## Molecular Structure of 3-Trifluoroacetamidobenzoyltrifluoroacetone Enol Form

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**Abstract**—3-Trifluoroacetamidobenzoyltrifluoroacetone formed in the reaction of 3-aminoacetophenone with an excess of methyl trifluoroacetate crystallizes in the *cis*-enol form with a hydroxy group located at the carbon atom bound with the trifluoromethyl substituent. Analysis of geometric characteristics indicate the presence of both intramolecular hydrogen bond in the enol fragment and intermolecular H…O contacts in the crystal of the compound.

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A characteristic feature of  $\beta$ -diketones is the increased mobility of the hydrogen atoms attached to the central carbon atom [1, 2]. This causes a high degree of enolization:



Enols exist in the cis- and trans-forms. In solutions, the two tautomeric forms can be determined from the vibrational and electronic spectra, as well as from the data of NMR spectroscopy. The keto-enol equilibrium is strongly affected by the nature of the substituents in the molecule of  $\beta$ -diketone, by temperature and solvent. The presence of electron-withdrawing groups changes the electron density distribution in the molecule and contributes to the relative content of the enol. Hydrogen bond, which is thus formed, stabilizes this form. Thus, fluorinated  $\beta$ -diketones are mainly in the enol form, the percentage of enol tautomer increases with increasing degree of fluorination [3]. For example, a molecule hexafluoroacetylacetone is enolyzed to 100%. The presence of aromatic substituents leads to an increase in the degree of enolization by the formation of a single  $\pi$ -electron conjugated chain between the benzene ring and the six-membered enol

cycle. In the case of asymmetrically substituted  $\beta$ -diketones two different enol forms can exist.

Alkyl substituents at the central carbon atom reduce the enol content to almost 0%. For example, acetylacetone at room temperature contains 81% of the enol, while in 3-methylacetylacetone the enol content is only 28%. Content of keto form increases with increasing temperature.

An important factor is the nature of the solvent. In inert environments the less polar enol form dominates due to the formation of intramolecular hydrogen bond. In contrast, polar solvents increase the content of ketone in the tautomeric mixture due to the solvation of the carbonyl groups by the polar solvent molecules.

We have previously shown [4] that the interaction of 3-aminoacetophenone with an excess of methyl trifluoroacetate and sodium hydride leads to the formation of 3-trifluoroacetamidobenzoyltrifluoroacetone instead of the expected 3-aminobenzoyltrifluoroacetone.

According to elemental analysis and <sup>1</sup>H NMR spectroscopy, the  $\beta$ -diketone **IV** isolated after reprecipitation with hexane contains one molecule of ether. Sublimation in a vacuum results in the removal of the associated (C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>O molecules. 3-Trifluoroacetamido-acetophenone **III** is an intermediate in this process. Compound **III** is formed rapidly and in high yield in the reaction of 3-aminoacetophenone with methyl trifluoroacetate in the absence of sodium hydride.



It was shown that compound IV exists in acetone $d_6$  and chloroform-d solutions as a mixture of enol and ketone forms in a ratio of 15:1. It was assumed that the compound is in the *cis* form, the hydroxy group is located mainly at the carbon atom linked to the most electronegative trifluoromethyl substituent (isomer IVa), although the existence of an alternative isomer IVb is also possible. The presence of enol IVa and/or IVb is confirmed by the presence in the <sup>1</sup>H NMR spectrum of the signal at 6.91 ppm (C–H), and the existence of the diketone follows from the presence of a singlet signal of two protons of the CH<sub>2</sub> group at 4.81 ppm. The HPLC data also showed in favor of the presence of the two forms of  $\beta$ -diketone IV in aceto-nitrile solution.

The molecular structure of compound IV established by the method of X-ray diffraction (Fig. 1) showed that after removal of the ether molecules by sublimation in a vacuum it crystallized from the solution in toluene as enol IVa. The enol fragment  $O^1C^{2-4}O^2$  is flat, the average deviation of the atoms from the plane is 0.011 Å. The dihedral angle between the planes of the fragment  $O^1C^{2-4}O^2$  and six-membered



**Fig. 1.** General view of the molecule of 3-(trifluoroacetamido)benzoyltrifluoroacetone **IVa**. Hydrogen atoms are not shown, except for  $H^{1A-3A}$ . Thermal ellipsoids are shown with 30% probability.

