

tion of the absolute configurations at high  $R$  is quite risky in some cases even though the structure contains heavy atoms.

We thank Dr Masaji Kasai, Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd, for providing (A).

#### References

- ARORA, S. K. (1979). *Life Sci.* **24**, 1519-1526.
- FRENZ, B. A. (1982). *Enraf-Nonius Structure Determination Package CAD-4 SDP-Plus*. Version 1.0. College Station, Texas, USA.
- FRENZ, B. A. (1983). *Enraf-Nonius Structure Determination Package CAD-4 SDP-Plus*. Version 1.1. College Station, Texas, USA.
- HIRAYAMA, N. & SHIRAHATA, K. (1984). *Acta Cryst.* **A40**, C73.
- HORNEMANN, U. & AIKMAN, M. J. (1973). *J. Chem. Soc. Chem. Commun.* pp. 88-89.
- HORNEMANN, U., KEHRER, J. P., NUNEZ, C. S. & RANIERI, R. L. (1974). *J. Am. Chem. Soc.* **96**, 320-321.
- International Tables for X-ray Crystallography* (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)
- JOHNSON, C. K. (1976). *ORTEP*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
- MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1982). *MULTAN11/82. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain-la-Neuve, Belgium.
- OGAWA, K., NOMURA, A., FUJIWARA, T. & TOMITA, K. (1979). *Bull. Chem. Soc. Jpn.* **52**, 2334-2338.
- SHIRAHATA, K. & HIRAYAMA, N. (1983). *J. Am. Chem. Soc.* **105**, 7199-7200.
- TULINSKY, A. & VAN DEN HENDE, J. H. (1967). *J. Am. Chem. Soc.* **89**, 2905-2911.
- UZU, K., HARADA, Y. & WAKAKI, S. (1964). *Agric. Biol. Chem.* **28**, 388-393.
- YAHASHI, R. & MATSUBARA, I. (1976). *J. Antibiot.* **29**, 104-106.
- YAHASHI, R. & MATSUBARA, I. (1978). *J. Antibiot.* **31**, corrections.
- YAO JIA-XING (1981). *Acta Cryst.* **A37**, 642-644.

*Acta Cryst.* (1987). **B43**, 559-562

## Theoretical Studies of Solid-State Reactivity by Packing Density and Potential-Energy Maps: Hydrogen Transfer in 5-Nitro-3-thiophenecarboxaldehyde Crystals

BY A. GAVEZZOTTI

*Dipartimento di Chimica Fisica ed Elettrochimica e Centro CNR, Università di Milano, Via C. Golgi 19, I-20133 Milano, Italy*

(Received 1 June 1987; accepted 17 July 1987)

#### Abstract

Packing-density maps and potential-energy maps for hydrogen migration in the title crystal are described. The two kinds of information are similar and complementary to one another. This resemblance could be exploited to trace non-van der Waals interactions in crystals. It is proposed that the packing-density-potential-energy methodology offers a sound and systematic basis for the discussion of intermolecular effects in solid-state reactivity.

#### Introduction and purpose

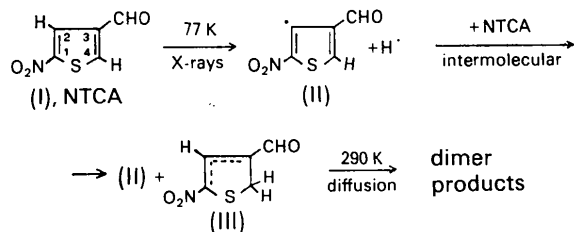
It is well known that irradiation by X-rays causes damage in organic crystals, usually by formation of radicals, that can also diffuse in the crystalline matrix, leading to a variety of products. These reactions can have very low conversion factors, so that the photolytic guest is unnoticed in ordinary X-ray diffraction analyses [but see Wei & Einstein (1981), who detected the presence of such a compound during the usual refinement procedures]. Spin resonance spectroscopies are, however, sensitive enough to give considerable structural and chemical information on

these systems, whose theoretical importance lies in the fact that they provide models for the first stages of reaction, where the products are trace impurities and the crystal matrix is largely unperturbed. Such cases provide unique insight on the crystal-lattice constraints on the path of solid-state organic reactions.

