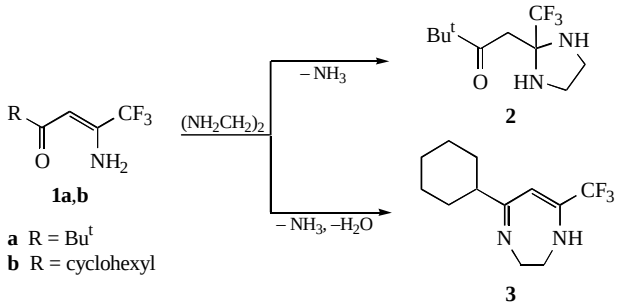
A novel synthesis of 2-acylmethyleneimidazolidines

Vyacheslav Ya. Sosnovskikh* and Michail Yu. Mel'nikov

Department of Chemistry, A. M. Gor'ky Urals State University, 620083 Ekaterinburg, Russian Federation. Fax: +7 3432 61 5978; e-mail: Vyacheslav.Sosnovskikh@usu.ru

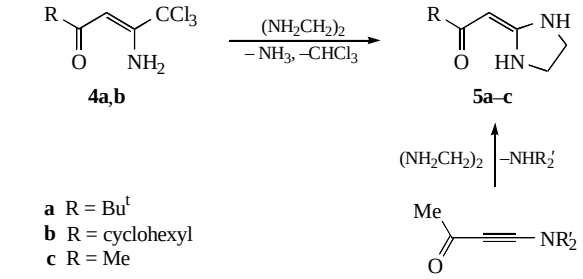
The reaction of aliphatic β-amino-β-trichloromethyl vinyl ketones with ethylenediamine gives 2-acylmethyleneimidazolidines.

We have shown recently[1] that the reactions of aliphatic β-amino-β-trifluoromethyl vinyl ketones with ethylenediamine are very sensitive to steric factors under conditions of kinetic control (at room temperature without a solvent). For example, aminoenone **1a** obtained from pinacolone and trifluoroacetonitrile affords, under these conditions, imidazolidine **2**, whereas aminoenone **1b** with a cyclohexyl substituent at the carbonyl group results in the formation of dihydrodiazepine **3**.



a R = Bu^t
b R = cyclohexyl

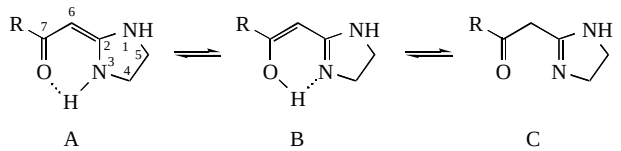
Taking into account these results and the ability of the CCl_3 group to be substituted under the action of N-nucleophiles,[2] we studied the reactions of aliphatic β-amino-β-trichloromethyl vinyl ketones **4a**,**b** with ethylenediamine and found that this reaction occurs as a double nucleophilic attack at the β-carbon atom. However, unlike CF_3-containing aminoenones, it is accompanied by substitution of the amino and trichloromethyl groups resulting in the formation of 2-acylmethyleneimidazolidines **5a**,**b**. The yields of compounds **5a**,**b** are 48% and 50%, respectively, since the reaction is complicated by the formation of by-products, which were not studied in detail.



a R = Bu^t
b R = cyclohexyl
c R = Me

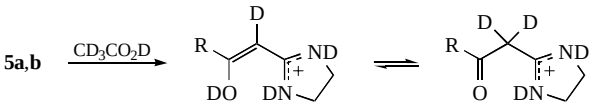
Compound **5c** was previously[3] obtained by the reactions of ethylenediamine with 4-dialkylamino-3-butyn-2-ones, which allows one to consider aminoenones **4** as synthetic equivalents of the relatively inaccessible β-aminoethynyl ketones.

Theoretically, imidazolidines **5**, as β-aminovinyl ketones, can exist in three tautomeric forms: ketoenamine (A), iminoenole (B) and ketoimine (C), and the content of the latter, based on the absence of the *exo*-methylene group signal in the ^{1}H NMR spectra, does not exceed 5%.



The compound **5c** was described in ref. 3 as an enolic tautomer B, by analogy with 1-benzyl-2-(2-hydroxyprop-1-enyl)-4,5-dihydroimidazole **6**, to which structure B was ascribed on the basis of the spectroscopic and crystallographic data.[†,4] It is noteworthy that the data presented in refs. 3 and 4 for compounds **5c** and **6** do not contradict the ketoenamine tautomer A, since the bands at 3300 and 3270 cm^{-1} and the chemical shifts at 9.1 and 9.5 ppm assigned to the OH group can also be attributed to the hydrogen-bonded NH, and the crystallographic data only indicate the delocalised character of the C(2)–C(6) and C(6)–C(7) bonds in the crystals of dihydroimidazole **6**. Furthermore, the Me group signals in these compounds are described as singlets implying the lack of the expected allylic coupling between the Me and =CH groups in **5c** and **6** (which should be present in the enolic form B).[5]

