Organic Chemistry

3-Acetyl-2-amino-4-hydroxy-1,3-pentadienecarbonitrile: *E,Z*-isomerism and the ability to form chelates*

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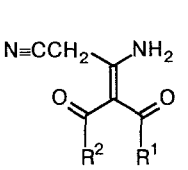
The Ni acetylacetonate-catalyzed addition of acetylacetone to malononitrile was shown to afford 3-acetyl-2-amino-4-hydroxy-1,3-pentadienecarbonitrile. The diphenyl boron chelate of the latter with a β-diketone-type structure was obtained. *E,Z*-isomerism of the chelate and the free ligand were investigated. The *Z*-isomers were found to dominate in low polarity solvents.

Key words: 3-acetyl-2-amino-4-hydroxy-1,3-pentadienecarbonitrile, diphenylboron chelate, *E,Z*-isomerism.

Functionalized β-diketones and β-ketoimines (enaminones) form boron chelates, which differ in reactivity from the parent free ligands, thus opening new opportunities in the synthesis of nitrogen-containing heterocycles.[1–5] For this reason, we are involved in the search for new chelate-forming derivatives of β-diketones and enaminones and the preparation of their boron complexes. Recently, a synthesis of enaminones (**1**), which contain a cyanomethyl group, by the reaction of β-dicarbonyl compounds with malononitrile (MN) in the presence of a catalytic amount of Ni acetylacetonate ($Ni(acac)_2$) was published[6]. (Spectral data for compound **1** are not presented.) We were interested in preparing the corresponding boron chelates (**2**) from enaminones **1**.

In connection with this aim we tried to synthesize the ligand from acetylacetone (acacH) and MN under the conditions reported in Ref. 6 (refluxing in $CHCl_3$ in the presence of 1 mol. % of $Ni(acac)_2$). However, the adduct of acacH to the C≡N bond of malononitrile appeared to have the structure of enaminonitrile **3**, not enaminone **1** ($R^1 = R^2 = Me$). In solution, the obtained adduct exists as a mixture of the *E*- and *Z*-isomers (about the C=C bond of the enamine fragment).

In the IR spectra of this compound recorded both in solution ($CHCl_3$) and in the solid state (KBr), an intense band of the conjugated C≡N group is observed (2200



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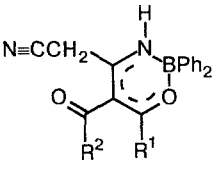

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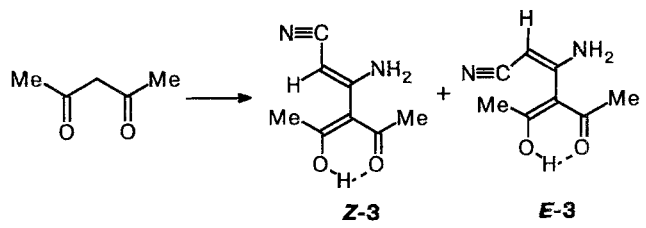


Reagents and conditions: MN, 1 mol. % of $Ni(acac)_2$, $CHCl_3$, Δ.

cm^{-1}). In the ^1H NMR spectra of compound **3** in different solvents two sets of signals are presented, which can be assigned to the protons of the CH= and NH_2 groups, two Me groups, and the enol proton considering their δ values and integral intensities (see Table 1). The ^{13}C NMR data are also in accordance with the structure of **3** (see chemical shifts (δ) of the CH= doublets in Table 2), confirming the existence of this compound as a mixture of *Z*- and *E*-isomers.

The assignment of the signals in ^1H NMR spectra to the *E*- and *Z*-forms was made using the nuclear Overhauser effect (NOE) data. Irradiation of protons of the NH_2 group gives rise to NOE enhancement (3.9±0.5 %) of the N≡C—CH= signal of the minor isomer in the spectrum of an equilibrium mixture of the isomers (in $CDCl_3$). However, no enhancement of the corresponding signal of the major isomer is observed. Thus, for compound **3** in $CDCl_3$ the *Z*-form predominates. In this form the =CH proton is more shielded than the corresponding proton of the *E*-isomer.

Compound **3** can be considered as 3-substituted 3-aminoacrylonitrile, therefore the data obtained are in accordance with the study of *E,Z*-isomerism of enaminonitriles of the $N{\equiv}C{-}CH{=}(R)NH_2$ type (R = Alk, Ar in Ref. 7). It was shown that the CH= protons are, as a rule, more shielded in the *Z*-isomers and that the *Z*-form is preferable (85—100 %) in low polarity solvents, if R = Ar. The process of isomerization of compound **3** is reversible. In more polar solvents (CD_3CN, DMSO-d_6) the content of the *E*-isomer in **3** increases and this isomer becomes predominant (Table 1). The study of the temperature dependence of the ^1H NMR spectrum of **3** in DMSO-d_6 demonstrates that heating to 60 °C leads to gradual broadening of the signals of both isomers, with restoration of the spectral pattern after subsequent cooling. Note that the $Z \rightleftharpoons E$ equilibrium is achieved practically immediately after preparation of the solution at 20 °C in all of the solvents studied.

