Russian Journal of General Chemistry, Vol. 75, No. 11, 2005, pp. 1821–1829. Translated from Zhurnal Obshchei Khimii, Vol. 75, No. 11, 2005, pp. 1907–1915.

3,5-Dimethylpyrazole Complexes with Strong Carboxylic Acids

S. F. Bureiko, N. S. Golubev, G. S. Denisov, S. Yu. Kucherov, and P. M. Tolstoi

Fok Research Institute of Physics, St. Petersburg State University, St. Petersburg, Russia

Received March 10, 2005

Abstract—3,5-Dimethylpyrazole and halogen-containing carboxylic acids in solution give rise to equilibrium between the free molecules and 1 : 1 and 1 : 2 H-complexes. These complexes either have a ion pair-like structure with two equivalent hydrogen bonds $O^{-}\cdots HN^{+}$ (1 : 1) or include homoconjugate anion with strong hydrogen bond C–O–H···O–C (1 : 2). At low temperatures, 2 : 1 complexes were detected. The structure and harmonic vibration frequencies of the complexes were calculated in terms of the density functional theory.

An important role of strong hydrogen bonds in enzymatic catalysis [1–3] and molecular self-organization [4–6] stimulates studies in this line. The problem is complicated by the fact that H-bond systems involved in both cases strongly interact with each other and are dependent on the molecular environment. Pyrazoles are promising model compounds and convenient components for building up supramolecular systems. Due to the presence of an =NN(H) fragment, pyrazole derivatives possess a unique ability to form various self-associates (linear chains, cyclic dimers, trimers, and tetramers, and complexes with proton donor and proton acceptors) in the gaseous phase, in crystal, and in solution [7–10]. Structural diversity of such associates and considerable differences in their spectral parameters make it possible to examine the effect of substituents on the geometry and thermodynamic properties of the complexes, interactions between several hydrogen bonds, and specific behavior of IR absorption bands typical of N–H stretching vibrations, chemical shifts and coupling constants in NMR spectra, and H/D-isotope effects.

In the present work we examined H-complexes derived from 3,5-dimethylpyrazole (**I**) and a number of strong carboxylic acids: trifluoroacetic acid (**II**), trichloroacetic acid (**III**), and dichloroacetic acid (**IV**). Molecule **I** possesses lone electron pairs on the nitrogen atom and proton-donor NH group, which could ensure formation of cyclic complexes involving the hydroxy and carbonyl groups of carboxylic acids, as well as of more complex cyclic associates consisting of more than one molecule of one or another component. Practical importance of our study follows from wide application of pyrazole derivatives in pharmacology as nonnarcotic analgetics. In order to attain the best effect, composite preparations including several compounds of this group (sometimes in combination with barbiturates or caffein [11]) are used.

We previously studied self-association of 3,5-dimethylpyrazole (**I**) and its complex formation with proton donors in solution and in the gaseous and solid phases. According to the IR data and quantum-chemical calculations [12], in methylene chloride free 3,5-dimethylpyrazole molecules occur in equilibrium with the corresponding trimer. Interaction with a strong proton donor, pentachlorophenol, gives rise to open-chain dimers with OH···N hydrogen bond, while the reaction of **I** with HBr leads to formation of H-bonded ion pairs consisting of one or two pyrazole molecules **I** and one HBr molecule. The complex derived from **I** and AcOH has a cyclic structure with two hydrogen bonds: OH···N and C=O···HN. The spectral data indicated proton transfer in the reaction of **I** with trifluoroacetic acid (**II**); on the other hand, the calculations predicted that the molecular structure is preferred. We also studied interactions of pyrazole **I**, diphenyltriazene, and substituted amidines with various acids by NMR and IR spectroscopy [13, 14] and found that the energies of hydrogen bonds in the cyclic complex of **I** with formic acid are 33 (OH···N) and 13 $kJ\,mol^{-1}$ (NH···O=C [14]; these values satisfactorily agree with the overall enthalpy of complex formation equal to 45 ± 4 $kJ\,mol^{-1}$ [13].

The goal of the present work was to study the structure and spectral and thermodynamic parameters of Hcomplexes derived from 3,5-dimethylpyrazole and halogenated carboxylic acids RCO2H (R = CF3, CCl_3, $CHCl_2$) in solution using IR and low-temperature ^{1}H and ^{15}N NMR spectroscopy, as well as quantum-chemical calculations.

We examined the IR spectra of solutions of pyrazole **I** and acid **II** in methylene chloride. The concentration of compound **I** was maintained constant, while the concentration of acid **II** was varied from less than equimolar amount to excess. The spectra of