The ^{1}H NMR spectrum of compound **5a** exhibits two multiplets AA′BB′ due to the spin system of the CH_2 group protons of the imidazolidine ring with centres at 3.51 and 3.67 ppm, a singlet due to the vinyl proton at 4.89 ppm, and broadened signals due to the NH protons at 4.83 and 9.34 ppm, the latter belonging to the hydrogen atom involved in the formation of the intramolecular hydrogen bond. When deuterioacetic acid is added, the signals of the vinyl and NH protons disappear and the multiplets of the CH_2 groups merge to form a singlet at 3.82 ppm indicating a fast H/D exchange and formation of a symmetrically delocalised imidazolinium monocation **7a**. A similar situation was observed for imidazolidine **5b**.[‡]



† *2-(2-Hydroxyprop-1-enyl)-4,5-dihydroimidazole* **5c**.[3] ^{1}H NMR (100 MHz, $CDCl_3$) δ: 1.90 (s, 3H, Me), 3.55 (m, 4H, CH_2CH_2), 4.67 (s, 1H, =CH), 9.09 (s, 1H, OH). IR (KBr disc, ν/cm^{-1}): 3300 (OH), 1620 (C=C).

1-Benzyl-2-(2-hydroxyprop-1-enyl)-4,5-dihydroimidazole **6**.[4] The bond lengths C(2)–C(6) and C(6)–C(7) are both 1.39 Å, intermediate between a double and a single bond. ^{1}H NMR (100 MHz, $CDCl_3$) δ: 2.0 (s, 3H, Me), 3.2–3.7 (m, 4H, CH_2CH_2), 4.3 (s, 2H, CH_2Ph), 4.85 (s, 1H, =CH, exchanges with D_2O), 7.4 (s, 5H, Ph), 9.5 (br. s, 1H, OH, exchanges with D_2O). IR (KBr disc, ν/cm^{-1}): 3280, 1605, 1530 (br.).

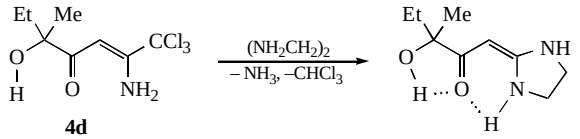
‡ *2-Pivaloylmethyleneimidazolidine* **5a**. Aminoenone **4a** (305 mg, 1.25 mmol) was dissolved in 300 μl (270 mg, 4.5 mmol) of ethylenediamine, and the reaction mixture was kept for 6–7 days at room temperature. The resulting crystals of imidazolidine **5a** were washed with water and recrystallised from CCl_4, yield 100 mg (48%), mp 183–184 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.12 (s, 9H, Bu^t), 3.51 (m, 2H, CH_2), 3.67 (m, 2H, CH_2), 4.83 (br. s, 1H, NH), 4.89 (s, 1H, =CH), 9.34 (br. s, 1H, NH); after addition of CD_3CO_2D: 1.13 (s, 9H, Bu^t), 3.82 (s, 4H, CH_2CH_2). IR (Vaseline oil, ν/cm^{-1}): 3300, 3240, 3150 (NH), 3040 (=CH), 1620 (C=O), 1545 (br., C=C, NH). Found (%): C, 64.10; H, 9.81; N, 16.66. Calc. for $C_9H_{16}N_2O$ (%): C, 64.25; H, 9.59; N, 16.65.

2-Cyclohexylcarbonylmethyleneimidazolidine **5b**. Yield 50%, mp 162–163 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.1–1.8 (m, 10H, cyclohexyl), 2.1 (m, 1H, CH of cyclohexyl), 3.51 (m, 2H, CH_2), 3.67 (m, 2H, CH_2), 4.55 (br. s, 1H, NH), 4.72 (s, 1H, =CH), 9.30 (br. s, 1H, NH); after addition of CD_3CO_2D: 1.1–1.8 (m, 10H, cyclohexyl), 2.3 (m, 1H, CH of cyclohexyl), 3.80 (s, 4H, CH_2CH_2). IR (Vaseline oil, ν/cm^{-1}): 3310, 3230, 3140 (NH), 1620 (C=O), 1545 (br, C=C, NH). Found (%): C, 67.69; H, 9.36; N, 14.50. Calc. for $C_{11}H_{18}N_2O$ (%): C, 68.01; H, 9.34; N, 14.42.

