

Structure, Basicity, and Thermodynamic Properties of 3,5-Bis(trifluoromethyl)-1,2,4-triazole with Regard to 1,2,4-Triazole: The Trifluoromethylation Effect

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Received June 8, 1993 (Revised Manuscript Received November 30, 1993*)

Thermodynamic properties (enthalpies of sublimation, gas-phase basicity) of 3,5-bis(trifluoromethyl)-1,2,4-triazole have been measured. These properties are discussed in the larger framework of two other triazoles, the parent compound and 3(5)-(trifluoromethyl)-1,2,4-triazole, thanks to *ab initio* calculations at the MP2/6-31G**/6-31G* level of accuracy. The calculations provide (i) an excellent description of the vibrational frequencies of 1H-1,2,4-triazole; (ii) a geometry for this compound more consistent with the microwave results; (iii) a description of the trifluoromethyl group as a substituent in theazole series; (iv) an excellent accord with the experimental proton affinity, and (v) an understanding of the interesting properties of the title compound.

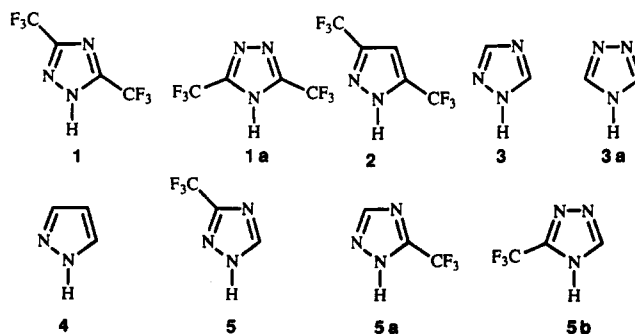
1. Introduction

The study of aromatic five-membered rings carrying trifluoromethyl substituents has been the subject of much interest in the last years. These studies included oxazoles,^{1,2} thiazoles,¹ imidazoles,^{1,3,4} furans,⁵ isoxazoles,^{6,7} isothiazoles,⁸ pyrazoles,⁷⁻¹³ 1,2,4-triazoles,¹⁴⁻¹⁶ 1,3,4-oxadiazoles,¹⁶ and tetrazoles.¹⁷ Nevertheless, all the reported publications dealt with synthetic aspects and the only report concerning the physicochemical properties of (trifluoromethyl)azoles concerns the influence of the CF₃ substituent on the acid-base properties of NH-pyrazoles.¹⁸ We decided to broaden the scope of these studies by

examining some relevant physical and chemical properties of 3,5-bis(trifluoromethyl)-1,2,4-triazole (1).¹⁵ Thus, we determined its enthalpy of sublimation and its gas-phase basicity relative to ammonia, ΔGB(1), defined as the standard Gibbs energy change for reaction 1:



To analyze the data obtained for 1, three more compounds are necessary: 3,5-bis(trifluoromethyl)pyrazole (2), 1,2,4-triazole (3), and pyrazole (4). Some other properties



which are not easily amenable to experiment, such as the relative stabilities of the different tautomers, the preferred protonation site, or the structure of the different protonated species, will be investigated theoretically in the framework of the *ab initio* MO theory. In order to better rationalize the trifluoromethyl substituent effects on the relative stability of the different tautomers as well as on their intrinsic basicities, we have considered it to be of

- * Abstract published in *Advance ACS Abstracts*, January 15, 1994.
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Table 1. Vapor Pressures of 3,5-Bis(trifluoromethyl)-1,2,4-triazole (1)^a

<i>T</i> , K	<i>t</i> , s	Δm , mg	<i>p</i> , Pa	$10^2 \Delta p/p$
270.56	21720	2.15	0.621	+0.675
273.02	18180	2.38	0.824	-1.30
275.49	16680	2.97	1.12	-0.454
278.06	14700	3.59	1.55	+1.56
280.46	12180	3.79	1.99	-1.42
283.16	11520	4.97	2.77	+0.754

^a $\log(p, \text{Pa}) = -B(T, \text{K})^{-1} + A$, $A = 14.38 \pm 0.16$, $B = 3946.4 \pm 42.9$, $\Delta H_{\text{sub}}^0(276.86) = 75.6 \pm 0.8 \text{ kJ mol}^{-1}$.

interest to include in this theoretical survey the corresponding monosubstituted derivatives, namely 3-(trifluoromethyl)-1*H*-1,2,4-triazole (5), 5-(trifluoromethyl)-1*H*-1,2,4-triazole (5a) and 3-(trifluoromethyl)-4*H*-1,2,4-triazole (5b). The discussion will proceed in the following order: gas-phase basicities, thermodynamic data, theoretical calculations, and general conclusions.

Experimental Section

The sample¹⁵ purity of 1 was determined to be 97.76% by differential scanning calorimetry, DSC (scan rate, 2.50 deg/min, mp 340.95 K).

Enthalpies of Sublimation. The enthalpies of sublimation were obtained from vapor pressures determined by the Knudsen effusion method, using the technique and procedure previously described.^{19,20} The apparatus consisted, essentially, of a stainless-steel sublimation chamber immersed in a jacket and connected to a high-vacuum system (1×10^{-4} Pa). The temperature of the jacket was maintained constant to within ± 0.005 K for each vapor-pressure experiment and was measured with a calibrated platinum resistance thermometer. The enthalpies of sublimation were computed from the relationship between pressure and temperature. The characteristics of the orifice employed in the sublimation experiment: orifice area (4.44 ± 0.02) $\times 10^{-4}$ cm² and Clausing coefficient $W_a = 0.943 \pm 0.012$.

