A Comparative Spectroscopic Investigation of Two Polymorphs of 4'-Methyl-2'-nitroacetanilide using Solid-state Infrared and High-resolution Solid-state Nuclear Magnetic Resonance Spectroscopy

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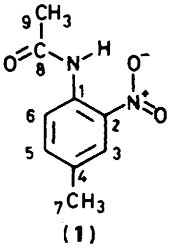
The low-temperature i.r. and high-resolution solid-state ^{13}C n.m.r. spectra of two polymorphs of 4'-methyl-2'-nitroacetanilide are presented and discussed with reference to their structures as determined by *X*-ray crystallography.

The existence of certain organic compounds in different polymorphic forms has been well known for many years. Many of these forms have been characterised by solid-state spectroscopic techniques, including vibrational spectroscopy[1] and, more recently, n.m.r.[2]

In the present work, spectroscopic investigations, by both i.r. and high-resolution solid-state n.m.r., of two polymorphic forms of 4'-methyl-2'-nitroacetanilide (1) of known crystal structure have been undertaken. We hoped to be able to rationalise the observed spectroscopic differences on the basis of the crystal structures, and also to compare the merits of the two techniques for the characterisation of polymorphs.



(1)

White and yellow polymorphs of the anilide (1) were first reported by Gattermann[3] in 1885, and the crystal structures of both forms have since been determined by single-crystal *X*-ray diffraction techniques.[4] Crystals of the white form are tabular and monoclinic (a = 10.421, b = 9.980, c = 9.568 Å, β = 99.51°), and belong to the $P2_1/c$ space group. There is one molecule in the asymmetric unit and there are four in the unit cell. The molecular conformation may be broadly described by three planes: one formed by all the ring carbon atoms, a second by the amide group and the ring carbon atom to which it is bonded, and a third by the nitro group and the ring carbon atom to which it is bonded. The only large deviation from these individual planes involves the amide hydrogen atom. In the white form both the amide and the nitro planes make an angle of 44.0° to the ring plane, suggesting restricted conjugation of the substituents with the aromatic ring. The close approach of the amide hydrogen atom of one molecule to the amide oxygen atom of the adjacent molecule (1.95 Å) confirms Skulski's proposal that intermolecular hydrogen bonding occurs in the white form.[5] All other intermolecular distances are greater than the sums of the relevant van der Waals radii. Molecules in the white form are related by c-glide planes, forming chains along the c direction. These chains are constructed by antiparallel molecular stacking, involving molecules related by inversion.

Crystals of the yellow form are filamentary and triclinic (a = 17.956, b = 12.908, c = 4.039 Å, α = 93.13°, β = 83.71°, γ = 90.77°), and in the space group $P\bar{1}$. There are two distinct molecules in the asymmetric unit, which will be referred to as Y(1) and Y(2), and four in the unit cell. The molecular conformations may again be described by the same three planes and, once again, the only significant deviation from these individual planes in both Y(1) and Y(2) occurs for the amide hydrogen atom.

In the case of Y(1), the nitro plane makes an angle of 12.3° with the ring and the amide plane an angle of 18.0°; thus the whole system is much closer to overall planarity than the white form. The amide hydrogen atom approaches one of the oxygen atoms in the nitro group to a distance of 1.95 Å, suggesting intramolecular hydrogen bonding. No intermolecular hydrogen bonding is apparent, the closest approach being one of 2.63 Å between the amide hydrogen atom of Y(1) and one of the oxygen atoms of the nitro group in Y(2). In Y(2) the nitro plane makes an angle of 18.0° with the ring, and the amide plane an angle of 30.6°. Intramolecular hydrogen bonding is again apparent between the amide and the nitro groups (closest approach 1.98 Å).

The two types of molecule in the yellow form pack in columns of either Y(1) or Y(2) molecules along the c direction. In both cases the plane of the benzene ring is inclined at 30° to the c axis, and the small ring–ring interplanar spacings (3.5 Å) are believed to be stabilised by some form of weak π-electron interaction. This is thought to account for the needle-like crystals of the yellow form, and its colour.

A third form of the anilide (1), the amber form, has been isolated and its structure determined.[6] This form is closely related to the yellow polymorph in that the amide group forms intramolecular hydrogen bonds with the nitro group. Neither i.r. nor solid-state n.m.r. spectra of the pure amber form free from contamination with the other polymorphs have been satisfactorily obtained, owing to its instability to pressure or to processes such as grinding.

