STRUCTURE OF 4-UNDECYLPYRAZOLE IN THE SOLID STATE: A ^{13}C AND ^{15}N CPMAS NMR SPECTROSCOPY STUDY

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ABSTRACT:

CPMAS NMR spectroscopy and semi-empirical calculations (AM1 and PM3) were used to determine the structure in the solid state of 4-undecylpyrazole. The conclusion is that this compound probably exists as a cyclic trimer.

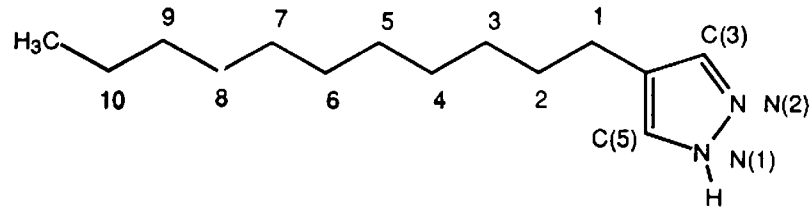
INTRODUCTION

We have used a combination of crystallography and high-resolution solid-state NMR (^{13}C and ^{15}N) to determine the structure of *N*H-pyrazoles in the solid state (1-6). However, in some cases monocrystals cannot be obtained and the structure must be deduced from NMR spectroscopy alone; this is the case with 4-undecylpyrazole **1**. This compound owing to the aliphatic chain at position 4 has not only a low melting point but also a plastic character which prevents its crystallisation in good conditions. Although the compound has not the expected mesogenic properties it has, nevertheless, some physical properties which are rather peculiar.

EXPERIMENTAL

1. Chemistry

The compound was prepared according to Theorell *et al.* (7) in a four-step procedure (these authors have prepared **1** to test it as an inhibitor of alcohol dehydrogenase). The compound, an oil wich solidifies, melt at 63-64°C (lit., m.p. 62.5-63.5°C) (6). ^1H NMR: in $CDCl_3$, the terminal methyl group appears at 0.86 ppm (triplet), the CH_2 at position 1 at 2.46 ppm (triplet), the CH_2 at position 2 at 1.54 ppm (quintet), the remaining CH_2 at 1.24 ppm (multiplet), pyrazole protons at C(3) and C(5) at 7.38 ppm (singlet).



2. NMR Spectroscopy

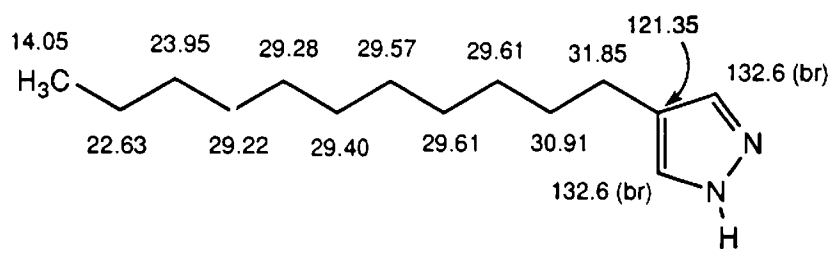
The ^{1}H and ^{13}C NMR spectra in solution ($CDCl_3$) were recorded in a Varian Unity 300 spectrometer (Zaragoza) working at 299.95 MHz (^{1}H) and 75.43 MHz (^{13}C). The procedure to record the solid-state ^{13}C NMR spectra [Cross-Polarization/MaginAngle Spinning (CPMAS) technique and TOSS sequence] have already been described (5,8); the spectrometres used were a Bruker AC200 (UNED) working at 50.32 MHz and a Bruker MSL 400 (CSIC) working at 100.63. The ^{15}N CPMAS NMR spectrum was recorded in a Bruker MSL 300 spectrometer (Berlin) working at 30.41 MHz (9); ^{15}N chemical shifts are referred to solid $^{15}NH_4Cl$.

3. Theoretical calculations

The calculations were carried using the AM1 (10) and PM3 (11) Hamiltonians within the MOPAC 6.0 package (12).