The results of the Knudsen effusion experiments are summarized in Table 1, in which values of temperature, time, and mass-sublimed substance are collected. The vapor pressures were calculated by means of eq 2. The symbols of eq 2 have the same

$$p = (\Delta m/W_a t)(2\pi RT/M)^{1/2} \quad (2)$$

meaning as in ref 20. The highest percentage of error for the vapor pressure in Table 1 is 0.05 and has been computed as the sum of the estimated errors of all quantities in eq 2. An equation of the type $\log(p, \text{Pa}) = -B(T, \text{K})^{-1} + A$, was fitted to the results of Table 1 by the least-squares method. The values $10^2 \Delta p/p$ are the fractional deviations of the experimental vapor pressures from those computed using the preceding equation. The uncertainties assigned to the values of $\Delta_{\text{sub}}H^0$ are based on the standard deviations of *B* values.

The sublimation enthalpy at 298.15 K has been computed using the same equation as in ref 21. The $C_{p,m}^0(\text{Cs})$ values have been determined by DSC whereas the $C_{p,m}^0(\text{g})$ values were calculated using the group-contribution scheme of Rihany and Donaiswamy.²² The $\Delta_{\text{sub}}H^0$ (298.15 K) is $74.7 \pm 0.8 \text{ kJ mol}^{-1}$.

FTICR Experiments. These were performed on a modified Bruker CMS-47 mass spectrometer under conditions similar to those used in previous work.²³ In every case, the attainment of equilibrium was established by means of double resonance experiments. It is noteworthy that, notwithstanding the relatively high volatility of 1, severe difficulties were met because of adsorption effects.

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Computational Details. The geometries of 1*H*-1,2,4-triazole (3), 4*H*-1,2,4-triazole (3a), as well as those of their mono- and disubstituted CF₃ derivatives and their protonated species have been fully optimized at the HF level of theory by using a 6-31G* basis set.²⁴ The harmonic vibrational frequencies were obtained by analytical second derivative techniques and used both to characterize the corresponding minima and to evaluate zero-point energies (ZPE), which were scaled by the empirical factor 0.893.²⁵ Electron correlation effects have been taken into account by evaluating the energies at the second-order Møller-Plesset theory (MP2),²⁶ keeping the core electron frozen. These post-SCF calculations have been performed also at the 6-31G* level for the most-stable protonated species. All theoretical calculations have been carried out with the Gaussian-90 series of programs.²⁷

Protonation energies were evaluated as the energy difference between the corresponding protonated and unprotonated species. The protonation energies defined in this way are affected by the so-called basis set superposition error (BSSE), which has been estimated by using the counterpoise method of Boys and Bernardi,²⁸ at the MP2/6-31G* level.

To analyze the effects of the CF₃ substituent on the electronic properties of the triazole we have carried out a topological analysis of the charge density, ρ , and its Laplacian, $\nabla^2\rho$, for all systems included in this study. As it has been shown by Bader and co-workers,²⁹ $\nabla^2\rho$ identifies regions of space where the electronic charge of a given system is locally concentrated ($\nabla^2\rho < 0$) or depleted ($\nabla^2\rho > 0$). In general, negative values of $\nabla^2\rho$ are typical of covalent bonds, where the electronic charge is concentrated in the interatomic region leading to a lowering of the energy associated with the predominance in this region of the potential energy density. On the contrary, positive values of $\nabla^2\rho$ are associated with interactions between closed-shell systems, where the electronic density is concentrated in the atomic basins. The depletion of charge in the interatomic region leads then to a predominance of the kinetic energy density. Therefore, an analysis of the topological properties of $\nabla^2\rho$ will provide information on possible bond activations within the system upon protonation and, in general, on the charge redistribution associated with CF₃ substitution. To obtain a more quantitative information on these effects we have also located the relevant bond critical points (bcp), i.e., points where the electronic charge density, ρ , has one positive curvature (λ_3) and two negative ones (λ_1, λ_2). This allows us to estimate, when necessary, the ellipticity of a given bond, which is defined as $\epsilon = (\lambda_1/\lambda_2) - 1$. According to the definitions of λ_1 and λ_2 , the ellipticity will be exactly zero for single and triple bonds, and different from zero for those linkages which do not present cylindrical symmetry.

Results and Discussion

Gas-Phase Basicity. $\Delta\text{GB}(1)$ was determined by means of Fourier transform ion cyclotron resonance mass spectrometry (FTICRMS).³⁰ In these experiments, the standard Gibbs energy changes, $\delta\Delta G_{\text{H}^+}(\text{g})$, pertaining to

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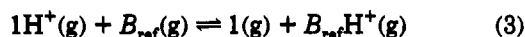
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Table 2. Experimental Data Pertaining to the Determination of $\Delta GB(1)^a$

B_{ref}	$\Delta G(B_{\text{ref}})^{a,b}$	$\delta\Delta G_{\text{H}^+}(\text{g})^a$	$\Delta GB(1)^a$
<i>n</i> -PrCHO	-59.4	+10.9 ± 0.4	-49.4
<i>n</i> -PrSH	-56.5	+5.4 ± 0.4	-51.0
<i>i</i> -PrSH	-47.7	-2.5 ± 0.4	-50.2

^a All values in kJ mol⁻¹. ^b Reference 26.

the proton-exchange reaction between 1 and three reference bases (eq 3),³¹ were measured:



In every case, $\Delta GB(1)$ was calculated as:

$$\Delta GB(1) = \Delta G(B_{\text{ref}}) + \delta\Delta G_{\text{H}^+}(\text{g}) \quad (4)$$

The experimental results, $\Delta GB(1)$ as well as $\Delta G(B_{\text{ref}})$ are summarized in Table 2.

From these data we deduce the average value $\Delta GB(1) = -50.2 \pm 0.8$ kJ mol⁻¹. The proton affinity of 1 relative to ammonia, $\Delta PA(1)$, that is, the standard enthalpy change for reaction 1, cannot be obtained directly from ICR data. Use is often made of entropy changes estimated from changes in symmetry numbers.³² Our *ab initio* calculations allow, however, a direct calculation of the entropy change pertaining to reaction 1: $\Delta S[1] = -30.96$ J mol⁻¹ K⁻¹. At the nominal temperature of the experiment, 333 K, $T\Delta S[1] = -10.3$ kJ mol⁻¹ and hence, $\Delta PA[1] = -60.5$ kJ mol⁻¹.