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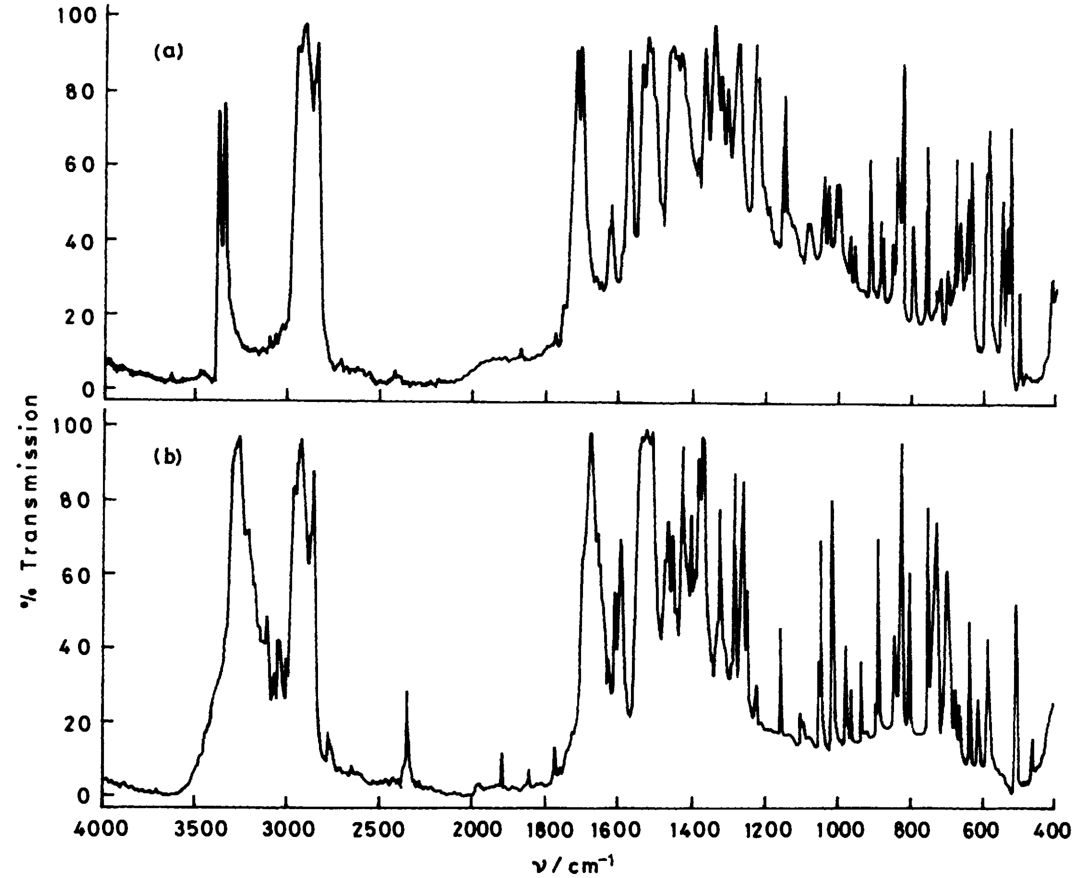


Figure 1. I.r. spectra of 4′-methyl-2′-nitroacetanilide (**1**) (Nujol mulls at 77 K): (a) yellow form, (b) white form; spectra represented in an inverted mode with respect to the transmission scale

Experimental

The white form of the anilide (**1**) was produced by cooling an aqueous ethanolic solution, and the yellow form by cooling a solution in light petroleum (b.p. 60—80 °C).

I.r. spectra were recorded in the range 4 000—400 cm^{-1} with a Perkin-Elmer 580B dispersive spectrometer. The yellow form of (**1**) was found to be relatively unstable to pressure at low temperatures, so the spectra (Figure 1) were recorded for Nujol mulls at 77 K, rather than KBr discs.

Solution-state ^{13}C n.m.r. spectra were recorded at 25 MHz for samples in a range of solvents, with a JEOL FX 100 high-resolution spectrometer.