The fast exchange for deuterium of the NH and vinyl protons is expected as such behaviour is consistent with the tautomerism observed in various heterocyclic systems containing exocyclic β-carbonyl moieties.[4,6]

Unfortunately, based on the ^{1}H NMR spectroscopic data, we cannot choose unambiguously between structures A and B for compounds **5a**,**b**; however, taking into account the fact that ≥ 95% of β-aminovinyl ketones exist in the ketoenamine form, which has a greater ability to stabilise as compared to imino-enols,[7] we prefer the enamine tautomer A, a choice favoured by the comparison of the IR and ^{1}H NMR spectra of imidazolidine **5a** and the corresponding β-aminovinyl ketone (5-amino-2,2-dimethyl-4-hexen-3-one[§,8]). The IR spectra of these compounds in Vaseline oil contain an intense absorption band in the region of 1620–1625 cm^{-1}, which is characteristic of the C=O group coupled with the enamine fragment. In compounds **5b**,**c**, this band is observed at 1620 cm^{-1}, whereas for dihydroimidazole **6**[4] it lies at 1605 cm^{-1}.

We have additionally confirmed the conclusion about the predominant contribution of the ketoenamine form A to the tautomeric equilibrium by the reaction of ethylenediamine with aminoenone **4d**[9] resulting in the formation of imidazolidine **5d**.[¶]



4d **5d**

Unlike **5a**–**c**, compound **5d** contains a hydroxyl group in the α-position relative to the carbonyl and hence the keto form A stabilised by two intramolecular hydrogen bonds is more preferable *a priori*.

Similar spectral parameters for **5a**–**c** and **5d** make it possible to assign the ketoenamine structure A to all these compounds, while the reaction of aminoenones **4a**,**b**,**d** with ethylenediamine described in this work is a new and simple synthetic route to 2-acylmethyleneimidazolidines.

This work was supported by the Russian Foundation for Basic Research (grant no. 96-03-33373).

References

1 V. Ya. Sosnovskikh, M. Yu. Mel'nikov and I. A. Kovaleva, *Izv. Akad. Nauk, Ser. Khim.*, 1998, 2305 (*Russ. Chem. Bull.*, 1998, **47**, 2234).
2 M. Cönen, J. Faust, S. Ringel and R. Mayer, *J. Prakt. Chem.*, 1965, **27**, 239.
3 I. G. Ostroumov, A. E. Tsil'ko, I. A. Maretina and A. A. Petrov, *Zh. Org. Khim.*, 1988, **24**, 1165 [*J. Org. Chem. USSR* (*Engl. Transl.*), 1988, **24**, 1050].
4 M. W. Anderson, M. J. Begley and R. S. F. Jones, *J. Chem. Soc., Perkin Trans. 1*, 1984, 2599.
5 R. Mondelli and L. Merlini, *Tetrahedron*, 1966, **22**, 3253.
6 G. R. Malone and A. I. Meyers, *J. Org. Chem.*, 1974, **39**, 713.
7 G. O. Dudek and R. H. Holm, *J. Am. Chem. Soc.*, 1962, **84**, 2691.
8 V. Ya. Sosnovskikh and I. S. Ovsyannikov, *Zh. Org. Khim.*, 1990, **26**, 2086 [*J. Org. Chem. USSR* (*Engl. Transl.*), 1990, **26**, 1850].
9 V. Ya. Sosnovskikh, *Zh. Org. Khim.*, 1992, **28**, 1307 [*J. Org. Chem.* (*Engl. Transl.*), 1992, **28**, 1250].

§ *5-Amino-2,2-dimethyl-4-hexen-3-one*.[8] ^{1}H NMR (80 MHz, $CDCl_3$) δ: 1.10 (s, 9H, Bu^t), 1.93 (s, 3H, Me), 5.1 (br. s, 1H, NH), 5.20 (s, 1H, =CH), 9.8 (br. s, 1H, NH). IR (Vaseline oil, ν/cm^{-1}): 3300, 3160 (NH_2), 1625 (C=O), 1600, 1540 (C=C, NH_2).

¶ *2-(1-Hydroxy-1-methylpropyl)carbonylmethyleneimidazolidine* **5d**. Yield 32%, mp 142–143 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 0.83 (t, 3H, Me, *J* 7.3 Hz), 1.29 (s, 3H, Me), 1.61 (q, 1H, MeC*H*H, *J* 7.3 Hz), 1.62 (q, 1H, MeCH*H*, *J* 7.3 Hz), 3.57 (m, 2H, CH_2), 3.72 (m, 2H, CH_2), 4.73 (s, 1H, =CH), 4.81 (br. s, 1H, OH), 4.89 (br. s, 1H, NH), 8.87 (br. s, 1H, NH); after addition of CD_3CO_2D: 0.82 (t, 3H, Me, *J* 7.3 Hz), 1.28 (s, 3H, Me), 1.62 (q, 2H, MeCH_2, *J* 7.3 Hz), 3.69 (s, 4H, CH_2CH_2). IR (Vaseline oil, ν/cm^{-1}): 3380, 3270, 3220 (OH, NH), 1615 (C=O), 1560 (br., C=C, NH). Found (%): C, 58.35; H, 8.66; N, 15.06. Calc. for $C_9H_{16}N_2O_2$ (%): C, 58.67; H, 8.75; N, 15.21.

Received: Moscow, 2nd July 1998
Cambridge, 29th September 1998; Com. 8/05566A