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^1H, ^{13}C and ^{19}F NMR Studies on the Structure of the Intramolecularly Hydrogen Bonded *cis*-Enols of 2-Trifluoroacetylcycloalkanones

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Summary. The ^1H, ^{13}C and ^{19}F NMR spectra of some 2-trifluoroacetylcycloalkanones comprising five-, six-, seven-, and eight-membered ring systems have been studied. These systems have been shown by ^{19}F NMR spectroscopy to be over 90% enolized. The effects of ring size on the ^1H, ^{13}C and ^{19}F chemical shifts and ^{13}C-^{19}F coupling constants are discussed. The direction of enolization in these systems was investigated by ^1H, ^{13}C and ^{19}F NMR spectroscopy and evidences were presented in favour of a dominant exocyclic enol form in the five- and an endocyclic enol form in the six-, seven- and eight-membered ring systems.

Keywords. Fluorinated β-diketones; NMR; Enol forms; Intramolecular hydrogen bond.

^1H-, ^{13}C- und ^{19}F-NMR-Untersuchungen zur Struktur der intramolekularen Wasserstoffbindung in den *cis*-Enolen von 2-Trifluoracetylcycloalkanonen

Zusammenfassung. Die ^1H-, ^{13}C- und ^{19}F-NMR-Spektren einiger 2-Trifluoracetylcycloalkanone mit fünf-, sechs-, sieben- und achtgliedrigen Ringsystemen wurden untersucht. Mittels ^{19}F-NMR konnte über 90% Enolisierung nachgewiesen werden. Der Effekt der Ringgröße auf die chemischen Verschiebungen in den ^1H-, ^{13}C- und ^{19}F-NMR-Spektren und auf die ^{13}C-^{19}F-Kopplungskonstanten werden diskutiert. Die Enolisierungsrichtung dieser Systeme wurde unter Einsatz der NMR-Spektren untersucht: dabei ergab sich eine dominierende exocyclische Enolform für die Fünfringe und eine endocyclische Enolform für die sechs-, sieben- und achtgliedrigen Ringe.

Introduction

Although the structures of intramolecularly hydrogen bonded *cis*-enols of β-diketones have been extensively investigated by a diversity of techniques [1–11], there has been a conflict of evidence among these reports as to the symmetry of the intramolecular hydrogen bond. A symmetric enol with linear hydrogen bond was proposed for acetylacetone [1], trifluoroacetylacetone [2] and hexafluoroacetylacetone [3] to account for the short O...O non-bonded distances (238–255 pm) obtained by a gas phase electron diffraction technique. However, the accuracy of these measurements has been critisized [4] because of failure to maintain tautomeric equilibrium during evaporation of the sample. Alternatively, x-ray diffraction studies on benzoylacetone [5] and dibenzoylmethane [6] have predicted an asymmetric enol form with non-linear hydrogen bond. The asymmetric nature of the enol of acetylacetone and related molecules has been ascertained by measurements of ^{13}C and ^{2}H spin relaxation time and deuterium quadrupole coupling constants [7], and UV [4], IR [8, 9], NMR [4, 10] and x-ray photoelectron [11] spectra.

In connection with our work [12, 13] on fluorinated β-diketones and their metal chelates, we have prepared a series of 2-trifluoroacetylcycloalkanones comprising five-, six-, seven-, and eight-membered ring systems. These systems have been shown [12] to exist in solution as equilibrium mixtures of the tautomeric forms (compare the formula scheme).

The rate of uncatalyzed keto-enol interconversion is usually slow. Hence, the keto and enol forms are clearly distinguishable by a variety of chemical and physical techniques. On the other hand, the two possible *cis*-enol forms (see formula scheme) in the present series of fluorinated β-diketones interconvert very rapidly by intramolecular chelate proton transfer. Thus, the two enol forms are only distinguishable as individuals in the electronic and vibrational spectra [12], whereas the NMR spectra correspond to a weighted average of the two species as a consequence of the rapid interconversion in comparison with the NMR time scale. The main thrust of the present work was to provide further insight into the structure of the intramolecularly hydrogen bonded *cis*-enol forms in these systems using ^{1}H, ^{13}C and ^{19}F NMR spectroscopy.

Experimental

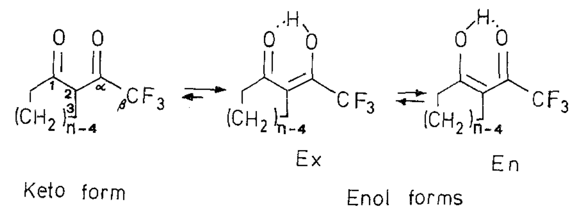
The compounds examined have been described previously [12]. The ^{1}H and ^{19}F NMR spectra were recorded on a JEOL-100-FT spectrometer at 100 and 94 MHz, respectively. The ^{1}H spectra were recorded at a digital resolution of 0.244 Hz/point. The proton-decoupled ^{13}C NMR spectra were recorded on a JEOL JNM-FX-90 Q spectrometer at 22.6 MHz. The ^{1}H and ^{13}C NMR spectra of 10–15% solution in $CDCl_3$ were measured relative to internal *TMS*. The ^{19}F NMR spectra were measured for the neat liquids, using $CFCl_3$ as external reference in a sealed capillary. The ^{19}F chemical shifts refer to $CFCl_3$ with positive shifts to high frequency of the reference. All samples were measured at ambient temperature. The deuterium signal of the solvent was used as an internal lock signal.