Thermodynamic Data. Table 3 summarizes data for compounds 1–4. Given, in particular are, the experimental enthalpies of fusion ($\Delta_{\text{fus}}H$) and sublimation ($\Delta_{\text{sub}}H$) as well as the calculated (through eq 5) enthalpies of

$$\Delta_{\text{vap}}H \approx \Delta_{\text{sub}}H - \Delta_{\text{fus}}H \quad (5)$$

vaporization ($\Delta_{\text{vap}}H$). We also present the corresponding melting points and the equilibrium vapor pressures of these compounds at 298.16 K.

The boiling point of 1 and the molar volumes for both trifluoromethyl derivatives are not available, so they have been estimated as follows: for the boiling point, we have taken $\text{bp}(1) = \text{bp}(3) + [\text{bp}(2) - \text{bp}(4)]$, that is, we have assumed that bis-trifluoromethylation has the same effect on the boiling points of 3 and 4. For the molar volumes, V , as subcooled liquids at 298.16 K, we have assumed $V(3) \approx V(4)$ and taken a contribution of 57.5 mL/CF₃.³³ With these approximations, estimates of Hildebrand's solubility

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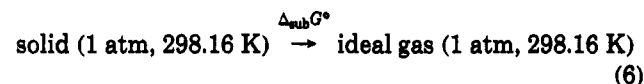
parameter, δH ,³⁶ and vaporization entropies of the liquids at their boiling points, were obtained.

Recent work by Marcus³⁷ shows how sketchy is our understanding of the link between thermodynamics and structuredness in condensed phases. This notwithstanding, the following can be deduced from the results collected in Table 3.

(i) $\Delta_{\text{sub}}H$ for triazoles are always larger than those for the corresponding pyrazoles, possibly reflecting the larger dipolarity of the former (the gas-phase microwave dipole moments of pyrazole and 1,2,4-triazole are 2.21 and 2.71 D).³⁹

(ii) In both series, the presence of the trifluoromethyl groups lowers the enthalpies of sublimation by an average of 7.7 kJ mol⁻¹, quite comparable to the reduction of 5.6 kJ mol⁻¹ in $\Delta_{\text{fus}}H$. The effect on $\Delta_{\text{vap}}H$ is thus quite small. A referee has rightly pointed out that, inasmuch as fluorination generally has a negligible effect on heats of vaporization,³⁹ one would expect $\Delta_{\text{vap}}H$ for compounds 1 and 2 to be close to those for the corresponding dimethylated derivatives which, on the basis of a carefully study by Chickos, Hyman, Ladon, and Liebman,⁴⁰ should be some 9 kJ mol⁻¹ higher than those of the parent compounds 3 and 4. Experimentally, one finds that $\Delta_{\text{sub}}H$ for 3,5-dimethylpyrazole is indeed 9.3 kJ mol⁻¹ higher than pyrazole.¹⁸ However, as shown in Table 3, the actual values for the sublimation and vaporization enthalpies of 1 and 2 are substantially smaller than those for the parent compounds. The difference with respect to the predicted values is clearly related to the weakening of the self-association brought about by the bis-trifluoromethylation.

(iii) At 298.16 K, vapor pressures of these solids are small and well below 0.101 MPa (1 atm), so that the standard Gibbs energy change for reaction 6 is always positive. In both cases, data in Table 3 shows that the



sublimation process is more endergonic for triazoles than for pyrazoles. Assuming ideal gas behavior, the sublimation of triazole is more endergonic than that of pyrazole by 11.9 kJ mol⁻¹.⁴¹ Interestingly, this is practically the same difference in $\Delta_{\text{sub}}H$ values. The difference in Gibbs energies for the trifluoromethyl derivatives is smaller, 2.66 kJ mol⁻¹. Considering the couples (1)/(3) and (2)/(4) we see that bis-trifluoromethylation favors reaction 6 by 11.1 and 1.9 kJ mol⁻¹, respectively.

(iv) Consideration of $\rho = \Delta_{\text{vap}}S/R$ shows extremely similar values for all these compounds. Without exception, they are larger than 10. Thus, according to Trouton's rule, they are "structured" liquids. In fact, their ρ values are larger than those for water, alkanols, glycerol, and HMPA and close to that for dibutyl phthalate.³⁸ In

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(41) Taking into account that $V = (\partial G/\partial P)_T$ and using the state equation for ideal gases.

Table 3. Relevant Thermodynamic Data for Compounds 1-4

compound	mp ^a	bp ^a	V ^b	$\Delta_{\text{sub}}H^c$	$\Delta_{\text{fus}}H^c$	$\Delta_{\text{vap}}H^c$	P ^d	δ_H^e	$\Delta_{\text{vap}}S/R^f$
1 ^g	340.95 ^h	494	149.6	74.7 ± 0.8	8.48	66.2	13.92	20.6	16.1
2 ^h	352.6	421	149.6	67.9 ± 0.6	11.03	56.9	40.45	19.1	16.3
3 ^h	395.0	533	61.6	84.0 ± 0.2	16.38	67.6	0.16	32.5	15.3
4 ^h	340.9	460	61.6	74.0 ± 0.4	14.41	59.6	18.97	30.4	15.6

^a In K. ^b In mL mol⁻¹, estimated as indicated in ref 33. ^c In kJ mol⁻¹. ^d In Pa. ^e In MPa^{1/2}. ^f Dimensionless. ^g All values from this work. ^h From this work and ref 18. ⁱ According to refs 34 and 35 this compound melts at 349–350 K; an examination of its DSC reveals a maximum at 350.03 K but with a very progressive melting. A linear extrapolation gives 340.95 K.