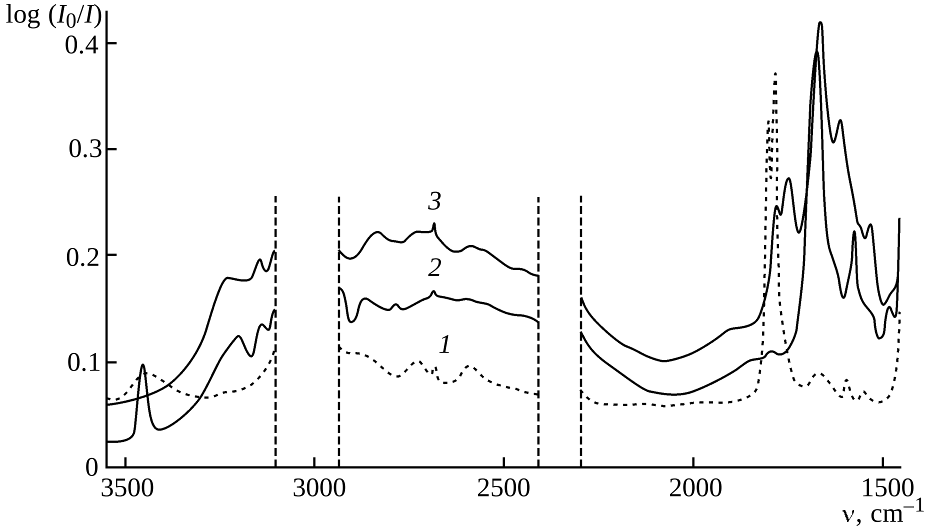

Fig. 1. IR spectra of solutions in CH_2Cl_2 containing (*1*) 0.02 mol l^{-1} of **II**, (2) 0.02 mol l^{-1} of **I** and 0.02 mol l^{-1} of **II**, and (*3*) 0.02 mol l^{-1} of **I** and 0.04 mol l^{-1} of **II** (vertical dashed lines bound the solvent absorption regions).

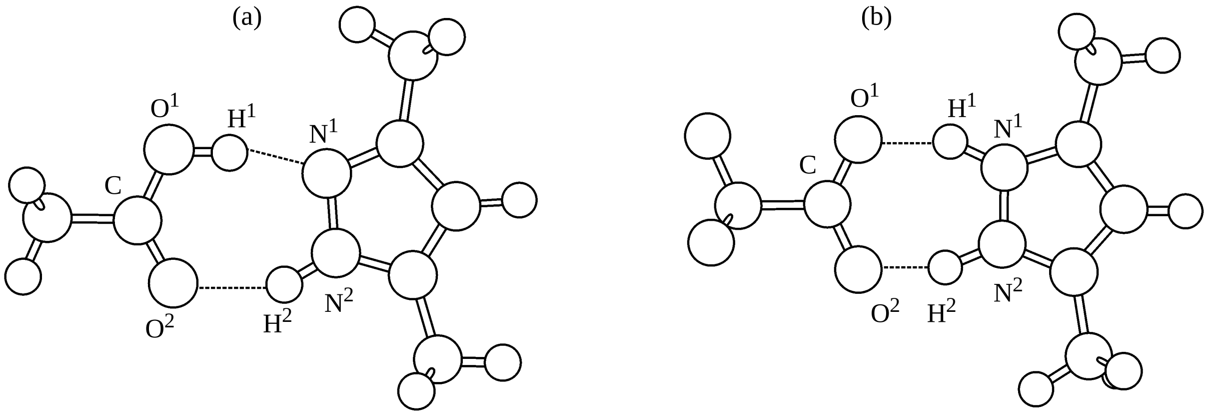

Fig. 2. Structures of the (a) molecular and (b) ionic **I**–**II** complexes according to the B3LYP/6-31G**+ calculations.

solutions with excess pyrazole **I** (Fig. 1) contain a broad band in the region 3300–2100 cm^{-1}, which may be assigned to longitudinal vibration of the hydrogen atom in the $O^-\cdots HN^+$ hydrogen bond [12]. This suggests formation of a 1 : 1 complex by compounds **I** and **II** with proton transfer from acid **II** to base **I**. As shown in [12, 14], such structure of the complex (Fig. 2b) is intrinsic just to complexes of difunctional nitrogen-centered bases with strong carboxylic acids, in contrast to complexes of **I** with acetic and chloroacetic acids, which have a cyclic molecular structure. The formation of H-bonded ion pair in solution is additionally supported by the presence in the IR spectrum of a band at 1680 cm^{-1}, which belongs to $\nu_{as}(CO_2^-)$ vibrations in the trifluoroacetate ion [15].

Addition of excess acid to a solution of compound **I** leads to appearance in the IR spectrum of $\nu_{as}(CO_2)$ bands at 1800 and 1785 cm^{-1} due to monomeric acid **II** and its dimer, respectively; this means that the solution contains free molecules of acid **II**, i.e., those not involved in complex formation with pyrazole **I**. Addition of acid also induces other changes in the spectral pattern, in particular, increase of background absorption in the range from 2000 to 500 cm^{-1} (which is typical of a considerable contribution of proton motion), complete disappearance of the band at 1570 cm^{-1} belonging to free base **I**, appearance of several new broad bands at 1750, 1665, 1608, 1540, and 1350 cm^{-1}, and low-frequency shift of the band at 1680 cm^{-1}. These findings suggest formation of a new complex. Presumably, it has a composition of 1 : 2, i.e., two molecules of acid **II** per molecule of pyrazole **I**. The existence of such complex is confirmed by quantum-chemical calculations (see below), and its structure is shown in Fig. 3.

The spectral patterns characterizing intermolecular interactions in solution with acids **III** and **IV** as proton donors are similar to that described above. We can conclude that, according to the IR spectral data, 3,5-dimethylpyrazole (**I**) with acids **II**–**IV** in solution at room temperature gives rise to 1 : 1 and 1 : 2 H-complexes which have the structure of H-bonded ion pairs formed via proton transfer from the acid to the nitrogen atom of pyrazole **I**.

Low-temperature NMR spectra. The behavior of the pyrazole **I**–acid systems at low temperatures was studied by analyzing the ^{1}H and ^{15}N NMR spectra of a mixture of compound **I** and acid **III** in a Freon mixture.