RESULTS AND DISCUSSION

The ^{13}C NMR spectrum in solution (solvent $CDCl_3$) has the following chemical shifts:



The broadening of the signals of C(3) and C(5) pyrazole carbon atoms, which appear at 132.6 ppm, is due to a slow prototropic exchange of the NH-proton between positions N(1) and N(2). This phenomenon, although not very common in $CDCl_3$, has been observed for other pyrazoles (4).

In the solid state the spectra were recorded, at room temperature, with two instruments, one working at 50 MHz (Fig. 1a) and the other at 100 MHz (Fig. 1b); for all practical purposes the 100 MHz spectrum corresponds to a lower temperature.

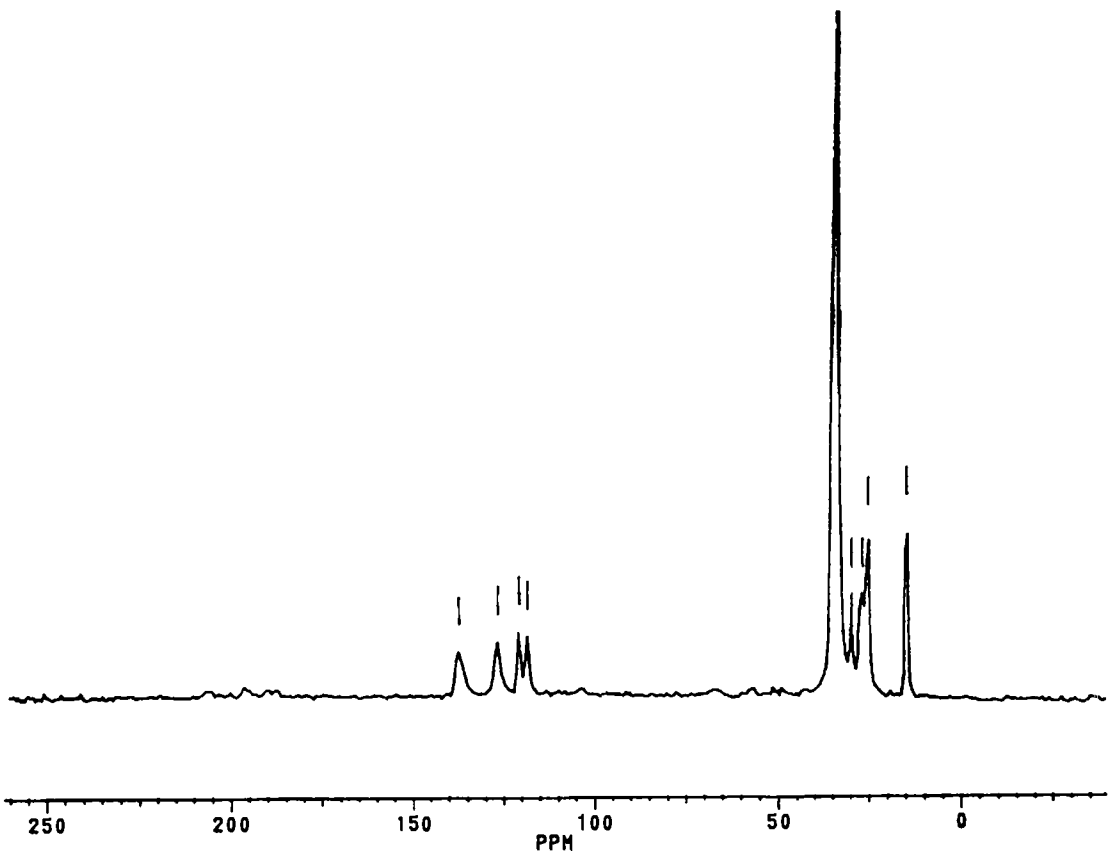
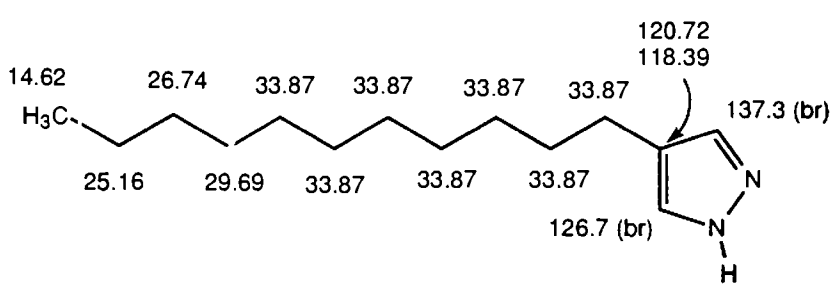


