Chelate synthesis of 1-alkyl-5-trifluoromethyl-1,6-naphthyridine-(1*H*)-4-ones

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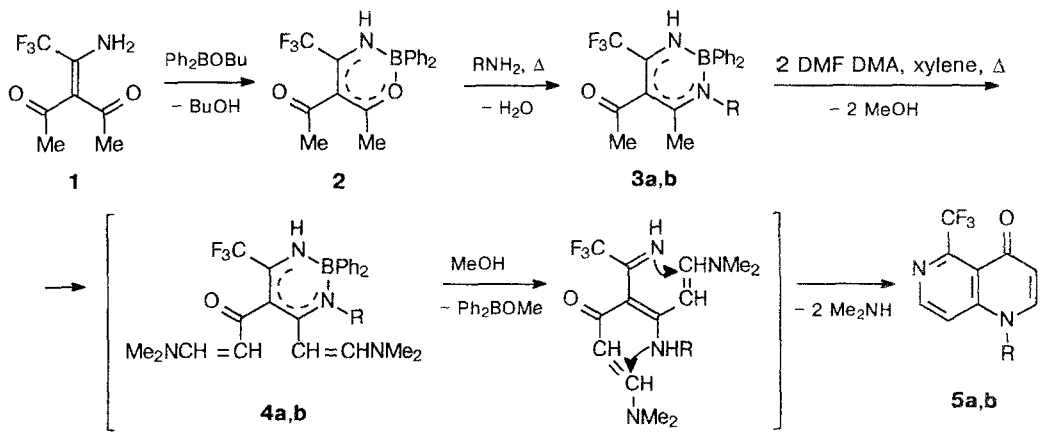
Recently, a convenient synthesis of 3-acetyl-4-amino-5,5,5-trifluoro-3-pentene-2-one (**1**), an important building block for the preparation of heterocyclic compounds (in particular, pyrimidines) with a CF_3 moiety was described.[1] We have found that cyclic systems can also be formed from enaminone **1** using "chelate methodology". In the present communication we propose an original and effecient approach to the synthesis of the 1,6-naphthyridine system from **1** *via* its chelate complexes with boron. Treatment of compound **1** with Ph_2BOBu gives rise to the diphenylboron chelate **2**, which upon heating with primary amines is transformed into complexes **3a,b**. The latter react with 2 moles of dimethylformamide dimethylacetal (DMF DMA) in boiling xylene to give the hitherto unknown 5-trifluoromethyl-1,6-naphthyridine-(1*H*)-4-ones (**5a,b**) in 77—87 % yield (Scheme).

The intermediate chelates (**4a,b**) are probably formed from β-diiminates **3** and DMF DMA as a result of condensation at the methyl groups. The methanol evolved causes the deborylation of complexes **4** accompanied by the cyclization of the ligands as a result of the elimination of two molecules of Me_2NH. The structures of chelates **2**, **3a,b**, and naphthyridines **5a,b** were confirmed by elemental analysis data and spectral methods (IR-, ^1H-, ^{13}C NMR, and MS).

All operations were carried out under nitrogen.

Diphenylboron complex of 3-acetyl-4-amino-5,5,5-trifluoro-3-pentene-2-one (2). A mixture of 9.0 g (46 mmol) of **1** and 12.06 g (50.7 mmol) of Ph_2BOBu in 75 mL of ether was stirred for 3 h and allowed to stand for 12 h. The solvent and BuOH were evaporated *in vacuo*, 100 mL of pentane were added to the residue, and the precipitate was filtered off and washed with pentane yielding 93.5% of chelate **2** (15.36 g), m.p. 132—133.5 °C. MS, *m/z*: 359 $[M]^{+\cdot}$; 282 $[M-Ph]^+$. IR spectrum (CH_2Cl_2, ν/cm^{-1}): 3375 (NH), 1700 (CO). ^1H NMR spectrum ($CDCl_3$, δ, ppm): 2.32 (s, 3 H, MeCO); 2.43 (s, 3 H, MeCOB); 7.25—7.40 (m, 10 H, 2Ph), 7.58 (b.s, 1 H, NH). ^{13}C NMR spectrum ($CDCl_3$, δ, ppm, *J*/Hz): 24.24 (q, MeCOB, J = 130); 32.34 (b.q, MeCO, J = 129); 111.50 (b.s, AcCAc); 118.85 (q, CF_3, $J_{C,F}$ = 281); 155.61 (q, CF_3C); 127.16; 127.57; 131.74; 146.0 (2Ph); 187.80 (q, COB); 196.83 (q, C=O). ^{11}B NMR spectrum ($CDCl_3$, δ, ppm): +3.9.