Liquid Freons and their mixtures are convenient solvents for low-temperature NMR studies; they are inert, transparent, and low-viscous down to 100 K and lower [16]. The temperature range from 100 to 150 K ensures slow migration of protons between molecules in a complex; therefore, resonance signals from complexes having different compositions can be observed separately. The stoichiometry of the complexes was determined via partial deuteration (replacement of labile protons by deuterium). A small weakening of hydrogen bond as a result of deuteration leads to change of the strength of the neighboring bonds, and the ^{1}H NMR spectrum displays additional splitting of signals due to vicinal [10] isotope effects.

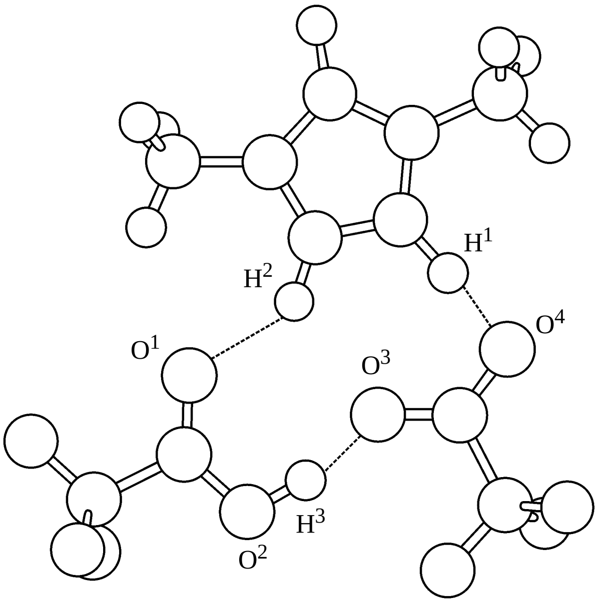

Fig. 3. Structure of the 1 : 2 pyrazole **I**–2RCO$_2$H complex.

Figure 4 shows the ^{1}H and ^{15}N NMR spectra of a solution containing acid **III** and pyrazole **I** labeled with ^{15}N at both nitrogen atoms. The solution contains several different complexes whose ratio depends on the concentration ratio of acid **III** and pyrazole **I**. Addition of acid **III** to a solution of **I** in Freons leads

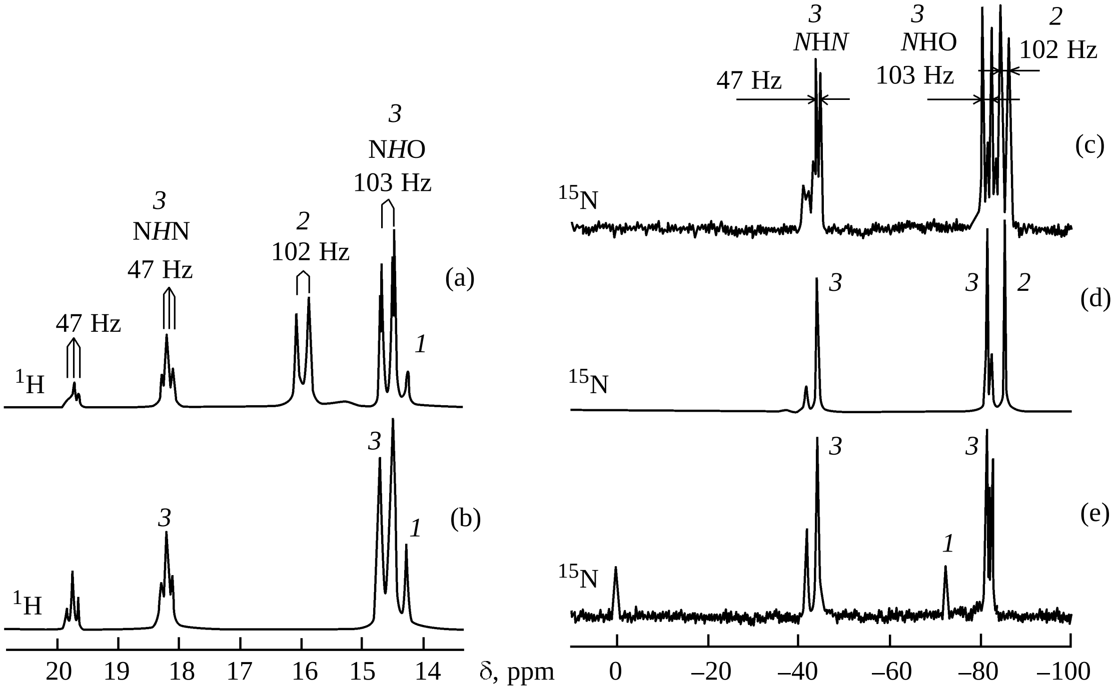

Fig. 4. (a, b) ^{1}H and (c–d) ^{15}N NMR spectra of (*1*) pyrazole **I** homoassociates, (*2*) 1 : 1 complex **I**–**III**, and (*3*) 2 : 1 complex **I**–**III** [0.02 mol l^{-1} of **I** and (a, c, d) 0.03 and (b, d) 0.05 mol l^{-1} of **III**].