We have previously undertaken the packing analysis of photochemical reactions in crystals (Gavezzotti & Bianchi, 1986; Gavezzotti, 1987). We present in this paper some calculations for the hydrogen transfer after radicalization in 5-nitro-3-thiophenecarboxaldehyde (NTCA) crystals, a reaction that has been studied by ESR and ENDOR as a function of temperature (Geoffroy, Celalyan-Berthier, Reddy, Bernardinelli & Papadopoulos, 1985). This is one of the few, but rapidly increasing in number, cases in which a full X-ray structure determination was carried out. Our results confirm (or, at least, do not contradict) the conclusions drawn from the spectroscopic study, and illustrate the potential applications of a simultaneous use of packing-density and packing-energy methods in mapping the most favourable reaction paths in organic crystals.

### Outline of the problem

The reaction scheme is as follows (Geoffroy *et al.*, 1985):



According to the authors, homolytic scission of the C(2)–H bond is followed by attack on C(4) of a neighbouring molecule, with formation of the allyl radical (III); at higher temperatures, a diffusion-controlled dimerization takes place. The C(4)··H(2) intermolecular distance in the crystal of (I) is 3.6 Å. The key step is in any case the hydrogen-transfer process that leads to the formation of the (II)–(III) radical pair. If, and what, this process has to do with the crystal packing of (I) will be analyzed in the following.

### Packing analysis of the NTCA crystal

The NTCA molecule has a free surface,  $S_M$ , of 144 Å<sup>2</sup>, a volume of 111 Å<sup>3</sup> and a packing coefficient of 0.700. The number of valence electrons,  $Z_V$ , is 52. With these parameters, the statistical values for the packing energy are (Gavezzotti, 1985):

$$PE = (0.0767 S_M + 1.448) \times 4.187 = 52.3 \text{ kJ mol}^{-1}$$

$$PE = (0.202 Z_V + 3.472) \times 4.187 = 58.6 \text{ kJ mol}^{-1}$$

while the value actually computed by pairwise summation of atom–atom non-bonded energies (see below for details) is 56.9 kJ mol<sup>-1</sup> (at 7 Å cutoff). The difference is thus less than 10%. There are no patent deviations from the average for any of the packing-statistics parameters for NTCA; but it is well known that no such deviations are needed for a crystal to be reactive. There are two weak hydrogen bonds, one of them involving the allegedly reactive hydrogen. They do not pose a serious problem in the evaluation of the packing energy (but see below).

Packing diagrams (Fig. 1) and packing-density maps (Fig. 2) reveal more. The arrows in Fig. 1 show the two symmetric and equivalent direct hydrogen-transfer paths, and the dotted line marks the weak H bond to the carboxaldehyde group of a neighbouring molecule. The packing-arrangement across the centrosymmetrical couple of molecules joined by the arrows in Fig. 1. Void zones appear in the neighbourhood of both H(2) and H(4); cavities A and B surround the hydrogen-bonded O··H couples. A plausible path

for the hydrogen-radical migration is traced by the arrows in Fig. 2, which point out the channel that runs between the aldehyde O(3) atom of the molecule at 2–x, 1–y, 1–z and the C(3') atom of the target molecule, at 1–x, 1–y, 1–z. By following this channel, the radical can squeeze past the main obstacles on its course to C(4').

The reaction path above is that proposed from experiment. But the maps clearly show that an

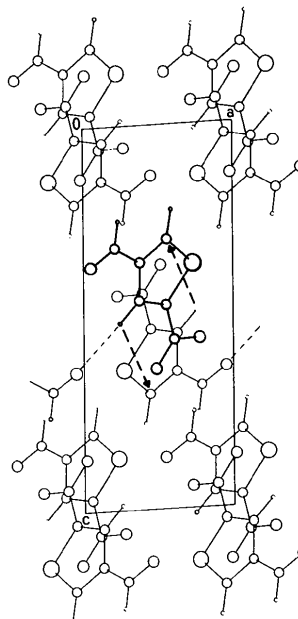


Fig. 1. Packing diagram for NTCA (projection on *b*). The arrows denote the direct path for hydrogen migration, the dotted line is the hydrogen bond (after the structure determination by Geoffroy *et al.*, 1985).