Diphenylboron complex of 3-(1'-amino-2',2',2'-trifluoro)ethylidene-4-butyliminopentane-2-one (3a). A mixture of 1.0 g (2.8 mmol) of **2** and 0.4 g (5.6 mmol) of



1 **2** **3a,b** **4a,b** **5a,b**

R = *n*-Bu (**a**), $PhCH_2$ (**b**)

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n-$BuNH_2$ in 5 mL of THF was refluxed for 6 h. The solvent was evaporated and the residue was chromatographed on a column of SiO_2 (eluent: C_6H_6) resulting in 0.85 g (73.5%) of chelate **3a**, m. p. 116.5—117 °C. IR spectrum (CH_2Cl_2, ν/cm^{-1}): 3396 (NH), 1690 (C=O). ^1H NMR spectrum ($CDCl_3$, δ, ppm): 0.57 (t, 3 H, Me); 0.90 (m, 2 H, CH_2); 1.10 (m, 2 H, CH_2); 2.18 (s, 3 H, MeCO); 2.36 (s, 3 H, MeCN); 3.29 (m, 2 H, CH_2N); 6.21 (b.s, 1 H, NH); 7.2—7.4 (m, 10 H, 2Ph). ^{13}C NMR spectrum ($CDCl_3$, δ, ppm, *J*/Hz): 13.13 (q, Me, J = 124); 18.24 (q, MeCN, J = 130); 20.00 (t, CH_2); 30.55 (t, CH_2); 33.39 (q, MeCO, J = 126); 50.57 (t, CH_2N); 108.88 (s, AcC); 120.12 (q, CF_3, $J_{C,F}$ = 279); 126.68; 127.32; 133.24; 148 (2Ph); 147.93 (CF_3C); 165.54 (C=N); 199.38 (CO).

Diphenylboron complex of 3-(1'-amino-2',2',2'-trifluoro)ethylidene-4-benzyliminopentane-2-one (3b) was obtained from **2** and $PhCH_2NH_2$ using the procedure described for the preparation of chelate **3a**. Yield 65%, m.p. 139—140 °C.

1-Butyl-5-trifluoromethyl-1,6-naphthyridine-(1*H*)-4-one (5a). A mixture of 0.36 g (0.87 mmol) of chelate **3a** and 0.31 g (2.61 mmol) of DMF DMA in 15 mL of xylene was refluxed for 3 h. The solvent was evaporated *in vacuo* and the residue was chromatographed on a column of SiO_2 (eluent: C_6H_6 — $CHCl_3$) resulting in 0.20 g (87%) of naphthyridinone **5a**, m.p. 143—145 °C. MS, *m/z*: 270 $[M]^{+\cdot}$. IR spectrum (CH_2Cl_2, ν/cm^{-1}): 1655 (C=O). ^1H NMR spectrum ($CDCl_3$, δ, ppm): 0.99 (t, 3 H, Me); 1.43 (m, 2 H, CH_2); 1.82 (m, 2 H, CH_2); 4.09 (t, 2 H, CH_2N); 6.33 (d, 1 H, H-3); 7.43 (d, 1 H, H-8); 7.49 (d, 1 H, H-2); 8.67 (d, 1 H, H-7). ^{13}C NMR spectrum ($CDCl_3$, δ, ppm, *J*/Hz): 13.37 (q, Me, J = 126); 19.68 (t, CH_2, J = 125); 30.40 (t, CH_2, J = 126); 33.16 (t, CH_2N, J = 139); 113.10 (d, C-8, J = 165); 115.01 (d, C-3, J = 168); 120.13 (C-4a); 121.54 (q, CF_3, $J_{C,F}$ = 275); 143.02 (d, C-2, J = 177); 146.81 (m, C-8a); 147.63 (d, C-7, J = 184); 148.05 (q, C-5); 175.14 (d, C=O).

1-Benzyl-5-trifluoromethyl-1,6-naphthyridine-(1*H*)-4-one (5b) was obtained from **3b** using the procedure described for the preparation of **5a**. Yield 77%, m.p. 175—176 °C.

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References

1. V. A. Dorokhov, A. V. Komkov, L. S. Vasil'ev, O. G. Azarevich, and M. F. Gordeev, *Izv. AN SSSR. Ser. khim.*, 1991, 2639 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1991, **40**, 2311].

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