High-resolution solid-state ^{13}C n.m.r. spectra were recorded with a purpose-built system consisting of an Oxford Instruments super-conducting magnet operating at 4.7 T (200.0 MHz for ^{1}H, 50.3 MHz for ^{13}C) and a Bruker double-resonance 'magic-angle-rotation' probe, with radiofrequency and computing hardware virtually identical with that previously described for a lower-field spectrometer built[7] at the University of East Anglia. Samples were packed in rotors of the Andrew-Beams type, and a small amount of KBr was added to each to allow setting of the 'magic angle'. Adamantane was used as an external secondary reference for peak positions (δ 37.7). Throughout the discussion, locants will refer to atomic numbering as in structure (**1**), *i.e.* primes will be omitted.

Results and Discussion

Infrared Investigation.—Theoretically, the anilide (**1**) has 66 normal modes of vibration, of which 30 can be related to vibrations associated with the benzene ring skeleton, *i.e.* the hydrogen atoms of the benzene ring and the atoms of the substituents directly attached to the ring. As an aid to the assignment of the i.r. spectra the model due to Varsanyi[8] for a 1,2,4-trisubstituted benzenoid was used. The results for the white and yellow forms of (**1**) are given in Table 1.

The *X*-ray crystallographic study cites hydrogen bonding as an intermolecular effect in the white and an intramolecular effect in the yellow form of (**1**) and this is supported by the i.r. data. It is likely, however, that the nitro group will perturb the normal amide bands to varying degrees in both forms. The amide I band in simple secondary amides, in the solid state, appears[9] in the range 1 680—1 630 cm^{-1}. The i.r. bands of the two polymorphs suggest that the hydrogen bonding in both cases is comparatively weak, particularly in the case of the yellow form, and its effect is obscured by the much larger nitro effect.

As already mentioned, the yellow form is known to have an asymmetric unit containing two distinct molecules with different molecular conformations. This property is reflected in the i.r. spectra: the amide NH and carbonyl stretching frequencies each show two bands. The crystallographic results[4] suggest that the shortest distances for intramolecular interactions involving the amide hydrogen atoms and the oxygen atoms of the nitro group are 1.95 and 1.98 Å, which probably correspond to the two i.r. amide NH stretching vibrations of 3 359 and 3 385 cm^{-1}, respectively. The comparatively long interatomic distances and high NH stretching frequencies are consistent with very weak intramolecular hydrogen bonds. Intermolecular hydrogen bonding is discounted on the basis of crystallographic considerations. Indeed,

Table 1. Infrared data for the white and yellow forms of the anilide (**1**) (spectra recorded at 77 K)[a]

	Yellow	White
ν(NH)	3 385s, 3 359s	3 260s
ν(CH arom.)	3 108w, 3 078w, 3 042w	3 105w, 3 067w, 3 043w
ν(CO)	1 720s, 1 708s	1 672s
ν(C=C)	1 623m, 1 579s	1 608m, 1 589m
$\nu_{as}(NO_2)$	1 544s	1 535s
ν(C=C)	1 529s, 1 518s	1 508s, 1 449m
Amide II	1 438s	1 524s
$\nu_s(NO_2)$	1 348s	1 369s
Amide III	1 233s	1 321s
δ(C–H)	1 310m	
ν(C=C)	1 283s	1 282s, 1 261s
δ(C–X)	1 152m	1 155m
δ(C–H)	1 087w	1 099w, 1 090w
$\delta(C–CH_3)$ rock	1 048w, 1 032w	1 049w, 1 043m
$\delta(C–CH_3)$ rock	1 013w, 1 002w	1 012s, 978w
$\nu(C–CH_3)$	920m	933w
γ(C=CH)	889w	888s
$\delta_s(NO_2)$	852w, 842m	841m
δ(C=CH)	839m, 829s	823s
ν(C–C) skel.	798w	801m
$\gamma_s(NO_2)$	759m, 681m	752s, 700m
γ(NH)	650w	710w
δ(CO)	639m	638m
γ(CO)	591m	611w
$\delta_{as}(NO_2)$	550m	588m
δ(C–C–C)	537w, 529m, 503w	508m, 503m

[a] Data in cm^{-1}, with spectra recorded in % transmission.

