The first synthesis of tetrahydrobenzo[b]pyrrolo[2,1-*f*][1,6]naphthyridine by the Michael addition of butyn-2-one to 1-(2-methoxycarbonylvinyl)tetrahydrobenzo[*b*][1,6]naphthyridine

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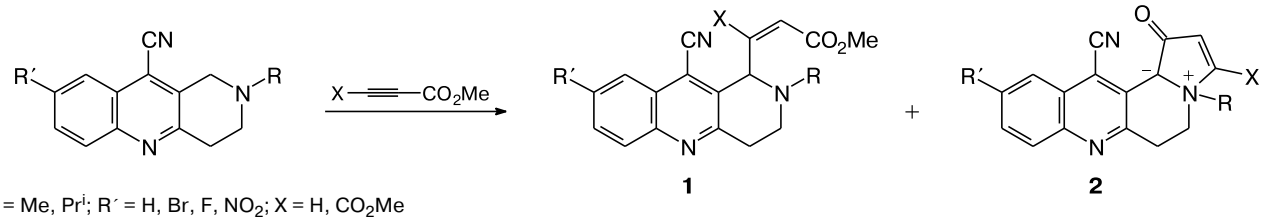
The reaction of 10-cyanotetrahydrobenzo[*b*][1,6]naphthyridines with activated alkynes results in a mixture of 1-methoxycarbonyl- or 1,2-dimethoxycarbonylvinyl-substituted tetrahydrobenzonaphthyridines **1** and ammonium ylides derived from tetrahydrobenzo[*b*]pyrrolo-[2,1-*f*][1,6]naphthyridine **2**.[1] The formation of the latter is caused by the Stevens rearrangement or by attack of the anionic center on the ester group in the intermediate ylide (Scheme 1).

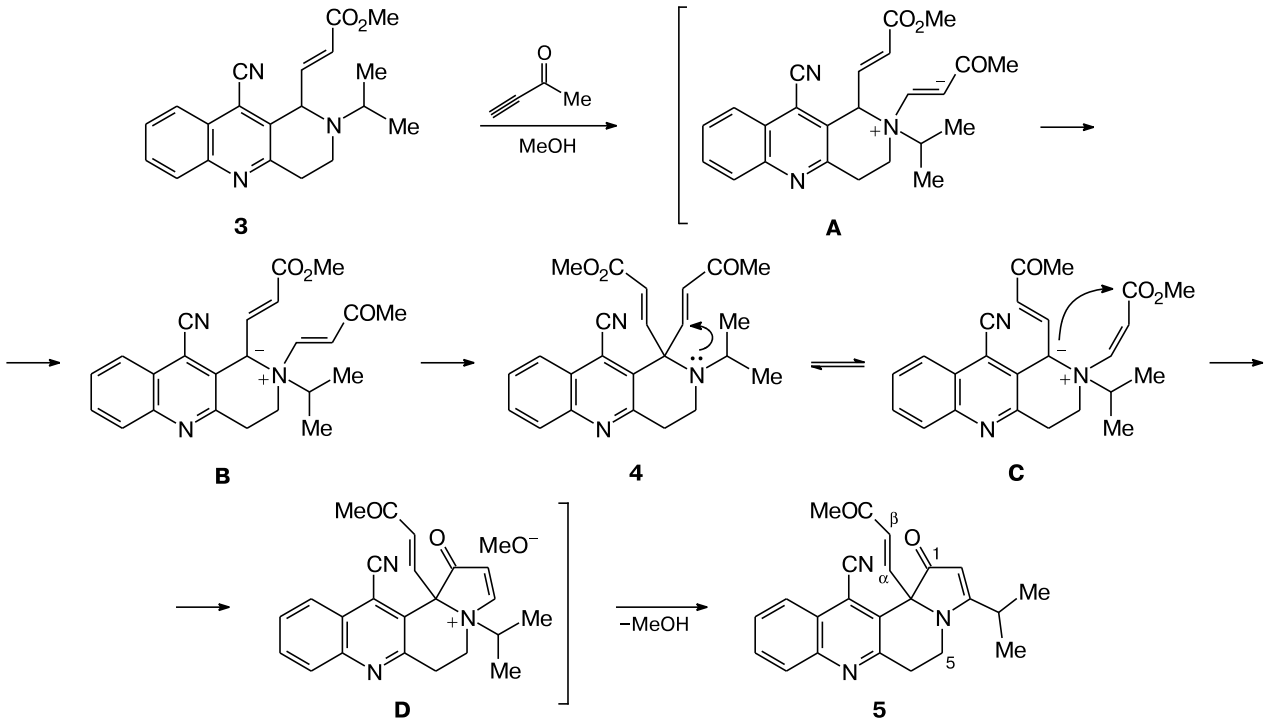
It was of interest to prepare 1,1-di(vinyl)-substituted benzonaphthyridines using the reaction of compounds **1** with activated alkynes and to carry out the synthesis of