Thus, compound **3** is a 3-substituted 2,4-pentanedione, existing in the enol form. Hence, there is an opportunity to prepare the acetylacetonate-type boron chelates using this ligand. However, one cannot exclude the possibility of isomerization of ligand **3** into the type **1** enaminone and the subsequent formation of chelate **2** ($R^1 = R^2 = Me$) with N,O-coordination of the B atom (chelate systems of such derivatives of β-diketones as diacetylketene aminals and *N,S*-acetals[1—3]).

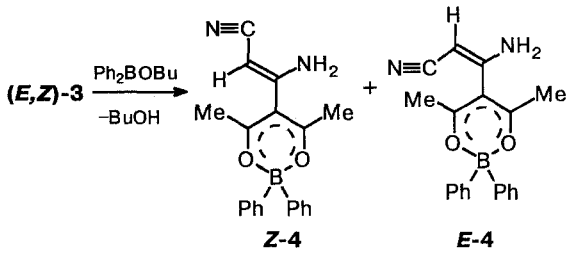
The reaction of butoxydiphenylborane with compound **3** afforded the chelate in 85 % yield. According to IR, ^1H, and ^{13}C NMR data the chelate has the structure of acetylacetonate **4**, and also exists in solution as a mixture of *E*- and *Z*-isomers.

Table 1. ^1H NMR data of compounds **3** and **4** (δ, ppm)

Compound	Solvent	Isomer	Relative content of isomer (%)*	2 Me	=CH	NH_2	2 Ph	OH
3**	C_6D_6	*Z*	80	1.69	3.31	3.85	—	17.03
		E	20	1.92	3.78	3.03	—	17.25
	$CDCl_3$	*Z*	75	2.19	3.99	4.93	—	16.57
		E	25	2.23	4.48	4.58	—	16.66
	CD_3CN	*Z*	40	2.13	3.93	4.45	—	16.63
		E	60	2.17	4.43	4.45	—	16.70
	DMSO-d_6	*Z*	25	2.10	3.84	6.84	—	16.63
		E	75	2.12	4.31	6.84	—	16.63
4	C_6D_6	*Z*	85	1.57	3.05	3.48	7.20—8.00	—
		E	15	1.81	3.55	2.51	7.20—8.00	—
	$CDCl_3$	*Z*	70	2.35	3.94	4.77	7.20—7.50	—
		E	30	2.40	4.48	4.28	7.20—7.50	—
	CD_3CN	*Z*	40	2.32	3.80	5.40	7.15—7.50	—
		E	60	2.35	4.48	5.50	7.15—7.50	—
	DMSO-d_6	*Z*	30	2.31	3.64	6.97	7.10—7.50	—
		E	70	2.32	4.37	6.97	7.10—7.50	—

*Based on integral intensities of the signals.

Additionally, in the spectra of compound **3 signals with low intensities (from 5 to 7 %) were observed that can be assigned to the CH_2 and CH_3 groups of the isomer of type **1** ($R^1 = R^2 = Me$) or to an impurity of unknown structure.



In the mass spectrum of complex **4** a weak peak of the molecular ion and an intense peak of the $[M-Ph]^+$ ion are observed. In the IR spectrum ($CHCl_3$) of **4** intense absorption bands of the conjugated C≡N group (2205 cm^{-1}), the chelate ring (1590 and 1475 cm^{-1}), and the free NH_2 group (3500 and 3492 cm^{-1}) are present. As in the case of ligand **3**, in the ^1H and ^{13}C NMR spectra of chelate **4** two sets of signals of the *E*- and *Z*-isomers are observed (Tables 1 and 2). However, the $Z \rightleftharpoons E$ equilibrium in the case of complex **4** is achieved much more slowly (*ca.* 3 days).

Assignment of signals of the *Z*- and *E*-isomers of **4** was also performed using the NOE technique. Irradiation of the NH_2 protons of the minor isomer in the ^1H NMR spectrum of a solution of **4** (in $CDCl_3+C_6D_6$) gives NOE enhancement (3.6±0.5 %) of the CH signal and, therefore, the *Z*-isomer is predominant. The transition to more polar solvents results in a significant decrease in the percentage of *Z*-isomer in the equilibrium mixture, *e.g., ca.* 30 % in DMSO-d_6. The isomeric composition of chelate **4** and free ligand **3** in different solvents are practically the same.