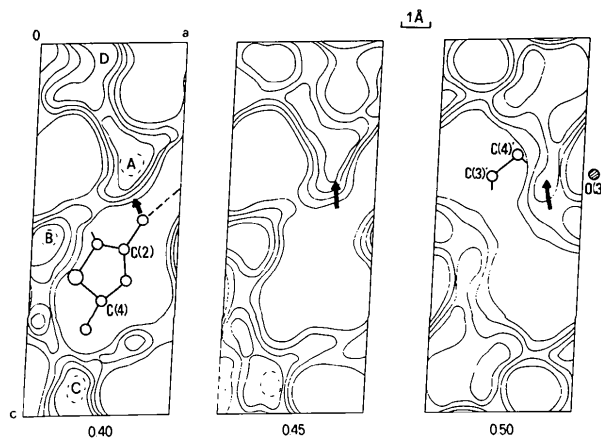


Fig. 2. Packing-density maps (Gavezzotti, 1983) for NTCA, *xz* sections, *y* (fractional) as shown below each section. Elementary volume 0.32 Å<sup>3</sup>, isodensity curves from zero (dotted line) to 80% in steps of 20%. Unprimed atom labels are for the starting molecule, primed labels for the target molecule. Arrows show the approximate direction of the exiting H atom. O(3), shaded circle, is the aldehyde O atom with which an H bond was formed (compare with the molecular diagram in Fig. 1).

Table 1. Fractional coordinates of atoms, for use in the examination of Figs. 2 and 3

Cell dimensions for NTCA (Geoffroy *et al.*, 1985) are  $a = 5.199$ ,  $b = 9.238$ ,  $c = 13.217$  Å;  $\beta$  (omitted in the paper and recalculated from the density) is  $93.3^\circ$ . Space group  $P2_1/n$ ,  $Z = 4$ .

	<i>x</i>	<i>y</i>	<i>z</i>
C(2)	0.6267	0.3456	0.5432
C(4)	0.4418	0.3408	0.6993
H(2)	0.763	0.381	0.484
H(4)	0.392	0.352	0.769
O(3 <sup>iv</sup> )	1.0471	0.4196	0.3665
C(4 <sup>i</sup> )	0.5582	0.6592	0.3007
C(3 <sup>i</sup> )	0.3769	0.5958	0.3576
C(4 <sup>ii</sup> )	1.4418	0.3408	0.6993
S <sup>iii</sup>	1.2698	0.21076	0.63531
C(4 <sup>iii</sup> )	0.4418	0.3408	-0.3007

Symmetry code: (i)  $1-x, 1-y, 1-z$ ; (ii)  $1+x, y, z$ ; (iii)  $x, y, z-1$ ; (iv)  $2-x, 1-y, 1-z$ .

alternative path could be taken by the H radical into cavity *B* of the cell at  $+1$  in *x*, atom C(4<sup>ii</sup>) of the  $1+x, y, z$  molecule being only  $4.5$  Å away (the S atom of this same molecule would however be in the way). Another possible diffusion course is again through cavity *A*, but this time following channel *D* all the way to cavity *C* in the cell at  $-1$  on *z*, thus reaching atom C(4<sup>iii</sup>) on the  $x, y, z-1$  molecule. For easy reference, Table 1 collects the fractional coordinates of all the atoms which have been mentioned so far.

It should be noted that reasoning based on available space cannot distinguish between the diffusion of H(2) to C(4) and H(4) to C(2), since any path which is easy for one is *ipso facto* an easy path for the other.

### Packing potential-energy calculations

The packing energy of NTCA and the potential-energy variations after H detachment have been calculated as follows. Non-bonded intermolecular interactions were accounted for by pairwise summations using standard potentials (see, for the choice, Gavezzotti, 1983). No electrostatic contributions have been included – which is a crude approximation if precise values of sublimation energies are required. We do not think that these forces are strictly necessary if an evaluation of the rough shape and steepness of the reaction cavity is sought. Most of our arguments concern regions of the potential-energy surface where repulsive dispersion forces are the overwhelmingly largest contribution, and electrostatic terms could only be a small modulation of the total potential. We do not argue that these forces do not exist; we assume that they are spectator forces for the processes we are interested in.