Figure 1a: ^{13}C-CPMAS-NMR spectra of 4-undecylpyrazole at 50 MHz.

The spectrum at 50 MHz can be summarized like this:



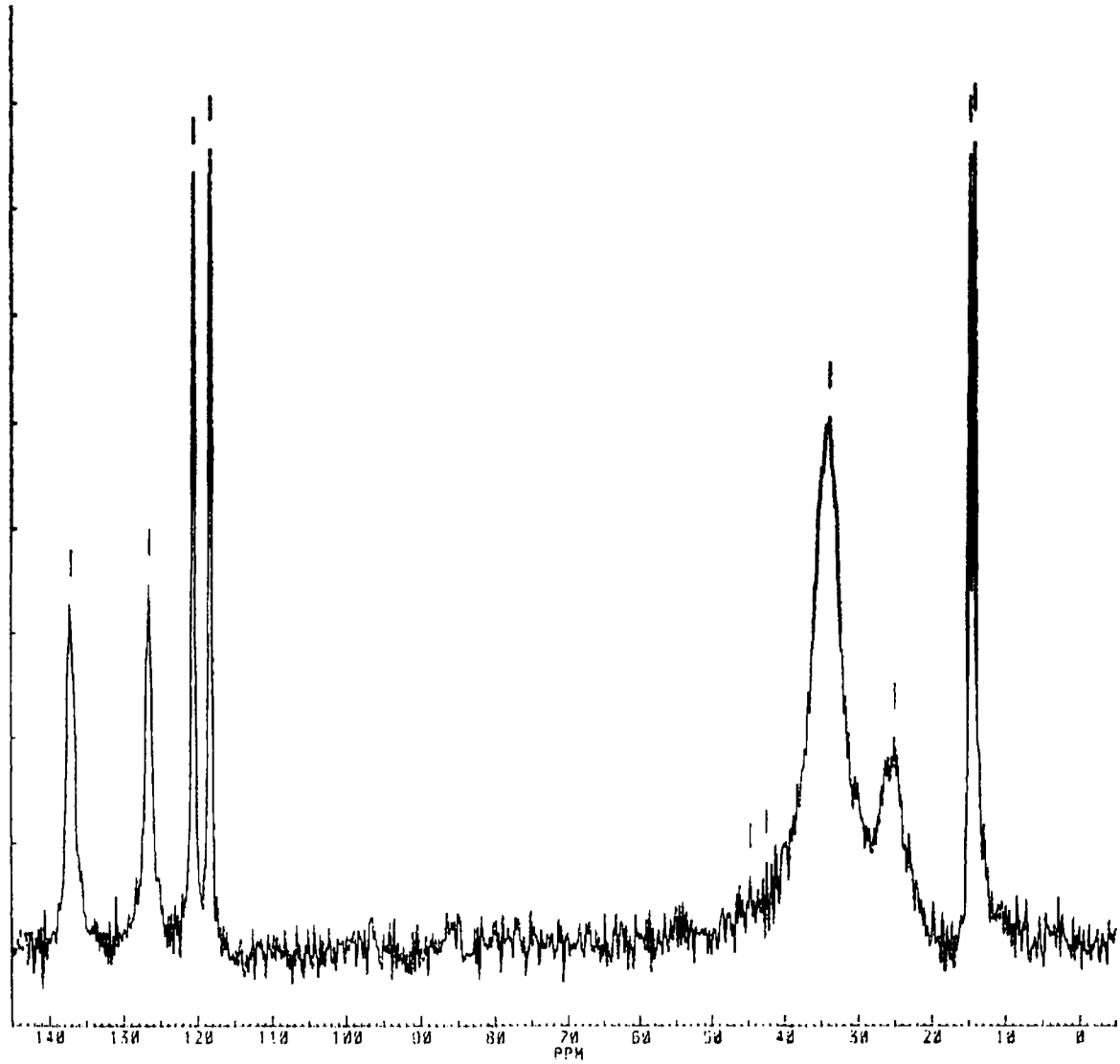
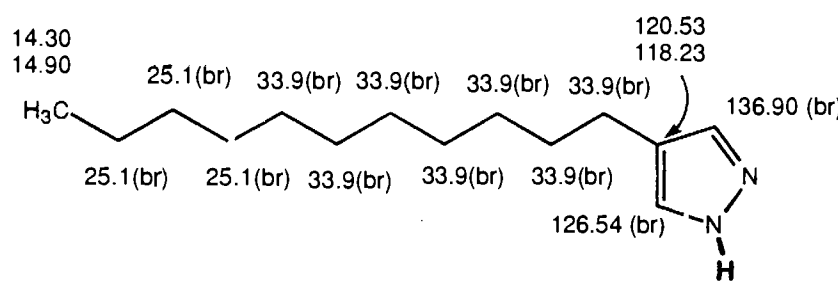