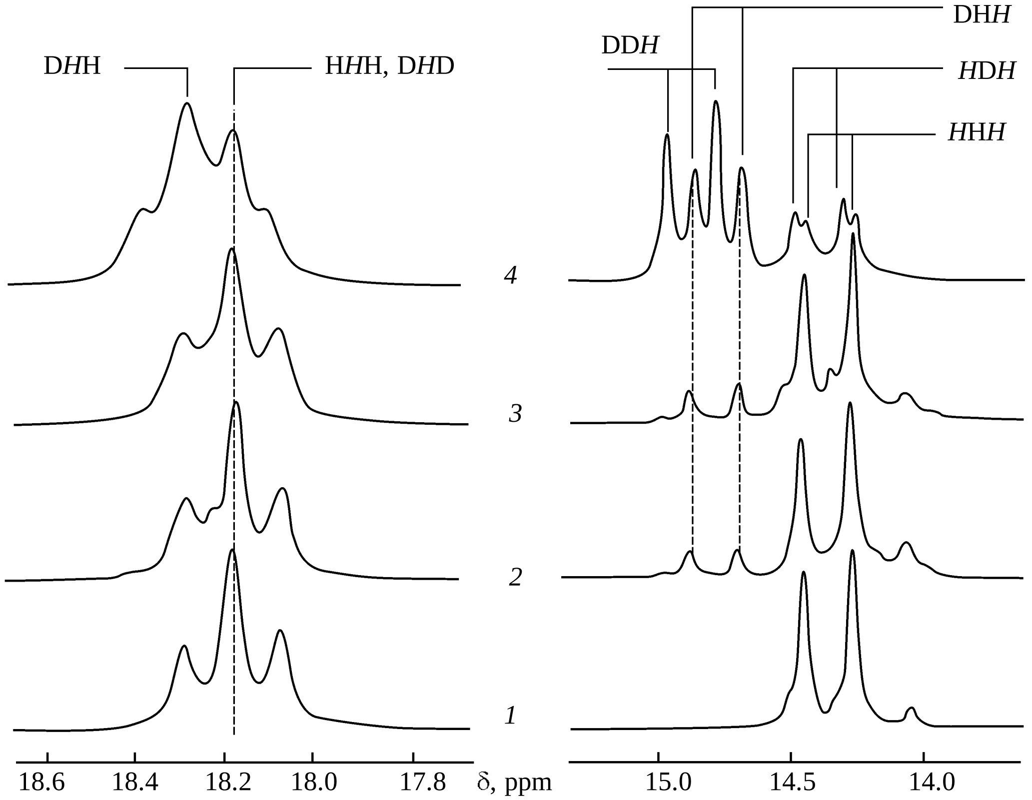

Fig. 5. ^{1}H NMR spectra of solutions of deuterated complexes **I–III** in Freons at 110 K; deuterium concentration, %: (*1*) 0, (*2*) 15, (*3*) 25, and (*4*) 70.

to formation of 1 : 1 complexes including two equivalent $O^{-}\cdots HN^{+}$ hydrogen bonds, as follows from the presence in the ^{1}H NMR spectrum of a doublet at δ 16 ppm with $^{1}J_{NH}$ = 102 Hz (Fig. 4a). Molecule **I** is protonated by acid **III** to give Hbonded ion pair. In the ^{15}N NMR spectrum, we observe a signal at δ_N –85.5 ppm due completely protonated nitrogen atom (Fig. 4c, d).

Systems **I**–**III** containing excess pyrazole **I** also showed in the low-temperature NMR spectra signals of complexes consisting two molecules of **I** and one molecule of acid **III**. Proton transfer from the acid gives rise to ion pair with homoconjugate bisdimethylpyrazolium. The H-bond ring includes one NH···N and two $O^{-}\cdots HN^{+}$ hydrogen bonds. Two signals are present in the ^{1}H NMR spectrum (Figs. 4a, 4b). The signal at δ 18.2–17.9 ppm corresponds to the NH···N bridging proton, and it is split into a triplet ($^{1}J_{NH}$ = 47 Hz) due to fast motion of the proton in a symmetric potential with two potential wells. The other signal at δ ~14.5 ppm is a doublet ($^{1}J_{NH}$ = 103 Hz); it was assigned to the bridging protons in the $O^{-}\cdots HN^{+}$ bond. The intensity ratio of these signals (1 : 2) suggests the presence of 2 : 1 complexes of **I** with **III**, which is fully consistent with the ^{15}N NMR spectra (Figs. 4c–4e). In fact, the 2 : 1 complex shows in the ^{15}N NMR spectrum a doublet with $^{1}J_{NH}$ = 103 Hz in the region corresponding to completely protonated nitrogen atom (δ_N –82 ppm) and a doublet at δ_N –44 ppm ($^{1}J_{NH}$ 47 = Hz), i.e., in the region intermediate between those typical of protonated and nonprotonated nitrogen atoms.

Cooperativity of hydrogen bonds in the 2 : 1 complex was additionally studied by partial deuteration. As a result, three new signals appeared in the ^{1}H NMR spectrum (Fig. 5, Table 1). These signals were assigned to different isotopomers by calculating their relative intensities upon variation of the overall concentration od deuterium and H/D ratio. Taking into account symmetric structure of the complex and the fact that the completely deuterated complex gives no signals in the ^{1}H NMR spectrum, we can observe five isotopomers: HHH, DHH, HDH, DDH, and DHD (here, the first and the last symbols refer to the $O^{-}\cdots HN^{+}$ hydrogen bonds, and the middle, to the central NH···N bond). Four isotopomers (HHH, DHH, HDH, and DDH) contribute to the signal at δ ~14.5 ppm, and three isotopomers (HHH, DHH, DHD), to that at δ ~18.2 ppm (Fig. 5). The $O^{-}\cdots HN^{+}$ hydrogen bridges are strongly interacting bonds since deuteration of one of these necessarily leads to considerable change in the position of the signal from the other: the signals of DDH and DHH are displaced downfield by ~0.6 ppm relative to that of the HHH isotopomer.