benzene ring  $C^{5-10}$  is 6.7°. The hydrogen atom  $H^{2A}$  is located at the oxygen atom  $O^1$  and is turned in the direction of the oxygen atom  $O^2$ . The distance  $O^2 \cdots H^{2A}$ 1.86(3) Å is significantly shorter than the  $O \cdots H$ hydrogen bond (2.1 Å) [5]. The angle at the hydrogen atom  $O^2 \cdots H^{2A} - O^1$  is 139.1°, and is in the range of similar values characteristic of hydrogen bonds (100– 180°) [6, 7]. Thus, the analysis of geometric characteristics indicates the presence of intramolecular hydrogen bond  $O^2 \cdots H^{2A}$  in the enol fragment **IVa** of the compound. Bond lengths  $O^2 - C^4$  and  $C^2 - C^3$  [1.229(2) and 1.350(3) Å, respectively] are noticeably shorter than the distances  $O^1 - C^2$  [1.316(2) Å] and  $C^3 - C^4$ [1.454(3) Å], indicating that the  $O^1 C^{2-4} O^2$  fragment is in the enol form (Table 1).

In the crystal of compound **IVa** we found short intermolecular O···H contacts (Fig. 2). The contacts  $O^{2A}$ ···H<sup>2AE</sup> and  $O^{2E}$ ···H<sup>2AA</sup>,  $O^{2B}$ ···H<sup>2AF</sup> and  $O^{2F}$ ···H<sup>2AB</sup>,  $O^{2C}$ ···H<sup>2AG</sup> and  $O^{2G}$ ···H<sup>2AC</sup> form dimeric fragments of the molecules of compound **IVa** in the crystal. The distances of these contacts are 2.17(3) Å, and angles at the hydrogen atoms are 135.3°. Dimeric fragments are connected to each other through intermolecular contacts  $O^{3A}$ ···H<sup>1AB</sup> and  $O^{3F}$ ···H<sup>1AE</sup>,  $O^{3B}$ ···H<sup>1AC</sup> and  $O^{3G}$ ···H<sup>1AF</sup>, the distances are equal to 2.02(1) Å. The

**Table 1.** Selected bond lengths (*d*) and bond angles ( $\omega$ ) in compound IVa

Bond	d, Å	Angle	ω, deg
$N^1 - C^{11}$	1.336(3)	$O^1 C^2 C^3$	127.3(2)
$N^{1}-C^{7}$	1.427(3)	$C^2C^3C^4$	119.4(2)
$O^1 - C^2$	1.316(2)	$C^{3}C^{4}C^{5}$	120.7(2)
$O^2 - C^4$	1.229(2)	$O^2C^4C^3$	119.5(2)
$O^{3}-C^{11}$	1.215(2)	$C^7 N^1 C^{11}$	124.0(2)
$C^2 - C^3$	1.350(3)	$O^3C^{11}N^1$	126.7(2)
$C^{3}-C^{4}$	1.454(3)	$N^{1}C^{11}C^{12}$	115.9(2)
$C^{4}-C^{5}$	1.487(3)		
$C^{5}-C^{6}$	1.396(3)		
$C^{6}-C^{7}$	1.386(3)		

angle at the hydrogen atoms in these contacts is  $154.6^{\circ}$ . According to their geometric characteristics, the short intermolecular O····H contacts in the crystal of compound **IVa** are intermolecular hydrogen bonds O···H [5–7].

## **EXPERIMENTAL**

The IR spectra of compounds as liquid films between KBr plates or as suspensions in mineral oil were recorded on a FTIR spectrometer FSM 1201. <sup>1</sup>H



Fig. 2. Fragment of crystal packing of 3-(trifluoroacetamido)benzoyltrifluoroacetone IVa. Thermal ellipsoids are shown with 30% probability.

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Parameter	Value	
Empirical formula	$C_{12}H_7F_6NO_3$	
Molecular weight	327.19	
Crystal system	Monoclinic	
Space group	P2(1)/n	
<i>a</i> , Å	5.0639(7)	
b, Å	13.4610(19)	
<i>c</i> , Å	18.325(3)	
β, deg	92.790(3)	
V, Å <sup>3</sup>	1247.6(3)	
Ζ	4	
$d_{\rm calc},~{ m g~cm^{-3}}$	1.742	
$\mu$ , mm <sup>-1</sup>	0.182	
<i>F</i> (000)	656	
$2\theta_{max}$ , deg	52	
Number of measured reflections	9933	
Number of independent reflections	2434	
$R_{\rm int}$	0.0461	
Q-factor	1.030	
$R_1$ [for reflections with $I > 2\sigma(I)$ ]	0.0452	
$wR_2$ [for reflections with $I > 2\sigma(I)$ ]	0.0990	
$R_1$ (for all reflections)	0.0682	
$wR_2$ (for all reflections)	0.1073	
Residual electron density peaks, max/min, e Å <sup>-3</sup>	0.249/-0.204	