Figure 1b: ^{13}C-CPMAS-NMR spectra of 4-undecylpyrazole at 100 MHz.

On the other hand the 100 MHz spectrum (Fig. 1b) corresponds to the following assignment:



At 50 MHz, see Fig. 1a, the signals belonging to carbons C(3) and C(5) are broad due to a slow (in the NMR time scale) prototropic exchange **in the solid state**. We have observed this particular behaviour only in the case of pyrazoles which crystallized in cyclic structures (dimers, trimers and tetramers) (1,2) and never in pyrazoles which crystallize in long chains (catamers). At 100 MHz, the signals are narrower but still a little broad, see Fig. 1b. Increasing the field correspond to cooling down the solution, thus the prototropic exchange becomes slower.

The undecyl substituent exists probably in two conformations and the dynamic of interconversion is quite fast in the NMR time scale. At 50 MHz (Fig. 1a), two signals corresponding to C(4) atom are observed, one corresponding to the terminal methyl group and a series of **narrow** signals corresponding to the polymethylene chain. At 100 MHz (Fig. 1b), the resolution is better: not only C(4) is splitted but also the methyl group; on the contrary, the polymethylene chain is **very broad**. We assign the observed spectra to the existence of two interconverting conformations of the undecyl chain. It can be imagined as a skipping rope with its two ends fixed at C(4) and CH_3 existing in two conformations (for instance, in-plane and out-of-plane with regard to the pyrazole ring) which explain the splittings of C(4) and CH_3, but moving fast between these two conformations, which explain why the broadening increases on going from 50 to 100 MHz.

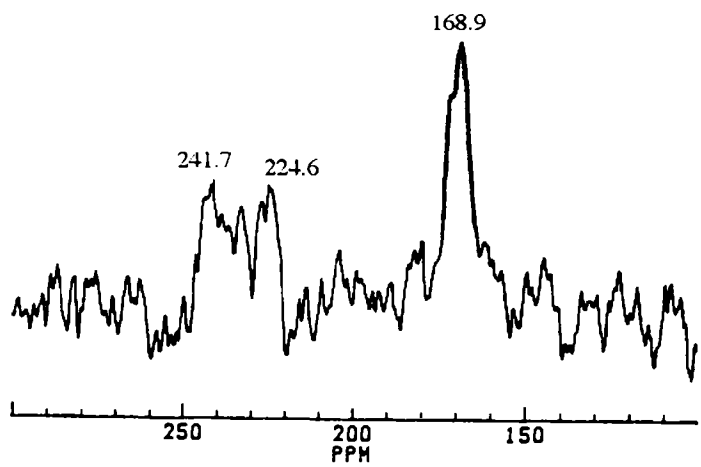
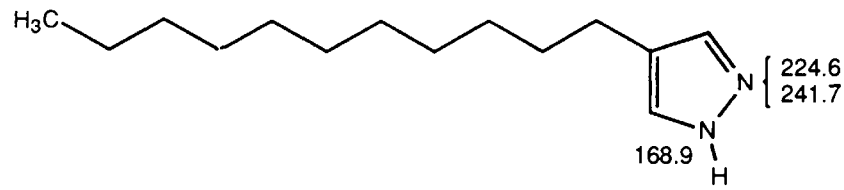