Table 4. Total Energies (hartrees), ZPE (kJ mol⁻¹), Dipole Moments (D), and Protonation Energies (PA) in kJ mol⁻¹^a

compound	HF/6-31G*	ZPE	MP2/6-31G*/6-31G	μ	PA
3	-240.80415	171.5	-241.53912	2.99	860.5
3a	-240.79298	169.4	-241.52766	5.96	888.7
3(4H)	-241.16196	208.8	-241.88247		
3(2H)	-241.14469	206.3	-		
5	-576.42171	187.0	-577.78612	5.42	829.0
5a	-576.41923	187.0	-577.78543	1.99	827.5
5b	-576.40849	184.9	-577.77346	5.43	860.4
5(4H)	-576.76146	223.8	-578.11731		
5(2H)	-576.74434	221.7	-		
5a(4H)	-576.75828	223.8	-		
1	-912.03437	202.1	-914.03025	3.79	786.2
1a	-912.02146	200.0	-914.01759	4.12	819.6
1(4H)	-912.35703	238.5	-914.34571		
1(2H)	-912.34319	236.4	-		

^a Values obtained at the MP2/6-31G*/6-31G* level and including the ZPE correction, scaled by the empirical factor 0.893, the thermal corrections, and the BSSE correction evaluated at the MP2 level.

Marcus-Bennetto-Caldin terms,^{37,42} they are quite "ordered" liquids.

(v) As regards δ_H values, some important features appear: for the parent compounds 3 and 4, they are larger than for alcohols and ethylene glycol and only moderately smaller than for glycerol. Bis-trifluoromethylation reduces δ_H by ca. 37% in 1 and 2. These compounds then become comparable to materials like benzene and ethyl acetate. Physically, this is a consequence of the fact that the large increase in size of the molecules brought about by substitution offsets the moderate increase in dipole moments⁴³ and the feeble dispersive interactions provided by the six weakly polarizable fluorine atoms.⁴⁴ Thus, cavity formation and vaporization of 1 and 2, materials of lower "stiffness"^{37,42} are facilitated.

Theoretical Calculations. The HF and MP2 total energies of the systems under investigation are listed in Table 4. This table contains also the corresponding ZPE and the dipole moments evaluated at the HF level, as well as the protonation energies evaluated at the MP2/6-31G*/6-31G* level. It must be noticed that the protonated species have been identified by giving the number of the neutral molecule from which they derive and by indicating within parentheses the position which undergoes protonation. For instance, 5(4H) identifies the cation obtained by protonation of 5 at the N4 atomic center.

The corresponding optimized structures have been schematized in Figure 1. The geometrical parameters

obtained for both tautomers of 1,2,4-triazole (3 and 3a) are not very different from those reported earlier,⁴⁵ which were obtained at the 6-31G level. The greatest deviations are observed for the N1-N2 and C3-N4 bond distances of 3, which are much shorter when the basis set includes polarization functions. Although the data obtained by microwave spectroscopy (MW)⁴⁶ are only partial, they show that 3 is more stable than 3a in the gas-phase and that the 6-31G* optimized geometry is closer to that reported by Bolton *et al.*⁴⁶ which was estimated from data for related heterocyclic systems (pyrrole, pyrazole, and imidazole) and then systematically varied to fit the experimental rotational constants. Our value for the N1-N2 bond distance (1.341 Å) is shorter than that estimated in ref 44 (1.381 Å), although it is in reasonably good agreement with the value obtained by neutron diffraction by Jeffrey *et al.* (1.356 Å).⁴⁷ It cannot be disregarded, however, that a geometry optimization including electron correlation effects could have some influence on the lengths of these particular bonds. Nevertheless, the agreement between our calculated rotational constants (10523, 10175, and 5173 MHz) and the experimental ones (10245, 9832, and 5015 MHz) is also fairly good. On the other hand, both our scaled harmonic vibrational frequencies and assignments for 1H-1,2,4-triazole (3) are in remarkably good agreement with those experimentally observed in the 400–4000 cm⁻¹ region for the vapor-phase spectrum (Table 5).⁴⁸ Similarly, our calculated dipole moment (2.99 D) is also in very good accord with the experimental value obtained by MW (2.71 D).^{38,46}

For the remaining compounds we have not found either experimental or theoretical information on their geometries. Figure 1 clearly illustrates that a CF₃ substituent has an almost negligible effect on the azole ring. In fact, bond lengths change by less than 0.01 Å and endocyclic bond angles by less than 0.4°. This is ratified by the topological characteristics of the Laplacian of the charge densities of compounds 3, 5, and 1. As shown in Figure 2 and Table 6, substitution of one or the two hydrogen atoms of 3 by CF₃ groups leaves the charge density associated with the azole ring practically unperturbed. This seems to indicate that the conjugation of the CF₃ with the aromatic system of the azole is very small. Moreover, CF₃ substitution does not alter either the ellipticity of the ring bonds in a significant manner (see Table 6) and only the bonds contiguous to the substituted carbon (C3-N2 and C3-N4) show a slight π -polarization. All these characteristics agree with the predictions of the

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(43) According to STO-3G calculations reported in ref 18, compounds 2 and 4 have very similar dipole moments: 2.24 and 2.15 D, respectively. Those of compounds 1 and 3 are discussed with the theoretical part of the present paper.

(44) Assuming spherical molecular shapes, this is tantamount to an increase of the molecular radius, increase which is also mirrored in the Laplacians of their charge densities (see Figures 2 and 3). This weakens the intermolecular interactions. See, e.g. Hirschfelder, J. O.; Curtiss, C. F.; Bird, R. B. *The Molecular Theory of Gases and Liquids*; John Wiley: New York, 1967, particularly Chapter 13.