Results and Discussion

^{1}H *NMR Spectra*

The ^{1}H NMR spectra of compounds **1**–**4** exhibit complex multiplets at lower frequencies (δ = 1.5–2.9 ppm) for the ring methylene hydrogens but no appreciable signal for the methyne hydrogen (C_1 H) which indicate the predominance of the enol forms in these systems. The chemical shift and half width ($\Delta_{1/2}$ in Hz) of the enolic O – H proton provide a proper measure of the strength of the intramolecular hydrogen bond in these systems [14–16].

In 2-trifluoroacetylcyclopentanone (**1**), the enolic proton is found at δ 13.01 ppm, whereas in the six-, seven-, and eight-membered ring systems (compounds **2**–**4**) the enolic proton signal appears at δ 15.06, 15.91, and 16.10 ppm, respectively. For comparison, the enolic proton signal of enolic 2-acetylcyclopentanone is found at δ 13.08 ppm [17], whereas that of 2-acetylcyclohexanone is found at δ 15.9 ppm [18], and in general, the chemical shift of the chelated enolic proton of non-aromatic β-diketones appears at δ 13–18 ppm [17, 18].



Compound	n
1	5
2	6
3	7
4	8

In compounds **1**–**4** the enolic proton signal undergoes an appreciable high frequency shift from the five- to the six-membered ring system, but only slightly so through the series. These changes correspond to a decrease in acidities (pK_a values are 6.75, 7.18, 8.38, and 8.3 for compounds **1**–**4**, respectively) [19], and presumably an increase in the strength of the intramolecular hydrogen bond of the enols through the series. It is also of interest to note that the five-membered ring system (compound **1**) which is the most acidic enol of the series and thus has the least firmly bound enolic hydrogen, displays the broadest signal with $\Delta_{1/2} \sim 13.7$ Hz.

These observations suggest that the placement of the enolic hydrogen between the two oxygens is such that the electron-withdrawing influence of the CF_3 group is maximum in the five-membered ring system via an exocyclic enol (Ex) (comp. formula scheme). These findings are fully consistent with our recent MINDO/3 calculations [20] on these systems. Such calculations have established a non-planar enolic chelate ring with a substantially weaker intramolecular hydrogen bond in the exocyclic enol of 2-trifluoroacetylcyclopentanone (compound **1**) in comparison with other ring systems.

A further interesting feature of the enolic proton signals of compounds **1**–**4** is the observation of long-range coupling effects which are more pronounced in the seven-membered ring system (compound **3**) to give a well resolved quartet ($J \sim 0.97$ Hz). For comparison, the enolic proton signals in medium ring enols of 2-acetylcycloalkanones [19] and 2-ethoxycarbonylcycloalkanones [16] revealed fine splitting in the form of a triplet ($J \sim 0.5$–1.5 Hz) which was ascribed [16] to long-range coupling between the enolic proton and the ring methylene hydrogens.

^{13}C *NMR Spectra*

The ^{13}C chemical shifts and ^{13}C-^{19}F coupling constants for compounds **1**–**4** are summarized in Table 1. The presence of $^{n}J(C-F)$ couplings has made the assignments unambiguous. Only the carbonyl carbons (C_1 and C_α) of compounds **1**–**4** show large and consistent changes in the chemical shifts with ring size and are therefore discussed here in detail.

Shapet'ko and coworkers [21] have observed large and additive substituent effects on the ^{13}C chemical shifts of the *cis*-enol of acyclic β-diketones. However, early interpretation of these data in terms of a symmetrical enol form has been later abandoned by these authors [22] in favour of an asymmetrical enol form,

Table 1. ^{13}C NMR spectral data of compounds **1–4**

Compound no.	Chemical shifts δ (ppm)										Coupling constants (Hz)		
	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_α	C_β	$^4J(C_3-F)$	$^2J(C_\alpha-F)$	$^1J(C_\beta-F)$
1	209.30	110.96	25.74	20.86	37.11				160.97	119.36	2.44	35.0	278.3
2	190.01	105.22	22.21	21.18	21.94	32.13			170.00	117.81	2.44	35.0	286.9
3	204.74	111.88	25.35	31.37	25.08	28.99	40.58		170.18	119.25	2.44	35.0	283.2
4	199.76	108.96	23.74	29.09	26.93	26.22	31.53	35.71	174.30	119.14	2.44	35.0	285.4

and as Robinson et al. [10] pointed out, the large and approximately additive substituent effects observed by Shapet'ko [21] may arise from the influence of substituents on the inter-enol equilibrium. In order to test the additivity of substituent effects upon the ^{13}C chemical shifts of the carbonyl carbons in the present series of cyclic β-diketones, it is necessary to define a further parameter, R^n, to account for the influence of ring size on these systems. Thus, for $\delta(C_\alpha)$, the following relation is used,