Figure 2: ^{15}N-CPMAS-NMR spectra of 4-undecylpyrazole.

The ^{15}N CPMAS NMR spectrum is represented in Fig. 2 and corresponds to the following assignment:



The NH signal at 168.9 ppm is quite normal, for other NH-pyrazoles it appears at 170.3 (pyrazole itself) and 166.8 (3,5-dimethylpyrazole) (9). One of the signals of the -N= atom, that at 241.7 ppm is also in the expected range: pyrazole itself 247.6 ppm and 3,5-dimethylpyrazole 241.3 ppm (9). We have shown (9,13) that the -N= signal is much more sensitive to the strength of the N-H···N hydrogen bond (HB) than the -NH- signal; thus the other -N= signal, at about 224.6 ppm, corresponds probably to a different situation regarding the HB network. One possibility is that the two conformations of the undecyl chain correspond to two different types of HBs.

All these data pointed out to a proton transfer in the solid state, that is to a cyclic dimer, trimer or tetramer. Since the X-ray structure cannot be obtained, we have carried out semi-empirical calculations on these cyclic n-mers (n = 2, 3, 4). To simplify, we have replaced the undecyl chain by a methyl (2, 4-methylpyrazole) and a butyl chain (3, 4-butylpyrazole). The optimized geometries for the dimer, trimer and tetramer of compound 3 are represented below (Figs. 3a-3c). Note the extended -all-*trans*- conformation of the alkyl chains.

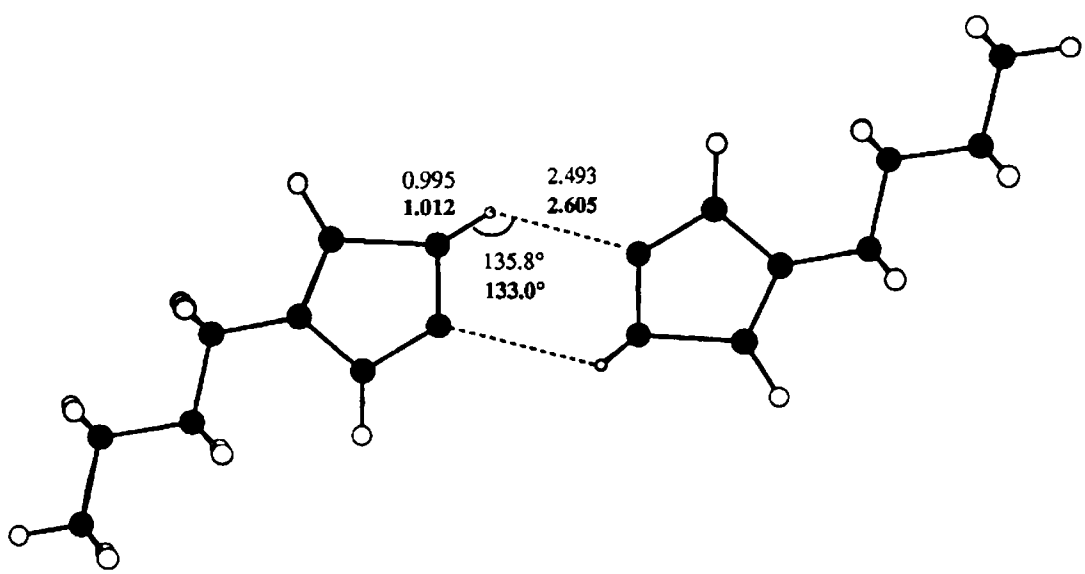


Figure 3a: Optimized geometry of 4-undecylpyrazole: dimer.