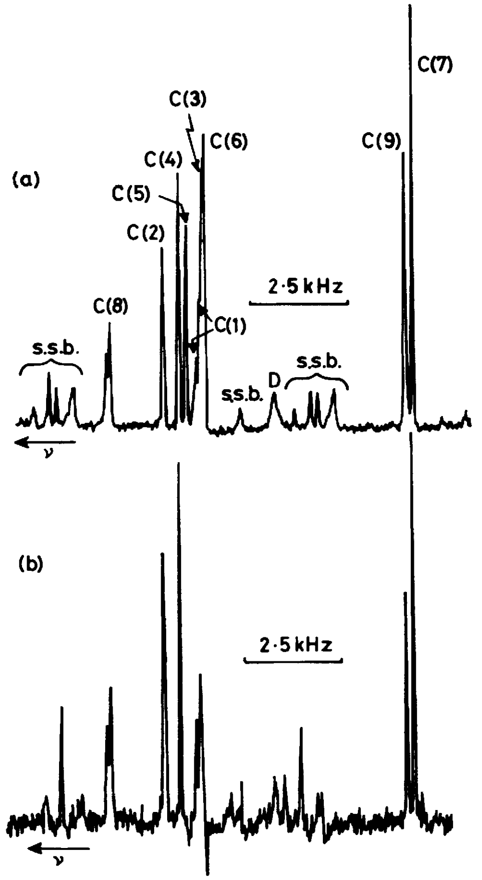


Figure 2. ^{13}C N.m.r. spectrum of the white form of 4′-methyl-2′-nitroacetanilide (**1**): (a) from a cross-polarisation magic-angle-rotation experiment; (b) from a non-quaternary suppression experiment (s.s.b. indicates spinning sideband, and D the peak assigned to Delrin in the rotor)

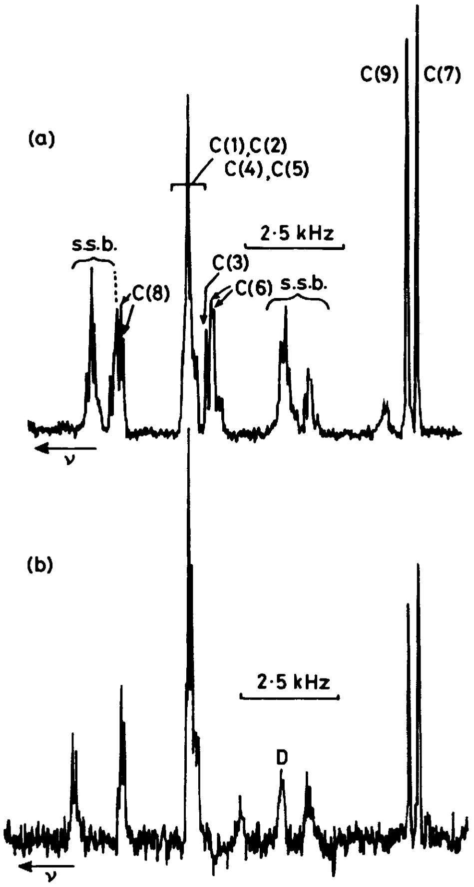


Figure 3. ^{13}C N.m.r. spectrum of the yellow form of 4′-methyl-2′-nitroacetanilide (**1**): (a) from a cross-polarisation magic-angle-rotation experiment; (b) from a non-quaternary suppression experiment (s.s.b. indicates spinning sideband, and D the peak assigned to Delrin in the rotor)

there is no evidence for any such intermolecular effects in the i.r. spectrum. The weak intramolecular hydrogen-bonding effects shown by the yellow form may also in part be reflected in the amide I carbonyl stretching frequencies of 1 720 and 1 708 cm^{-1}. The very high CO stretching frequencies are indeed in the direction opposite to those expected for hydrogen-bonding effects, and it seems that the effects of the nitro group dominate electronically and/or sterically. The amide I carbonyl stretching frequencies observed in the solid-state i.r. spectra of acetanilide, 2′-nitroacetanilide, and 3′-nitroacetanilide correspond to 1 660, 1 703, and 1 677 cm^{-1}, respectively, also indicating the dominant effect of the nitro group *ortho* to the secondary amide.

The NO_2 group is planar and its stretching frequencies show[10] little variation on hydrogen bonding. The antisymmetric $\nu(NO_2)$ vibration is essentially uncoupled to any other mode and is observed at 1 544 and 1 535 cm^{-1} for the yellow and white polymorphs, respectively. The lower-frequency $\nu(NO_2)$ stretching vibration is more likely to show coupling with modes associated with the aromatic skeleton, the values for yellow and white forms of (**1**) being 1 348 and 1 369 cm^{-1} respectively. In view of the weak nature of the hydrogen bonding, it is not possible to correlate these frequencies with crystallographic data.