The negative sign of the above vicinal effect proves the existence of a 2 : 1 complex between **I** and *III*: The $O^{-}\cdots HN^{+}$ hydrogen bonds are anticooperative. On the other hand, their interactions with the NH···N bond are much weaker: the signals from the HDH and HHH isotopomers are poorly resolved. An analogous pattern is observed for the NH···N hydrogen bridge. Presumably, H–D exchange almost does not affect the remaining nondeuterated hydrogen bonds provided that the symmetry of the 2 : 1 complex does not change.

Specific interaction between different hydrogen bonds in the 2 : 1 complex can also be illustrated by the ^{15}N NMR spectra. Insofar as we failed to distinguish signals from different isotopomers in the region corresponding to completely protonated nitrogen atoms ($O^{-}\cdots HN^{+}$ bonds), let us consider the δ_N range from –50 to –40 ppm which is typical of nitrogen atoms involved in the NH···N bond (Fig. 6). The expected intensities of signals from each isotopomer can be estimated using a simple statistic model, according to which the intensity of a signal is proportional to the population of the corresponding isotopomer; the latter were measured as $(1 - x_D)^3$ for HHH, $2(1 - x_D)^2x_D$ for DHH, $(1 - x_D)x_D^2$ for HDH, $2(1 - x_D)x_D^2$ for DDH, $(1 - x_D)x_D^2$ for DHD, and x_D^3 for DDD, where x_D is the concentration of deuterium, %. The signal in the ^{15}N NMR spectrum were assigned on the basis of the above listed populations (Fig. 6). As in the ^{1}H NMR spectra, symmetric H/D-exchange (HHH – DHD) does not change the position of the ^{15}N signal to an appreciable extent. The secondary isotope effect δ_N(HDH) – δ_N(HHH) is positive, and its absolute value approaches that of the negative vicinal isotope effect δ_N(DHH) – δ_N(HHH). Thus, both effects in the DDH isotopomer compensate each other, and the DDH signal position is close to that of HHH.

Quantum-chemical calculations of the complexes. Calculation of 1 : 1 and 1 : 2 complexes of pyrazole **I** with carboxylic acids is a difficult task, for these systems include more than 25 atoms. Therefore, all calculations were performed in two steps. In the first step, stationary geometric parameters of the complexes were calculated at a relatively low level, and the parameters thus obtained were used in the second step to calculated more precisely their structure and vibrational frequencies in the harmonic approximation.

Table 1. NMR spectra of the 2 : 1 **I–III** complex

Parameter	Isotopomer	Value
Hydrogen bond NH···N		
$\delta(^1H)$ ±0.02, ppm	HHH	18.16
	DHH	18.25
	DHD	18.16
$^1J_{NH}$ ±1, Hz	HHH	48
	DHH	47
	DHD	48
$\delta(^{15}N)$ ±0.1, ppm	HHH	–44.6
	DHH	–35.9
	HDH	–53.1
	DHD	–44.9
	DDH	–45.5
	DDD	–55.0
Hydrogen bond $O^{-}\cdots HN^{+}$		
$\delta(^1H)$ ±0.02, ppm	HHH	14.31
	DHH	14.78
	HDH	14.36
$^1J_{NH}$ ±1, Hz	DDH	14.90
	HHH	104
	DHH	101
	HDH	102
	DDH	101
$\delta(^{15}N)$ ±0.1, ppm	HHH	–81.8
	DHH	[a]
	HDH	[a]
	DHD	[a]
	DDH	[a]
	DDD	[a]

[a] Unresolved bands.

Optimization of the electronic energy of **I**–RCO_2H complexes gave two equilibrium configurations: RCO_2H + **I** (Fig. 2a) and $RCOO^{-}$ + **I**·H^{+} (Fig. 2b). The first of these corresponds to the molecular complex [according to the B3LYP/6-31G+** calculations, the O–H bond length *R*(OH) is 1.06 Å], while the second is a ionic structure with *R*(OH) = 1.50 Å.

Different basis sets were used in the calculations of 1 : 1 **I**–RCO_2H complexes. As shown in [12], the shape of the potential energy surface is quite sensitive to the basis set used and the calculation procedure. According to the results obtained for bimolecular complexes using different basis sets, such complexes could have either only molecular (complex **I**–**IV**) or both molecular and ionic structure (**I**–**II** and **I**–**III**).

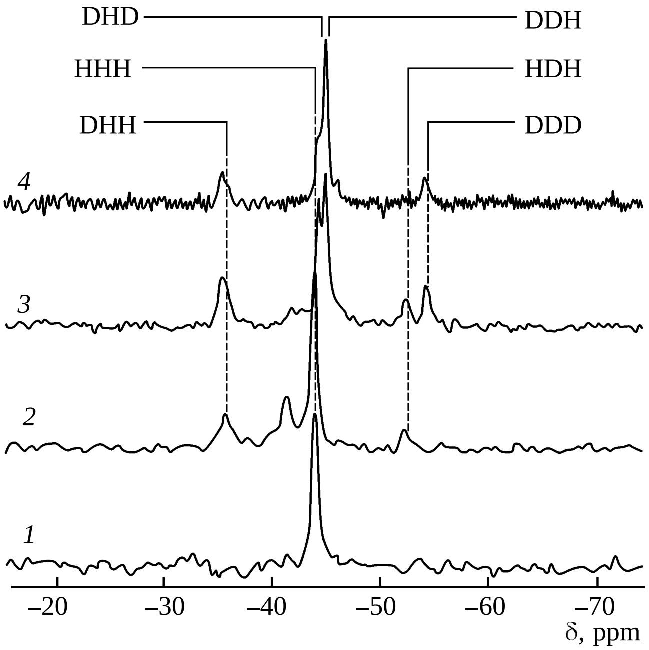

Fig. 6. ^{15}N NMR spectra of solutions of deuterated complexes **I**–**III** in Freons at 110 K; deuterium concentration, %: (*1*) 0, (*2*) 20, (*3*) 70, and (*4*) 85.