It is known that the value of the $^1J_{C-H}$ coupling constant depends on the orientation of the substituents (*cis—trans*) about the double bond.[8] In the ^{13}C NMR spectra of ligand **3** and chelate **4** this $^1J_{C-H}$ also differs significantly for the *E*- and *Z*-isomers (see Table 2).

Chelate **4** is a white crystal solid, readily soluble in organic solvents except petroleum ether.

Experimental

The ^1H NMR spectra were recorded with a Bruker WM-250 instrument (250.13 MHz), and the ^{13}C NMR spectra were recorded with a Bruker AM-300 instrument (75.47 MHz). Chemical shifts are given relative to tetramethylsilane. The nuclear Overhauser effect (NOE) experiments were performed with a Bruker WM-250 spectrometer using the NOE MULT procedure (Bruker) in a difference mode in $CDCl_3$ (for ligand **3**) and in $CDCl_3+C_6D_6$ (for chelate **4**). The IR spectra were recorded with an UR-20 instrument. Mass spectra were obtained with a Varian MAT CH-6 spectrometer.

All of the operations were performed under dry nitrogen.

3-Acetyl-2-amino-4-hydroxy-1,3-pentadienecarbonitrile (3). A mixture of MN (0.33 g, 5 mmol), acacH (0.5 g, 5 mmol), and anhydrous $Ni(acac)_2$ (0.013 g, 0.05 mmol) in anhydrous $CHCl_3$ (15 mL) was refluxed for 8 h (*cf.* Ref. 6). The solvent was evaporated, the oily residue containing **3**, unchanged acacH, and a polymeric material was chromatographed on a column with SiO_2 (eluent: benzene; benzene—chloroform, 1 : 1; chloroform) to give nitrile **3** (0.35 g, 42 %), m.p. 89.5—90.5 °C (from a benzene—hexane mixture). Found (%): C, 57.93; H, 6.07; N, 16.74. $C_8H_{10}N_2O_2$. Calculated (%): C, 57.82; H, 6.07; N, 16.86. Mass spectrum, *m/z*: 166 $[M]^+$. IR (CH_2Cl_2, ν/cm^{-1}): 3514 and 3405 (NH_2), 3280—3000 (OH, CH), 2200 (C≡N), 1625, 1599, 1410.

Diphenylboron chelate of compound 3 (4). Butoxydiphenylborane (3.5 g, 15 mmol) was added with stirring to a solution of **3** (1.5 g, 9 mmol) in $CHCl_3$ (25 mL) and the mixture was stirred at 20 °C for 2 h. The solvent was removed *in vacuo* and the oily residue was triturated with an ether—hexane mixture (1 : 1). The crystals formed were filtered off to give chelate **4** (2.8 g, 85 %), m.p. 144—149 °C (decomp., from a benzene—hexane mixture). Found (%): C, 72.76; H, 5.99; B, 3.09. $C_{20}H_{19}BN_2O_2$. Calculated (%): C, 72.75; H, 5.80;

Table 2. ^{13}C NMR data of compounds **3** and **4** (δ, ppm, J_{CH}/Hz)

Compound	Solvent	Isomer	2 Me	=CH	CN	MeCOC	N—C=	2 CO	2 Ph
3	$CDCl_3$	*Z*	22.95	67.20 (181)	118.55	111.30	158.37	191.20	
		E	22.74	69.67 (167)	120.02	110.05	158.91	191.36	
	DMSO-d_6	*Z*	22.79	62.82 (178)	119.53	112.29	158.90	190.59	
		E	22.49	64.84 (168)	121.29	110.83	160.10	190.67	
4	$CDCl_3$	*Z*	22.69	68.14 (180)	117.91	112.07	155.66	190.10	126.78; 126.92; 127.05; 127.54; 131.51; 130.99; 147.00
		E	22.66	70.51 (168)	119.30	110.65	156.20	190.22	
	DMSO-d_6	*Z*	22.73	63.58 (180)	119.02	112.90	156.63	189.68	126.37; 126.46; 126.90; 127.09
		E	22.58	65.75 (168)	120.63	110.38	157.96	189.54	130.92; 130.25; 147.50

B, 3.27. Mass spectrum, *m/z*: 330 $[M]^+$, 253 $[M-Ph]^+$. IR (CH_2Cl_2, ν/cm^{-1}): 3500, 3492 (NH_2), 2205 (C≡N), 1622, 1592, 1477. ^1H and ^{13}C NMR spectra of compounds **3** and **4** are given in Tables 1 and 2.

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