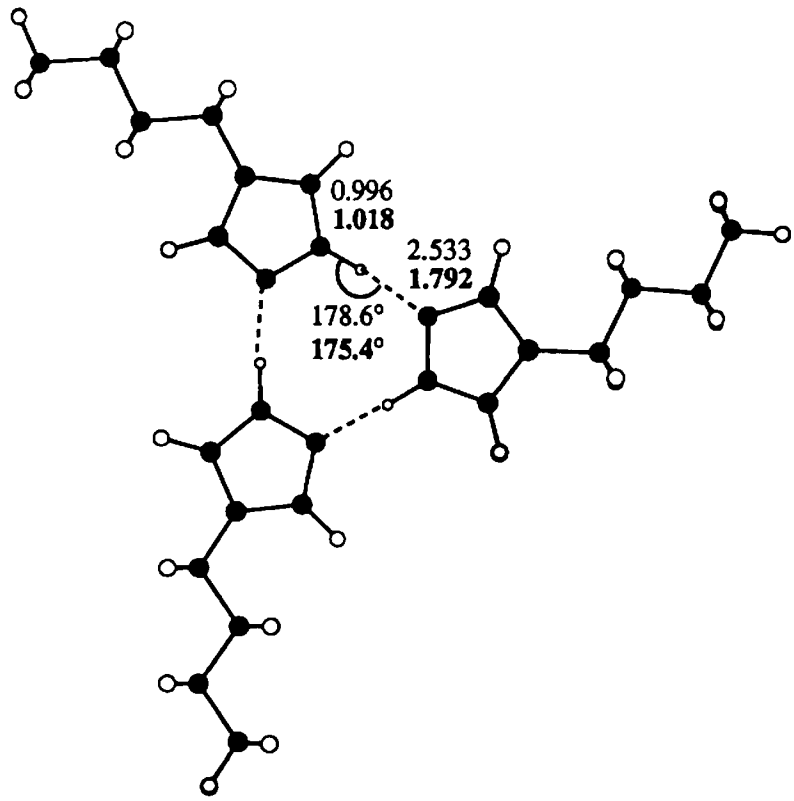


Figure 3b; Optimized geometry of 4-undecylpyrazole: trimer.

The results of the calculated heats of formation (in kcal mol^{-1}) are reported in Table 1 whereas the energies of the hydrogen bonds and the energy per one hydrogen bond (in parentheses) are reported in Table 2 (all values in kcal mol^{-1}). The energy per HB results of dividing the interaction energy by n.

TABLE 1: Calculated heats of formation

	4-methylpyrazole **2**		4-butylpyrazole **3**	
n	AM1	PM3	AM1	PM3
1	57.42	39.40	38.04	24.41
2	110.84	75.40	72.08	45.41
3	165.18	103.38	107.03	58.36
4	220.03	145.60	142.51	85.60