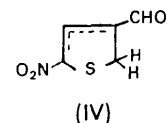
Quite a problem is posed by intramolecular interactions of the leaving H radical with the parent molecule. We do not wish to calculate bond-breaking energies. We assume that interactions with the parent molecule are relevant only if they become significantly

repulsive, or, in other words, we require that the H radical cannot diffuse against its own starting molecule. In practice, the intermolecular potential energy for the H radical in the lattice was calculated as if it were an H atom, and was supplemented with intramolecular terms by (i) neglecting all C(2)–H(2) interactions, and (ii) including interactions with other atoms of the parent molecule only if they contribute a net repulsive energy. These last contributions were computed by the same potential functions as for the intermolecular energies – usually an incorrect procedure, justified in this case by the consideration that the leaving H radical quickly becomes an intermolecular object to its parent molecule. The calculation of the potential energy is thus less accurate in close proximity to the original molecule, but this is a region where nothing relevant to our purposes happens.

The hydrogen bonds have been treated as ordinary intermolecular interactions. This crude assumption is partly justified by the fact that, after the H bonds have been broken, the non-bonded potentials provide a reasonable estimate of the repulsive energies, while the attractive ones are uninteresting if the main bond-breaking drive is provided by photochemical excitation. Thus, the small energy content of the weak H bond is incorporated in the overall bond-breaking energy, which was neglected altogether.

As is customary, ring H atoms were located at C–H =  $1.08$  Å along the ring-bond-angle bisector, and the aldehyde H atom was placed at C–H =  $1.0$  Å.

In preliminary calculations, we took the following species to probe the crystal site in which the radical will find itself:



This species incorporates both 'defects', a missing H atom on C(2) and an extra H atom on C(4). The packing energy of (I) is  $-124.8$  kJ mol<sup>-1</sup>; substitution of one molecule of (IV) in the crystal of (I) produces a destabilization of less than  $0.42$  kJ mol<sup>-1</sup>; a crystal entirely made of (IV) is again about  $0.42$  kJ mol<sup>-1</sup> less stable than the pure crystal of (I). From this we conclude that little or no intermolecular correlation is to be expected between reacted sites. This conclusion is a safe one, since it relies on a comparison of calculations in which the long-range electrostatic terms are equal, as is the destabilization energy that comes from the rupture of the intermolecular H bond at H(2).

The packing potential energy of the H radical in the crystal was evaluated by placing an H atom at the points of a grid with steps of  $\sim 0.5$  Å in *x*, *y*, *z*, in the presence of the counter radical and of the

surrounding undamaged molecules (whose position was not optimized). The resulting relative energy maps are shown in Fig. 3. They are given only up to  $y = 0.5$  fractional, since after that a substantial semi-bonding interaction with  $C(4^i)$  must begin, and we provide no means of accounting for it. A spurious repulsion would result by treating the  $H-C(4^i)$  interaction as a normal non-bonded contact.

A clear exit channel for the H radical is outlined in Fig. 3, which also shows that it meets a barrier not higher than  $63 \text{ kJ mol}^{-1}$  as it proceeds towards the reaction terminus. A remarkable mobility (in an intermolecular sense) is thus evident, and the barrier could be further lowered by a small reorganization of the immediate neighbours. As already noted, the mapping of the transfer path may not be used to discriminate between  $C(2)-H$  and  $C(4)-H$  bond cleavage, a choice which is dictated almost exclusively by intramolecular factors. It does, however, confirm that the proposed path for the solid-state reaction is indeed a practicable one. But the maps also point out that the crystal can accommodate a guest  $H^{\cdot}$  in many locations at a rather low energy cost; the reaction is intermolecularly less constrained than it might be thought, and hydrogen exchange may not be restricted to occur among nearest neighbours. The possibility of multisite reaction cannot be ruled out.