The white form of (**1**) exhibits a crystal structure based on intermolecular hydrogen bonding.[4] The O $\cdots$ H distance is 1.95 Å and the O $\cdots$ H–N angle 172.8°. The i.r. spectra confirm the relative strengths of hydrogen bonding in the two forms, with the symmetric NH stretching frequency and amide I band shifted by *ca.* 100 and 50 cm^{-1}, respectively, to lower

Table 2. Solution-state ^{13}C n.m.r. data for the anilide (**1**)

	Shift from Me_4Si (p.p.m.)								
Solvent	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)
CD_2Cl_2	132.6	136.6	125.4	133.6	136.6	122.2	20.6	168.6	25.5
CD_3CN	132.1	136.3	125.8	134.8	136.5	123.7	20.4	169.5	25.0
CD_3OD	130.9	141.5	125.5	136.3	135.8	125.9	20.5	171.3	24.0
$CDCl_3$	132.2	136.2	125.2	133.1	136.4	121.9	20.4	168.4	25.4
CD_3COCD_3	132.3	138.2	125.6	134.3	136.2	123.5	20.3	168.9	24.8
CD_3SOCD_3	130.3	143.6	126.6	136.3	135.7	126.0	21.6	169.6	24.9

Table 3. Solid-state ^{13}C n.m.r. data for white and yellow forms of the anilide (**1**)

	Shift from Me_4Si (p.p.m.)								
Form	C(1)[a]	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)[a]	C(9)
White	127.7	144.1	124.3	135.9	132.3	123.2	19.2	172.8	23.0
	125.3							171.1	
Yellow	132.0	135.9	125.1	134.7	136.9	122.4	20.1	170.6	24.8
	131.4	133.0				121.8	19.7	168.9	
	129.8							167.3	

[a] The resonance positions given for these carbon atoms are the components of nitrogen-split doublets (plus crystallographic splittings for the yellow form) and are thus not true chemical shifts. The nitrogen-split 2:1 doublets have the more intense line of the pair at the lower frequency.

wavenumber in the case of the white form, as compared with the yellow.

The distinct differences in the geometries of the amide groups in the two polymorphs may reflect competition for the amide NH lone-pair electrons between the adjacent carbonyl group and the nitro group. Hence, the white form, where interaction by the carbonyl group predominates, shows a normal amide I frequency and a greater degree of hydrogen bonding. The amide group geometry is similar to that in acetanilide, and the variations in carbonyl stretching for acetanilide (1 660 cm^{-1}) and the white form of (**1**) (1 672 cm^{-1}) probably reflect the presence of intermolecular hydrogen bonding in each case.

The high-resolution i.r. spectrum of the yellow form is more complex than that of the white. The fact that there are two molecules in the asymmetric unit of the yellow form is reflected in the splittings observed for the NH stretching and amide I bands as well as for several of the skeletal deformation modes in the fingerprint region of the spectrum.

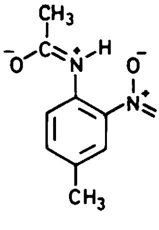
N.m.r. Investigation.—(a) *Solution state.* Solution-state ^{13}C n.m.r. spectra of the anilide (**1**) have been recorded in a range of solvents;[11] the results are summarised in Table 2 for comparison with the solid-state results.

(b) *Solid state.* Proton T_1 values were determined at 60 MHz using a conventional high-power pulse spectrometer, and were found to be 60 s for the white form and 45 s for the yellow. With these values in mind ^{13}C cross-polarisation magic-angle-rotation spectra were obtained using a recycle time of 60 s and a contact time of 5 ms for both forms. In addition, non-quaternary suppression spectra of both forms were obtained under identical conditions, using a dipolar dephasing 'window' of 40 μs. The 'flip-back' technique was used for both the cross-polarisation magic-angle-rotation and non-quaternary suppression[12] spectra. In all cases spectra with good signal-to-noise ratios were obtained in 1 000 transients (Figures 2 and 3).

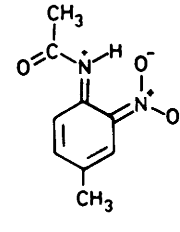
Assignments of peak positions based on the identification of quaternary carbon signals and on comparison with solution-state values are given in Table 3.