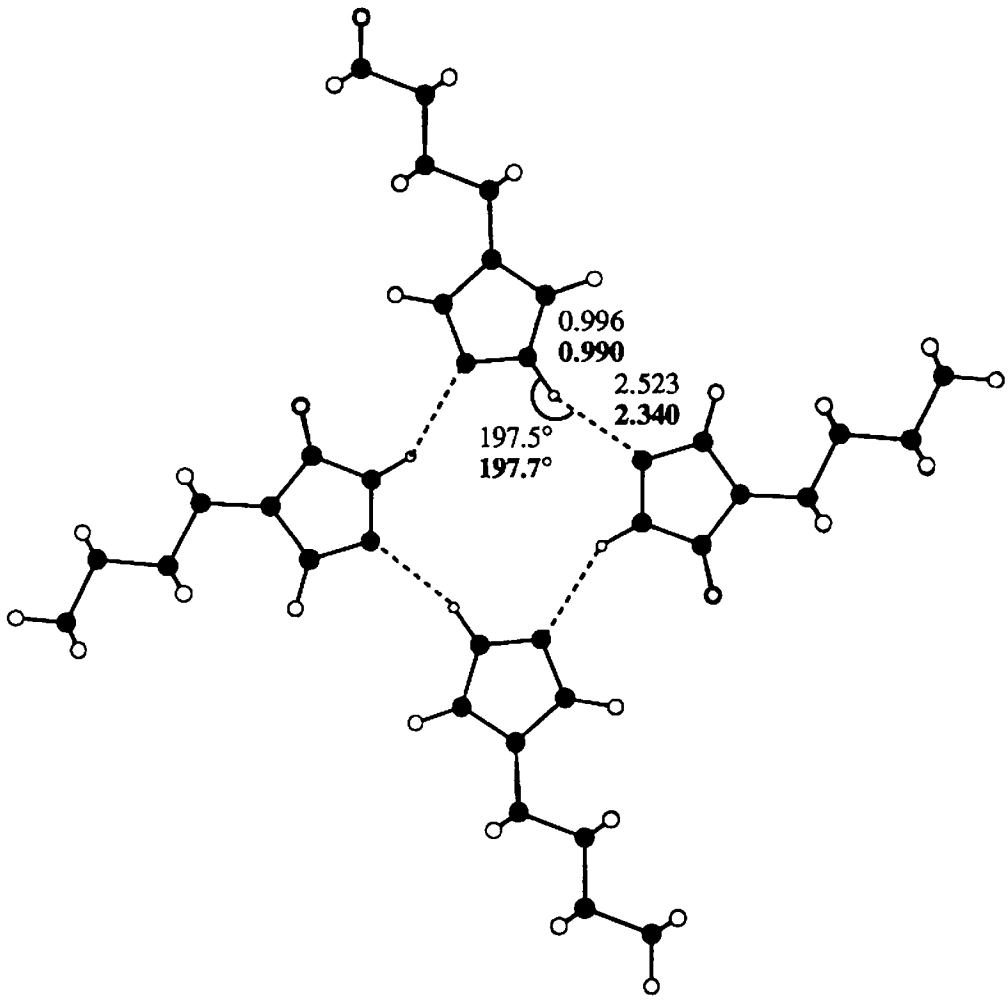


Figure 3c: Optimized geometry of 4-undecylpyrazole: tetramer.

TABLE 2: Energies per HB

	4-methylpyrazole **2**		4-butylpyrazole **3**	
n	AM1	PM3	AM1	PM3
2	4.00 (2.00)	3.40 (1.70)	4.00 (2.00)	3.41 (1.70)
3	7.08 (2.36)	14.82 (4.94)	7.09 (2.36)	14.87 (4.96)
4	9.65 (2.41)	12.00 (3.00)	9.65 (2.41)	12.04 (3.01)

It is extremely satisfactory that the calculations for **2** and **3** (Table 2) are almost identical, thus one can safely assume that it will be the same for **1**. On the other hand, the calculations are quite different depending on the semi-empirical method used. According to AM1 calculations, the stabilization gained by HB favours trimers and tetramers (2.4 kcal mol^{-1}) with regard to dimers (2.0 kcal mol^{-1}). The PM3 method clearly points out to trimers (5.0 kcal mol^{-1}) being better than tetramers (3.0 kcal mol^{-1}) and those, in turn, being better than dimers (1.7 kcal mol^{-1}).

The PM3 values seems more consistent with the idea that the most stable n-mer should be that with the straighter HB: trimer (N-H···N angle = 177°) > tetramer (N-H···N angle = 163°) > dimer (N-H···N angle = 133°). A linear dimer (N-H···N angle = 165°) has an HB energy of 3.85 kcal mol^{-1}, higher than the cyclic dimer (1.70 kcal mol^{-1}) but lower than the cyclic trimer (4.96 kcal mol^{-1}). It has been recently reported[14] that PM3 is superior to AM1 to represent geometries and energies of hydrogen-bonded complexes.

In conclusion, it appears that 4-undecylpyrazole **1**, in the solid state, exists as a mixture of two cyclic trimers (similar to Fig. 1b), differing in the HBs, which exchange the three N-H protons in a concerted mechanism.

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