Scheme 1



R = Me, Pr^i; R′ = H, Br, F, NO_2; X = H, CO_2Me

Scheme 2



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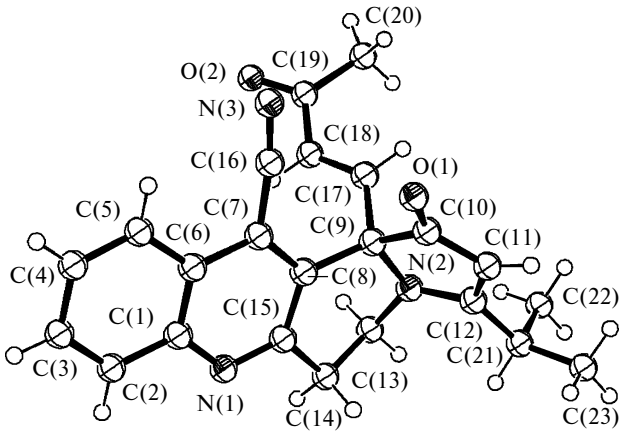

Fig. 1. X-Ray structure of compound **5**.

tetrahydrobenzonaphthyridines spiroannulated at the position 1 through transformation of functional groups of the vinyl substituents.

However, the reaction of 1-(1-methoxycarbonylvinyl)-substituted tetrahydronaphthyridine **3** with an excess of acetylacetylene at 20 °C in MeOH led to (3-oxobutenyl)-substituted tetrahydrobenzo[b]pyrrolo[2,1-*f*][1,6]naphthyridine **5** instead of the expected divinyl-substituted compound **4** (Scheme 2).

By analogy with our studies,[1,2] the formation of intermediate **4** *via* zwitterion **A** and ylide **B** could be supposed. Presumably, the transformation of compound **4** proceeds through the retro-Stevens rearrangement with formation of ylide **C**, which transforms into quaternary salt **D** upon intramolecular cyclization. The migration of the isopropyl group from the nitrogen atom to the α-position of the pyrrole ring followed by elimination of a methanol molecule leads to benzopyrrolonaphthyridine **5**, whose structure was established by X-ray analysis (Fig. 1).

Experimental

The mass spectrum (ESI) was obtained on an Agilent 1100 Series LC/MSD Trap System VL spectrometer. The ^{1}H NMR spectrum was recorded on a Varian Unity 400 spectrometer (the operating frequency is 400 MHz) in $CDCl_3$, using the solvent signals as the internal standard. X-ray crystallographic data were collected at 293 K using a Bruker P4 diffractometer (Mo-Kα-radiation). All subsequent calculations were performed using the complex of programs SHELX-97.[3]

3-Isopropyl-1-oxo-12b-[(1*E*)-3-oxobuten-1-yl]-1,5,6,12b-tetrahydrobenzo[*b*]pyrrolo[2,1-*f*]-1,6-naphthyridine-12-carbonitrile (5). A solution of 1-methoxycarbonylvinyl-substituted naphthyridine **3** (2.0 g, 6 mmol) and acetylacetylene (0.6 g, 12 mmol) in 20 mL of dry methanol was stirred for 2 weeks at 20 °C (the reaction was monitored by TLC (Silufol, ethyl acetate)). After disappearance of the starting compound the solvent was evaporated, the remained pale brown oil was recrystallized from ether to obtain 0.26 g (11%) of compound **5** as pale yellow crystals, m.p. 111—113 °C. ^{1}H NMR (chloroform-d, δ, *J*/Hz): 1.29 (d, 3 H, $\underline{Me_2}CH$, J = 7.5); 1.31 (d, 3 H, $\underline{Me_2}CH$, J = 7.5); 2.08 (s, 3 H, O=C—CH_3); 2.89—2.91 (m, 1 H, $Me_2\underline{CH}$); 3.22—3.31 (m, 2 H, C(6)H_2); 4.00—4.03 (m, 2 H, C(5)H_2); 5.21 (s, 1 H, C(2)H); 6.16 (d, 1 H, CH-β, J = 12.5); 6.54 (d, 1 H, CH-α, J = 12.5); 7.71—7.81 (m, 2 H, C(9)H+C(10)H); 8.06 (d, 1 H, C(11)H, J = 8.9); 8.31 (d, 1 H, C(8)H, J = 8.9). Mass spectrum, *m/z*: 388 $[M + H]^+$. Found (%): C, 74.28; H, 5.46; N, 10.91. $C_{24}H_{25}O_2$. Calculated (%): C, 74.37; H, 5.70; N, 11.31.

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