BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 49 (6), 1719—1720 (1976)

A Proton Magnetic Resonance Study of the Molecular Configurations of 2′,5′-Dichloroacetoacetanilide in Various Solvents

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(Received September 25, 1975)

Synopsis. It has been found by ^{1}H NMR spectroscopy that 2′,5′-dichloroactoacetanilide (**1**) exists predominantly in the *keto* form containing an intramolecular hydrogen bond between the amide proton and the carbonyl oxygen at the γ-position in chloroform solutions. In pyridine, the line broadening of signals suggests a rapid interconversion between the *keto* and *enol* forms. Configurations of the *enol* form are discussed.

It is well known that β-diketones undergo *keto-enol* tautomerism in solution. ^{1}H NMR studies of such tautomerism have been carried out for a number of derivatives of acetylacetone and acetoacetic acid,[1] but only a few studies have been done on acetoacetamide derivatives.[2]

The *keto-enol* equilibrium is sensitive to many factors, such as the temperature, the concentration, and the solvent, as well as to the presence of substituents. Acetylacetone, *N*,*N*-dimethylacetoacetamide, and ethyl acetoacetate show a successively decreasing contribution of *enol* form.[1,2]

It is an interesting subject to determine which of the many possible conformations are actually reallized in the case of each compound. This paper will be concerned with the molecular configuration of 2′,5′-dichloroacetoacetanilide (**1**), which is revealed to exist predominantly in the *keto* form in $CDCl_3$.

Experimental

Commercial 2′,5′-dichloroacetoacetanilide (**1**) was purified by recrystallization from CCl_4.

The ^{1}H NMR spectra were recorded on a Varian T-60A spectrometer, using TMS as the internal standard. The concentrations of the samples were 6% (w/v) unless otherwise noted.

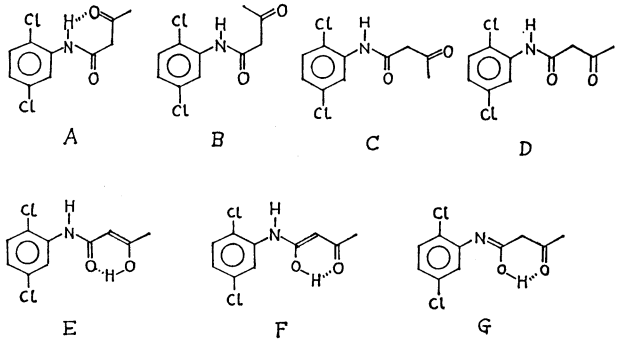
The IR and UV spectra were measured on a Hitachi infrared spectrophotometer, Model G-3, and a Hitachi spectrophotometer, Model 356, respectively.

Results and Discussion

The ^{1}H NMR spectra of **1** in various solvents are relatively simple and seem to be composed of two kinds of signals. Raising the temperature of a DMSO solution of **1** up to 100 °C caused no new signals to appear, but there was a slight upfield shift of the amide proton signal.

The signal at δ 3.64 (in $CDCl_3$, for example) corresponding to *ca.* 2H can be ascribed to the methylene protons in *keto* forms on the basis of its chemical shift. The broad signal at δ 9.77 corresponding to *ca.* 1H may be attributed to the amide proton. The alternative assignment of this signal to an enolic OH in the G structure can be eliminated on the basis of the close resemblance in the IR spectra of **1** and 2′, 5′-dichloroacetanilide (**2**) in $CDCl_3$ (Table 1). The amide bands at about 1600 and 1700 cm^{-1} were clearly observed at about same positions. The UV spectra of **1** and **2** in 1,2-dichloroethane solutions are very similar to each other. These facts seem to allow us to rule out the contribution of G in the present case.

The ABX spectral pattern of the aromatic ring protons permits an unequivocal assignment of H-6′ because of the presence of two chlorine atoms. The similarity in the δ values for the ring protons of **1** and **2** enables us to assign forms A to D with the *trans* configuration about the amide bond to *keto* tautomers for **1**, because the *trans* configuration of **2** has been proved on the basis of the diagnostic acetylation-deshielding shift.[3] The corresponding *cis* configurations were dificult to realize, judging from the generally known fact that amide bonds (or peptide bonds) predominantly exist in the *trans* form.[4]



The amide proton of **1** resonates at a field lower by about 2.14 ppm than does that of **2**. This pronounced downfield shift can be interpreted in terms of the A configuration, wherein an intramolecular hydrogen bond is formed between the amide proton and the γ-carbonyl oxygen, though the contributions of B, C, and D can not be neglected. The concentration dependence of the amide proton signal was negligible, as was to be expected from the intramolecular hydrogen bond formed. The broad band at 2900—3400 cm^{-1} in the IR spectrum of **1** may also be ascribed to the amide proton intramolecularly hydrogen-bonded.

