solvent and HMDS as internal reference.

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