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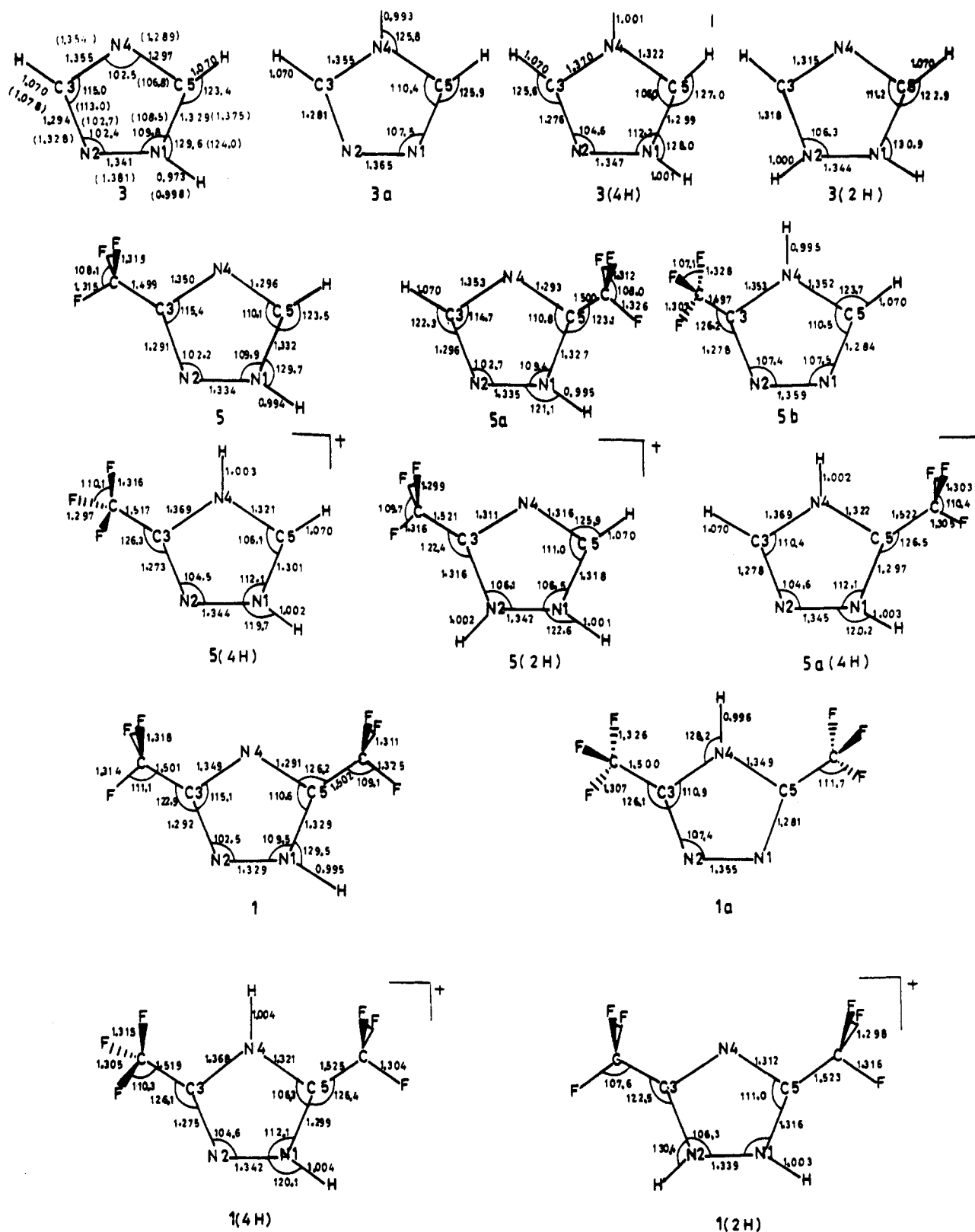


Figure 1. 6-31G* Optimized geometries. Bond angles in degrees and bond lengths in angstroms. For 1H-1,2,4-triazole (3), the values within parentheses correspond to the estimated structure (see text) reported in ref. 44.

Topsom-Taft's model⁴⁹ to account for substituent effects on relative stabilities. The Taft-Topsom formalism indicates that the electronegativity parameter σ_x amounts to -0.02 , indicating that the charge-transfer to or from the ring is very small ($\sigma_x = 0.00$ for H and $\sigma_x = 0.70$ for F).

The resonance parameter $\sigma_{R^+} = 0.00$ (for the protonated form) while $\sigma_R = 0.07$ (for the neutral form). The latter is comparable to the values for the methyl group ($\sigma_R = 0.03$; $\sigma_{R^+} = -0.08$).⁴⁹

Notice that field and polarizability contributions for CF_3 are sizeable ($\sigma_F = 0.44$, $\sigma_a = -0.25$), but they have little bearing on charge-transfer to or from the ring and

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Table 5. Harmonic Vibrational Frequencies (cm⁻¹) of 1*H*-1,2,4-Triazole (3)

$\bar{\nu}(\text{cald})^a$	$\bar{\nu}(\text{exptl})$	assignment
3508	3510	N-H stretch
3098	3140	C3-H stretch
3090		C5-H stretch
1573	1503	(C5-N4 + N2-C3) stretch <i>op</i> ^b + NH bend + CH bend
1465	1430	(N1-C5 + N4-C3) stretch <i>op</i> + NH bend + CH bend
1399	1360	(C5-N4 + C3-N2) stretch <i>ip</i> ^c + NH bend + CH bend
1303	1280	(C3-N4 + N1-N2) stretch <i>op</i> + NH bend + CH bend
1257	1260	CH bend + NH bend + ring breathing
1145	1155	ring breathing
1109	1103	(C3-N4 + N1-C5) stretch <i>ip</i>
1050	1040	N1-N2 stretch + CH bend
959	970	N1-C5-N4 bend
939		N2-C3-N4 bend
931	883	C3-H out of plane
905	842	C5-H out of plane
675	678	ring torsion
656		ring torsion
522	538	NH out of plane