An analogous situation was observed in CCl_4 solutions. In DMSO, it is not clear from only the position of the amide proton signal whether or not this configuration remains unchanged, because that of **2** also resonates at a low field due to the intermolecular hydrogen bonding with a DMSO molecule. However, the molecular planarity is considered to be lowered in DMSO, as suggested by the diagnostic upfield shift of the H-6′ signal as compared with that in $CDCl_3$.[5]

TABLE 1. SPECTRAL DATA FOR 2′,5′-DICHLOROACETOACETANILIDE (**1**) AND 2′,5′-DICHLOROACETANILIDE (**2**) IN VARIOUS SOLVENTS

NMR: Chemical shift in ppm										
Compd			CCl_4[a]		$CDCl_3$		DMSO-d_6		C_5D_5N	
	keto	enol	keto	enol	keto	enol	keto	enol	keto	enol
1	CH_3	CH_3	2.31	1.97	2.33	1.99	2.23	1.96	2.18	
	CH_2	CH	3.56	5.01	3.64	5.07	3.71	5.45	4.00	
	NH		9.73		9.77		9.87		10.47	
	H-3′	H-3′	7.30		7.33		7.53		7.35	
	H-4′	H-4′	6.99		7.03		7.25		7.07	
	H-6′	H-6′	8.52	8.58	8.47		8.05	7.93	8.60	
		OH		13.3		13.3		13.4		
Population			77	23	92	8	92	8		
2		CH_3			2.24		2.13			
		NH			7.63		9.60			
		H-3′			7.30		7.56			
		H-4′			7.02		7.26			
		H-6′			8.47		7.98			

UV (in dichloroethane) nm(ε)	
1	300(s)[b], 292(2400), 283(3040), 248(13500)
2	— 292(1200), 283(1200), 246(14000)
IR (in $CDCl_3$)[c] cm^{-1}	
1	3392, 3400—2900, 1712, 1690, 1587, 1525
2	3400, 3100, 1710, 1693, 1587, 1581, 1510

a) Saturated solution. b) Shoulder. c) Lower frequency bands are omitted.

In pyridine it is noted that the linewidths of the signals of the methyl and methylene protons are much broader than those in chloroform. Although no apparent signal ascribable to *enol* forms were observed, the broadening in the methylene proton signal suggests a rather rapid interconversion between the *keto* and *enol* forms. This could be ascribed to catalytic actions of pyridine.[1d]

The population of the *keto* form is much greater in this compound than in *N*,*N*-dimethylacetoacetamide.[2] The intramolecular hydrogen bonding between the amide proton and the γ-carbonyl oxygen may be responsible for this.

It is possible to imagine four configurations (E and F and the corresponding *cis* forms, E′ and F′) as *enol* forms. The fact that the chemical shift of H-6′ in the *enol* tautomer is very close to that for the *keto* tautomer favors the E and F structures, which have the oxygen atom in close proximity to H-6′, rather than E′ and F′, which have the olefinic proton in such proximity. The methyl signals of the *enol* tautomers were observed at fields higher than those of the *keto* tautomers in the solvents examined, as was also observed for a series of β-diketones and β-keto esters.[1e] The difference between the chemical shifts of the two tautomers of **1** is almost the same as that in the case of ethyl acetoacetate, but it is clearly larger than that of acetylacetone. If the *enol* molecule assumes the F form, the chemical shift of the acetyl protons should not be very different from that in the *keto* form. Furthermore, if a rapid interconversion between E and F is supposed, the chemical shift difference between the *keto* and *enol* forms should be equal to the corresponding difference in acetylacetone. The argument given above leads one to the conclusion that the molecular configuration of the *enol* tautomer is E.

The olefinic proton signal of the *enol* tautomer was observed at δ 5.07 in $CDCl_3$, higher by −0.51 ppm than that of acetylacetone, but almost the same as that of ethyl acetoacetate. The enolic OH proton resonates at δ 13.3 in $CDCl_3$. The corresponding values for acetylacetone and ethyl acetoacetate are δ 15.6 and 12.2 in pure liquid respectively.[1e] These facts also support the argument presented above.

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