**Table 2.** The main crystallographic characteristics, parameters of X-ray diffraction experiment, and refinement of compound IVa

NMR spectra were recorded on a Bruker Avance DPX-200 instrument (200 MHz) at 25°C, internal reference TMS. Electron absorption spectra were recorded on a Perkin Elmer Lambda 25 spectrophotometer.

The XRD data for compounds **IVa** were obtained on a Smart APEX diffractometer (graphite monochromator, Mo $K_{\alpha}$  radiation,  $\lambda = 0.71073$  Å,  $\omega$ - and  $\varphi$ scans, T = 100 K). The extinction was accounted for using the SADABS software [8]. The structure of compounds **IVa** was solved by the direct method and refined by the least squares method with respect to  $F_{hkl}^2$ in anisotropic approximation for all nonhydrogen atoms. Hydrogen atoms attached to the carbon atoms  $C^6$  and  $C^{8-10}$  were placed in geometrically calculated positions and refined in the *rider* model [ $U_{iso}(H) =$  $1.2U_{eq}(C)$ ]. The positions of hydrogen atoms  $H^{1A-3A}$  at the nitrogen atoms N<sup>1</sup>, oxygen O<sup>1</sup>, and carbon C<sup>3</sup>, respectively, were found from the difference Fourier synthesis of electron density and refined in isotropic approximation. All calculations were performed using the software package SHELXTL v.6.12 [9]. The main crystallographic characteristics, parameters of X-ray diffraction experiment and refinement for compound **IVa** are shown in Table 2.

We used sodium hydride as a 60% suspension in mineral oil of Acros. 3-Aminoacetophenone (I) (Acros) and methyl trifluoroacetate (II) (PIM Invest) were used without pretreatment.

3-(Trifluoroacetamidobenzoyl)trifluoroacetone (IV). A three-neck flask equipped with a stirrer, a dropping funnel, and a reflux condenser was heated to 100°C in a stream of argon, and then a solution of 3.0 g (0.075 mol) of NaH in 100 ml of water-free diethyl ether was charged to it, and 19.2 g (0.15 mol) of compound II was added dropwise with stirring. Then a solution of 5.0 g (0.037 mol) of 3-aminoacetophenone (I) in 20 ml of ether was added, the mixture was stirred for 3 h, and 10% H<sub>2</sub>SO<sub>4</sub> solution was added in portions till neutral reaction. The ether layer was separated, dried over Na<sub>2</sub>SO<sub>4</sub>, diketone was isolated and recrystallized from diethyl ether-hexane. 10.1 g of the  $IV \cdot O(C_2H_5)_2$  etherate was obtained. <sup>1</sup>H NMR spectrum [(CD<sub>3</sub>)<sub>2</sub>CO], δ, ppm: 1.10 t (6H, C<u>H</u><sub>3</sub>CH<sub>2</sub>, J 7.03), 3.34-3.45 q (4H, CH<sub>3</sub>CH<sub>2</sub>, J 7.03). After sublimation in a vacuum 9.4 g (78%) of diketone IV was isolated. Colourless crystals of IVa were grown from a saturated solution in toluene at room temperature. IR spectrum, v, cm<sup>-1</sup>: 3300 (NH), 3087 (C=CH), 1716 (amide I), 1614, 1550 (C=O, C=COH), 1590 (amide II), 1489, 1458, 1282, 1221, 1188, 1150, 1120 (CF<sub>3</sub>), 788. <sup>1</sup>H NMR spectrum [(CD<sub>3</sub>)<sub>2</sub>CO],  $\delta$ , ppm (J, Hz): 4.81 s (2H, CH<sub>2</sub>, diketone) 6.91 s (1H, CH, enol), 7.66 t (1H arom., J 8.03), 8.02-8.04 m (1H, Ph), 8.08-8.10 m (1H, Ph), 8.44 s (1H, Ph), 10.49 s (NH). Found, %: C 43.20, H 2.15. C<sub>12</sub>H<sub>7</sub>F<sub>6</sub>NO<sub>3</sub>. Calculated, %: C 44.04, H 2.16.

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