Table 2 contains the parameters of moleular and ionic complexes formed by compounds **I** and **II**, calculated at the B3LYP/6-31G+** level. The molecular complex is more energetically favorable by 5.5 kJ mol^{-1}. In the ionic structure, both protons are located more closely to the nitrogen atom, i.e., it is an ion pair with two intermolecular hydrogen bonds (Fig. 2b).

Table 2. Calculated (DFT/B3LYP/6-31G**+) geometric parameters of the 1 : 1 **I**–**II** complexes

Parameter	Molecular complex[a]	Ionic complex[b]	
		isolated structure	calculation according to the Onsager model
R(O^1–H^1), Å	1.06	1.51	1.71
R(H^1–N^1), Å	1.52	1.09	1.04
R(O^2–H^2), Å	2.02	1.60	1.69
R(H^2–N^2), Å	1.01	1.06	1.05
R(O^1–N^1), Å	2.57	2.55	2.68
R(O^2–N^2), Å	2.86	2.59	2.67
R(C–O^1), Å	1.30	1.26	1.25
R(C–O^2), Å	1.22	1.25	1.25
$\angle$O^{1}H^{1}N, deg	172.5	160.0	155.4
$\angle$O^{2}H^{2}N^2, deg	139.9	155.6	155.4
$\angle$H^{1}N^{1}N^2, deg	112.9	113.5	115.1
$\angle$H^{2}N^{2}N^1, deg	116.8	113.5	115.1
$\angle$O^{1}CO^2, deg	127.9	128.8	130.2

[a] See Fig. 2a. [b] See Fig. 2b.

According to the calculations performed with the use of the Onsager and Tomasi models, both minima in the two-well potential or the minimum corresponding to the molecular complex become deeper, and an additional minimum due to the ionic complex appears (if the isolated complex has a single-minimum potential). Such behavior of the system is normal, for proton transfer from the donor to the acceptor (provided that solvent effect is taken into account) requires a lesser energy since the relative depth of the potential minima and the height of the barrier change. For example, the B3LYP/6-31G** calculation with account taken of the solvent effect according to the Onsager model (CH_2Cl_2, ε = 8.9) gives a minimum corresponding to the ionic **I**–**II** complex, which is lower by 6 kJ mol^{-1} than that corresponding to the molecular complex. In the calculations according to the Tomasi model using the same dielectric constant, the ionic structure of the **I**–**III** complex is more favorable than the molecular one by 7.6 kJ mol^{-1}. The geometric parameters of the ionic **I**–**II** complex, calculated according to the Onsager model, are give in Table 2; it is seen that the intermolecular hydrogen bonds are extended.

As shown above, the experimental data indicate the existence of complexes consisting of two acid molecules and one molecule of pyrazole **I** in solution containing excess acid. The 1 : 2 complex **I**–2**II** was calculated by the DFT/B3LYP/6-31G** method. We thus obtained three different configurations **A**, **B**, and **C** which are shown in Fig. 7. All these structures include **I** · H$^+$ cation and bis-trifluoroacetate homoconjugate with a very short and strong O^2–H^3···O^3 hydrogen bond, the distance R(O^2···O^3) being 2.45–2.51 Å. Complex **C** is energetically more stable, and it has an asymmetric structure. The calculated energy of formation of structure **C** is 165 kJ mol^{-1}, while the energies of formation of isomers **A** and **B** are lower by 19 and 21 kJ mol^{-1}, respectively. Complex **C** is characterized by the smallest dipole moment (μ = 8 D) and the shortest O–H bond (1.03 Å) in the O–H···O hydrogen bond, but the latter is not linear.

Calculations of vibration frequencies in the harmonic approximation revealed a series of strong bands in the region 1700–1200 cm^{-1} (Table 3); however, only isomer **C** gives rise to five strong bands in that region. Their intensity is determined by the joint contribution of vibrations of the CO_2^- group and proton in the O–N···O hydrogen bond.

Table 3. Calculated and experimental frequencies and intensities (in parentheses, km/mol) of harmonic vibrations of isomers **A**–**C** of the 1:2 **I**–**II** complex

A		**B**		**C**		Experiment
calculation, cm^{-1}	assignment	calculation, cm^{-1}	assignment	calculation, cm^{-1}	assignment	
1820 (290)	$\nu(CO_{as})_s + \nu(OH)$	1800 (1070)	$\nu(CO_{as})_{as}$	1810 (580)	$\nu(CO_{as})_s + \delta(OH)$	1753
1700 (620)	$\delta(NH_{as}) + \nu(OH) + \nu(CO_{as})_{as}$	1660 (110)	$\delta(NH_{as})$	1700 (360)	$\delta(NH_{as})$	1665
1680 (840)	$\delta(NH_{as}) + \delta(OH)$	1620 (500)	$\delta(NH_s) + \delta(OH)$	1680 (370)	$\nu(CO_{as})_{as} + \delta(NH_{as}) + \delta(OH)$	1608
1610 (170)	$\delta(NH_s)$	1550 (90)	$\delta(NH_{as}) + \delta(OH)$	1590 (90)	$\delta(NH_s)$	1540
570 (0)	$\delta(OH)$	–	–	1535 (20)	$\delta(OH)$	–

Table 4 contains the geometric parameters of 1:2 complexes for all the examined acids (for atom numbering, see Fig. 3). It is seen that the lengths of hydrogen bonds and the corresponding bond angles in the complexes formed by acids **II**, **III**, and **IV** differ only slightly. On the other hand, the N–H bond in the $O^{-}\cdots H–N^{+}$ moiety of the 1:2 complexes (**I**–$2RCO_2H$) is longer than in monomeric, dimeric, and trimeric species of **I** [12]. The O–H component of the O–H···O hydrogen bond in the complexes is longer by 0.06 Å than that in the unassociated acid molecules and is 1.03 Å.