^a Scaled by the empirical factor 0.893. ^b *op* stands for out-of-phase. ^c *ip* stands for in-phase.

mostly contribute to the destabilization and stabilization, respectively, of the protonated form. This is also reflected in the relative stabilities of the different isomers. Our MP2/6-31G*//6-31G* results, after including the ZPE correction, indicate that tautomer 3 is 6.7 kcal mol⁻¹ (28 kJ mol⁻¹) more stable than 3a, while the energy gaps between 5 and 5b and between 1 and 1a are 7.5 kcal mol⁻¹ (31.4 kJ mol⁻¹) and 7.8 kcal mol⁻¹ (32.6 kJ mol⁻¹), respectively. Quite interestingly, this implies that the energy gap between 5 and 5b is slightly greater than that between 3 and 3a, even though in 5b an F...H intramolecular hydrogen bond (IMHB) should be possible. Something similar can be said of 1a with respect to 1, since in the former there is the possibility of formation of two IMHBs while in the latter only one is possible. However, a topological analysis of the electronic charge densities of these systems reveals that no critical points exist between the fluorine atoms and the NH protons. Therefore, in none of these systems a true IMHB exists, explaining the aforementioned energetics. This explains also the fact that 5a is only 0.3 kcal mol⁻¹ (1.3 kJ mol⁻¹) less stable than 5.

Gas phase protonation has, on the contrary, a sizeable effect on the azole system. As illustrated in Figure 3 and Table 6, N4 protonation of 3, 5, and 1 implies an activation of N4-C3, N4-C5, and C-CF₃ bonds, while C3-N2 and C5-N1 linkages become slightly reinforced. This is a direct consequence of the significant charge transfer which takes place from the azole to the incoming proton. This charge transfer involves primarily the nitrogen lone-pair. However, since the nitrogen atom is highly electronegative, it recovers part of the charge by depopulating the bonds in which it participates (C3-N4 and N4-C5, see Table 6). This charge depletion is transmitted, to some extent, to C3 and C5, which depopulate the C-CF₃ bonds and polarize the bonding charge of the C3-N4 and C5-N1 linkages toward them. The ellipticity values also show that the π -system is the one which becomes more strongly affected since these depopulations are also accompanied by a sizeable decrease in the ellipticity of the bonds. These charge redistributions upon protonation are also mirrored in the changes observed in the corresponding bond lengths.

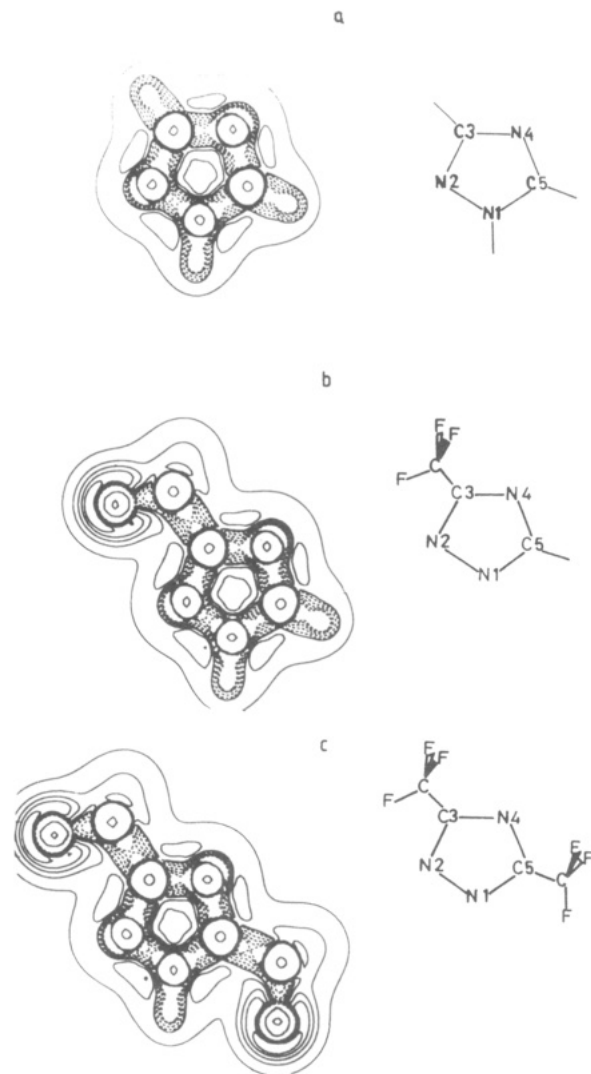


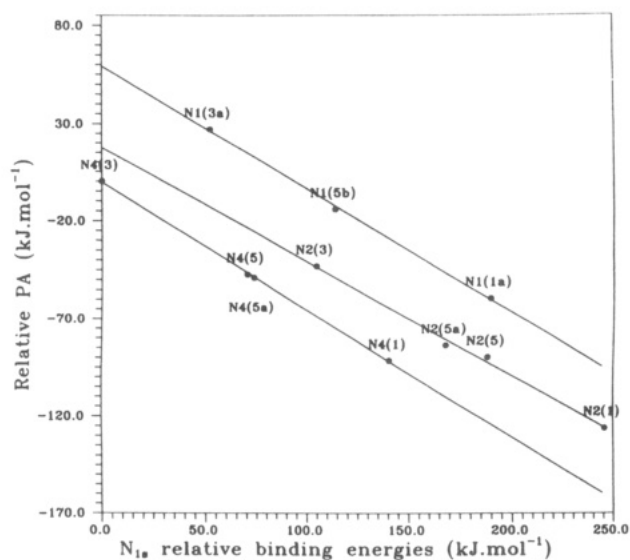
Figure 2. Contour map of the Laplacian of the charge density of (a) 1*H*-1,2,4-triazole (3), (b) 3-(trifluoromethyl)-1*H*-1,2,4-triazole (5), and (c) 3,5-bis(trifluoromethyl)-1,2,4-triazole (1). Positive values of $\nabla^2\rho$ are denoted by full lines and negative values by dashed lines. Contour values in au are ± 0.05 , ± 0.25 , ± 0.50 , ± 0.75 , and ± 0.95 .