One rather striking feature of our results is the close resemblance of the maps in Figs. 2 and 3. To an astonishing degree of detail, isoenergetic curves at  $62.8 \text{ kJ mol}^{-1}$  intervals resemble isodensity curves at 20% intervals. An H atom can therefore be used as a probe of crystal packing density, just like a point charge exploring an electric field. This idea is not new (see for instance Moore, Nassimbeni, Niven & Taylor, 1986), and it is almost obvious that van der Waals potential energy and van der Waals envelopes give the same qualitative information on intermolecular interactions. It would be interesting to compare packing-density maps with packing-energy maps obtained with more refined potentials, including for instance electrostatic interactions. An appreci-

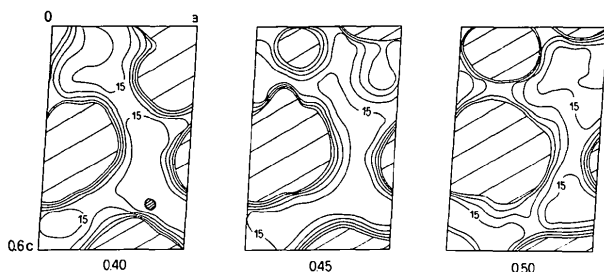


Fig. 3. Potential-energy maps for the H atom, as described in the text. Isoenergy curves at  $62.8 \text{ kJ mol}^{-1}$  ( $15 \text{ kcal mol}^{-1}$ ) intervals.  $xz$  sections,  $y$  (fractional) as shown below each section. Note that the map goes only to 0.6 fractional along  $c$ . The shaded circle is the original position of the undetached H atom (compare with molecular diagrams in Figs. 1 and 2).

ation (qualitative or quantitative) of the differences could trace the location and the directional properties of non-van der Waals forces in crystals.

### Final remarks

Admittedly, this paper does not add much to the elucidation of the reaction path in NTCA, which was accomplished in a satisfactory way by spectroscopic techniques. It uses, *a posteriori*, the crystallographic and spectroscopic information of Geoffroy *et al.* (1985) to improve and illustrate the methodology for the theoretical analysis of such reactions. That the results are not in conflict with experiment is, in a sense, a required side result. We wish, on the other hand, to emphasize the import of this methodology to the general field of organic solid-state reactivity. It does offer a sound and systematic basis for the discussion of intermolecular factors, incorporating in a simple way and by an inexpensive procedure all the necessary information. The reader may appreciate the substantial increase in quality and detail of the intermolecular information on going from the packing scheme in Fig. 1 to the maps in Figs. 2 and 3.

We thank Dr R. Bianchi and Dr T. Pilati for the use of graphic programs. Partial financial support came from Fondi Ministero della Pubblica Istruzione 40%.

### APPENDIX

The packing potential energy for fragments in crystals was computed according to the prescriptions in Gavezzotti (1987). Formula (3) in that paper is, however, in error. It should read:

$$\text{PPE} = \text{PPE}(\text{lattice, aggregate}) + \sum_{ij} E(\text{fragment } i, \text{fragment } j),$$

while the packing energy is

$$\text{PE} = \frac{1}{2} \text{PPE}(\text{lattice, aggregate}) + \sum_{ij} E(\text{fragment } i, \text{fragment } j).$$

### References

- GAVEZZOTTI, A. (1983). *J. Am. Chem. Soc.* **105**, 5220-5225.
- GAVEZZOTTI, A. (1985). *J. Am. Chem. Soc.* **107**, 962-967.
- GAVEZZOTTI, A. (1987). *Tetrahedron*, **43**, 1241-1251.
- GAVEZZOTTI, A. & BIANCHI, R. (1986). *Chem. Phys. Lett.* **128**, 295-299.
- GEOFFROY, M., CELALYAN-BERTHIER, A., REDDY, M. V. V. S., BERNARDINELLI, G. & PAPADOPOULOS, M. (1985). *J. Chem. Phys.* **82**, 4850-4855.
- MOORE, M. H., NASSIMBENI, L. R., NIVEN, M. L. & TAYLOR, M. W. (1986). *Inorg. Chim. Acta*, **115**, 211-217.
- WEI, C. H. & EINSTEIN, J. R. (1981). *Acta Cryst.* **B37**, 410-414.