Table 4. Calculated (B3LYP/6-31G**) geometric parameters of the 1:2 **I**–acid complexes, monomeric acids, and cyclic self-associates **I**

Parameter	RCO_2H		
	IV	**III**	**II**
$R(N–H^1)$, Å	1.10	1.08	1.09
$\angle(NH^2O)$, deg	144.7	145.0	144.2
$R(O^2–O^3)$, Å	2.52	2.51	2.51
$R(O^2–H^3)$, Å	1.02	1.03	1.03
	Acid		
$\angle(COH)$, deg	106.9	106.8	107.1
$R(O–H)$, Å	0.97	0.97	0.97
	I [12]		
	Monomer	Dimer	Trimer
$R(N–H)$, Å	1.01	1.02	1.04

The results of our quantum-chemical calculations confirmed the possibility for formation of a 2:1 complex from pyrazole **I** and trichloroacetic acid (**III**), which was detected by NMR spectroscopy (see above). The structure of that complex is similar to the structure of the complex of **I** with HBr, which was described in [12]. The complex contains three hydrogen bonds: one NH···N and two $O^{-}\cdots HN^{+}$. According to

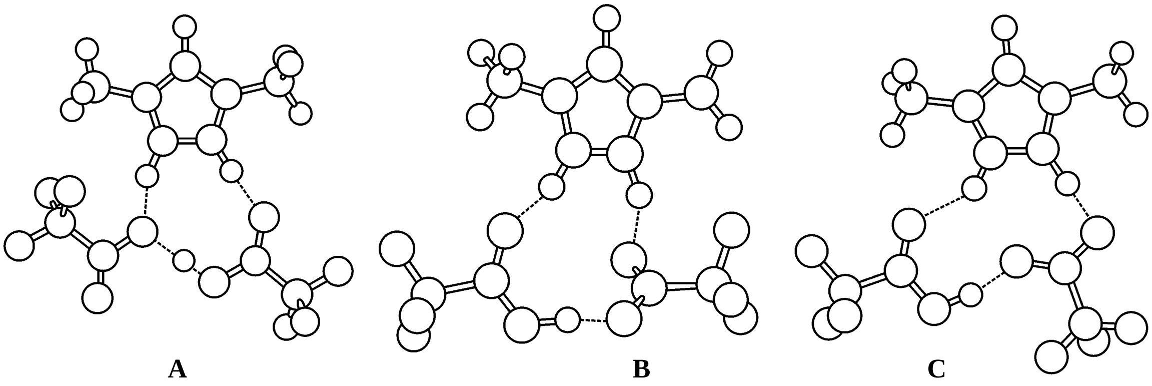
A **B** **C**

Fig. 7. Structures of isomers **A**–**C** of the **I**–$2RCO_2H$ complex.

the B3LYP/6-31G** calculations, the NH···N hydrogen bond is asymmetric and almost linear: ∠NHN = 175°, *R*(N–H) = 1.08 Å, *R*(N···N) = 2.72 Å. The molecules of **I** in the 2 : 1 complex 2**I**–**III** do not lie in a single plane: the corresponding dihedral angle is 29°; therefore, the arrangement of the acid molecule is also nonplanar.

EXPERIMENTAL

The IR spectra of solutions were recorded in the frequency range from 4000 to 370 cm^{-1} on a Bruker IFS-28 Fourier spectrometer at a resolution of 1 cm^{-1} (20°C). Samples were placed in standard cells with KBr or fluorite windows (layer thickness 0.125 to 0.55 mm). Methylene chloride or carbon tetrachloride were used as solvents. The NMR spectra were obtained on a Bruker AMX-500 spectrometer from solutions in a Freon mixture (CDF_3 + CDF_2Cl) in the temperature range from 150 to 110 K [13]; the ^{15}N chemical shifts were measured relative to the signal from the nonprotonated nitrogen atom in self-associate **I**.

3,5-Dimethylpyrazole and 1,2-[^{15}N]$_2$-3,5-dimethylpyrazole (from Aldrich) were used without additional purification; the acids were purified and dried if necessary. Deuterated samples of compound **I** for NMR studies were prepared by repeated dissolution of **I** in methanol-*d*, followed by distillation of the solvent under reduced pressure. Trihaloacetic acids were deuterated in a similar way. The overall concentration of deuterium in the hydroxy group of the acids was determined from the OH/CH_3 signal intensity ratio in the ^{1}H NMR spectra.

Quantum-chemical calculations were performed in terms of the density functional theory (DFT/B3LYP/6-31G**) using GAUSSIAN-98 software package [17]. The B3LYP hybrid exchange functional [18–20] with the extended 6-31G Gauss-type basis set was supplemented by heavy-atom d orbitals, hydrogen *p*-orbitals, and diffuse functions; the latter were Gauss functions with very small exponents, which slowly decreased as the distance from the nucleus increased (they are important for correct description of anions and weak hydrogen bonds). The calculations were limited to vibrational frequencies in the harmonic approximation. Solvent effects were taken into account using the Onsager and Tomasi models [21, 22] which ensured fairly good results (i.e., consistent with the experimental data) even when applied to large systems [23].