$$\delta(C_\alpha) = 191.5 + \Delta_x + R^n,$$

where the constant 191.5 ppm is the corresponding value of the chemical shift of the carbonyl carbon of the *cis*-enol of acetylacetone [21] and Δ_x and R^n are parameters for the influence of substituent and ring size, respectively. From Shapet'ko's work [21], $\Delta_x = -14.9$ ppm for the CF_3 group. Using the data of Table 1 for $\delta(C_\alpha)$ in compounds **1**–**4** and the corresponding data for 2-acetylcycloalkanones [19], the R^n parameter has been evaluated for the various ring systems. The results presented in Table 2 show reasonable additivity relation for the two series of cyclic β-diketones. In the five-membered ring systems, the large R^n value (-15.44 ppm) reflects the influence of this highly strained ring system on the position of the inter-enol equilibrium.

The predominance of the exocyclic enol form (Ex) in the five-membered ring system (compound **1**) is consistent with the following observations: Firstly, the ^{13}C signal of the trifluoroacetyl carbon (C_α) is observed at lower frequencies in the five-membered ring system [$\delta(C_\alpha) = 160.97$ ppm in **1**] in comparison with other ring systems. Secondly, the ^{13}C signal of the ring carbonyl (C_1) in the five-membered ring system (compound **1**) approaches closely the expected value of an unenolized carbonyl group [$\delta(C_1) = 209$ ppm in **1**], and finally, $^1J(C-F)$ has a value of 278 Hz in the five-, and ~ 285 Hz in the six-, seven-, and eight-membered ring systems (Table 1). Examination of the literature data [23–25] on $^1J(C-F)$ in trifluoromethyl substituted compounds reveal that the magnitude of $^1J(C-F)$ for $CF_3-C=C-$ and $CF_3-C=O$ type of environments are ~ 270 and ~ 285 Hz,

Table 2. Substituent and ring size effects on the ^{13}C chemical shift of the acetyl carbon (C_α) in 2-acetylcycloalkanones and 2-trifluoroacetylcycloalkanones

Ring size (n)	R^n	2-Trifluoroacetylcycloalkanones $X = CF_3$; $\Delta_x = -14.9$ ppm[a] $\delta(C_\alpha)$		2-Acetylcycloalkanones $X = CH_3$; $\Delta_x = 0.0$ ppm[a] $\delta(C_\alpha)$	
		Calc.	Obs.[b]	Calc.	Obs.[c]
5	−15.44	161.16	160.97	176.06	176.25
6	−7.84	168.76	170.00	183.66	182.42
7	−6.47	170.13	170.18	185.03	184.97
8	−2.95	173.65	174.30	188.55	187.90

[a] From Shapet'ko's work [21]

[b] This work

[c] Ref. [19]

Table 3. ^{19}F NMR spectral data of compounds **1**–**4**

Compound	^{19}F Chemical Shifts (δ)[a]		
	Enol form	Keto form	Enol %
1	−74.95[b]	−80.96	98.0%
2	−71.89	−80.50	90.7%
3	−71.81	−80.45	90.5%
4	−72.99	−79.90	93.9%

[a] In ppm relative to $CFCl_3$; negative values indicate lower frequencies
[b] Resolved as a triplet ($J = 2.4$ Hz)

respectively. Thus, the magnitude of $^1J(C-F)$ in compound **1** clearly suggests the presence of the $CF_3-C=C$ moiety of an exocyclic enol form.

^{19}F *NMR Spectra*

The ^{19}F NMR spectra of compounds **1**–**4** exhibit two well-separated sharp singlets corresponding to the trifluoromethyl group in the keto and enol tautomers. The position of the keto-enol equilibrium was determined by intensity measurements of the two signals. Table 3 summarizes the ^{19}F chemical shifts and enol% which indicate over 90% enolization in all cases.

The ^{19}F resonances of a CF_3 group in the enol forms of acyclic fluorinated β-diketones [25–29] are typically found in the region −76 to −78 ppm. For example, the corresponding ^{19}F resonances of 1,1,1-trifluoroacetylacetone [26], ethyl 1,1,1-trifluoroacetylacetate [27], and hexafluoroacetylacetone [28] are observed at −77.5, −76.14, and −77 ppm, respectively. These values reflect the noted tendency of these systems to enolize predominantly toward the trifluoroacetyl group.

In the present series of cyclic fluorinated β-diketones **1**–**4** the direction of enolization is markedly dependent on ring size. Thus, in contrast with enolic 2-trifluoroacetylcyclopentanone (**1**), where fluorine resonates at −74.95 ppm in accord with a dominant enolization toward the trifluoroacetyl group (an exocyclic enol form), the ^{19}F resonances of the six-, seven-, and eight-membered ring systems (compounds **2**–**4**) are observed at relatively higher frequencies (−71.8– −72.99 ppm) consistent with a dominant endocyclic enol form in these ring systems.

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