(c) *Discussion.* The doublet structure of the peaks arising from C(1) and C(8) [for numbering see formula (**1**)], α to the amide nitrogen atom, in the white form, is due to dipolar coupling with the quadrupolar ^{14}N nucleus. This effect has been well documented elsewhere[13] but it is worth noting that the sizes of these splittings at this field strength confirm the far from symmetric electronic environment of this nitrogen atom. Similar effects are observed in the yellow form but are complicated by the existence of the two conformationally distinct molecules in the asymmetric unit. The fact that only three peaks are observed for both C(1) and C(8) in the yellow form is presumably due to accidental degeneracies in both cases.

It has been mentioned already that one of the major differences in electronic distribution between the polymorphs may be due to competition for the lone pair on the amide nitrogen atom by the adjacent carbonyl group and the ring/nitro system. The extreme resonance possibilities in addition to that shown (**1**) may be represented by the two canonical forms (**2**) and (**3**). Consideration of these possibilities



(**2**)



(**3**)

with regard to the crystal structures of the two polymorphs shows that (**2**) is more likely to be favoured in the white form, where hydrogen bonding is intermolecular (involving the carbonyl oxygen atom) and the larger interplanar angles make delocalisation through the ring less favourable. On the other hand, the yellow form is more likely to favour (**3**), since in this polymorph hydrogen bonding is intramolecular (involving the nitro oxygen atom) and there is much greater coplanarity of the three groups, making delocalisation through the ring more favourable.

Very large differences in chemical shift between the two polymorphs are indeed observed at C(1) (amide-bonded ring carbon atom) and at C(2) (nitro-bonded ring carbon atom). The resonance for C(1) is *ca.* 5 p.p.m. to lower frequency for the white polymorph than for the yellow, while that for C(2) is *ca.* 9.6 p.p.m. to higher frequency in the white than in the yellow. The idea that these changes are due to competition for the amide nitrogen lone pair, as already described, is supported by the solution-state n.m.r. data.

Although the changes in chemical shifts observed on change of solvent [2.3 p.p.m. for C(1) and 7.4 p.p.m. for C(2)] are not as great as the differences observed between polymorphs, the overall trend clearly supports the idea of competition for the amide nitrogen lone pair, with different results in the two polymorphs, and the same idea can be used to explain other observed differences [*e.g.* at C(8) and C(5)].

Apart from these large differences between the spectra of the two polymorphs, differences between the two molecules in the asymmetric unit of the yellow form are apparent in the spectra. This has already been mentioned for C(1) and C(8), but differences can be seen more clearly for C(2), C(6), and C(7). The splitting on C(7) is presumably due to steric interaction with neighbouring molecules, and indeed the C(4)–C(7) bond is found to differ in length between the two non-congruent molecules. The splitting at C(2) can probably be explained by the differing degrees of ring/nitro conjugation in the two molecules (as affected by variations in torsion angles) and may therefore be thought of as having an origin similar to that of the splittings for C(1) and C(8). However it may also be linked with a change in the electronic environment of the nitrogen in the nitro group, leading to observable residual dipolar splittings. The splitting on C(6) is again a steric effect, but in this case the effect is intramolecular, being caused by the difference in interatomic distances between the hydrogen atom which is bonded to C(6) and the carbonyl oxygen atom which is bonded to C(8) in the two forms (2.26 and 2.32 Å). This difference is almost certainly accompanied by a change in geometry at C(6).

Conclusion

The results show that both techniques readily distinguish the gross differences between the two polymorphs of the anilide (**1**), but n.m.r. is possibly more sensitive to the smaller differences between the two crystallographically non-equivalent molecules in the asymmetric unit of the yellow form. It has been possible to rationalise most of the changes observed in both types of spectra on the basis of the crystallographic data and competition for the lone pair of electrons on the amide nitrogen atom between the amide and ring/nitro groups. It seems that the two techniques must be regarded as complementary in this field since i.r. is sensitive to changes in bond polarity while n.m.r. seems more sensitive to changes in electron density at a given nucleus.

Acknowledgements

We thank Professor N. Sheppard, F.R.S., and Dr. G. I. Gregory for discussions. A. M. K. thanks Glaxo Research Ltd. for financial support. The S.E.R.C. has provided finances for purchase of the solid-state n.m.r. equipment.

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Received 13*th November* 1985; *Paper* 5/1996