As shown in Figure 1, for the three species 3, 5, and 1, N4 protonation is accompanied by a significant lengthening of the C3-N4, N4-C5 and C-CF₃ bonds, a shortening of both C3-N2 and C5-N1 linkages and, in many cases, protonation induces an internal rotation of one of the CF₃ groups. Similarly as we pointed out above for the neutral species, we have not found, in the topological analysis of the charge densities of the protonated species, any bond critical point between the fluorine atoms and the protons of the ring which might put in evidence the existence of IMHBs. We must conclude then, coherently with the characteristics of $\nabla^2\rho$ in these regions (see Figure 3), that there is only an electrostatic interaction between the net negative charge at the fluorine atoms and the net positive charge at the azole hydrogens. This would explain why protonation is accompanied by a rotation of the CF₃ group in an effort by the system to decrease the average distances between the three negatively charged fluorine atoms and the incoming proton.

The calculated protonation affinities, obtained as the energy difference between protonated and unprotonated species after including ZPE, thermal, and MP2/6-31G*

Table 6. Bond Characteristics of 1,2,4-Triazole and its Mono- and Bisubstituted CF₃ Neutral and Protonated Species (σ in e/au³ and $\nabla^2\rho$ in e/au³)

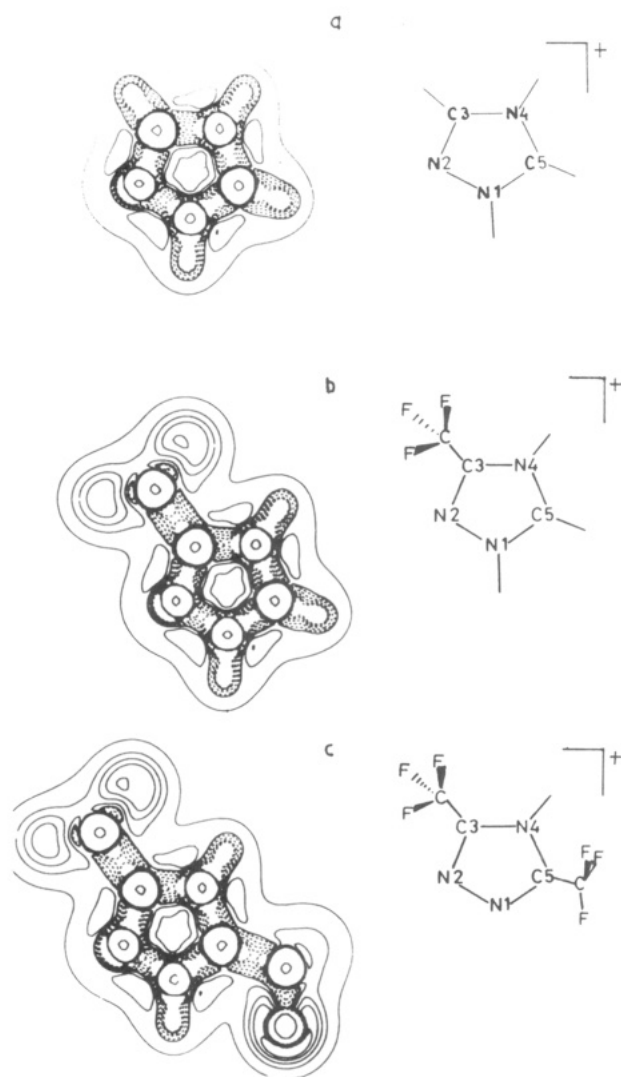
bond	ρ	$\nabla^2\rho$	ϵ	ρ	$\nabla^2\rho$	ϵ	ρ	$\nabla^2\rho$	ϵ	ρ	$\nabla^2\rho$	ϵ	ρ	$\nabla^2\rho$	ϵ	ρ	$\nabla^2\rho$	ϵ
N1-N2	0.382	-0.883	0.104	0.378	-0.879	0.070	0.389	-0.917	0.107	0.381	-0.895	0.072	0.393	-1.848	0.106	0.382	-0.898	0.070
N2-C3	0.378	-0.437	0.284	0.369	-0.537	0.198	0.382	-0.448	0.347	0.400	-0.562	0.379	0.381	-0.450	0.348	0.400	-0.581	0.371
C3-N4	0.343	-0.986	0.124	0.352	-0.638	0.126	0.348	-1.034	0.157	0.312	-0.455	0.088	0.346	-0.945	0.159	0.311	-0.426	0.084
N4-C5	0.387	-0.989	0.237	0.309	-0.422	0.052	0.386	-0.934	0.238	0.352	-0.617	0.123	0.390	-0.931	0.278	0.353	-0.633	0.139
C5-N1	0.338	-0.379	0.150	0.397	-0.584	0.336	0.336	-0.384	0.146	0.367	-0.547	0.190	0.340	-0.423	0.208	0.370	-0.546	0.221
N1-H	0.349	-1.854	0.038	0.309	-0.422	0.052	0.347	-1.852	0.063	0.337	-1.827	0.045	0.345	-1.848	0.035	0.342	-1.816	0.029
C3-X ^a	0.297	-1.201	0.038	0.344	-1.695	0.018	0.295	-0.954	0.031	0.285	-0.900	0.018	0.295	-0.949	0.062	0.284	-0.896	0.027
C5-X	0.298	-1.200	0.031	0.299	-1.316	0.030	0.298	-1.218	0.037	0.299	-1.325	0.028	0.294	-0.941	0.062	0.279	-0.880	0.043
C-F	-	-	-	-	-	-	0.286	0.253	0.149	0.306	0.207	0.095	0.292	0.219	0.132	0.303	0.173	0.082
N4-H	-	-	-	0.330	-1.782	-	-	-	-	0.332	-1.773	0.022	-	-	-	0.329	-1.761	0.021