ACKNOWLEDGMENTS

The authors are thankful to A.V. Shurukhina for her help in the experimental studies and Kh.-Kh. Limbakh for providing the possibility for recording NMR spectra and performing calculations at the Institute of Chemistry, Free University of Berlin.

This study was performed under financial support by the Russian Foundation for Basic Research and by the Federal Education Agency of the Russian Federation.

REFERENCES

1. Bevilacqua, P.C., *Biopolymers*, 2004, vol. 73, no. 1, p. 90.
2. Frey, P., *J. Phys. Org. Chem.*, 2004, vol. 17, nos. 6–7, p. 511.
3. Schowen, K.B., Limbach, H.-H., Denisov, G.S., and Schowen, R.L., *Biochim. Biophys. Acta*, 2000, vol. 1458, no. 1, p. 43.
4. Paraschiv, V., Crego-Calama, M., Fokkens, R.H., Padberg, C.J., Timmerman, P., and Rainhourt, D.N., *J. Org. Chem.*, 2001, vol. 66, no. 25, p. 8297.
5. Archer, E.A., Gong, H., and Krische, M.J., *Tetrahedron*, 2001, vol. 57, no. 7, p. 1139.
6. Desiraju, G.R., *Acc. Chem. Res.*, 2002, vol. 35, no. 7, p. 565.
7. Klein, O., Aguilar-Parrilla, F., Lopez, J.M., Jagerovic, N., Elguero, J., and Limbach, H.-H., *J. Am. Chem. Soc.*, 2004, vol. 126, no. 37, p. 11718.
8. Boldog, I., Rusanov, E.B., Sieler, J., and Domasevitch, K.V., *New J. Chem.*, 2004, vol. 28, no. 6, p. 756.
9. Claramunt, R.M., Lopez, C., Garcia, M.A., Denisov, G.S., Alkorta, I., and Elguero, J., *New J. Chem.*, 2003, vol. 27, no. 4, p. 734.
10. Detering, K., Tolstoi, P.M., Golubev, N.S., Denisov, G.S., and Limbakh, Kh.-Kh., *Dokl. Ross. Akad. Nauk*, 2001, vol. 379, no. 3, p. 353.
11. Saratikov, A.S., Prishchep, T.P., and Yavorovskaya, V.E., *Protivovospalitel'nye sredstva gruppy pirazola* (Antiphlogistic Agents of the Pyrazole Series), Tomsk: Tomsk. Univ., 1975.
12. Castaneda, J.P., Denisov, G.S., Kucherov, S.Yu., Schreiber, V.M., and Shurukhina, A.V., *J. Mol. Struct.*, 2003, vol. 660, p. 25.
13. Bureiko, S.F., Golubev, N.S., and Chernyshova, I.V., *Khim. Fiz.*, 1987, vol. 6, no. 2, p. 176.
14. Bureiko, S.F. and Chernyshova, I.V., *Zh. Fiz. Khim.*, 1993, vol. 63, no. 2, p. 319.
15. Bellamy, L.J., *The Infra-red Spectra of Complex Molecules*, London: Methuen, 1958.
16. Golubev, N.S. and Denisov, G.S., *J. Mol. Struct.*, 1992, vol. 270, p. 263.
17. Frisch, M.J., Trucks, G.W., Schlegel, H.B., Scu-

seria, G.E., Robb, M.A., Cheeseman, J.R., Zakrzewski, V.G., Montgomery, J.A., Stratmann, R.E., Burant, J.C., Dapprich, S., Millam, J.M., Daniels, A.D., Kudin, K.N., Strain, M.C., Farkas, O., Tomasi, J., Barone, V., Cossi, M., Cammi, R., Mennucci, B., Pomelli, C., Adamo, C., Clifford, S., Ochterski, J., Petersson, G.A., Ayala, P.Y., Cui, Q., Morokuma, K., Malick, D.K., Rabuck, A.D., Raghavachari, K., Foresman, J.B., Cioslowski, J., Ortiz, J.V., Stefanov, B.B., Liu, G., Liashenko, A., Piskorz, P., Komaromi, I., Gomperts, R., Martin, R.L., Fox, D.J., Keith, T., Al-Laham, M.A., Peng, C.Y., Nanayakkara, A., Gonzalez, C., Challacombe, M., Gill, P.M.W., Johnson, B.G., Chen, W., Wong, M.W., Andres, J.L., Head-Gordon, M., Replogle, E.S., and Pople, J.A., *GAUSSIAN-98. Rev. A.1*, Pittsburgh: Gaussian, 1998.

18. Becke, A.D., *J. Chem. Phys.*, 1993, vol. 98, no. 7, p. 5648.
19. Lee, C., Yang, W., and Parr, R.G., *Phys. Rev. B: Condens. Matter Mater. Phys.*, 1988, vol. 37, no. 2, p. 785.
20. Becke, A.D., *Phys. Rev. A: At., Mol., Opt. Phys.*, 1988, vol. 38, no. 6, p. 3098.
21. Onsager, L., *J. Am. Chem. Soc.*, 1936, vol. 58, no. 8, p. 1486.
22. Wong, M.W., Frisch, M.J., and Wiberg, K.B., *J. Am. Chem. Soc.*, 1991, vol. 113, no. 13, p. 4776.
23. Yan Zh. and Sebastian, J.F., *Tetrahedron*, 2004, vol. 60, no. 48, p. 10 899.