^a X = H, CF₃.**Figure 3.** Contour map of the Laplacian of the charge density of the protonated forms of (a) 1*H*-1,2,4-triazole (3(4H)), (b) 3-(trifluoromethyl)-1*H*-1,2,4-triazole (5(4H)), and (c) 3,5-bis-(trifluoromethyl)-1,2,4-triazole (1(4H)). Same conventions as in Figure 2.

BSSE corrections, have been summarized in Table 4. The first conspicuous fact is the good agreement between our estimated gas-phase proton affinity of 1 and the experimental value reported in the previous section which shows that this compound is *ca* 17.7 kcal mol⁻¹ (74 kJ mol⁻¹) and 18 kcal mol⁻¹ (75 kJ mol⁻¹) less basic than 1,2,4-triazole (3) and ammonia, respectively. Significantly, the mono-substituted derivative 5 presents a calculated gas-phase basicity about 7.5 kcal mol⁻¹ (31 kJ mol⁻¹) smaller than the unsubstituted compound 3, which indicates that CF₃ substitution effects are practically additive, a fact already noted for pyrazoles.¹⁸ From the values in Table 4 it can be seen that, as is the case for the parent compound, 5 and its tautomer 5b, 5a and 5b, and 1 and 1a yield common cations upon protonation. Consider, for instance, the most complex case, that of the mono-substituted derivative 5 where three different neutral molecules and three different cations exist (Scheme 1).

The results of Scheme 1 (HF/6-31G* differences in energy in kJ mol⁻¹ with respect to the most stable tautomer are given between parentheses) show that the most-stable neutral tautomer 5 upon protonation yields the most-stable cation 5(4H). Tautomer 5a is only slightly less stable than tautomer 5 (the difference decreases to 1.3 kJ mol⁻¹ when MP2/6-31G*/ZPE energies are used).

Our results show that N4 is the most-basic center disregarding the degree of substitution as it is predicted

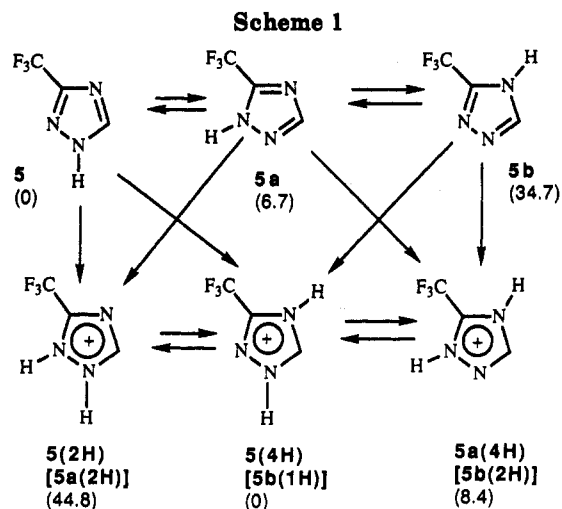
**Figure 4.** Linear correlations between the protonation energies and N_{1s} orbital energies. All values relative to 1*H*-1,2,4-triazole.

by the corresponding value of the 1s binding energy. The existence of a linear relationship between gas-phase proton affinities and inner-shell ionization potentials is well established,⁵⁰⁻⁵² provided that protonation does not cause significant structural changes and that the different atomic

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centers present similar hybridization patterns.⁵³ This is clearly illustrated in Figure 4 which shows that the linear correlations between relative protonation energies and relative *1s* orbital energies (taken in absolute value as a measure of the *1s* binding energy according to Koopman's theorem) are grouped in three different sets. These sets correspond respectively to (a) the most basic center (N4) of 1*H*-1,2,4-triazole (3) and their mono- and disubstituted CF₃ derivatives (5, 5a, 1); (b) the alternative basic center (N2) of 1*H*-1,2,4-triazole, which corresponds to the most

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basic center of the mono- and disubstituted CF₃ derivatives of 4*H*-1,2,4-triazole (3a), that is, 5b and 1a, and (c) the less basic center of 3a, 5b, and 1a.

Concluding Remarks

The crystal structure of compound 1 could not be determined because the crystals sublime very quickly even when sealed in a Lindeman capillary tube (the effect of the radiation on the evaporation rate could be important). Nevertheless, some information was obtained: compound 1 crystallizes in the *Pbca* space group with *Z* = 8, unit cell volume of 1537.6 Å³, density = 1.77 g cm⁻³. Only two types of structure are compatible with these values, a cyclic dimer or a polymer chain, all bis(trifluoromethyl)-1,2,4-triazole molecules being identical in the crystal. 1,2,4-Triazole (3) also crystallizes in the *Pbca* group, *Z* = 8, has a density of 1.394 g cm⁻³, and forms infinite corrugated sheets.^{45,54} Thus, the structure could be quite similar with 1 having a higher density than 3.

Acknowledgment. The work of Drs. C. Foces-Foces and A.L. Llamas-Saiz, who carried out the crystallographic determinations (I. Rocasolano) is warmly acknowledged. Work by E.B. was supported by a grant from CSIC. This work was partially supported by the DGICYT Project No. PB90-0228-C02. M.E. gratefully acknowledges a post-doctoral fellowship from the Ministerio de Educación y Ciencia of Spain.

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